# Biomolecules & Biomedicine

**Biomolecules and Biomedicine** 

ISSN: 2831-0896 (Print) | ISSN: 2831-090≯ Journal Impact Factor® (2023): 3.1

CiteScore®(2023):7.4 www.biomolbiomed.com | www.blog.bjbms.org

The BiomolBiomed publishes an "Advanced Online" manuscript format as a free se authors in order to expedite the dissemination of scientific findings to the research comm soon as possible after acceptance following peer review and corresponding modificatior appropriate). An "Advanced Online" manuscript is published online prior to copyediting, for for publication and author proofreading, but is nonetheless fully citable through its Digita Identifier (doi®). Nevertheless, this "Advanced Online" version is NOT the final version manuscript. When the final version of this paper is published within a definitive issue of the with copyediting, full pagination, etc., the new final version will be accessible through the doi and this "Advanced Online" version of the paper will disappear.

## **META - ANALYSIS**

Anwaier et al: Maternal diabetes and fetal epicardial fat thickness

## Influence of maternal diabetes during pregnancy

## on ultrasound-measured fetal epicardial fat

## thickness: A meta-analysis

## Apizi Anwaier<sup>1</sup>, Jian Li<sup>1</sup>, Wei Liu<sup>1</sup>, Liangjie Dong<sup>1</sup>, Yunfei Ding<sup>1</sup>, and Zhaoxia Yu<sup>1\*</sup>

<sup>1</sup>Department of Critical Care Medicine, the First affiliated Hospital of Xinjiang Medical University, Urumqi, China;

\*Correspondence to Zhaoxia Yu zhaoxiayu xjah@hotmail.com

DOI: https://doi.org/10.17305/bb.2025.11909

#### ABSTRACT

Maternal diabetes during pregnancy, including gestational diabetes mellitus (GDM) and pregestational diabetes mellitus (PDM), has been linked to alterations in fetal development. This meta-analysis aimed to investigate the impact of maternal diabetes on fetal epicardial fat thickness (fEFT), measured via ultrasound—a potential marker of cardiometabolic risk. A systematic search of PubMed, Embase, and Web of Science was conducted to identify observational studies assessing fEFT in pregnant women with and without diabetes. A random-effects model was used to calculate the mean difference (MD) in fEFT between groups. Heterogeneity was evaluated using the I<sup>2</sup> statistic, and sensitivity, subgroup, and meta-regression analyses were performed to explore sources of variability. Data from ten studies, comprising twelve datasets and 1,303 participants, were pooled. Women with diabetes during pregnancy had significantly higher fEFT compared to those without diabetes (MD: 0.37 mm, 95% confidence interval [CI]: 0.26 to 0.49, p < 0.001), with moderate heterogeneity ( $I^2 = 69\%$ ). Sensitivity analyses, conducted by excluding one dataset at a time, confirmed the robustness of the findings (all *p*-values < 0.05). Meta-regression revealed a positive correlation between gestational age (GA) at fEFT measurement and fEFT differences (coefficient = 0.040, p = 0.005), accounting for 83.2% of the heterogeneity. Subgroup analyses demonstrated consistent results across study designs, maternal diabetes types, and demographic factors but highlighted greater fEFT differences in studies where GA at fEFT measurement was > 26 weeks. In conclusion, maternal diabetes during pregnancy is associated with increased fEFT, particularly in later gestation.

**Keywords:** Gestational diabetes mellitus; GDM; pregestational diabetes mellitus; PDM; fetal epicardial fat thickness; fEFT; metabolism; meta-analysis.

#### **INTRODUCTION**

Diabetes mellitus (DM) is a common metabolic disorder that poses significant health challenges worldwide, with increasing prevalence among women of childbearing age (1, 2). Gestational diabetes mellitus (GDM), defined as glucose intolerance first recognized during pregnancy (3), and pregestational diabetes mellitus (PDM), which encompasses type 1 or type 2 diabetes diagnosed before pregnancy (4), affect a substantial proportion of pregnancies globally. GDM alone has been reported to affect approximately 14% of pregnancies (5), while PDM incidence varies geographically, largely reflecting the prevalence of diabetes in the general population (6). Both conditions are associated with a range of adverse maternal and fetal outcomes, including preeclampsia, preterm delivery, fetal macrosomia, and perinatal complications (7-9). These complications underscore the importance of understanding and mitigating the effects of maternal DM on pregnancy and offspring health. Emerging evidence highlights the potential influence of maternal DM on the cardiometabolic risk of offspring, which may manifest in both fetal development and later life (10, 11). Fetal exposure to maternal hyperglycemia is thought to disrupt normal metabolic programming, predisposing offspring to obesity, insulin resistance, and type 2 diabetes in adolescence and adulthood (12). These observations have led to a growing interest in identifying early markers of cardiometabolic risk in fetuses exposed to maternal DM (13). Among these, fetal epicardial fat thickness (fEFT) has emerged as a promising candidate. Epicardial fat is a metabolically active visceral fat depot that envelops the myocardium and coronary arteries, and its thickness has been linked to cardiometabolic disorders in adults (14, 15). Measuring fEFT via ultrasound provides a non-invasive method to assess fetal adiposity and may offer insights into early alterations in metabolic pathways influenced by maternal factors (16). Increased fEFT in fetuses and neonates correlates with higher birth weight, greater adiposity, and metabolic markers indicating early dysfunction, such as hyperinsulinemia (17-20). These findings suggest that elevated fEFT in utero could serve as an early marker of cardiometabolic risk. Despite the biological plausibility and clinical significance of these associations, research on the influence of maternal DM on fEFT remains relatively limited. Some observational studies have demonstrated increased fEFT in fetuses of women with GDM or PDM compared to non-diabetic pregnancies (21-28).

Given the growing interest in fEFT as a potential early marker of fetal cardiometabolic risk, understanding its association with maternal diabetes is crucial. While individual studies have explored this relationship, findings remain inconsistent due to variations in study design, measurement methods, and sample characteristics. Therefore, we conducted this systematic review and meta-analysis to quantitatively assess the impact of maternal diabetes (both GDM and PDM) on ultrasound-measured fEFT and explore potential sources of heterogeneity, providing a comprehensive synthesis of the available evidence. Additionally, we sought to investigate the modifying effects of study characteristics, such as gestational age (GA) at the time of fEFT measurement, maternal BMI, and the type of maternal DM, on this association.

#### MATERIAL AND METHODS

This meta-analysis adhered to the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) (29, 30) and the Cochrane Handbook for Systematic Reviews of Interventions (31) throughout its design, data collection, statistical analysis, and interpretation of results. This meta-analysis was registered with PROSPERO under the identifier CRD42024618929. Initially, the protocol focused on pregnancies complicated by GDM compared to controls. However, prior to data extraction, the protocol was amended to include both GDM and PDM to comprehensively evaluate the influence of maternal diabetes on fetal epicardial fat thickness. The amendment was submitted and approved by PROSPERO, in accordance with standard meta-analysis procedures.

#### Literature search

To identify studies relevant to the meta-analysis, we conducted a systematic search of PubMed, Embase, and Web of Science using comprehensive search terms, including ("epicardial adipose tissue" OR "epicardial fat" OR "pericardial adipose tissue" OR "pericardial fat" OR "cardiac adipose tissue" OR "cardiac fat" OR "subepicardial adipose tissue" OR "subepicardial fat" OR "heart fat" OR "heart adipose tissue") AND ("gestational diabetes" OR "GDM" OR "pregestational diabetes" OR ("gestational" OR "pregnancy" OR "pregnant") AND ("diabetes" OR "diabetic" OR "hyperglycemia")). The search was restricted to studies involving humans and published as full-length articles in peer-reviewed English-language journals. Additionally, references from relevant original and review articles were manually screened to identify potentially eligible studies. The literature search covered publications from database inception to November 12, 2024. Detailed search terms and strategies for each database are provided in **Supplemental Data**.

#### Inclusion and exclusion criteria

The inclusion criteria for eligible studies were as follows: (1) observational studies published as full-length articles; (2) included pregnant women with DM, either GDM or PDM, and healthy pregnant women without DM, all with singleton pregnancies; (3) assessed fEFT via ultrasound in women with and without DM; and (4) reported or allowed the calculation of differences in fEFT between women with and without DM during pregnancy. The diagnostic criteria for GDM or PDM were based on those used in the included studies. Exclusion criteria were: (1) studies that did not include pregnant women; (2) studies including pregnant women with other clinical conditions, such as pregnancy-induced hypertension or preeclampsia; (3) studies

that did not measure fEFT; and (4) preclinical studies, reviews, or editorials. In cases of overlapping populations, the study with the largest sample size was included in the meta-analysis.

#### Study quality evaluation and data extraction

The processes of literature search, study identification, quality assessment, and data extraction were independently performed by two authors. Disagreements, if any, were resolved through consultation with the corresponding author. Study quality was evaluated using the Newcastle-Ottawa Scale (NOS) (32), which assesses three domains: selection of cases and controls, comparability between groups, and measurement of exposure. The NOS assigns scores ranging from 1 to 9, with higher scores indicating better quality. The following data were extracted from each study for analysis: study details (author, year, country, and design), participant characteristics (sample size, age, and BMI of pregnant women), median GA for fEFT measurement, type of maternal DM (GDM or PDM), and variables matched or adjusted in reporting the influence of maternal DM on fEFT.

#### **Statistical analysis**

The mean difference (MD) with corresponding 95% confidence intervals (CIs) was used to summarize the difference in fetal epicardial fat thickness (fEFT) between women with and without diabetes during pregnancy (33). Heterogeneity among studies was assessed using the Cochrane Q test and the I<sup>2</sup> statistic (33, 34). Heterogeneity was categorized as mild (I<sup>2</sup> < 25%), moderate (I<sup>2</sup> 25%–75%), or substantial (I<sup>2</sup> > 75%). A random-effects model was applied to pool the results, accounting for potential between-study variability (31). Sensitivity analyses were conducted by omitting one dataset at a time to evaluate the robustness of the findings (33). Predefined univariate meta-regression analyses were performed to assess the modifying effects of study characteristics on the outcomes, including sample size, mean maternal age, mean BMI, and NOS scores. Predefined subgroup analyses explored the influence of study characteristics, such as study design, type of maternal diabetes, mean maternal age, BMI, timing of fEFT measurement, and NOS scores. For subgroup definitions, medians of continuous variables were used as cutoffs. Publication bias was initially evaluated through funnel plot construction and visual assessment of symmetry (35), complemented by Egger's regression test (35). Statistical analyses were performed using RevMan (Version 5.1; Cochrane Collaboration, Oxford, UK) and Stata software (version 12.0; Stata Corporation, College Station, TX). A two-sided p-value of <0.05 was considered statistically significant.

#### RESULTS

#### **Study inclusion**

The study inclusion process is illustrated in Figure 1. Initially, 168 potentially relevant records were identified through a comprehensive search of the three databases. After removing 25 duplicates, 143 records remained. Screening of titles and abstracts excluded 123 studies, primarily because they did not align with the objectives of the meta-analysis. The full texts of the remaining 20 records were then assessed independently by two authors, leading to the exclusion of 10 studies for reasons detailed in Figure 1. Ultimately, 10 observational studies were deemed eligible for inclusion in the quantitative analysis (21-28, 36, 37).

#### Summary of study characteristics

Table 1 summarizes the characteristics of the included studies. In total, 10 observational studies were included, comprising six case-control studies (23, 24, 26-28, 36) and four cross-sectional studies (21, 22, 25, 37). These studies were published between 2016 and 2023 and were conducted in Turkey (22, 24, 27, 28, 36), the United States (21, 23), and India (25, 26, 37). Two studies (27, 28) provided separate datasets for women with GDM and PDM, resulting in 12 datasets included in the meta-analysis. A total of 1,303 women with singleton pregnancies were analyzed, with mean maternal ages ranging from 25.6 to 35.8 years and mean BMI from 27.9 to 31.3 kg/m<sup>2</sup>. The ultrasonic methods for measuring fEFT varied among the included studies, (e.g., left ventricular outflow tract, four-chamber, or apical views) and reference points for defining fEFT thickness, which are described in detail in **Table 1**. The median GA for ultrasound assessment of fEFT ranged from 20.0 to 34.5 weeks. Six studies included women with GDM (22, 24-26, 36, 37), one study included women with PDM (21), and three studies included both GDM and PDM populations (23, 27, 28). In all included studies, potential confounding factors, such as GA at the time of fEFT measurement, were matched between women with and without diabetes during pregnancy. The quality of the included studies, assessed using the Newcastle-Ottawa Scale (NOS), ranged from seven to nine stars, indicating overall good methodological quality (Table 2).

#### Results of overall meta-analysis and sensitivity analysis

Moderate heterogeneity was observed among the included studies ( $I^2 = 69\%$ ). Using a random-effects model, the pooled analysis demonstrated that fEFT was significantly greater in women with DM during pregnancy compared to those without DM (MD: 0.37 mm, 95% CI: 0.26 to 0.49, p < 0.001; Figure 2A). Sensitivity analyses, performed by excluding one dataset at a time, confirmed the robustness of the results (MD range: 0.32 to 0.40, all p < 0.05).

#### **Results of the meta-regression analysis**

Univariate meta-regression analysis indicated a positive correlation between median GA at fEFT measurement and the fEFT difference between women with and without DM during pregnancy (coefficient = 0.040, p = 0.005; Table 3 and Figure 2B), explaining a substantial proportion of heterogeneity (Adjusted R<sup>2</sup> = 83.2%). Other variables, such as sample size, mean maternal age, mean maternal BMI, and NOS scores, did not show significant effects (all p > 0.05; Table 3).

#### **Results of the subgroup analysis**

Subgroup analyses revealed consistent effects of maternal DM on fEFT across study designs (case-control and cross-sectional, *p* for subgroup difference = 0.18; Figure 3A), types of maternal DM (GDM and PDM, *p* for subgroup difference = 0.55; Figure 3B), mean maternal age categories (< 29 years vs.  $\ge$  29 years, *p* = 0.69; Figure 4A), and maternal BMI categories (< 30 kg/m<sup>2</sup> vs.  $\ge$  30 kg/m<sup>2</sup>, *p* = 0.59; Figure 4B). However, subgroup analysis by GA for fEFT measurement showed a significantly greater increase in fEFT in studies with GA > 26 weeks compared to those with GA  $\le$  26 weeks (0.54 mm vs. 0.23 mm, *p* for subgroup difference = 0.002; Figure 5A). Similar findings were observed in studies with varying NOS scores (*p* for subgroup difference = 0.09; Figure 5B).

#### **Publication bias**

Figure 6 presents the funnel plots for the meta-analysis evaluating the difference in fEFT between women with and without DM during pregnancy. The plots appear symmetrical upon visual inspection, suggesting a low risk of publication bias. This observation is further supported by Egger's regression test, which did not indicate significant publication bias (p = 0.58).

#### DISCUSSION

The results of this meta-analysis reveal a significant association between maternal DM during pregnancy and increased fEFT, with a mean difference of 0.37 mm compared to pregnancies without DM. This finding was consistent across sensitivity analyses, with moderate heterogeneity observed. Meta-regression analysis identified GA at the time of fEFT measurement as a significant source of heterogeneity, suggesting that the impact of maternal DM on fEFT becomes more pronounced as pregnancy progresses. Subgroup analyses further demonstrated consistent results across various study designs, maternal demographic factors, and study quality, underscoring the robustness of the observed association.

The influence of maternal DM on fEFT can be attributed to several pathophysiological mechanisms. Hyperglycemia-induced fetal hyperinsulinemia plays a central role, as elevated insulin levels stimulate the proliferation and hypertrophy of adipocytes, leading to increased fat deposition (38). Insulin acts as a growth-promoting hormone during fetal development, with high levels directly influencing the differentiation of preadipocytes into mature adipocytes, particularly in metabolically active depots such as epicardial fat (39). Epicardial fat, due to its proximity to the myocardium and coronary arteries, has a unique metabolic profile characterized by high lipolytic activity and the secretion of pro-inflammatory cytokines and adipokines (40). These characteristics make it particularly susceptible to the metabolic alterations associated with maternal DM. Additionally, maternal DM is associated with systemic inflammation and oxidative stress, which may exacerbate adipogenesis and impair normal fat distribution in the fetus (41). Hyperglycemia triggers the overproduction of reactive oxygen species (ROS) (42) and activates proinflammatory pathways such as nuclear factor- $\kappa$ B (NF- $\kappa$ B) (43). These processes lead to the upregulation of inflammatory cytokines, including tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) and interleukin-6 (IL-6), which can further promote adipose tissue expansion and dysfunction (44). In the fetal environment, these inflammatory signals may enhance the deposition of epicardial fat by promoting local adipocyte proliferation and hypertrophy (45). Maternal DM also affects placental function, further contributing to increased fEFT (46). The placenta acts as a mediator of nutrient transfer and endocrine signaling between the mother and fetus (47). In pregnancies complicated by DM, placental abnormalities such as increased vascular resistance and reduced mitochondrial function have been observed (47). These changes can alter the supply of glucose and lipids to the fetus, favoring excessive energy availability and fat deposition (47). Moreover, maternal hyperglycemia can upregulate placental transporters for glucose and fatty acids, leading to an increased flux of these substrates to the fetus and subsequent adipogenesis in depots such as epicardial fat (48). Finally, epigenetic modifications may also play a role in the influence of maternal DM on fEFT. Chronic hyperglycemia during pregnancy can induce changes in DNA methylation, histone modification, and noncoding RNA expression in the developing fetus (49). These epigenetic alterations can affect the expression of genes involved in adipogenesis and metabolism, potentially predisposing the fetus to increased fat deposition and cardiometabolic dysfunction later in life (50). Studies have demonstrated altered methylation patterns in genes regulating insulin signaling and lipid metabolism in offspring of diabetic pregnancies, which may contribute to the observed increase in fEFT (51, 52).

The results of the meta-regression and subgroup analyses offer important insights into the timing and magnitude of maternal DM's effects on fEFT. The positive correlation between GA and fEFT differences suggests that later gestation may represent a critical period for the influence of maternal DM on fetal adiposity. This finding has clinical implications, as it highlights the importance of early and sustained glycemic control throughout pregnancy to minimize the impact on fetal development (53). The consistency of results across study designs, maternal age, BMI, and study quality indicates that the observed association is robust and not confounded by these factors. This reinforces the validity of fEFT as a marker for assessing

the effects of maternal DM on fetal development. In addition, although our subgroup analysis did not reveal a significant difference in the effect of GDM versus PDM on fEFT, we acknowledge that these two conditions have distinct metabolic characteristics and may exert differential influences on fetal development (54). However, the shared pathophysiological pathways, including hyperglycemia-induced fetal hyperinsulinemia and inflammatory processes, likely contribute to similar changes in fEFT (55). Further studies are warranted to explore potential variations in fEFT progression between GDM and PDM pregnancies, particularly in relation to glycemic control and disease severity.

This meta-analysis has several strengths. It represents a comprehensive and up-to-date synthesis of the literature, incorporating data from multiple observational studies with matched or adjusted GA to ensure comparability. Rigorous methodological approaches, including sensitivity, subgroup, and meta-regression analyses, were employed to explore heterogeneity and identify key modifiers of the observed association (56). These analyses enhance the reliability of the findings and provide valuable insights into the factors influencing fEFT in pregnancies complicated by DM. Moreover, the inclusion of studies with high methodological quality, as assessed by the NOS scores, further supports the robustness of the results.

Despite these strengths, several limitations must be acknowledged. First, the meta-analysis included only observational studies, which are inherently subject to residual confounding despite adjustments for key variables (57). Second, unmeasured factors, such as maternal diet, physical activity, and genetic predispositions, may have influenced the results (58). Third, the study-level nature of the analysis limits the ability to explore individual-level data and precludes causal inferences. Additionally, while GA emerged as a significant modifier, the underlying mechanisms and precise role of GA in the observed association warrant further investigation. Another potential limitation is the variation in diagnostic criteria for GDM across the included studies. Most studies applied the International Association of the Diabetes and Pregnancy Study Groups (IADPSG) criteria (22-24, 26-28, 36, 37), while one study used the Diabetes In Pregnancy Study group India (DIPSI) criteria (25). Differences in diagnostic thresholds may introduce variability in the classification of GDM, potentially affecting the pooled estimates (59). However, due to the limited number of included studies, we were unable to assess the impact of these variations. Future metaanalyses incorporating a larger number of studies may allow for a more detailed evaluation of the influence of different GDM diagnostic criteria on fEFT. Finally, the included studies used different ultrasound techniques for fEFT measurement. These methodological differences may have contributed to heterogeneity in our meta-analysis. However, due to the absence of a standardized protocol for fEFT assessment, future studies should aim to establish uniform measurement criteria to enhance comparability across studies. The findings of this meta-analysis have potentially important clinical implications. Our findings suggest that increased fEFT may serve as an early indicator of fetal metabolic risk in pregnancies complicated by diabetes. Given its non-invasive nature, ultrasound-based fEFT assessment could be integrated into prenatal screening protocols to identify fetuses at risk of metabolic complications (60). Furthermore, optimizing maternal glycemic control may help mitigate excessive fetal fat accumulation, potentially improving longterm cardiometabolic health in offspring (12). Future studies should explore standardized thresholds for fEFT measurement and its predictive value in clinical practice. Routine assessment of fEFT in pregnancies complicated by DM could provide valuable information for risk stratification and guide targeted interventions to optimize fetal outcomes (61). The identification of GA as a key modifier underscores the need for close monitoring during later gestation, particularly in women with poor glycemic control. Although increased fEFT has been suggested as a marker of fetal metabolic compromise, including macrosomia (62), we were unable to assess its direct relationship with these outcomes due to limited available data. Future studies should explore whether fEFT could serve as an early predictor of fetal overgrowth and metabolic dysfunction, particularly in pregnancies complicated by diabetes. Future research should focus on elucidating the long-term implications of increased fEFT on offspring health and exploring interventions to mitigate these effects (63). Longitudinal studies investigating the trajectory of fEFT from fetal to postnatal life and its association with cardiometabolic outcomes in offspring would be particularly informative (63). Additionally, randomized controlled trials evaluating the effects of glycemic control and other maternal interventions on fEFT and offspring outcomes could provide critical insights into causal pathways and potential strategies for prevention.

#### CONCLUSION

In conclusion, this meta-analysis demonstrates that maternal DM during pregnancy is associated with increased fEFT, with the effect becoming more pronounced in later gestation. These findings highlight the importance of glycemic control and targeted monitoring in diabetic pregnancies to mitigate long-term cardiometabolic risks in offspring. Further research is needed to clarify the mechanisms underlying this association and to explore the clinical utility of fEFT as a prognostic marker in this high-risk population.

Conflicts of interest: Authors declare no conflict of interest.

**Funding:** This study was supported by "Tianshan Talents" Medical and Health High-level Talent Training Program (TSYC202301A039).

**Data availability:** The data that support the findings of this study are available from the corresponding author upon reasonable request.

Submitted: 22 December 2024

Accepted: 13 February 2025

Published online: 05 March 2025

#### REFERENCES

1. Ornoy A, Becker M, Weinstein-Fudim L, Ergaz Z. Diabetes during Pregnancy: A Maternal Disease Complicating the Course of Pregnancy with Long-Term Deleterious Effects on the Offspring. A Clinical Review. Int J Mol Sci. 2021;22(6).

2. Bashir M, Fagier Y, Ahmed B, C Konje J. An overview of diabetes mellitus in pregnant women with obesity. Best Practice & Research Clinical Obstetrics & Gynaecology. 2024;93:102469.

3. Sweeting A, Wong J, Murphy HR, Ross GP. A Clinical Update on Gestational Diabetes Mellitus. Endocr Rev. 2022;43(5):763-93.

4. Malaza N, Masete M, Adam S, Dias S, Nyawo T, Pheiffer C. A Systematic Review to Compare Adverse Pregnancy Outcomes in Women with Pregestational Diabetes and Gestational Diabetes. Int J Environ Res Public Health. 2022;19(17).

5. Modzelewski R, Stefanowicz-Rutkowska MM, Matuszewski W, Bandurska-Stankiewicz EM. Gestational Diabetes Mellitus-Recent Literature Review. J Clin Med. 2022;11(19).

6. Hunt KJ, Schuller KL. The increasing prevalence of diabetes in pregnancy. Obstet Gynecol Clin North Am. 2007;34(2):173-99, vii.

7. American Diabetes Association Professional Practice C. 15. Management of Diabetes in Pregnancy: Standards of Care in Diabetes—2024. Diabetes Care. 2023;47(Supplement\_1):S282-S94.

8. Ye W, Luo C, Huang J, Li C, Liu Z, Liu F. Gestational diabetes mellitus and adverse pregnancy outcomes: systematic review and meta-analysis. BMJ. 2022;377:e067946.

9. Shub A, Lappas M. Pregestational diabetes in pregnancy: Complications, management, surveillance, and mechanisms of disease-A review. Prenat Diagn. 2020;40(9):1092-8.

 Tam WH, Ma RCW, Ozaki R, Li AM, Chan MHM, Yuen LY, et al. In Utero Exposure to Maternal Hyperglycemia Increases Childhood Cardiometabolic Risk in Offspring. Diabetes Care. 2017;40(5):679-86.
 Hufnagel A, Dearden L, Fernandez-Twinn DS, Ozanne SE. Programming of cardiometabolic health:

the role of maternal and fetal hyperinsulinaemia. Journal of Endocrinology. 2022;253(2):R47-R63.

12. Seneviratne SN, Rajindrajith S. Fetal programming of obesity and type 2 diabetes. World J Diabetes. 2022;13(7):482-97.

13. Lurbe E, Ingelfinger J. Developmental and Early Life Origins of Cardiometabolic Risk Factors. Hypertension. 2021;77(2):308-18.

14. Braescu L, Gaspar M, Buriman D, Aburel OM, Merce AP, Bratosin F, et al. The Role and Implications of Epicardial Fat in Coronary Atherosclerotic Disease. J Clin Med. 2022;11(16).

15. Packer M. Epicardial Adipose Tissue May Mediate Deleterious Effects of Obesity and Inflammation on the Myocardium. Journal of the American College of Cardiology. 2018;71(20):2360-72.

16. Ikenoue S, Waffarn F, Sumiyoshi K, Ohashi M, Ikenoue C, Buss C, et al. Association of ultrasoundbased measures of fetal body composition with newborn adiposity. Pediatr Obes. 2017;12 Suppl 1(Suppl 1):86-93.

17. Yakut K, Öcal DF, Sanhal Yaşar C, Halıcı Öztürk F, Şanlı C, Çelen Ş. Fetal epicardial fat thickness in fetal growth restriction; effects on fetal heart function and relationship with the severity of disease. J Matern Fetal Neonatal Med. 2022;35(25):6946-52.

18. Doğru Ş, Akkuş F. Fetal epicardial fat thickness in non-severe idiopathic polyhydramnios: Its impact on fetal cardiac function and perinatal outcomes. J Clin Ultrasound. 2023;51(6):974-80.

19. Lu JLA, Jamhour M, Rizzo G. Is a fetal epicardial fat thickness a proxy of cardiac function? J Clin Ultrasound. 2023;51(6):981-2.

20. Dal Y, Akkuş F, Karagün Ş, Nessar AZ, Karaca SG, Kıllı M, et al. Fetal epicardial fat thickness and modified myocardial performance index in late-onset fetal growth restriction. J Clin Ultrasound. 2024;52(9):1321-8.

21. Jackson D, Deschamps D, Myers D, Fields D, Knudtson E, Gunatilake R. Fetal epicardial fat thickness in diabetic and non-diabetic pregnancies: A retrospective cross-sectional study. Obesity (Silver Spring). 2016;24(1):167-71.

22. Yavuz A, Akkurt MO, Yalcin S, Karakoc G, Varol E, Sezik M. Second Trimester Fetal and Maternal Epicardial Fat Thickness in Gestational Diabetic Pregnancies. Horm Metab Res. 2016;48(9):595-600.

23. Akkurt MO, Turan OM, Crimmins S, Harman CR, Turan S. Increased fetal epicardial fat thickness: A novel ultrasound marker for altered fetal metabolism in diabetic pregnancies. J Clin Ultrasound. 2018;46(6):397-402.

Iskender C, Yakut Yucel K, Dereli ML, Saglam E, Celen S, Caglar T, et al. Increased fetal epicardial fat thickness: A reflecting finding for GDM and perinatal outcomes. Echocardiography. 2022;39(8):1082-8.
Baria M, Bharpoda DU, Hihor KK, Kothiwala CC. Role of Epicardial Fat Thickness by ultrasound in diagnosis of Gestational diabetes: An observational study. European Journal of Cardiovascular Medicine. 2023;13(3):407-10.

26. Ghuman GK, Bagri N, Chandra R, Malik A, Misra R, Gaikwad HS. Role of ultrasonographic measurement of the fetal epicardial fat pad and cardiac interventricular septal thickness in predicting the outcome and prevent various complications of gestational diabetes mellitus. Egyptian Journal of Radiology and Nuclear Medicine. 2023;54(1):91.

27. Omeroglu I, Golbasi H, Bayraktar B, Golbasi C, Yildirim Karaca S, Demircan T, et al. Predicting adverse perinatal outcomes with fetal modified myocardial performance index and epicardial fat tissue thickness in diabetes-complicated pregnancies. Eur Rev Med Pharmacol Sci. 2023;27(21):10620-30.

28. Sever B, Bayraktar B, Adıyaman D, Gölbaşı H, Ömeroğlu İ, Çolak S, et al. Association of increased fetal epicardial fat thickness with maternal pregestational and gestational diabetes. J Matern Fetal Neonatal Med. 2023;36(1):2183474.

29. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372:n71.

30. Page MJ, Moher D, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. PRISMA 2020 explanation and elaboration: updated guidance and exemplars for reporting systematic reviews. BMJ. 2021;372:n160.

31. Higgins J, Thomas J, Chandler J, Cumpston M, Li T, Page M, et al. Cochrane Handbook for Systematic Reviews of Interventions version 6.2. The Cochrane Collaboration. 2021;www.training.cochrane.org/handbook.

32. Wells GA, Shea B, O'Connell D, Peterson J, Welch V, Losos M, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses.

2010;http://www.ohri.ca/programs/clinical\_epidemiology/oxford.asp.

33. Higgins J, Green S. Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0. The Cochrane Collaboration. 2011;<u>www.cochranehandbook.org</u>.

34. Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. Stat Med. 2002;21(11):1539-58.

35. Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. BMJ. 1997;315(7109):629-34.

36. Aydin S, Fatihoglu E. Fetal Epicardial Fat Thickness: Can It Serve as a Sonographic Screening Marker for Gestational Diabetes Mellitus? J Med Ultrasound. 2020;28(4):239-44.

37. Singh A, Josan AS, Gupta K, Pahwa S. Fetal Epicardial Fat Thickness: Its Role as Marker for Gestational Diabetic Mellitus. Indian J Radiol Imaging. 2023;33(3):302-8.

38. Karcz K, Królak-Olejnik B. Impact of Gestational Diabetes Mellitus on Fetal Growth and Nutritional Status in Newborns. Nutrients. 2024;16(23).

39. Lewitt MS. The Role of the Growth Hormone/Insulin-Like Growth Factor System in Visceral Adiposity. Biochem Insights. 2017;10:1178626417703995.

40. Iacobellis G, Bianco AC. Epicardial adipose tissue: emerging physiological, pathophysiological and clinical features. Trends Endocrinol Metab. 2011;22(11):450-7.

41. Jiménez-Osorio AS, Carreón-Torres E, Correa-Solís E, Ángel-García J, Arias-Rico J, Jiménez-Garza O, et al. Inflammation and Oxidative Stress Induced by Obesity, Gestational Diabetes, and Preeclampsia in Pregnancy: Role of High-Density Lipoproteins as Vectors for Bioactive Compounds. Antioxidants (Basel). 2023;12(10).

42. Busik JV, Mohr S, Grant MB. Hyperglycemia-induced reactive oxygen species toxicity to endothelial cells is dependent on paracrine mediators. Diabetes. 2008;57(7):1952-65.

43. Tsalamandris S, Antonopoulos AS, Oikonomou E, Papamikroulis GA, Vogiatzi G, Papaioannou S, et al. The Role of Inflammation in Diabetes: Current Concepts and Future Perspectives. Eur Cardiol. 2019;14(1):50-9.

44. Yuan T, Yang T, Chen H, Fu D, Hu Y, Wang J, et al. New insights into oxidative stress and inflammation during diabetes mellitus-accelerated atherosclerosis. Redox Biology. 2019;20:247-60.
45. Talman AH, Psaltis PJ, Cameron JD, Meredith IT, Seneviratne SK, Wong DTL. Epicardial adipose tissue: far more than a fat depot. Cardiovascular Diagnosis and Therapy; Vol 4, No 6 (December 25, 2014):

Cardiovascular Diagnosis and Therapy. 2014.

46. Calvo MJ, Parra H, Santeliz R, Bautista J, Luzardo E, Villasmil N, et al. The Placental Role in Gestational Diabetes Mellitus: A Molecular Perspective. touchREV Endocrinol. 2024;20(1):10-8.

47. Kramer AC, Jansson T, Bale TL, Powell TL. Maternal-fetal cross-talk via the placenta: influence on offspring development and metabolism. Development. 2023;150(20).

48. Long NM, Rule DC, Zhu MJ, Nathanielsz PW, Ford SP. Maternal obesity upregulates fatty acid and glucose transporters and increases expression of enzymes mediating fatty acid biosynthesis in fetal adipose tissue depots. J Anim Sci. 2012;90(7):2201-10.

49. Dłuski DF, Wolińska E, Skrzypczak M. Epigenetic Changes in Gestational Diabetes Mellitus. Int J Mol Sci. 2021;22(14).

50. Pant R, Firmal P, Shah VK, Alam A, Chattopadhyay S. Epigenetic Regulation of Adipogenesis in Development of Metabolic Syndrome. Front Cell Dev Biol. 2020;8:619888.

51. Ott R, Melchior K, Stupin JH, Ziska T, Schellong K, Henrich W, et al. Reduced Insulin Receptor Expression and Altered DNA Methylation in Fat Tissues and Blood of Women With GDM and Offspring. The Journal of Clinical Endocrinology & Metabolism. 2019;104(1):137-49.

52. Petropoulos S, Guillemin C, Ergaz Z, Dimov S, Suderman M, Weinstein-Fudim L, et al. Gestational Diabetes Alters Offspring DNA Methylation Profiles in Human and Rat: Identification of Key Pathways Involved in Endocrine System Disorders, Insulin Signaling, Diabetes Signaling, and ILK Signaling. Endocrinology. 2015;156(6):2222-38.

53. Buhary BM, Almohareb O, Aljohani N, Alzahrani SH, Elkaissi S, Sherbeeni S, et al. Glycemic control and pregnancy outcomes in patients with diabetes in pregnancy: A retrospective study. Indian J Endocrinol Metab. 2016;20(4):481-90.

54. Karcz K, Królak-Olejnik B. Impact of Gestational Diabetes Mellitus on Fetal Growth and Nutritional Status in Newborns. Nutrients [Internet]. 2024; 16(23).

55. Plows JF, Stanley JL, Baker PN, Reynolds CM, Vickers MH. The Pathophysiology of Gestational Diabetes Mellitus. Int J Mol Sci. 2018;19(11).

56. Parr NJ, Schweer-Collins ML, Darlington TM, Tanner-Smith EE. Meta-analytic approaches for examining complexity and heterogeneity in studies of adolescent development. J Adolesc. 2019;77:168-78.

57. Mathur MB, VanderWeele TJ. Methods to Address Confounding and Other Biases in Meta-Analyses: Review and Recommendations. Annu Rev Public Health. 2022;43:19-35.

58. Iacobellis G. Epicardial fat links obesity to cardiovascular diseases. Prog Cardiovasc Dis. 2023;78:27-33.

59. Tehrani FR, Naz MSG, Bidhendi-Yarandi R, Behboudi-Gandevani S. Effect of Different Types of Diagnostic Criteria for Gestational Diabetes Mellitus on Adverse Neonatal Outcomes: A Systematic Review, Meta-Analysis, and Meta-Regression. Diabetes Metab J. 2022;46(4):605-19.

60. Lorenzo-Almorós A, Hang T, Peiró C, Soriano-Guillén L, Egido J, Tuñón J, et al. Predictive and diagnostic biomarkers for gestational diabetes and its associated metabolic and cardiovascular diseases. Cardiovascular Diabetology. 2019;18(1):140.

61. Zisser HC, Biersmith MA, Jovanovič LB, Yogev Y, Hod M, Kovatchev BP. Fetal risk assessment in pregnancies complicated by diabetes mellitus. J Diabetes Sci Technol. 2010;4(6):1368-73.

62. Iskender C, Yakut Yücel K, Dereli ML, Sağlam E, Çelen Ş, Çağlar T, et al. Increased fetal epicardial fat thickness: A reflecting finding for GDM and perinatal outcomes. Echocardiography. 2022;39(8):1082-8.
63. Calcaterra V, Mannarino S, Garella V, Rossi V, Biganzoli EM, Zuccotti G. Cardiovascular Risk in Pediatrics: A Dynamic Process during the First 1000 Days of Life. Pediatr Rep. 2023;15(4):636-59.

14

### TABLES AND FIGURES WITH LEGENDS

#### Table 1. Characteristics of the included studies

Study	Country	Design	No. of women included	Maternal age (years)	Maternal BMI (kg/m <sup>2</sup> )	fEFT measuring timing	Methods for fEFT measuring	Median GA of fEFT measuring (weeks)	Type of maternal diabetes	No. of women with DM	Variables matched or adjusted
Yavuz 2016	Turkey	CS	80	27.7	27.9	GA: 24- 28 weeks	Via ultrasound at end- diastole over 3 cardiac cycles from the RV wall, recording the highest value per cycle	26	GDM (IADPSG)	40	Maternal age, BMI, GA, fetal gender, and fetal abdominal circumference
Jackson 2016	USA	CS	56	28.8	30.8	GA: 20- 28 weeks	Via ultrasound using LVOT views near the aortic valve, selecting the image that best	23.5	PDM	28	Maternal age, BMI, GA, and fetal abdominal circumference

Ś

							delineated the epicardial				
							fat border	Ċ			
							Via ultrasound using the LVOT view, identifying				
							the hypoechogenic fat				Maternal BMI,
Akkurt		66	212	20.2	21.2	GA: 24-	layer over the RV, and	28.2	GDM	100	ethnicity, GA,
2018	USA	LL.	212	29.2	31.5	35 weeks	point near a reference	28.2	(IADPSG)	100	fetal sex, and
							line drawn through the				fetal abdominal
							descending aorta and				circumference
							aortic annulus				
							Via ultrasound using the				Maternal age,
Aydin	Turkey	CC	120	32.1	20	GA: 18-	standardized four-	20	GDM	60	BMI, GA, and
2020	TUIKEy	cc	120	32.1	27	22 weeks	fEFT at the midpoint of	20	(IADPSG)	00	fetal abdominal
							the ventricular wall				circumference

Iskender 2022	Turkey	CC	80	28	29.1	GA: 28- 39 weeks	Via ultrasound using the apical five-chamber view, measuring the hypoechoic area on the free wall of the RV with a reference line drawn from the descending aorta through the aortic annulus	34.5	GDM (IADPSG)	40	Maternal age, gravidity, and GA
Baria 2023	India	CS	70	35.8	NR	GA: 24- 28 weeks	Via ultrasound using the LVOT view, identifying the hypoechogenic area between the visceral pericardium and myocardium along the right ventricle, measured	26	GDM (DIPSI)	35	Maternal age and GA

							during end-systole				
Ghuman 2023	India	CC	70	25.6	NR	GA: 24- 32 weeks	Via ultrasound using a standardized four- chamber view at end- diastole over three cardiac cycles, measuring the hypoechoic space just outside the myocardium on the right ventricular free wall	28	GDM (IADPSG)	35	Maternal age, BMI, and GA
Omeroglu 2023 GDM	Turkey	CC	135	29	30.4	GA: 28- 39 weeks	Via ultrasound using the LVOT view, measuring the hypoechoic area between the myocardium and visceral pericardium on the RV	32	GDM (IADPSG)	90	GA

Omeroglu 2023 PDM	Turkey	CC	90	28	29.9	GA: 28- 39 weeks	Via ultrasound using the LVOT view, measuring the hypoechoic area between the myocardium and visceral pericardium on the RV	32	PDM	45	GA
Singh 2023	India	CS	60	26.4	NR	GA: 24- 28 weeks	Via ultrasound using the LVOT view, measuring the hypoechoic area between the visceral pericardium and myocardium along the right ventricle at end- diastole	26	GDM (IADPSG)	30	Maternal age and GA
Sever 2023	Turkey	CC	165	29.9	30	GA: 24- 28 weeks	Via ultrasound using cardiac long-axis views	26	GDM (IADPSG)	110	Maternal BMI, GA, parity,

GDM						of the LVOT near the				gravidity, and
						aortic valve, measuring	Ċ			fetal sex
						the thickest hypoechoic				
						area at end-diastole				
						Via ultrasound using				
Sover						cardiac long-axis views				Maternal BMI,
	T 1	 165	20.6	20.1	GA: 24-	of the LVOT near the	26		110	GA, parity,
2023	Turkey	165	30.6	30.1	28 weeks	aortic valve, measuring	26	PDM	110	gravidity, and
PDM						the thickest hypoechoic				fetal sex
					2	area at end-diastole				

 Table 2. Study quality evaluation via the Newcastle-Ottawa Scale

	Adequate definition of the cases	Representativeness of the cases	Selection of Controls	Definition of Controls	Controlled for GA	Controlled for other confoundings	Ascertainment of the exposure	Same method of ascertainment of exposure for cases and controls	Non- response rate	Overall
Yavuz 2016	1	0	1	1		1	1	1	1	8
Jackson 2016	1	1	1	1	1	1	1	1	1	9
Akkurt 2018	0	0		1	1	1	1	1	1	7
Aydin 2020	1	1	1	1	1	1	1	1	1	9
Iskender	1	1	1	1	1	1	1	1	1	9

2022										
Baria 2023	1	0	1	1	1	1	1	1	1	8
Ghuman 2023	1	0	1	1	1	1	5	1	1	8
Omeroglu										
2023	1	0	1	1	1	0	1	1	1	7
GDM										
Omeroglu	1	0	1	1	1	0	1	1	1	7
2023 PDM										
Singh	1	0	1	1	1	1	1	1	1	8
2023	_									-
Sever										
2023	1	0	1	1	1	1	1	1	1	8
GDM										
Sever	1	0	1	1	1	1	1	1	1	8
2023 PDM										

## Table 3. Results of univariate meta-regression analysis

Variables	MD of fEFT	between women with and with	out DM in pregn	ancy
	Coefficient	95% CI	p values	Adjusted R <sup>2</sup>
Sample size	-0.00061	-0.00360 to 0.00237	0.65	-14.9%
Mean maternal age (years)	0.0035	-0.0614 to 0.0684	0.91	-14.5%
Mean maternal BMI (kg/m <sup>2</sup> )	0.041	-0.111 to 0.194	0.56	-10.8%
Median GA at fEFT measuring (weeks)	0.040	0.015 to 0.066	0.005	83.2%
NOS	-0.15	-0.32 to 0.03	0.09	28.7%



Figure 1. Flowchart illustrates the process of database search and study identification

	DM p	regnar	icy	Non-DI	A pregni	ancy		Mean Difference	Mea	n Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	IV. Ra	indom, 95% Cl
avuz 2016	1.34	0.25	40	1.13	0.19	40	12.2%	0.21 [0.11, 0.31]		-
ackson 2016	1.43	0.37	28	1.16	0.3	28	10.1%	0.27 [0.09, 0.45]		
kkurt 2018	1.45	0.98	106	1.1	0.72	106	8.6%	0.35 [0.12, 0.58]		
ydin 2020	1.05	0.77	60	0.9	0.58	60	8.3%	0.15 [-0.09, 0.39]		
skender 2022	1.9	0.53	40	1.4	0.65	40	7.9%	0.50 [0.24, 0.76]		
laria 2023	1.8	0.59	35	1.1	1.18	35	4.5%	0.70 [0.26, 1.14]		
ihuman 2023	1.54	0.33	35	1.15	0.59	35	8.8%	0.39 [0.17, 0.61]		
meroglu 2023 GDM	1.83	1.2	90	1.19	0.28	45	7.8%	0.64 [0.38, 0.90]		
meroglu 2023 PDM	2.04	0.86	45	1.19	0.28	45	7.8%	0.85 [0.59, 1.11]		
ingh 2023	1.7	1.1	30	1.5	0.55	30	4.4%	0.20 [-0.24, 0.64]		
ever 2023 GDM	1.4	0.86	110	1,19	0.36	55	9.8%	0.21 [0.02, 0.40]		
iever 2023 PDM	1.47	0.87	110	1.19	0.36	55	9.8%	0.28 [0.09, 0.47]		_
otal (95% CI)			729			574	100.0%	0.37 [0.26, 0.49]		•
leterogeneity: Tau <sup>2</sup> = (	0.02; Chi	= 35.2	23. df =	11 (P = 0	.0002); (	2 = 69%		N 12 (S		1 1



**Figure 2.** Forest plots for the meta-analysis comparing fEFT between women with and without DM in **pregnancy and plots of the meta-regression analysis for the influence of GA of fEFT assessment**; A, forest plots for the overall meta-analysis; and B, meta-regression for the influence of GA of fEFT assessment on the results;

	Dm p	regnar	icy	NON-DA	a pregn	ancy		mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV. Random, 95% CI	IV. Random. 95% Cl
1.2.1 Case-control									
Akkurt 2018	1.45	0.98	106	1.1	0.72	106	8.6%	0.35 [0.12, 0.58]	
Aydin 2020	1.05	0.77	60	0.9	0.58	60	8.3%	0.15 [-0.09, 0.39]	
Iskender 2022	1.9	0.53	40	1.4	0.65	40	7.9%	0.50 [0.24, 0.76]	
Ghuman 2023	1.54	0.33	35	1,15	0.59	35	8.8%	0.39 [0.17, 0.61]	
Omeroglu 2023 GDM	1.83	1.2	90	1.19	0.28	45	7.8%	0.64 [0.38, 0.90]	
Omeroglu 2023 PDM	2.04	0.86	45	1.19	0.28	45	7.8%	0.85 [0.59, 1.11]	
Sever 2023 GDM	1.4	0.86	110	1.19	0.36	55	9.8%	0.21 [0.02, 0.40]	
Sever 2023 PDM	1.47	0.87	110	1.19	0.36	55	9.8%	0.28 10.09, 0.471	
Subtotal (95% CI)	1.197.61	1081	596	0.502.1	-503.50	441	68.8%	0.41 [0.26, 0.56]	•
Heterogeneity: Tau <sup>2</sup> = ( Test for overall effect: 2	0.03; Chi Z = 5.30 (	<sup>2</sup> = 24.1 P < 0.0	53, df = 00001)	7 (P = 0.0	0009); I²	= 71%		2770 - B	
1.2.2 Cross-sectional									
Yavuz 2016	1.34	0.25	40	1.13	0.19	40	12.2%	0.21 [0.11, 0.31]	-
Jackson 2016	1.43	0.37	28	1.16	0.3	28	10.1%	0.27 [0.09, 0.45]	
Baria 2023	1.8	0.59	35	1.1	1.18	35	4.5%	0.70 [0.26, 1.14]	
Singh 2023	1.7	1.1	30	1.5	0.55	30	4.4%	0.20 [-0.24, 0.64]	
Subtotal (95% CI)			133			133	31.2%	0.27 [0.13, 0.41]	•
Heterogeneity: Tau <sup>2</sup> = 0 Test for overall effect: 2	0.01; Chř Z = 3.88 (	<sup>e</sup> = 4.76 P = 0.0	8, df = 3 0001)	(P = 0.19	9); I <sup>2</sup> = 3	7%			
Total (95% CI)			729			574	100.0%	0.37 (0.26.0.49)	•
Loran factor cul				11/0 - 0	00031-1	2 - 60%	100.070	and, famo, and	
Heterogeneity: Tau <sup>a</sup> = ( Test for overall effect: 2 Test for subaroup differ	0.02; Chi Z = 6.46 ( nences: C	r = 35.2 P < 0.( hi² = 1	.81. df = .81. df =	= 1 (P = 0	.18). P =	44.9%			-1 -0.5 0 0.5 1 Lower fEFT in DM Higher fEFT in
Heterogeneity: Tau <sup>a</sup> = ( Test for overall effect: 2 Test for subaroup differ	0.02; Chi Z = 6.46 ( nences: C DM p	regnar	.3, df = )0001) .81. df = 1cy	1 (P = 0 1 (P = 0 Non-DM	.18). P = A pregn	44.9% ancy		Mean Difference	-1 -0.5 0 0.5 1 Lower fEFT in DM Higher fEFT in I Mean Difference
Heterogeneity: Tau <sup>2</sup> = ( Test for overall effect: 7 Test for subaroup differ Study or Subgroup	0.02; Chi Z = 6.46 ( rences: C DM p <u>Mean</u>	r = 35.3 P < 0.( hi <sup>2</sup> = 1 regnar SD	.3, df = )0001) .81, df = ncy <u>Total</u>	1 (P = 0 1 (P = 0 Non-DM Mean	.18). P = A pregn SD	44.9% ancy Total	Weight	Mean Difference IV. Random. 95% CI	-1 -0.5 0 0.5 1 Lower fEFT in DM Higher fEFT in Mean Difference IV, Random, 95% CI
Heterogeneity: Tau <sup>2</sup> = ( Test for overall effect: 7 Test for subaroup differ Study or Subgroup 1.3.1 GDM versus nor	0.02; Chi Z = 6.46 ( rences: C DM p <u>Mean</u> n-DM	r = 35.2 P < 0.( hi <sup>2</sup> = 1 regnar SD	3, df = )0001) 81, df = ncy Total	1 (P = 0 1 (P = 0 Non-DM Mean	.18), (* = 18),	44.9% ancy Total	Weight	Mean Difference IV. Random, 95% CI	-1 -0.5 0 0.5 1 Lower fEFT in DM Higher fEFT in I Mean Difference IV, Random, 95% CI
Heterogeneity: Tau <sup>2</sup> = ( Test for overall effect: 2 Test for subgroup differ Study or Subgroup 1.3.1 GDM versus nor Yavuz 2016	0.02; Chi Z = 6.46 ( nences: C DM p <u>Mean</u> 1-DM 1.34	r = 35.2 P < 0.0 th <sup>2</sup> = 1 regnar SD 0.25	(3, df = )0001) (81, df = ncy Total 40	1 (P = 0 Non-Di Mean 1.13	18), P = A pregn SD 0.19	44.9% ancy <u>Total</u> 40	Weight 13.0%	Mean Difference IV. Random, 95% CI 0.21 [0.11, 0.31]	-1 -0.5 0 0.5 1 Lower fEFT in DM Higher fEFT in I Mean Difference IV, Random, 95% CI
Heterogeneity: Tau <sup>2</sup> = ( Test for overall effect: 2 Test for subgroup differ Study or Subgroup 1.3.1 GDM versus nor Yavuz 2016 Aydin 2020	0.02; Chi <sup>2</sup> z = 6.46 ( DM p <u>Mean</u> 1-DM 1.34 1.05	<ul> <li>= 35.2</li> <li>P &lt; 0.0</li> <li>chi<sup>2</sup> = 1</li> <li>regnar</li> <li>SD</li> <li>0.25</li> <li>0.77</li> </ul>	(3, df = )0001) (81, df = ncy <u>Total</u> 40 60	1 (P = 0 Non-DM Mean 1.13 0.9	.18). P = 18). P = 10,19 0.19 0.58	44.9% ancy <u>Total</u> 40 60	Weight 13.0% 9.1%	Mean Difference IV. Random. 95% CI 0.21 [0.11, 0.31] 0.15 [-0.09, 0.39]	-1 -0.5 0 0.5 1 Lower fEFT in DM Higher fEFT in I Mean Difference IV, Random, 95% CI
Heterogeneity: Tau <sup>2</sup> = ( Test for overall effect: 2 Test for subgroup differ Study or Subgroup	0.02; Chi Z = 6.46 ( rences: C DM p Mean n-DM 1.34 1.05 1.9	* = 35.2 P < 0.0 :hi <sup>2</sup> = 1 regnar SD 0.25 0.77 0.53	3, df = 10001) 81, df = 1000 100	1.13 1.4	18). P = 18). P = 18). P = 10, 19 0.19 0.58 0.65	44.9% ancy <u>Total</u> 40 60 40	Weight 13.0% 9.1% 8.7%	Mean Difference IV. Random. 95% CI 0.21 [0.11, 0.31] 0.15 [-0.09, 0.39] 0.50 [0.24, 0.76]	-1 -0.5 0 0.5 1 Lower fEFT in DM Higher fEFT in I Mean Difference IV, Random, 95% CI
Heterogeneity: Tau <sup>2</sup> = ( Test for overall effect: 2 Test for subaroup differ Study or Subgroup 1.3.1 GDM versus nor Yavuz 2016 Aydin 2020 Iskender 2022 Baria 2023	0.02; Chi Z = 6.46 ( rences: C DM p Mean 1-DM 1.34 1.05 1.9 1.8	* = 35.3 P < 0.0 bir <sup>2</sup> = 1 regnar SD 0.25 0.77 0.53 0.59	3, df = 10001) 81, df = 1cy Total 40 60 40 35	Non-DM Mean 1.13 0.9 1.4 1.1	16). P = 16). P = 16). P = 16). P = 10022, 1 10022,	44.9% ancy <u>Total</u> 40 60 40 35	Weight 13.0% 9.1% 8.7% 5.1%	Mean Difference <u>IV. Random, 95% CI</u> 0.21 [0.11, 0.31] 0.15 [-0.09, 0.39] 0.50 [0.24, 0.76] 0.70 [0.26, 1.14]	-1 -0.5 0 0.5 1 Lower fEFT in DM Higher fEFT in I Mean Difference IV, Random, 95% CI
Heterogeneity: Tau <sup>2</sup> = ( Test for overall effect: 2 Test for subaroup differ Study or Subgroup 1.3.1 GDM versus nor Yavuz 2016 Aydin 2020 Iskender 2022 Baria 2023 Ghuman 2023	0.02; Chi Z = 6.46 ( mences: C DM p <u>Mean</u> 1-DM 1.34 1.05 1.9 1.8 1.54	*= 35.7 P < 0.0 hi <sup>2</sup> = 1 regnar SD 0.25 0.77 0.53 0.59 0.33	(3, df = )0001) 81, df = <b>tcy</b> <b>Total</b> 40 60 40 35 35	Non-DM Mean 1.13 0.9 1.4 1.1 1.15	16). P = A pregn SD 0.19 0.58 0.65 1.18 0.59	44.9% ancy <u>Total</u> 40 60 40 35 35	Weight 13.0% 9.1% 8.7% 5.1% 9.6%	Mean Difference IV. Random, 95% CI 0.21 [0.11, 0.31] 0.15 [-0.09, 0.39] 0.50 [0.24, 0.76] 0.70 [0.26, 1.14] 0.39 [0.17, 0.61]	-1 -0.5 0 0.5 1 Lower fEFT in DM Higher fEFT in I Mean Difference IV, Random, 95% CI
Heterogeneity: Tau <sup>2</sup> = ( Test for overall effect: 2 Test for subgroup	0.02; Chi <sup>2</sup> Z = 6.46 ( mences: C DM p <u>Mean</u> 1-DM 1.34 1.05 1.9 1.8 1.54 1.83	*= 35.4 P < 0.0 hit <sup>2</sup> = 1 regnar SD 0.25 0.77 0.53 0.59 0.33 1.2	(3, df = )0001) 81, df = <b>tcy</b> <b>Total</b> 40 60 40 35 35 90	1 (P = 0 Non-DM Mean 1.13 0.9 1.4 1.1 1.15 1.19	18). P = 18). P = 19 0.19 0.58 0.65 1.18 0.59 0.28	44.9% ancy <u>Total</u> 40 60 40 35 35 45	Weight 13.0% 9.1% 8.7% 5.1% 9.6% 8.7%	Mean Difference IV. Random, 95% CI 0.21 [0.11, 0.31] 0.15 [-0.09, 0.39] 0.50 [0.24, 0.76] 0.70 [0.26, 1.14] 0.39 [0.17, 0.61] 0.64 [0.38, 0.90]	-1 -0.5 0 0.5 1 Lower fEFT in DM Higher fEFT in I Mean Difference IV, Random, 95% CI
Heterogeneity: Tau <sup>2</sup> = ( Test for overall effect: 2 Test for subaroup differ Study or Subgroup 1.3.1 GDM versus nor Yavuz 2016 Aydin 2020 Iskender 2022 Baria 2023 Ghuman 2023 Omeroglu 2023 GDM Singh 2023	0.02; ChiP Z = 6.46 ( rences: C DM p 1.0M 1.34 1.05 1.9 1.8 1.54 1.83 1.54	P < 0.0 P < 0.0 bir <sup>2</sup> = 1 regnar SD 0.25 0.77 0.53 0.59 0.33 1.2 1.1	(3, df = )0001) 81, df = 1cy Total 40 60 40 35 35 90 30	1 (P = 0 Non-DA Mean 1.13 0.9 1.4 1.1 1.15 1.19 1.5	18). P = 18). P = 19 0.19 0.58 0.65 1.18 0.59 0.28 0.55	44.9% ancy Total 40 60 40 35 35 45 30	Weight 13.0% 9.1% 8.7% 5.1% 8.7% 5.1%	Mean Difference IV. Random, 95% CI 0.21 [0.11, 0.31] 0.15 [-0.09, 0.39] 0.50 [0.24, 0.76] 0.70 [0.26, 1.14] 0.39 [0.17, 0.61] 0.64 [0.38, 0.90] 0.20 [-0.24, 0.64]	-1 -0.5 0 0.5 1 Lower fEFT in DM Higher fEFT in I Mean Difference IV, Random, 95% CI
Heterogeneity: Tau <sup>2</sup> = ( Test for overall effect: 2 Test for subgroup 1.3.1 GDM versus nor Yavuz 2016 Aydin 2020 Iskender 2022 Baria 2023 Ghuman 2023 Omeroglu 2023 GDM Singh 2023 Sever 2023 GDM	0.02; ChiP Z = 6.46 ( mences: C DM p Mean 1.34 1.05 1.9 1.8 1.54 1.83 1.54 1.83 1.7	P < 0.0 P < 0.0 bir <sup>2</sup> = 1 regnar SD 0.25 0.77 0.53 0.59 0.33 1.2 1.1 0.86	(3, df = )0001) 81, df = 1cy Total 40 60 40 35 35 90 30 110	1.13 1.13 0.9 1.4 1.15 1.15 1.5 1.19	18). P = 18). P = 19, Pregn. 5D 0.19 0.58 0	44.9% ancy Total 40 60 40 35 35 45 30 55	Weight 13.0% 9.1% 8.7% 5.1% 9.6% 8.7% 5.1%	Mean Difference IV. Random, 95% CI 0.21 [0.11, 0.31] 0.15 [-0.09, 0.39] 0.50 [0.24, 0.76] 0.70 [0.26, 1.14] 0.39 [0.17, 0.61] 0.64 [0.38, 0.90] 0.20 [-0.24, 0.64] 0.21 [0.02, 0.40]	-1 -0.5 0 0.5 1 Lower fEFT in DM Higher fEFT in I Mean Difference IV, Random, 95% CI
Heterogeneity: Tau <sup>2</sup> = ( Test for overall effect: 2 Test for subgroup 1.3.1 GDM versus nor Yavuz 2016 Aydin 2020 Iskender 2022 Baria 2023 Ghuman 2023 Omeroglu 2023 GDM Singh 2023 Sever 2023 GDM Subtotal (95% CI)	0.02; ChiP Z = 6.46 ( mmces: C DM p <u>Mean</u> 1-DM 1.34 1.05 1.9 1.8 1.54 1.83 1.7 1.4	P < 0.0 hi <sup>2</sup> = 1 regnar SD 0.25 0.77 0.53 0.59 0.33 1.2 1.1 0.86	(3, df = (20001) 81, df = (10) 100 100 100 100 100 100 100	1.13 0.9 1.13 0.9 1.4 1.15 1.19 1.5 1.19	18). P = 18). P = 19 0.19 0.58 0.65 1.18 0.59 0.28 0.36	44.9% ancy Total 40 60 40 35 35 45 30 55 340	Weight 13.0% 9.1% 8.7% 5.1% 9.6% 8.7% 5.1% 10.7% 69.9%	Mean Difference IV. Random, 95% CI 0.21 [0.11, 0.31] 0.16 [-0.09, 0.39] 0.50 [0.24, 0.76] 0.70 [0.26, 1.14] 0.39 [0.17, 0.61] 0.64 [0.38, 0.90] 0.20 [-0.24, 0.64] 0.21 [0.02, 0.40] 0.35 [0.21, 0.48]	-1 -0.5 0 0.5 1 Lower fEFT in DM Higher fEFT in I Mean Difference IV, Random, 95% CI
Heterogeneity: Tau <sup>2</sup> = ( Test for overall effect: 2 Test for subgroup 1.3.1 GDM versus nor Yavuz 2016 Aydin 2020 Iskender 2022 Baria 2023 Ghuman 2023 Ghuman 2023 Ghuman 2023 Sever 2023 GDM Singh 2023 Sever 2023 GDM Subtotal (95% CI) Heterogeneity: Tau <sup>2</sup> = (	0.02; ChiP Z = 6.46 ( mences: C DM p Mean 1-DM 1.34 1.05 1.9 1.8 1.54 1.83 1.54 1.83 1.7 1.4	P < 0.0 P < 0.0 hi <sup>2</sup> = 1 regnar SD 0.25 0.77 0.53 0.59 0.33 1.2 1.1 0.86	3, df = )0001) .81, df = 1cy Total 40 60 40 35 35 90 30 110 440 26, df =	1.13 1.13 0.9 1.4 1.15 1.19 1.5 1.19 1.5 1.19 1.5 1.19 1.7 1.7 1.7 1.7 1.7 1.7 1.7 1.7	18). P = 18). P = 19, 19 0.19 0.58 0.65 1.18 0.59 0.28 0.55 0.36 0.1; P =	44.9% ancy Total 40 60 40 35 35 45 30 55 340 62%	Weight 13.0% 9.1% 8.7% 5.1% 9.6% 8.7% 5.1% 10.7% 69.9%	Mean Difference IV. Random, 95% CI 0.21 [0.11, 0.31] 0.15 [-0.09, 0.39] 0.50 [0.24, 0.76] 0.70 [0.26, 1.14] 0.39 [0.17, 0.61] 0.64 [0.38, 0.90] 0.20 [-0.24, 0.64] 0.21 [0.02, 0.40] 0.35 [0.21, 0.48]	-1 -0.5 0 0.5 1 Lower fEFT in DM Higher fEFT in I Mean Difference IV, Random, 95% CI
Heterogeneity: Tau <sup>2</sup> = ( Test for overall effect: 2 Test for subaroup differ Study or Subaroup differ 1.3.1 GDM versus nor Yavuz 2016 Aydin 2020 Iskender 2022 Baria 2023 Ghuman 2023 Ghuman 2023 Ghuman 2023 Ghuman 2023 GDM Singh 2023 Sever 2023 GDM Subtotal (95% CI) Heterogeneity: Tau <sup>2</sup> = ( Test for overall effect: 2	0.02; Chiř Z = 6.46 ( mences: C DM p <u>Mean</u> 1-DM 1.34 1.05 1.9 1.8 1.54 1.83 1.54 1.83 1.7 1.4	P < 0.0 P < 0.0 thi <sup>2</sup> = 1 0.25 0.77 0.53 0.59 0.33 1.2 1.1 0.86 I = 18.2 P < 0.0	(3, df = (00001) 81, df = (100 100 100 100 100 100 100 10	Non-DM Mean 1.13 0.9 1.4 1.1 1.15 1.19 1.5 1.19 7 (P = 0.0	18). P = 18). P = 18). P = 10,19 0.58 0.58 0.65 1.18 0.59 0.28 0.55 0.36 11); P =	44.9% ancy Total 40 60 40 35 35 35 35 340 55 340 52%	Weight 13.0% 9.1% 8.7% 5.1% 8.7% 5.1% 10.7% 69.9%	Mean Difference IV. Random, 95% CI 0.21 [0.11, 0.31] 0.15 [-0.09, 0.39] 0.50 [0.24, 0.76] 0.70 [0.26, 1.14] 0.39 [0.17, 0.61] 0.64 [0.38, 0.90] 0.20 [-0.24, 0.64] 0.21 [0.02, 0.40] 0.35 [0.21, 0.48]	-1 -0.5 0 0.5 1 Lower fEFT in DM Higher fEFT in I Mean Difference IV, Random, 95% CI
Heterogeneity: Tau <sup>2</sup> = ( Test for overall effect: 2 Test for subaroup differ Study or Subaroup differ 1.3.1 GDM versus nor Yavuz 2016 Aydin 2020 Iskender 2022 Baria 2023 Ghuman 2023 Omeroglu 2023 GDM Singh 2023 Sever 2023 GDM Subtotal (95% CI) Heterogeneity: Tau <sup>2</sup> = ( Test for overall effect: 2 1.3.2 PDM versus non	0.02; Chi <sup>2</sup> Z = 6.46 ( mences: C DM p Mean 1-DM 1.34 1.05 1.9 1.8 1.54 1.83 1.7 1.4 0.02; Chi <sup>2</sup> Z = 5.14 (	P < 0.0 P < 0.0 thi <sup>2</sup> = 1 SD 0.25 0.77 0.53 0.59 0.33 1.2 1.1 0.86 * = 18.2 P < 0.0	(3, df = (00001) 81, df = (1000000000000000000000000000000000000	Non-DA Non-DA <u>Mean</u> 1.13 0.9 1.4 1.1 1.15 1.19 1.5 1.19 7 (P = 0.0	18). P = 18). P = 19 0.19 0.58 0.58 0.58 1.18 0.59 0.28 0.55 0.36 11); P =	44.9% ancy Total 40 60 40 35 35 45 30 55 340 52%	Weight 13.0% 9.1% 5.1% 9.6% 8.7% 5.1% 10.7% 69.9%	Mean Difference IV. Random. 95% CI 0.21 [0.11, 0.31] 0.15 [-0.09, 0.39] 0.50 [0.24, 0.76] 0.70 [0.26, 1.14] 0.39 [0.17, 0.61] 0.64 [0.38, 0.90] 0.20 [-0.24, 0.64] 0.21 [0.02, 0.40] 0.35 [0.21, 0.48]	-1 -0.5 0 0.5 1 Lower fEFT in DM Higher fEFT in I Mean Difference IV, Random, 95% CI
Heterogeneity: Tau <sup>2</sup> = ( Test for overall effect: 2 Test for subaroup differ Study or Subaroup differ 1.3.1 GDM versus nor Yavuz 2016 Aydin 2020 Iskender 2022 Baria 2023 Ghuman 2023 Ghu	0.02; Chiř Z = 6.46 ( mences: C DM p <u>Mean</u> 1.34 1.05 1.9 1.8 1.54 1.83 1.7 1.4 0.02; Chiř Z = 5.14 ( 1.43	= 35.7 P < 0.0 hi <sup>2</sup> = 1 regname SD 0.25 0.77 0.53 0.59 0.33 1.2 1.1 0.86 * = 18.2 P < 0.0	(3, df = (3, df = (3, df = (3, df = (40) (40) (40) (40) (35) (30) (30) (10) (440) (26, df = (30) (28)	1.13 1.13 0.9 1.4 1.13 1.13 1.15 1.19 1.5 1.19 7 (P = 0.0 1.16	18). P = 18). P = 18). P = 10,19 0.58 0.58 0.58 0.58 0.58 0.58 0.58 0.58 0.28 0.55 0.36 0.19 0.28 0.55 0.36	- 03 % 44.9% ancy Total 40 60 40 60 40 35 35 35 35 35 340 55 340 52%	Weight 13.0% 9.1% 8.7% 5.1% 9.6% 8.7% 5.1% 10.7% 69.9%	Mean Difference IV. Random, 95% CI 0.21 [0.11, 0.31] 0.15 [-0.09, 0.39] 0.50 [0.24, 0.76] 0.70 [0.26, 1.14] 0.39 [0.17, 0.61] 0.64 [0.38, 0.90] 0.20 [-0.24, 0.64] 0.21 [0.02, 0.40] 0.35 [0.21, 0.48] 0.27 [0.09, 0.45]	-1 -0.5 0 0.5 1 Lower fEFT in DM Higher fEFT in I Mean Difference IV, Random, 95% CI
Heterogeneity: Tau <sup>2</sup> = ( Test for overall effect: 2 Test for subaroup differ Study or Subaroup differ 1.3.1 GDM versus nor Yavuz 2016 Aydin 2020 Iskender 2022 Baria 2023 Ghuman 2023 Ghuman 2023 Ghuman 2023 Ghuman 2023 Ghuman 2023 Sever 2023 GDM Subtotal (95% Cl) Heterogeneity: Tau <sup>2</sup> = ( Test for overall effect: 2 1.3.2 PDM versus non Jackson 2016 Omerogiu 2023 PDM	0.02; Chiř Z = 6.46 ( mences: C DM p <u>Mean</u> 1.34 1.05 1.9 1.8 1.54 1.54 1.54 1.54 1.54 1.54 1.54 1.54	= 35.0 P < 0.0 hi <sup>2</sup> = 1 regnar <u>SD</u> 0.25 0.77 0.53 0.59 0.33 1.2 1.1 0.86 * = 18.2 P < 0.0	(3) of = (3) of = (3) 0001) (81, df = (40) 60 40 35 35 35 30 110 440 26, df = (00001) 28 45	1.13 0.9 1.43 0.9 1.4 1.13 1.13 1.15 1.19 1.5 1.19 7 (P = 0.0 1.16 1.19	18). P = 18). P = 18). P = 18). P = 19 0.19 0.58 0.65 1.18 0.59 0.28 0.55 0.36 11); P = 0.3 0.28	- 03 % 44.9% ancy Total 40 60 40 35 35 35 35 35 340 55 340 55 340 52%	Weight 13.0% 9.1% 8.7% 5.1% 9.6% 8.7% 5.1% 10.7% 69.9%	Mean Difference IV. Random, 95% CI 0.21 [0.11, 0.31] 0.15 [-0.09, 0.39] 0.50 [0.24, 0.76] 0.70 [0.26, 1.14] 0.39 [0.17, 0.61] 0.64 [0.38, 0.90] 0.20 [-0.24, 0.64] 0.21 [0.02, 0.40] 0.35 [0.21, 0.48] 0.27 [0.09, 0.45] 0.85 [0.59, 1.11]	-1 -0.5 0 0.5 1 Lower fEFT in DM Higher fEFT in I Mean Difference IV, Random, 95% CI
Heterogeneity: Tau <sup>2</sup> = ( Test for overall effect: 2 Test for subaroup differ Study or Subaroup differ 1.3.1 GDM versus nor Yavuz 2016 Aydin 2020 Iskender 2022 Baria 2023 Ghuman 2023 Sever 2023 PDM Sever 2023 PDM	0.02; Chiř Z = 6.46 ( mences: C DM p <u>Mean</u> 1.34 1.05 1.9 1.8 1.54 1.64 1.63 1.7 1.4 0.02; Chiř Z = 5.14 ( 1.43 2.04 1.47	= 35 P < 0.0 hi <sup>2</sup> = 1 regnar <u>SD</u> 0.25 0.77 0.53 0.59 0.33 1.2 1.1 0.86 * = 18.2 * = 18.2 0.37 0.86 0.87 0.86 0.87	(3, of = (3, of = (4, of = (3, of =) (4, of = (4, of =) (4,	1.13 0.9 1.4 1.13 0.9 1.4 1.1 1.5 1.19 7 (P = 0.0 1.16 1.19 1.19 1.19 1.11 1.19 1.19 1.19	16), P = 16), P	- 03 % 44.9% ancy Total 40 60 40 35 340 35 340 55 340 55 340 55 32%	Weight 13.0% 9.1% 8.7% 5.1% 9.6% 8.7% 5.1% 10.7% 69.9%	Mean Difference IV. Random, 95% CI 0.21 [0.11, 0.31] 0.15 [-0.09, 0.39] 0.50 [0.24, 0.76] 0.70 [0.26, 1.14] 0.39 [0.17, 0.61] 0.64 [0.38, 0.90] 0.20 [-0.24, 0.64] 0.21 [0.02, 0.40] 0.35 [0.21, 0.48] 0.27 [0.09, 0.45] 0.85 [0.59, 1.11] 0.28 [0.09, 0.47]	-1 -0.5 0 0.5 1 Lower fEFT in DM Higher fEFT in I Mean Difference IV, Random, 95% CI
Heterogeneity: Tau <sup>2</sup> = ( Test for overall effect: 2 Test for subdroup differ Study or Subdroup differ 1.3.1 GDM versus nor Yavuz 2016 Aydin 2020 Iskender 2022 Baria 2023 Ghuman 2023 Ghu	0.02; Chiř Z = 6.46 ( mences: C DM p <u>Mean</u> 1-DM 1.34 1.05 1.9 1.8 1.54 1.64 1.83 1.7 1.4 0.02; Chiř Z = 5.14 ( 1.43 2.04 1.47	= 36.0 P < 0.0 hi <sup>2</sup> = 1 regnar <u>SD</u> 0.25 0.77 0.53 0.59 0.33 1.2 1.1 0.86 0.87 0.37 0.86 0.87	28, df = 00001) 81, df = 00001) 81, df = 00001 40 60 40 35 35 90 30 110 440 26, df = 00001) 28 45 110 183	1.13 0.9 1.4 1.15 1.19 7 (P = 0.0 1.16 1.19 1.19	18). P = 18). P = 19, 19 0.19 0.58 0.65 1.18 0.59 0.28 0.36 0.36 0.36	- 03 % 44.9% ancy Total 40 60 40 35 35 35 35 35 35 35 35 35 35 35 32% 28 45 55 55 128	Weight 13.0% 9.1% 8.7% 5.1% 9.6% 5.1% 10.7% 69.9% 11.0% 8.6% 10.6% 30.1%	Mean Difference IV. Random, 95% CI 0.21 [0.11, 0.31] 0.15 [-0.09, 0.39] 0.50 [0.24, 0.76] 0.70 [0.26, 1.14] 0.39 [0.17, 0.61] 0.64 [0.38, 0.90] 0.20 [-0.24, 0.64] 0.21 [0.02, 0.40] 0.35 [0.21, 0.48] 0.27 [0.09, 0.45] 0.85 [0.59, 1.11] 0.28 [0.09, 0.47] 0.45 [0.13, 0.78]	-1 -0.5 0 0.5 1 Lower fEFT in DM Higher fEFT in I Mean Difference IV, Random, 95% CI
Heterogeneity: Tau <sup>2</sup> = ( Test for overall effect: 2 Test for subaroup differ Study or Subaroup differ 1.3.1 GDM versus nor Yavuz 2016 Aydin 2020 Iskender 2022 Baria 2023 Ghuman 2023 Subtotal (95% CI) Heterogeneity: Tau <sup>2</sup> = (	0.02; Chiř Z = 6.46 ( mnces: C DM p <u>Mean</u> 1.34 1.05 1.9 1.8 1.54 1.64 1.83 1.7 1.4 0.02; Chiř Z = 5.14 ( 1.43 2.04 1.47 0.07; Chiř	= 36.0 P < 0.0 hi <sup>2</sup> = 1 regnar <u>SD</u> 0.25 0.77 0.53 0.59 0.33 1.2 1.1 0.86 * = 18.2 9 < 0.0 0.37 0.86 0.87	(3, of = (3, of = (3, of = (3, of = (3, of = (3, of = (3, of = (40) (4	1.13 0.9 1.4 1.13 0.9 1.4 1.15 1.19 1.5 1.19 7 (P = 0.0 1.16 1.19 1.19 2 (P = 0.0	18), P = 18), P = 18), P = 18), P = 18), P = 0.19 0.58 0.58 0.65 1.18 0.59 0.28 0.36 0.19 0.28 0.36 0.36 0.36 0.36 0.36	- 03 % 44.9% ancy Total 40 60 40 35 345 345 345 340 55 55 340 55 340 55 340 55 55 340 55 55 340 55 55 340 55 55 55 55 55 55 55 55 55 55 55 55 55	Weight 13.0% 9.1% 8.7% 5.1% 9.6% 5.1% 10.7% 69.9% 11.0% 8.6% 10.6% 30.1%	Mean Difference IV. Random, 95% CI 0.21 [0.11, 0.31] 0.15 [-0.09, 0.39] 0.50 [0.24, 0.76] 0.70 [0.26, 1.14] 0.39 [0.17, 0.61] 0.64 [0.38, 0.90] 0.20 [-0.24, 0.64] 0.21 [0.02, 0.40] 0.35 [0.21, 0.48] 0.27 [0.09, 0.45] 0.85 [0.59, 1.11] 0.28 [0.09, 0.47] 0.45 [0.13, 0.78]	-1 -0.5 0 0.5 1 Lower fEFT in DM Higher fEFT in I Mean Difference IV, Random, 95% CI
Heterogeneity: Tau <sup>2</sup> = ( Test for overall effect: 2 Test for subaroup differ Study or Subaroup differ 1.3.1 GDM versus nor Yavuz 2016 Aydin 2020 Iskender 2022 Baria 2023 Ghuman 2023 Ghuman 2023 Ghuman 2023 Gomeroglu 2023 GDM Subtotal (95% Cl) Heterogeneity: Tau <sup>2</sup> = ( 1.3.2 PDM versus non Jackson 2016 Omeroglu 2023 PDM Subtotal (95% Cl) Heterogeneity: Tau <sup>2</sup> = ( Test for overall effect: 2	0.02; Chiř Z = 6.46 ( mences: C DM p Mean 1-DM 1.34 1.05 1.9 1.8 1.54 1.8 1.54 1.8 1.54 1.8 1.54 1.8 1.54 1.8 1.7 1.4 0.02; Chiř Z = 5.14 ( 1.43 2.04 1.47 0.07; Chiř Z = 2.75 (	= 36.0 P < 0.0 hi <sup>2</sup> = 1 regnar <u>SD</u> 0.25 0.77 0.53 0.59 0.33 1.2 1.1 0.86 * = 18.2 P < 0.0 0.37 0.86 0.87 * = 14.1 P = 0.0	28 45 40 60 40 35 30 110 440 26, df = 00001) 28 45 110 183 22, df = 006)	1.13 0.9 1.13 0.9 1.4 1.13 1.15 1.19 1.5 1.19 7 (P = 0.0 1.16 1.19 1.19 2 (P = 0.0	18), P = 18), P = 18), P = 18), P = 19, 19 0.19 0.58 0.58 0.58 0.58 0.58 0.58 0.59 0.28 0.36 0.19 0.28 0.36 0.28 0.36 0.28 0.36 0.28 0.36 0.28 0.36 0.28 0.36 0.28 0.36 0.28 0.36 0.28 0.36 0.28 0.36 0.28 0.36 0.28 0.36 0.28 0.36 0	- 03 % 44.9% ancy Total 40 60 40 35 35 35 35 35 340 55 340 52% 28 45 55 55 128 = 86%	Weight 13.0% 9.1% 8.7% 5.1% 10.7% 69.9% 11.0% 8.6% 10.6% 30.1%	Mean Difference IV. Random, 95% CI 0.21 [0.11, 0.31] 0.15 [-0.09, 0.39] 0.50 [0.24, 0.76] 0.70 [0.26, 1.14] 0.39 [0.17, 0.61] 0.64 [0.38, 0.90] 0.20 [-0.24, 0.64] 0.21 [0.02, 0.40] 0.35 [0.21, 0.48] 0.27 [0.09, 0.45] 0.85 [0.59, 1.11] 0.28 [0.09, 0.47] 0.45 [0.13, 0.78]	-1 -0.5 0 0.5 1 Lower fEFT in DM Higher fEFT in I Mean Difference IV, Random, 95% CI
Heterogeneity: Tau <sup>2</sup> = ( Test for overall effect: 2 Test for subgroup	0.02; Chiř Z = 6.46 ( mences: C DM p <u>Mean</u> 1.34 1.05 1.9 1.8 1.54 1.83 1.7 1.4 0.02; Chiř Z = 5.14 ( 1.43 2.04 1.47 0.07; Chiř Z = 2.75 (	= 35.0 P < 0.0 hi <sup>2</sup> = 1 regnar <u>SD</u> 0.25 0.77 0.53 0.59 0.33 1.2 1.1 0.86 * = 18.2 P < 0.0 0.37 0.86 0.87 * = 14.1 P = 0.0	(3), of = (3), of = (3), of = (3), of = (40) (40) (40) (40) (35) (90) (30) (10) (440) (45)	1.13 1.13 0.9 1.13 0.9 1.4 1.1 1.15 1.19 1.5 1.19 7 (P = 0.0 1.16 1.19 1.19 2 (P = 0.0	18), P = 18), P = 18), P = 18), P = 18), P = 18), P = 19, 19, 19, 19, 10, 10, 10, 10, 10, 10, 10, 10, 10, 10	- 03 % 44.9% ancy Total 40 60 40 35 35 35 45 30 55 340 55 340 52% 28 45 55 128 = 86%	Weight 13.0% 9.1% 8.7% 5.1% 10.7% 69.9% 11.0% 8.6% 10.6% 30.1% 100.0%	Mean Difference IV. Random. 95% CI 0.21 [0.11, 0.31] 0.15 [-0.09, 0.39] 0.50 [0.24, 0.76] 0.70 [0.26, 1.14] 0.39 [0.17, 0.61] 0.64 [0.38, 0.90] 0.20 [-0.24, 0.64] 0.21 [0.02, 0.40] 0.35 [0.21, 0.48] 0.27 [0.09, 0.45] 0.85 [0.59, 1.11] 0.28 [0.09, 0.47] 0.45 [0.13, 0.78] 0.38 [0.25, 0.50]	-1 -0.5 0 0.5 1 Lower fEFT in DM Higher fEFT in I Mean Difference IV, Random, 95% CI
Heterogeneity: Tau <sup>2</sup> = ( Test for overall effect: 2 Test for subaroup differ Study or Subaroup differ 1.3.1 GDM versus nor Yavuz 2016 Aydin 2020 Iskender 2022 Baria 2023 Ghuman 2023 Ghuman 2023 Ghuman 2023 Ghuman 2023 Ghuman 2023 Ghuman 2023 Ghuman 2023 Ghuman 2023 Ghuman 2023 Sever 2023 GDM Subtotal (95% Cl) Heterogeneity: Tau <sup>2</sup> = ( Test for overall effect: 2 Subtotal (95% Cl) Heterogeneity: Tau <sup>2</sup> = ( Test for overall effect: 2 Total (95% Cl)	0.02; Chiř Z = 6.46 ( mences: C DM p <u>Mean</u> 1.34 1.05 1.9 1.8 1.54 1.83 1.7 1.4 0.02; Chiř Z = 5.14 ( 1.43 2.04 1.47 0.07; Chiř Z = 2.75 ( 0.03; Chiř	= 35. <sup>3</sup> P < 0.0 hi <sup>2</sup> = 1 regnar <u>SD</u> 0.25 0.77 0.53 0.53 0.53 0.53 0.53 0.33 1.2 1.1 0.86 * = 18.2 P < 0.0 0.37 0.86 0.87 * = 14.1 P = 0.0	28 40 60 40 60 40 355 30 110 440 26, df = 00001) 28 45 110 183 12, df = 006) 623 13, df =	1.13 0.9 1.13 0.9 1.4 1.13 1.13 1.15 1.19 1.5 1.19 7 (P = 0.0 1.16 1.19 1.19 2 (P = 0.0 1.0 (P = 0.0)	.18), P = <b>A pregn.</b> <b>SD</b> 0.19 0.58 0.65 1.18 0.59 0.28 0.55 0.36 0.19; P = 0.28 0.55 0.36 0.19; P = 0.28 0.36 0.28 0.36 0.3	- 03 % 44.9% ancy Total 40 60 40 355 35 35 35 35 340 55 340 52% 28 45 55 128 = 86% 468 <sup>2</sup> = 72%	Weight 13.0% 9.1% 8.7% 5.1% 10.7% 69.9% 11.0% 8.6% 10.6% 30.1%	Mean Difference IV. Random, 95% CI 0.21 [0.11, 0.31] 0.15 [-0.09, 0.39] 0.50 [0.24, 0.76] 0.70 [0.26, 1.14] 0.39 [0.17, 0.61] 0.64 [0.38, 0.90] 0.20 [-0.24, 0.64] 0.21 [0.02, 0.40] 0.35 [0.21, 0.48] 0.27 [0.09, 0.45] 0.85 [0.59, 1.11] 0.28 [0.09, 0.47] 0.45 [0.13, 0.78] 0.38 [0.25, 0.50]	-1 -0.5 0 0.5 1 Lower fEFT in DM Higher fEFT in Mean Difference IV, Random, 95% CI

### Figure 3. Forest plots for the subgroup analyses comparing fEFT between women with and without

DM in pregnancy; A, subgroup analysis according to study design; and B, subgroup analysis according to

the type of DM in pregnancy;

<b>M</b>		egnal	T	HUIPDI	n progn	arroy		mean prinerence	ni Deni Onterence
Study or Subgroup	Mean	SD	otal	Mean	50	Total	Weight	IV. Random, 95% CI	IV. Random, 95% CI
1.4.1 Maternal age < 2	9 years								
Yavuz 2016	1.34	0.25	40	1.13	0.19	40	12.2%	0.21 [0.11, 0.31]	
Jackson 2016	1.43	0.37	28	1.16	0.3	28	10.1%	0.27 [0.09, 0.45]	
Iskender 2022	1.9	0.53	40	1.4	0.65	40	7.9%	0.50 [0.24, 0.76]	
Ghuman 2023	1.54	0.33	35	1.15	0.59	35	8.8%	0.39 [0.17, 0.61]	
Omeroglu 2023 PDM	2.04	0.86	45	1.19	0.28	45	7.8%	0.85 [0.59, 1.11]	
Singh 2023	1.7	1.1	30	1.5	0.55	30	4.4%	0.20 [-0.24, 0.64]	
Subtotal (95% CI)			218			218	51.2%	0.40 [0.21, 0.58]	•
Heterogeneity: Tau <sup>2</sup> = (	0.04; Chi	2 = 23.0	08, df =	5 (P = 0.0	0003); l <sup>2</sup>	= 78%			
Test for overall effect: 2	2 = 4.24 (	(P < 0.0	0001)		00000000000				
1.4.2 Maternal age ≥	29 years	1							
Akkurt 2018	1.45	0.98	106	1.1	0.72	106	8.6%	0.35 [0.12, 0.58]	
Avdin 2020	1.05	0.77	60	0.9	0.58	60	8.3%	0.15 (-0.09, 0.39)	
Baria 2023	1.8	0.59	35	1.1	1.18	35	4.5%	0.70 [0.26, 1.14]	
Omeroalu 2023 GDM	1.83	12	90	1.19	0.28	45	7.8%	0.64 [0.38, 0.90]	
Sever 2023 GDM	1.4	0.86	110	1 19	0.36	55	9.8%	0.21 [0.02, 0.40]	
Sever 2023 PDM	1 47	0.87	110	1 19	0.36	55	9.8%	0.28 [0.09, 0.47]	
Subtotal (95% CI)	1.41	0.07	511	1.10	0.00	356	48.8%	0.35 [0.20, 0.50]	•
Hataroganaity: Tau? = (	02- Chi	2 - 12 1	11 df -	5 /P = 0 /	13)- 12 - 4	50%		anan famat ananl	100 million (100 m
Test for overall effect: 2	2 = 4.48 (	(P < 0.0	00001)	3 (F = 0.0	Joj, 1 - 1	19 10			
Total (95% CI)			720			574	100.0%	0 37 10 26 0 491	•
			140			214	100.070	0.01 [0.60, 0.40]	
Hotoroonnoibu Tou? = (	102 Chi	2 - 25 4	-16 00	11 /D = 0	00031	2 - 60%			
Heterogeneity: Tau <sup>2</sup> = 0	0.02; Chi	a = 35.2	23, df =	11 (P = 0	.0002); I	<sup>a</sup> = 69%	i. L		-1 -0.5 0 0.5 1
Heterogeneity: Tau <sup>2</sup> = 0 Test for overall effect: 2	0.02; Chi Z = 6.46 (	<sup>a</sup> = 35.2 (P < 0.0	23, df =	11 (P = 0	.0002); 1	<sup>2</sup> = 69%	l l		-1 -0.5 0 0.5 1 Lower fEFT in DM Higher fEFT in
Heterogeneity: Tau <sup>2</sup> = 0 Test for overall effect: 2 Test for suboroup differ	0.02; Chi Z = 6.46 ( rences: C	² = 35.2 (P < 0.( Chi² = 0	23, df = 00001) .16. df =	11 (P = 0 = 1 (P = 0	.0002); I .691. I² =	² = 69% 0%	d <sup>erenderen</sup>		-1 -0.5 0 0.5 1 Lower fEFT in DM Higher fEFT in
Heterogeneity: Tau <sup>2</sup> = ( Test for overall effect: 2 Test for suboroup differ	0.02; Chi 2 = 6.46 ( rences: C	<sup>2</sup> = 35.2 (P < 0.0 Chi <sup>2</sup> = 0	23, df = 00001) .16. df =	11 (P = 0 = 1 (P = 0 Non-Di	.0002); I .69). I <sup>2</sup> =	<sup>2</sup> = 69% 0%		Mean Difference	-1 -0.5 0 0.5 1 Lower fEFT in DM Higher fEFT in
Heterogeneity: Tau <sup>2</sup> = ( Test for overall effect: 2 Test for suboroup differ	0.02; Chi 2 = 6.46 ( rences: C DM p Mean	² = 35.2 (P < 0.0 Chi² = 0 regnar	23, df = 00001) .16. df = ncy Total	11 (P = 0 = 1 (P = 0 Non-DI Mean	0002); 1 .691. 1² = W pregna SD	<sup>a</sup> = 69% 0% ancy Total	Weight	Mean Difference	-1 -0.5 0 0.5 1 Lower fEFT in DM Higher fEFT in Mean Difference
Heterogeneity: Tau <sup>2</sup> = ( Test for overall effect: 2 Test for subaroup differ Study or Subgroup	0.02; Chi 2 = 6.46 ( rences: C DM p <u>Mean</u>	<sup>2</sup> = 35.2 (P < 0.0 Chi <sup>2</sup> = 0 regnar <u>SD</u>	23, df = 00001) .16. df = ncy Total	11 (P = 0 = 1 (P = 0 Non-DI Mean	0002); I .69). I² = M pregn SD	* = 69% 0% ancy <u>Total</u>	Weight	Mean Difference	-1 -0.5 0 0.5 1 Lower fEFT in DM Higher fEFT in Mean Difference IV. Random, 95% CI
Heterogeneity: Tau <sup>2</sup> = 0 Test for overall effect: 2 Test for suboroup differ Study or Subgroup 1.5.1 Maternal BMI < 3	0.02; Chi z = 6.46 ( rences: C DM p <u>Mean</u> 10 kg/m2	<sup>2</sup> = 35.2 (P < 0.0 Chi <sup>2</sup> = 0 regnar <u>SD</u>	23, df = 00001) .16. df = ncy Total	11 (P = 0 = 1 (P = 0 Non-DI Mean	.0002); I .69). I <sup>2</sup> = M pregn SD	* = 69% 0% ancy Total	Weight	Mean Difference	-1 -0.5 0 0.5 1 Lower fEFT in DM Higher fEFT in Mean Difference IV. Random, 95% CI
Heterogeneity: Tau <sup>2</sup> = 0 Test for overall effect: 2 Test for suboroup differ Study or Subgroup 1.5.1 Maternal BMI < 3 Yavuz 2016	0.02; Chi 2 = 6.46 ( rences: C DM p <u>Mean</u> 10 kg/m2 1.34	e = 35.2 (P < 0.0 Chi <sup>2</sup> = 0 regnar SD 0.25	23, df = 00001) .16. df = ncy <u>Total</u> 40	11 (P = 0 = 1 (P = 0 Non-DI Mean 1.13	00002); I 069). I <sup>2</sup> = W pregna SD 0.19	<sup>2</sup> = 69% 0% ancy <u>Total</u> 40	Weight 14.5%	Mean Difference <u>IV. Random, 95% Cl</u> 0.21 [0.11, 0.31]	-1 -0.5 0 0.5 1 Lower fEFT in DM Higher fEFT in Mean Difference IV. Random, 95% CI
Heterogeneity: Tau <sup>2</sup> = 0 Test for overall effect: 2 Test for suboroup differ Study or Subgroup 1.5.1 Maternal BMI < 3 Yavuz 2016 Aydin 2020	0.02; Chi rences: C DM p <u>Mean</u> 0 kg/m2 1.34	<sup>a</sup> = 35.2 (P < 0.0 Chi <sup>2</sup> = 0 regnar SD 0.25 0.77	23, df = 00001) .16, df = ncy <u>Total</u> 40 60	11 (P = 0 = 1 (P = 0 Non-DI Mean 1.13 0.9	00002); I 069). I <sup>2</sup> = M pregna SD 0.19 0.58	<sup>2</sup> = 69% 0% ancy <u>Total</u> 40 60	Weight 14.5% 10.1%	Mean Difference <u>IV. Random, 95% Cl</u> 0.21 [0.11, 0.31] 0.15 [-0.09, 0.39]	-1 -0.5 0 0.5 1 Lower fEFT in DM Higher fEFT in Mean Difference IV. Random, 95% CI
Heterogeneity: Tau <sup>2</sup> = 0 Test for overall effect: 2 Test for suboroup differ Study or Subgroup 1.5.1 Maternal BMI < 3 Yavuz 2016 Aydin 2020 Iskender 2022	0.02; Chi rences: C DM p <u>Mean</u> 0 kg/m2 1.34 1.05 1.9	<sup>2</sup> = 35.2 (P < 0.0 Chi <sup>2</sup> = 0 regnat SD 0.25 0.77 0.53	23, df = 00001) .16, df = ncy <u>Total</u> 40 60 40	11 (P = 0 = 1 (P = 0 Non-DI Mean 1.13 0.9 1.4	00002); I 0.69). I <sup>2</sup> = M pregna SD 0.19 0.58 0.65	<sup>a</sup> = 69% 0% <u>ancy</u> <u>Total</u> 40 60 40	Weight 14.5% 10.1% 9.7%	Mean Difference <u>IV. Random, 95% C1</u> 0.21 [0.11, 0.31] 0.15 [-0.09, 0.39] 0.50 [0.24, 0.76]	-1 -0.5 0 0.5 1 Lower fEFT in DM Higher fEFT in I Mean Difference IV. Random. 95% CI
Heterogeneity: Tau <sup>2</sup> = 0 Test for overall effect: 2 Test for suboroup differ Study or Subgroup 1.5.1 Maternal BMI < 3 Yavuz 2016 Aydin 2020 Iskender 2022 Omerogiu 2023 PDM	0.02; Chi Z = 6.46 ( rences: C DM p <u>Mean</u> 10 kg/m2 1.34 1.05 1.9 2.04	<sup>2</sup> = 35.2 (P < 0.0 Chi <sup>2</sup> = 0 regnar 5D 0.25 0.77 0.53 0.86	23, df = 00001) .16, df = ncy <u>Total</u> 40 60 40 40 50 40 40 40 40 40 40 40 40 40 4	11 (P = 0 = 1 (P = 0 <u>Non-DI</u> <u>Mean</u> 1.13 0.9 1.4 1.19	0.0002); I 0.69). I <sup>2</sup> = W pregna SD 0.19 0.58 0.65 0.28	<sup>2</sup> = 69% 0% <u>Total</u> 40 40 45	Weight 14.5% 10.1% 9.7% 9.5%	Mean Difference IV. Random, 95% CI 0.21 [0.11, 0.31] 0.15 [-0.09, 0.39] 0.50 [0.24, 0.76] 0.85 [0.59, 1.11]	-1 -0.5 0 0.5 1 Lower fEFT in DM Higher fEFT in I Mean Difference IV. Random, 95% CI
Heterogeneity: Tau <sup>2</sup> = 0 Test for overall effect: 2 Test for suboroup differ Study or Subgroup 1.5.1 Maternal BMI < 3 Yavuz 2016 Aydin 2020 Iskender 2022 Omeroglu 2023 PDM Subtotal (95% CI)	0.02; Chii Z = 6.46 ( rences: C DM p <u>Mean</u> 10 kg/m2 1.34 1.05 1.9 2.04	<sup>2</sup> = 35.2 (P < 0.0 Chi <sup>2</sup> = 0 seegnat 0.25 0.77 0.53 0.86	23, df = 00001) .16, df = ncy <u>Total</u> 40 60 40 45 185	11 (P = 0 = 1 (P = 0 Non-DI Mean 1.13 0.9 1.4 1.19	0.0002); I 0.69). I <sup>2</sup> = W pregn: SD 0.19 0.58 0.65 0.28	<sup>2</sup> = 69% 0% <u>Total</u> 40 40 45 185	Weight 14.5% 10.1% 9.7% 9.5% 43.9%	Mean Difference <u>IV. Random, 95% Cl</u> 0.21 [0.11, 0.31] 0.15 [-0.09, 0.39] 0.50 [0.24, 0.76] 0.85 [0.59, 1.11] 0.41 [0.13, 0.70]	-1 -0.5 0 0.5 1 Lower fEFT in DM Higher fEFT in I Mean Difference IV. Random, 95% CI
Heterogeneity: Tau <sup>2</sup> = ( Test for overall effect: 2 Test for suboroup differ Study or Subgroup 1.5.1 Maternal BMI < 3 Yavuz 2016 Aydin 2020 Iskender 2022 Omeroglu 2023 PDM Subtotal (95% CI) Heterogeneity: Tau <sup>2</sup> = ( Test for overall effect: 2	0.02; Chi 2 = 6.46 ( rences: C DM p <u>Mean</u> 10 kg/m2 1.34 1.05 1.9 2.04 0.07; Chi 2 = 2.83 (	<sup>2</sup> = 35.2 (P < 0.0 Chi <sup>2</sup> = 0 oregnat SD 0.25 0.77 0.53 0.86 <sup>2</sup> = 23.6 (P = 0.0	23, df = 00001) 16, df = ncy <u>Total</u> 40 60 40 45 185 52, df = 005)	11 (P = 0 = 1 (P = 0 Non-DI Mean 1.13 0.9 1.4 1.19 3 (P < 0.0	.0002); i .69). i <sup>2</sup> = W pregn. SD 0.19 0.58 0.65 0.28 0001); i <sup>2</sup>	<sup>2</sup> = 69% 0% <u>Total</u> 40 60 40 45 185 = 87%	Weight 14.5% 10.1% 9.7% 9.5% 43.9%	Mean Difference IV. Random, 95% Cl 0.21 [0.11, 0.31] 0.15 [-0.09, 0.39] 0.50 [0.24, 0.76] 0.85 [0.59, 1.11] 0.41 [0.13, 0.70]	-1 -0.5 0 0.5 1 Lower fEFT in DM Higher fEFT in I Mean Difference IV. Random, 95% CI
Heterogeneity: Tau <sup>2</sup> = ( Test for overall effect: 2 Test for suboroup differ <u>Study or Subgroup</u> 1.5.1 Maternal BMI < 3 Yavuz 2016 Aydin 2020 Iskender 2022 Omeroglu 2023 PDM Subtotal (95% CI) Heterogeneity: Tau <sup>2</sup> = ( Test for overall effect: 2 1.5.2 Maternal BMI ≥	0.02; Chii 2 = 6.46 ( rences: C DM p <u>Mean</u> 1.34 1.05 1.9 2.04 0.07; Chii 2 = 2.83 ( 30 kg/m	<sup>2</sup> = 35.2 (P < 0.0 chi <sup>2</sup> = 0 <b>sp</b> 0.25 0.77 0.53 0.86 <sup>2</sup> = 23.6 (P = 0.0 2	23, df = 00001) 16, df = ncy Total 40 40 45 185 52, df = 005)	11 (P = 0 = 1 (P = 0 Non-DI Mean 1.13 0.9 1.4 1.19 3 (P < 0.0	.0002); I .69), I <sup>2</sup> = W pregna SD 0.19 0.58 0.65 0.28 0001); I <sup>2</sup>	<sup>2</sup> = 69% 0% <u>Total</u> 40 60 40 45 185 = 87%	Weight 14.5% 10.1% 9.7% 9.5% 43.9%	Mean Difference IV. Random, 95% Cl 0.21 [0.11, 0.31] 0.15 [-0.09, 0.39] 0.50 [0.24, 0.76] 0.85 [0.59, 1.11] 0.41 [0.13, 0.70]	-1 -0.5 0 0.5 1 Lower fEFT in DM Higher fEFT in I Mean Difference IV. Random. 95% CI
Heterogeneity: Tau <sup>2</sup> = 0 Test for overall effect: 2 Test for suboroup differ Study or Subgroup 1.5.1 Maternal BMI < 3 Yavuz 2016 Aydin 2020 Iskender 2022 Omeroglu 2023 PDM Subtotal (95% CI) Heterogeneity: Tau <sup>2</sup> = 0 Test for overall effect: 2 1.5.2 Maternal BMI ≥ Jackson 2016	0.02; Chii 2 = 6.46 ( rences: C DM p <u>Mean</u> 10 kg/m2 1.34 1.05 1.9 2.04 0.07; Chii 2 = 2.83 ( 30 kg/m 1.43	<sup>2</sup> = 35.2 (P < 0.0 chi <sup>2</sup> = 0 <b>SD</b> 0.25 0.77 0.53 0.86 <sup>2</sup> = 23.6 (P = 0.0 2 0.37	23, df = 00001) 16, df = ncy Total 40 40 45 185 52, df = 005) 28	11 (P = 0 = 1 (P = 0 Non-DI Mean 1.13 0.9 1.4 1.19 3 (P < 0.0 1.16	.0002); i .69), i <sup>2</sup> = W pregn: <u>SD</u> 0.19 0.58 0.65 0.28 0001); i <sup>2</sup> 0.3	<sup>2</sup> = 69% 0% <u>Total</u> 40 40 45 185 = 87%	Weight 14.5% 10.1% 9.7% 9.5% 43.9%	Mean Difference IV. Random, 95% CI 0.21 [0.11, 0.31] 0.15 [-0.09, 0.39] 0.50 [0.24, 0.76] 0.85 [0.59, 1.11] 0.41 [0.13, 0.70]	-1 -0.5 0 0.5 1 Lower fEFT in DM Higher fEFT in I Mean Difference IV. Random. 95% CI
Heterogeneity: Tau <sup>2</sup> = 0 Test for overall effect: 2 Test for suboroup differ Study or Subgroup 1.5.1 Maternal BMI < 3 Yavuz 2016 Aydin 2020 Iskender 2022 Omeroglu 2023 PDM Subtotal (95% CI) Heterogeneity: Tau <sup>2</sup> = 0 Test for overall effect: 2 1.5.2 Maternal BMI ≥ Jackson 2016 Akkurt 2018	0.02; Chii 2 = 6.46 ( rences: C DM p <u>Mean</u> 1.34 1.05 1.9 2.04 0.07; Chii 2 = 2.83 ( 30 kg/m 1.43 1.43 1.43	<sup>2</sup> = 35.2 (P < 0.0 chi <sup>2</sup> = 0 <b>sp</b> 0.25 0.77 0.53 0.86 <sup>2</sup> = 23.6 (P = 0.0 2 0.37 0.98	23, df = 00001) 16, df = ncy Total 40 40 40 45 185 52, df = 005) 28 106	11 (P = 0 = 1 (P = 0 Non-DI <u>Mean</u> 1.13 0.9 1.4 1.19 3 (P < 0.0 1.16 1.1	.0002); i .69). i <sup>2</sup> = W pregn: 5D 0.19 0.58 0.65 0.28 0001); i <sup>2</sup> 0.3 0.72	* = 69% 0% Total 40 60 40 45 185 = 87% 288	Weight 14.5% 10.1% 9.7% 9.5% 43.9% 12.2% 10.5%	Mean Difference IV. Random, 95% CI 0.21 [0.11, 0.31] 0.15 [-0.09, 0.39] 0.50 [0.24, 0.76] 0.85 [0.59, 1.11] 0.41 [0.13, 0.70] 0.27 [0.09, 0.45] 0.35 [0.12, 0.58]	-1 -0.5 0 0.5 1 Lower fEFT in DM Higher fEFT in I Mean Difference IV. Random, 95% CI
Heterogeneity: Tau <sup>2</sup> = 0 Test for overall effect: 2 Test for suboroup differ Study or Subgroup 1.5.1 Maternal BMI < 3 Yavuz 2016 Aydin 2020 Iskender 2022 Omeroglu 2023 PDM Subtotal (95% CI) Heterogeneity: Tau <sup>2</sup> = 0 Test for overall effect: 2 1.5.2 Maternal BMI ≥ Jackson 2016 Akkurt 2018 Omeroglu 2023 GDM	0.02; Chi 2 = 6.46 ( rences: C DM p Mean 10 kg/m2 1.34 1.05 1.9 2.04 0.07; Chi 2 = 2.83 ( 30 kg/m 1.43 1.45 1.82	<sup>2</sup> = 35.2 (P < 0.0 Chi <sup>2</sup> = 0 regnar 5D 0.25 0.77 0.53 0.86 (P = 0.0 2 0.37 0.37 0.37	23, df = 20001) 16, df = 1000 10	11 (P = 0 = 1 (P = 0 Non-DI <u>Mean</u> 1.13 0.9 1.4 1.19 3 (P < 0.0 1.16 1.1 1.19	0.0002); i 0.69), i <sup>2</sup> = W pregn: 0.19 0.58 0.65 0.28 0.001); i <sup>2</sup> 0.3 0.72 0.28	* = 69% 0% ancy Total 40 60 40 45 185 = 87% 28 106 45	Weight 14.5% 10.1% 9.7% 9.5% 43.9% 12.2% 10.5% 9.6%	Mean Difference IV. Random, 95% CI 0.21 [0.11, 0.31] 0.15 [-0.09, 0.39] 0.50 [0.24, 0.76] 0.85 [0.59, 1.11] 0.41 [0.13, 0.70] 0.27 [0.09, 0.45] 0.35 [0.12, 0.58] 0.64 [0 38, 0.90]	-1 -0.5 0 0.5 1 Lower fEFT in DM Higher fEFT in I Mean Difference IV. Random, 95% CI
Heterogeneity: Tau <sup>2</sup> = ( Test for overall effect: 2 Test for suboroup differ 1.5.1 Maternal BMI < 3 Yavuz 2016 Aydin 2020 Iskender 2022 Omeroglu 2023 PDM Subtotal (95% CI) Heterogeneity: Tau <sup>2</sup> = ( Test for overall effect: 2 1.5.2 Maternal BMI ≥ Jackson 2016 Akkurt 2018 Omeroglu 2023 GDM	0.02; Chi 2 = 6.46 ( rences: C DM p Mean 10 kg/m2 1.34 1.05 1.9 2.04 0.07; Chi 2 = 2.83 ( 30 kg/m 1.43 1.45 1.83 1.45 1.83	<sup>2</sup> = 35.2 (P < 0.0 Chi <sup>2</sup> = 0 <b>sp</b> 0.25 0.77 0.53 0.86 P = 0.0 2 0.37 0.98 1.2 0.98	23, df = 20001) 16, df = <b>Total</b> 40 60 40 45 185 52, df = 28 106 900 110	11 (P = 0 = 1 (P = 0 Non-DI Mean 1.13 0.9 1.4 1.19 3 (P < 0.0 1.16 1.1 1.19 1.19	0.0002); i .69). i <sup>2</sup> = W pregn. SD 0.19 0.58 0.65 0.28 0001); i <sup>2</sup> 0.3 0.72 0.28 0.28 0.28	* = 69% 0% ancy Total 40 60 40 45 185 = 87% 28 106 45 55	Weight 14.5% 10.1% 9.7% 9.5% 43.9% 12.2% 10.5% 9.6%	Mean Difference IV. Random, 95% CI 0.21 [0.11, 0.31] 0.15 [-0.09, 0.39] 0.50 [0.24, 0.76] 0.85 [0.59, 1.11] 0.41 [0.13, 0.70] 0.27 [0.09, 0.45] 0.35 [0.12, 0.58] 0.64 [0.38, 0.90] 0.21 [0.02, 0.40]	-1 -0.5 0 0.5 1 Lower fEFT in DM Higher fEFT in I Mean Difference IV. Random, 95% CI
Heterogeneity: Tau <sup>2</sup> = ( Test for overall effect: 2 Test for suboroup differ <u>Study or Subgroup</u> 1.5.1 Maternal BMI < 3 Yavuz 2016 Aydin 2020 Iskender 2022 Omeroglu 2023 PDM Subtotal (95% CI) Heterogeneity: Tau <sup>2</sup> = ( Test for overall effect: 2 1.5.2 Maternal BMI ≥ Jackson 2016 Akkurt 2018 Omeroglu 2023 GDM Sever 2023 GDM	0.02; Chi 2 = 6.46 ( rences: C DM p Mean 10 kg/m2 1.34 1.05 1.9 2.04 0.07; Chi 2 = 2.83 ( 30 kg/m 1.43 1.45 1.83 1.45	<sup>2</sup> = 35.2 (P < 0.0 Chi <sup>2</sup> = 0 regnar 0.25 0.77 0.53 0.86 P = 0.0 2 0.37 0.98 1.2 0.98 1.2 0.86	23, df = 20001) 16, df = <b>Total</b> 40 60 40 45 185 52, df = 28 106 90 110	11 (P = 0 = 1 (P = 0 Non-DI Mean 1.13 0.9 1.4 1.19 3 (P < 0.0 1.16 1.1 1.19 1.19 1.19 1.19	0.0002); i .69). i <sup>2</sup> = W pregna 0.19 0.58 0.65 0.28 0001); i <sup>2</sup> 0.3 0.72 0.28 0.3 0.72 0.28 0.36 0.28	* = 69% 0% ancy Total 40 60 40 45 185 = 87% 288 106 45 55 55	Weight 14.5% 10.1% 9.7% 9.5% 43.9% 12.2% 10.5% 9.6% 11.9%	Mean Difference IV. Random, 95% CI 0.21 [0.11, 0.31] 0.15 [-0.09, 0.39] 0.50 [0.24, 0.76] 0.85 [0.59, 1.11] 0.41 [0.13, 0.70] 0.27 [0.09, 0.45] 0.35 [0.12, 0.58] 0.64 [0.38, 0.90] 0.21 [0.02, 0.40] 0.24 [0.02, 0.40]	-1 -0.5 0 0.5 1 Lower fEFT in DM Higher fEFT in I Mean Difference IV. Random, 95% CI
Heterogeneity: Tau <sup>2</sup> = 0 Test for overall effect: 2 Test for suboroup differ Study or Subgroup 1.5.1 Maternal BMI < 3 Yavuz 2016 Aydin 2020 Iskender 2022 Omeroglu 2023 PDM Subtotal (95% CI) Heterogeneity: Tau <sup>2</sup> = 0 Test for overall effect: 2 1.5.2 Maternal BMI ≥ Jackson 2016 Akkurt 2018 Omeroglu 2023 GDM Sever 2023 GDM Sever 2023 PDM Subtotal (95% CI)	0.02; Chii 2 = 6.46 ( rences: C DM p Mean 10 kg/m2 1.34 1.05 1.9 2.04 0.07; Chii 2 = 2.83 ( 30 kg/m 1.43 1.45 1.83 1.4 1.47	<sup>2</sup> = 35.2 (P < 0.0 Chi <sup>2</sup> = 0 <b>regnar</b> 5D 0.25 0.77 0.53 0.86 (P = 0.0 2 0.37 0.98 1.2 0.86 0.87	23, df = 00001) 16, df = <b>Total</b> 40 60 40 45 185 52, df = 005) 28 106 90 110 110 444	11 (P = 0 1 (P = 0 Non-DI <u>Mean</u> 1.13 0.9 1.4 1.19 3 (P < 0.0 1.16 1.1 1.19 1.19 1.19	0.0002); i .69). i <sup>2</sup> = <b>V</b> pregn: <b>SD</b> 0.19 0.58 0.65 0.28 0.001); i <sup>2</sup> 0.3 0.72 0.28 0.36 0.36	* = 69% 0% ancy Total 40 60 40 45 185 = 87% 28 106 45 55 55 289	Weight 14.5% 10.1% 9.7% 9.5% 43.9% 12.2% 10.5% 9.6% 11.9% 56.1%	Mean Difference IV. Random, 95% CI 0.21 [0.11, 0.31] 0.15 [-0.09, 0.39] 0.50 [0.24, 0.76] 0.85 [0.59, 1.11] 0.41 [0.13, 0.70] 0.27 [0.09, 0.45] 0.35 [0.12, 0.58] 0.64 [0.38, 0.90] 0.21 [0.02, 0.40] 0.28 [0.09, 0.47] 0.33 [0.20, 0.46]	-1 -0.5 0 0.5 1 Lower fEFT in DM Higher fEFT in I Mean Difference IV. Random, 95% CI
Heterogeneity: Tau <sup>2</sup> = 0 Test for overall effect: 2 Test for suboroup differ 1.5.1 Maternal BMI < 3 Yavuz 2016 Aydin 2020 Iskender 2022 Omeroglu 2023 PDM Subtotal (95% CI) Heterogeneity: Tau <sup>2</sup> = 0 Test for overall effect: 2 1.5.2 Maternal BMI ≥ Jackson 2016 Akkurt 2018 Omeroglu 2023 GDM Sever 2023 GDM Sever 2023 PDM Subtotal (95% CI) Heterogeneity: Tau <sup>2</sup> = 0	0.02; Chi 2 = 6.46 ( rences: C DM p Mean 10 kg/m2 1.34 1.05 1.9 2.04 0.07; Chi 2 = 2.83 ( 30 kg/m 1.43 1.45 1.83 1.4 1.47 0.01; Chi	<sup>2</sup> = 35.2 (P < 0.0 Chi <sup>2</sup> = 0 regnar 5D 0.25 0.77 0.53 0.86 (P = 0.0 2 0.37 0.98 1.2 0.86 0.87 <sup>2</sup> = 7.64	23, df = 20001) 16, df = 1000 100 100 100 100 100 100 1	11 (P = 0 = 1 (P = 0 Non-DI Mean 1.13 0.9 1.4 1.19 3 (P < 0.0 1.16 1.1 1.19 1.19 1.19 1.19 (P = 0.1)	0.0002); i .69). i <sup>2</sup> = W pregn. SD 0.19 0.58 0.65 0.28 0.001); i <sup>2</sup> 0.3 0.72 0.28 0.36 0.36 0.36 1); i <sup>2</sup> = 4i	* = 69% 0% ancy Total 40 60 40 45 185 = 87% 28 106 45 55 55 289 3%	Weight 14.5% 10.1% 9.7% 9.5% 43.9% 12.2% 10.5% 9.6% 11.9% 11.9% 56.1%	Mean Difference IV. Random, 95% CI 0.21 [0.11, 0.31] 0.15 [-0.09, 0.39] 0.50 [0.24, 0.76] 0.85 [0.59, 1.11] 0.41 [0.13, 0.70] 0.27 [0.09, 0.45] 0.35 [0.12, 0.58] 0.64 [0.38, 0.90] 0.21 [0.02, 0.40] 0.28 [0.09, 0.47] 0.33 [0.20, 0.46]	-1 -0.5 0 0.5 1 Lower fEFT in DM Higher fEFT in I Mean Difference IV. Random. 95% CI
Heterogeneity: Tau <sup>2</sup> = 0 Test for overall effect: 2 Test for suboroup differ Study or Subgroup 1.5.1 Maternal BMI < 3 Yavuz 2016 Aydin 2020 Iskender 2022 Omeroglu 2023 PDM Subtotal (95% CI) Heterogeneity: Tau <sup>2</sup> = 0 Test for overall effect: 2 1.5.2 Maternal BMI ≥ Jackson 2016 Akkurt 2018 Omeroglu 2023 GDM Sever 2023 GDM Sever 2023 GDM Sever 2023 PDM Subtotal (95% CI) Heterogeneity: Tau <sup>2</sup> = 0 Test for overall effect: 2	0.02; Chii Z = 6.46 ( rences: C DM p <u>Mean</u> 1.34 1.35 1.9 2.04 0.07; Chii Z = 2.83 ( 30 kg/m 1.43 1.45 1.83 1.4 1.47 0.01; Chii Z = 5.09 (	<ul> <li><sup>2</sup> = 35.2 (P &lt; 0.0 chi<sup>2</sup> = 0</li> <li><sup>2</sup> = 0</li> <li>0.25 0.77 0.53 0.86</li> <li><sup>2</sup> = 23.6</li> <li>(P = 0.0</li> <li>2 0.37 0.98 1.2</li> <li>0.86 0.87</li> <li><sup>2</sup> = 7.64</li> <li>(P &lt; 0.0</li> </ul>	23, df = 00001) 16, df = <b>Total</b> 40 60 40 45 185 52, df = 005) 28 106 90 110 110 444 4, df = 4 00001)	11 (P = 0 Non-DI Mean 1.13 0.9 1.4 1.19 3 (P < 0.0 1.16 1.1 1.19	0.0002); i 0.69), i <sup>2</sup> = W pregna 0.19 0.58 0.65 0.28 0.001); i <sup>2</sup> 0.3 0.72 0.28 0.36 0.36 0.36 0.36 0.36 1); i <sup>2</sup> = 4i	* = 69% 0% ancy Total 40 60 40 45 185 = 87% 28 106 45 55 55 289 3%	Weight 14.5% 10.1% 9.7% 9.5% 43.9% 12.2% 10.5% 9.6% 11.9% 11.9% 56.1%	Mean Difference IV. Random, 95% C1 0.21 [0.11, 0.31] 0.15 [-0.09, 0.39] 0.50 [0.24, 0.76] 0.85 [0.59, 1.11] 0.41 [0.13, 0.70] 0.27 [0.09, 0.45] 0.35 [0.12, 0.58] 0.64 [0.38, 0.90] 0.21 [0.02, 0.40] 0.28 [0.09, 0.47] 0.33 [0.20, 0.46]	-1 -0.5 0 0.5 1 Lower fEFT in DM Higher fEFT in I Mean Difference IV. Random. 95% CI
Heterogeneity: Tau <sup>2</sup> = ( Test for overall effect: 2 Test for suboroup differ 1.5.1 Maternal BMI < 3 Yavuz 2016 Aydin 2020 Iskender 2022 Omeroglu 2023 PDM Subtotal (95% CI) Heterogeneity: Tau <sup>2</sup> = ( Test for overall effect: 2 1.5.2 Maternal BMI ≥ Jackson 2016 Akkurt 2018 Omeroglu 2023 GDM Sever 2023 GDM Sever 2023 GDM Sever 2023 GDM Subtotal (95% CI) Heterogeneity: Tau <sup>2</sup> = ( Test for overall effect: 2 Total (95% CI)	0.02; Chi Z = 6.46 ( irences: C DM p Mean 10 kg/m2 1.34 1.05 1.9 2.04 0.07; Chi Z = 2.83 ( 30 kg/m 1.43 1.45 1.83 1.4 1.47 0.01; Chi Z = 5.09 (	<sup>2</sup> = 35.2 (P < 0.0 Chi <sup>2</sup> = 0 regnar 3D 0.25 0.77 0.53 0.86 (P = 0.0 2 0.37 0.98 1.2 0.86 0.87 2 0.86 0.87 <sup>2</sup> = 7.64 (P < 0.0	23, df = 20001) 16, df = 1000 100 100 100 100 100 100 1	11 (P = 0 = 1 (P = 0 Non-Dl Mean 1.13 0.9 1.4 1.19 3 (P < 0.0 1.16 1.1 1.19	0.0002); i 0.69), i <sup>2</sup> = W pregna 0.19 0.58 0.65 0.28 0.001); i <sup>2</sup> 0.3 0.72 0.28 0.36 0.36 0.36 1); i <sup>2</sup> = 4(	* = 69% 0% ancy Total 40 60 40 45 185 = 87% 288 106 45 55 289 3%	Weight 14.5% 10.1% 9.7% 9.5% 43.9% 12.2% 10.5% 9.6% 11.9% 56.1% 100.0%	Mean Difference IV. Random, 95% CI 0.21 [0.11, 0.31] 0.15 [-0.09, 0.39] 0.50 [0.24, 0.76] 0.85 [0.59, 1.11] 0.41 [0.13, 0.70] 0.27 [0.09, 0.45] 0.35 [0.12, 0.58] 0.64 [0.38, 0.90] 0.21 [0.02, 0.40] 0.28 [0.09, 0.47] 0.33 [0.20, 0.46] 0.36 [0.23, 0.491]	-1 -0.5 0 0.5 1 Lower fEFT in DM Higher fEFT in I Mean Difference IV. Random. 95% CI
Heterogeneity: Tau <sup>2</sup> = ( Test for overall effect: 2 Test for suboroup differ 1.5.1 Maternal BMI < 3 Yavuz 2016 Aydin 2020 Iskender 2022 Omeroglu 2023 PDM Subtotal (95% CI) Heterogeneity: Tau <sup>2</sup> = ( Test for overall effect: 2 Jackson 2016 Akkurt 2018 Omeroglu 2023 GDM Sever 2023 GDM Sever 2023 GDM Sever 2023 PDM Subtotal (95% CI) Heterogeneity: Tau <sup>2</sup> = ( Test for overall effect: 2 Total (95% CI) Heterogeneity: Tau <sup>2</sup> = (	0.02; Chi Z = 6.46 ( rences: C DM p Mean 10 kg/m2 1.34 1.05 1.9 2.04 0.07; Chi Z = 2.83 ( 30 kg/m 1.43 1.45 1.83 1.4 1.47 0.01; Chi Z = 5.09 ( 0.03; Chi	<sup>2</sup> = 35.2 (P < 0.0 Chi <sup>2</sup> = 0 0.25 0.77 0.53 0.86 (P = 0.0 2 0.37 0.98 1.2 0.86 0.87 <sup>2</sup> = 7.64 (P < 0.0 <sup>2</sup> 2 = 31.5 <sup>2</sup>	23, df = 20001) 16, df = <b>Total</b> 40 60 40 45 185 52, df = 28 106 90 110 110 444 4, df = 4 20001) 629 39, df =	11 (P = 0 = 1 (P = 0 Non-Di Mean 1.13 0.9 1.4 1.19 3 (P < 0.0 1.16 1.1 1.19	(.0002); i $(.69)$ , $l^2 =$ W pregna 0.19 0.58 0.65 0.28 $0.001)$ ; $l^2$ 0.3 0.72 0.28 0.36 0.36 0.36 $1$ ; $l^2 = 41$ $0.001$ $l^2$	* = 69% 0% ancy Total 40 60 40 45 185 = 87% 288 106 45 55 289 3% 474 = 75%	Weight 14.5% 10.1% 9.7% 9.5% 43.9% 12.2% 10.5% 9.6% 11.9% 56.1% 100.0%	Mean Difference IV. Random, 95% CI 0.21 [0.11, 0.31] 0.15 [-0.09, 0.39] 0.50 [0.24, 0.76] 0.85 [0.59, 1.11] 0.41 [0.13, 0.70] 0.27 [0.09, 0.45] 0.35 [0.12, 0.58] 0.64 [0.38, 0.90] 0.21 [0.02, 0.40] 0.28 [0.09, 0.47] 0.33 [0.20, 0.46] 0.36 [0.23, 0.49]	-1 -0.5 0 0.5 1 Lower fEFT in DM Higher fEFT in I Mean Difference IV. Random, 95% CI

## Figure 4. Forest plots for the subgroup analyses comparing fEFT between women with and without

**DM in pregnancy**; A, subgroup analysis according to the mean maternal age; and B, subgroup analysis

according to the mean maternal BMI;

7



#### Figure 5. Forest plots for the subgroup analyses comparing fEFT between women with and without

DM in pregnancy; A, subgroup analysis according to the median GA of fEFT measurement; and B,

subgroup analysis according to the NOS scores;





### SUPPLEMENTAL DATA

## PubMed from inception to November 12, 2024

#	Searches	Results
1	"epicardial adipose tissue"[MeSH] OR "epicardial adipose tissue" OR	1553
	"epicardial fat" OR "pericardial adipose tissue" OR "pericardial fat"	
	OR "cardiac adipose tissue" OR "cardiac fat" OR "subepicardial	
	adipose tissue" OR "subepicardial fat" OR "heart fat" OR "heart	
	adipose tissue"	
2	("gestational diabetes"[MeSH] OR "gestational diabetes" OR "GDM"	3736
	OR "pregestational diabetes" OR (("gestational" OR	
	"pregnancy"[MeSH] OR "pregnant" OR "pregestational") AND	
	("diabetes"[MeSH] OR "diabetic" OR "hyperglycemia"[MeSH]))	
3	1 and 2	88

## Embase from inception to November 12, 2024

#	Searches	Results
1	'epicardial adipose tissue'/exp OR 'epicardial adipose tissue' OR	7542
	'cardiac adipose tissue' OR 'cardiac fat' OR 'subepicardial adipose	
	tissue' OR 'subepicardial fat' OR 'heart fat' OR 'heart adipose tissue'	
2	'gestational diabetes mellitus'/exp OR 'gestational diabetes' OR 'GDM'	31262
	OR 'pregestational diabetes' OR ('gestational' OR 'pregnancy'/exp OR	
	'pregnant' OR 'pregestational') AND ('diabetes'/exp OR 'diabetic' OR	

	'hyperglycemia'/exp)	
3	1 and 2	68
-		
4	Limit 3 to human	62
		-
5	Limit 4 to clinical study	60
5	Limit + to chine a study	00
6	Limit 5 to Embase	52
U		54

## Web of Science from inception to November 12, 2024

#	Searches	Results
1	TS="epicardial adipose tissue" OR "epicardial fat" OR "pericardial	5714
	adipose tissue" OR "pericardial fat" OR "cardiac adipose tissue" OR	
	"cardiac fat" OR "subepicardial adipose tissue" OR "subepicardial fat"	
	OR "heart fat" OR "heart adipose tissue"	
2	TS="gestational diabetes" OR "GDM" OR "pregestational diabetes"	11312
	OR ("gestational" OR "pregnancy" OR "pregnant" OR	
	"pregestational") AND ("diabetes" OR "diabetic" OR	
	"hyperglycemia")	
3	1 and 2	28