**Associations of High Body Mass Index and Excessive Gestational Weight Gain with Pregnancy Outcomes in Women with Type 1 Diabetes: A Systematic Review and Meta-analysis**

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**Running title:** BMI and GWG in pregnancies with type 1 diabetes

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The protocol of this review was registered in PROSPERO (ID CRD42023404436) <https://www.crd.york.ac.uk/PROSPERO/#searchadvanced>

**Twitter Summary:** Is weight important for #T1D pregnancy? Our latest paper shows that a healthy pre-pregnancy BMI & avoiding excessive weight gain in pregnancy are key ways to improve pregnancy outcomes. @ClaireMeek5.

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**Table: 1**

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**BACKGROUND**

The increased risk of pregnancy complications in type 1 diabetes is mainly attributed to maternal hyperglycemia. However, it is unclear if other potentially-modifiable factors, also contribute to risk in this population.

**PURPOSE**

To assess if high body-mass-index (BMI) and excessive gestational-weight-gain (GWG) are associated with perinatal complications in type 1 diabetes.

**DATA SOURCES**

We searched MEDLINE, Embase, PubMed, Scopus, Web of Science and Cochrane databases to January 2024.

**STUDY SELECTION**

Studies examining associations between periconception BMI or GWG and perinatal complications in type 1 diabetes were included.

**DATA EXTRACTION**

We used a predesigned data extraction template to extract study data including year, country, sample size, participants’ characteristics, exposure and outcomes.

**DATA SYNTHESIS**

We included 29 studies (18,965 pregnancies; 1978-2019) in the meta-analysis. A 1kg/m2 /1kgincrease in preconception BMI or GWG was associated with a 3% and 11% increase in perinatal complications respectively (BMI OR 1.03 (95%CI 1.01-1.06); GWG OR 1.11 (95%CI 1.04-1.18)). Preconception BMI ≥ 25kg/m2 or excessive GWG was associated with a 22% and 50% increase in perinatal complications respectively (BMI OR 1.22 (95%CI 1.11-1.34); GWG OR 1.50 (95%CI 1.31-1.73)).

BMI was associated with congenital malformation, preeclampsia, and neonatal-intensive-care-unit admission. Excessive GWG was associated with preeclampsia, Caesarean delivery, large-for-gestational-age and macrosomia.

**LIMITATIONS**

Retrospective study design, variable measurement for exposures /outcomes, small number of studies for some outcomes, no data from Asia and Africa.

**CONCLUSIONS**

Addressing maternal BMI pre-pregnancy and preventing excessive GWG should be key clinical priorities to improve outcomes in pregnant women with type 1 diabetes.

**Article highlights**

* Why did we undertake this study?

Despite improved glycemia through better access to diabetes technologies, pregnancy outcomes in women with type 1 diabetes remain suboptimal. BMI and GWG are important modifiable risk factors for suboptimal outcomes in the general antenatal population.

* What is the specific question(s) we wanted to answer?

Do elevated maternal BMI and excessive GWG contribute to suboptimal pregnancy outcomes in type 1 diabetes?

* What did we find?

A 1kg/m2 increase in pre-pregnancy BMI was associated with a 3% increase in the odds of perinatal complications. Excessive GWG was associated with a 50% increase in the odds of perinatal complications, especially pre-eclampsia and large-for-gestational-age.

* What are the implications of our findings?

Greater attention to maternal BMI and GWG is needed to improve pregnancy outcomes in type 1 diabetes.

Type 1 diabetes affects 5% to 10% of people with diabetes worldwide (1–3). Pregnant women with type 1 diabetes have a higher risk of suboptimal pregnancy outcomes affecting both mother and baby, such as pre-eclampsia and large-for-gestational age (4,5). Substantial improvements in access to diabetes technology in recent years have improved maternal glycemia but despite this, pregnancy outcomes remain suboptimal. Glycemia is recognised as a key modifiable factor for outcomes (5), but relatively few other modifiable factors have been assessed in this population.

In women without diabetes, obesity and excessive gestational weight gain (GWG) increase the risk of perinatal complications including preeclampsia, preterm labour, Caesarean delivery, large-for-gestational-age (LGA), macrosomia, admission to neonatal intensive care unit (NICU) and neonatal hypoglycemia (4,6,7). The combination of type 1 diabetes, high body mass index (BMI) and excessive GWG might have additive effects as risk factors for suboptimal pregnancy outcomes. The Institute of Medicine (IOM; now called National Academy of Medicine; NAM) recommends thresholds for GWG to optimize perinatal outcomes in pregnant women (8–10). The IOM/NAM guidelines were revised in 2009, however its recommendations are not tailored for special populations, such as women with type 1 diabetes (4).

In this systematic review and meta-analysis, we aimed to evaluate the association of maternal elevated BMI and excessive GWG with perinatal complications in type 1 diabetes.

**RESEARCH DESIGN AND METHODS**

This systematic review and meta-analysis were conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (11) and registered in PROSPERO (ID CRD42023404436).

**Search strategy**

We searched MEDLINE and Embase (using Ovid platform), PubMed, Scopus, Web of Science databases and Cochrane using a list of search terms related to maternal BMI, GWG, type 1 diabetes and suboptimal pregnancy outcomes (defined by a core outcome set) (12), including human studies in English. Details are presented in Supplementary Table 1.

We used Rayyan software (<http://rayyan.qcri.org>) to remove duplications and for title/abstract screening. Titles and abstracts were independently screened by three reviewers and the full texts were assessed against the eligibility criteria by two reviewers independently. Any disagreements were resolved by a third reviewer after independently examining the article against the inclusion criteria. The reference lists of the relevant articles were investigated for additional publications that might meet the eligibility criteria.

**Eligibility criteria**

For inclusion in this systematic review the published articles had to meet the following criteria: peer-reviewed analytical (trial, cohort, or case-control) studies, reporting the association between periconception BMI and/or GWG and perinatal outcomes in singleton pregnancies in women with type 1 diabetes.

Studies presenting a subgroup analysis of the above-mentioned association in a population of pregnant women with type 1 diabetes were also considered for inclusion in the meta-analysis.

The exposures of interest were BMI measured immediately before or after conception and GWG, defined as weight change between the first weight measured around the time of conception and the latest recorded weight before delivery. The outcomes of interest were maternal, neonatal, and obstetric outcomes (Supplementary Table 1). We excluded articles with no data on BMI, GWG, relevant perinatal complications or without disaggregated results in type 1 diabetes (PRISMA checklist; Supplementary Table 2).

**Data extraction and quality assessment**

Using a predesigned data extraction template (in Microsoft Excel), the following information (where available) was extracted: authors, publication year, country, sample size, inclusion and exclusion criteria, age, methods of assessing the exposure and the outcomes, data analysis, and confounders.

Studies reporting data from the same cohort were included if they reported different outcomes. Where two publications arose from the same dataset with the same outcome, the article that reported the largest sample size was used in this analysis.

In the included articles, the risk estimates were presented in different forms including odds ratios (ORs) and mean differences. If multiple risk estimates were presented in a study, the unadjusted risk estimates were selected for pooling in the meta-analysis. If needed, an attempt to retrieve incomplete or additional data in the primary article was made by email to the corresponding authors.

We used the Critical Appraisal Skills Program (CASP) tool (13) was used to assess the risk of bias in the individual articles. Different parts of the individual articles (including study objective and participants, exposure and outcome measures, confounding factors, result validity and applicability) were assessed using a descriptive approach. The Risk-of-bias VISualization (*robvis*) tool (14) was used to summarize and present results of the critical appraisal of the individual studies.

**Data synthesis and analysis**

Findings were synthesized by the type of exposure (periconception BMI or GWG) and outcome. In the selected studies, the GWG and BMI data were presented as either continuous or categorical measures. To combine the data in a meta-analysis, we opted for effect sizes (odds ratio and standard error) in the selected articles. If not provided, the primary OR was calculated using the data included in the manuscript.

Most primary studies reported pre-pregnancy BMI (n=18), and a minority (n=5) reported first trimester BMI (15–19). Most studies used the IOM/NAM guidelines to define optimal GWG (n=16), while four studies used different criteria (17,20–22).

Given the expected heterogeneity in the study populations and procedures, the random effects model was chosen for meta-analysis. Outcomes reported in a single primary study were excluded from meta-analysis. When two or more studies reported the same outcome, the results were pooled to estimate the OR for that particular outcome, and then all the outcomes were pooled together to give an overall OR for the effect of BMI or GWG on the occurrence of suboptimal perinatal outcomes.

The homogeneity assumptions of the effect sizes were assessed by the Cochran *Q* test, and the degree of heterogeneity were assessed using the *I2* statistics where an *I2* >50% indicates substantial heterogeneity. We explored source/s of heterogeneity through subgroup analysis and meta-regression. Variables related to study design (sample size and study time), population (country of study), and weight variable (continuous or categorical) were included in the meta-regression. Publication bias was investigated using Egger’s test and funnel plot. Sensitivity analysis was conducted to assess whether any of the included studies unduly influenced the results. Statistical significance was defined as two-sided p<0.05. All analyses were conducted in SPSS Statistics v.29 (IBM Corp. Released 2022. IBM SPSS Statistics for Windows, Version 29.0. Armonk, NY: IBM Corp).

**RESULTS**

**Study selection and characteristics**

The literature search initially identified 2,689 studies. After removing the duplicated studies, a total of 2,096 articles were included in the initial screening. After reviewing the titles and abstracts, 83 articles were retrieved for full-text review. Thirteen additional records were identified by checking the reference lists and considered for full-text review. After reviewing the 96 full-text records, 29 studies were included in this review (Fig.1; n=23 BMI; n=20 GWG). The reported perinatal outcomes were congenital malformation (n=2), preeclampsia (n=6), hypertensive disorders including gestational hypertension (n=3), preterm birth (n=5), Caesarean section (n=8), LGA (n=12), macrosomia (n=4), small for gestational age (SGA) (n=2), NICU admission (n=3), neonatal hypoglycemia (n=4), neonatal jaundice (n=4), respiratory distress syndrome (RDS) (n=2), perinatal death including stillbirth (n=3), and single studies for shoulder dystocia, one-minute APGAR (Appearance, Pulse, Grimace, Activity, Respiration) score<7, five-minute APGAR score<7 and neonatal polycythaemia.

A total of 18,965 pregnancies which occurred between 1978 and 2019 were included in this review. Most of the studies had a cohort design (both prospective and retrospective) and were published between 1987 and 2023. The characteristics of the included studies are summarised in Table 1.

**Periconception BMI and perinatal complication**

We pooled data from 22 studies (11,743 pregnancies) in a random effects meta-analysis of association between periconception BMI and suboptimal pregnancy outcomes (Fig. 2). The perinatal outcomes reported in the individual studies included congenital malformation (n=2), preeclampsia (n=4), preterm birth (n=5), Caesarean section (n=8), LGA (n=11), macrosomia (n=4), hypertensive disorders (n=3), perinatal death (n=3), neonatal hypoglycemia (n=2), NICU admission (n=2), and neonatal jaundice (n=2). Most of the studies reported more than one perinatal outcome.

Periconception BMI was associated with an increased odds of suboptimal perinatal outcomes in women with type 1 diabetes (OR 1.06, 95% CI 1.02-1.11). For the overall results the heterogeneity between studies was significant (*Q*=101.66, p<0.001) and substantial in magnitude (*I2*=65.5%) (Fig. 2).

Across the individual studies, BMI was presented either as a categorical or continuous variable. The subgroup analysis with BMI as a continuous variable (Supplementary Fig. 1) identified that a 1kg/m2 increase in maternal BMI was associated with a 3% increase in the odds of any perinatal complication (OR 1.03, 95% CI 1.01-1.06; *I2*=48.9%). In the studies that reported BMI as a categorical variable, subgroup analysis showed a significantly higher odds of suboptimal perinatal outcomes in women with periconception BMI≥25 kg/m2 (OR 1.22, 95% CI 1.11-1.34; *I2*=19.6%) (Supplementary Fig. 1).

**Periconception BMI and specific perinatal complications**

In women with type 1 diabetes, periconception BMI was associated with increased odds of congenital malformation (OR 1.22, 95% CI 1.02-1.47; *I2*=0), preeclampsia (OR 1.27, 95% CI 1.11-1.45; *I2*=0), and NICU admission (OR 1.08, 95% CI 1.03-1.13; *I2*=0; Fig. 2).

High BMI was not associated with hypertensive disorders (OR 1.10, 95% CI 0.96-1.27; *I2*=0%), preterm birth (OR 1.08, 95% CI 0.78-1.48; *I2*=87.6%), Caesarean section (OR 1.11, 95% CI 0.94-1.31; *I2*=79.3%), LGA (OR 1.05, 95% CI 1.00-1.10; *I2*=55.1%), macrosomia (OR 1.22, 95% CI 0.92 -1.62; *I2*=40.6%), perinatal death (OR 0.90, 95% CI 0.79-1.03; *I2*=26.6%), neonatal hypoglycemia (OR 1.03, 95% CI 0.95-1.11; *I2*=0), or neonatal jaundice (OR 0.95, 95% CI 0.70-1.28; *I2*=28.1%) (Fig. 2 and Supplementary Table 3).

**Gestational weight gain and perinatal complication**

To examine the relationship between GWG and suboptimal pregnancy outcomes, we pooled data from 20 studies (3560 pregnancies) in a meta-analysis (Fig. 3). The included studies are comparing the groups of women who had excessive GWG with those without excessive GWG. Because insufficient GWG was only reported in one cohort of participants, the insufficient GWG group was not suitable for inclusion in the meta-analysis. Perinatal outcomes investigated in the primary studies are preeclampsia (n=6), preterm birth (n=3), Caesarean section (n=7), LGA (n=12), macrosomia (n=4), neonatal hypoglycemia (n=4), NICU admission (n=3), neonatal jaundice (n=4); and SGA (n=2) and RDS (n=2). Most of the studies reported more than one perinatal outcome.

Women with type 1 diabetes who had excessive GWG were more likely to experience perinatal complication, overall (OR 1.41, 95% CI 1.26-1.59) (Fig. 4). The between-studies heterogeneity was substantial (*I2*=70.9%) and significant (*Q*=95.19, p<0.001). A subgroup analysis based on GWG measurement and presentation (categorical or continuous) highlighted that a 1 kg increase in maternal GWG was associated with 11% increase in the odds of perinatal complication (OR 1.11; 95% CI 1.04-1.18; *I2*=27.2%). Compared to those with adequate GWG women with excessive GWG were 50% more likely to experience perinatal complications (OR 1.50, 95% CI 1.31-1.73; *I2*=29.2%) (Supplementary Fig. 2).

**Gestational weight gain and specific perinatal complications**

In women with type 1 diabetes, excessive GWG was associated with an increased odds of preeclampsia (OR 1.10, 95% CI 1.04-1.16; *I2*=26.8%), Caesarean section (OR 1.70, 95% CI 1.28-2.25; *I2*=0%), LGA (OR 1.80, 95% CI 1.44-2.26; *I2*=44%) and macrosomia (OR 1.92, 95% CI 1.28-2.87; *I2*=39.5%). However, excessive GWG was not associated with preterm birth (OR 1.02, 95% CI 0.68-1.52; *I2*=0%), SGA (OR 0.65, 95% CI 0.21-2.02; *I2*=0), RDS (OR 1.81, 95% CI 0.78-4.20; *I2*=0%), neonatal hypoglycemia (OR 1.11, 95% CI 0.74-1.66; *I2*=0%), NICU admission (OR 0.91, 95% CI 0.59-1.41; *I2*=0%) or neonatal jaundice (OR 1.08, 95% CI 0.50-2.30; *I2*=66.4%) (Fig. 3 and Supplementary Table 3).

**Heterogeneity and publication bias**

The overall heterogeneity between the effect sizes in the meta-analysis for BMI was substantial (I2>50%). However, no heterogeneity was observed when the effect sizes pooled for congenital malformation, preeclampsia, neonatal hypoglycemia and NICU admission (Supplementary Table 3).

Some of the overall heterogeneity was explained by subgroup analysis. The subgroup analysis of the data based on the BMI measurement and presentation method (categorical or continuous variable) reduced the overall substantial heterogeneity (I2=65.5%) to lower levels (19.6% and 48.9% for categoric and continuous variables respectively).

To further evaluate the possible sources of heterogeneity, a meta-regression analysis was performed. The publication year (p<0.001) and sample size (p=0.019) also contributed to the overall heterogeneity (Supplementary Fig. 3).

The sensitivity analysis suggests that the overall results for the association between maternal BMI and perinatal outcomes are robust with minimal impact on the effect size of the pooled overall results. However, after removing the study by Small et al (19), the association between BMI and macrosomia became significant (OR 1.06, 95% CI 1.02-1.11; *I2*=0). This can be explained by the study period (1980-1984), publication year (1987) and case definitions (insulin dependent diabetes mellitus vs type 1 diabetes).

In the meta-analysis for the GWG, a substantial heterogeneity (*I2*=70.9%) for the overall results was observed. There was a low to moderate heterogeneity in effect sizes for LGA, and macrosomia but it was substantial for neonatal jaundice (Supplementary Table 3). A subgroup analysis of the data based on GWG reporting method (continuous or categorical variable) was performed. The levels of heterogeneity for the subgroups were reduced to *I2*=27.2% and *I2*=29.2% for continuous and categorical presentation of GWG respectively.

A meta-regression analysis was performed to further evaluate the possible sources of heterogeneity for the association between GWG and suboptimal perinatal outcomes. In addition to GWG reporting method and the perinatal outcomes, the meta-regression analysis showed that study year (p<0.001), country of study (p<0.001) and number of outcome cases (p=0.044) also contributed to the observed heterogeneity (Supplementary Fig. 4).

There was no evidence of publication bias in the funnel plot (Supplementary Fig. 5a) for association between BMI and the suboptimal perinatal outcomes (Egger’s intercept=0.03; p=0.237).

Visual inspection of the funnel plot for GWG and perinatal outcomes (Supplementary Fig. 5b) revealed evidence of publication bias which was supported by Egger’s test (Egger’s intercept=0.05, p=0.001). In a sensitivity analysis based on study period, excluding studies with data collection period before 2009 reduced the overall effect size slightly (OR 1.38, 95% CI 1.18 -1.62; *I2*=71.4%). However, the sensitivity analysis based on sample size and study design suggested that the meta-analysis results are robust with minimal impact on the effect size of the pooled results.

**Risk of bias**

In all included studies, with the exception of five (5,17,23–25), eligibility criteria were adequately described. The studies showed low risk to moderate of bias in relation to participant recruitment and follow-up, outcome measurement and reporting of results. However, there were disparities in the exposure measurements (both BMI and GWG). With the exception of six studies (17,19,21,23,24,26), the BMI and GWG groups were classified according to the World Health Organization (WHO) and IOM/NAM criteria. There were some inconsistencies in the thresholds used for the diagnosis of LGA, macrosomia, neonatal hypoglycemia and neonatal jaundice.

Overall, the majority of the studies demonstrated low to moderate risk of bias. Some of the studies had moderate to high bias risk due to self-reported periconception body weight, inconsistent case definitions, lack of precision of the results (large CIs), and insufficient control of the confounding variables. Supplementary Fig. 6 summarises the results of the critical appraisal of the individual studies.

**DISCUSSION**

This meta-analysis of 18,965 pregnancies demonstrates that maternal periconception BMI and GWG are important determinants of perinatal complications in type 1 diabetes pregnancy. A 1kg/m2 /1kg increase in preconception BMI or GWG was associated with a 3% and 11% increase in perinatal complications respectively. Preconception BMI ≥ 25kg/m2 or excessive GWG was associated with a 22% and 50% increase in perinatal complications respectively. Our data suggest that specific interventions to address maternal preconception BMI and prevent excessive GWG are likely to substantially improve pregnancy outcomes in women with type 1 diabetes.

**Strengths and Weaknesses**

There is limited published data about the association between perinatal outcomes and BMI and GWG in pregnancies with type 1 diabetes. Data from 29 primary studies including 18,965 pregnancies were pooled in the meta-analysis, but many studies were small with moderate risk of bias. In the primary studies, BMI and GWG were presented either as categorical or continuous variables. To maximise the number of studies in the meta-analysis, we included both continuous and categorical observational data, naturally prone to different types of bias. The critical appraisal indicates moderate bias risk in most of the primary studies, which included data between 1978 and 2019.

The use of novel technologies in type 1 diabetes is growing, although uptake is variable internationally. Although careful generalisation of our results to the contemporary cohorts is recommended, our sensitivity analysis demonstrated that study period did not substantially alter our results. Moreover, while the net GWG and role of factors such as gestational age, fluid retention (such as in preeclampsia) is challenging to measure accurately, this has not changed over time, and was not discussed in most of the primary studies. Most of the data pooled in this meta-analysis were from studies conducted in high-income countries, with no studies based in Asia or Africa. . Limiting our search to publications in English may have inadvertently excluded some published works in other languages.

As expected, some heterogeneity in this meta-analysis was observed, attributed to differences in outcome definitions, exposure / measurement timing , the use of continuous vs categorical variables. Our work highlights the need for further studies in cohorts of women with type 1 diabetes, using consistent definitions for outcomes and exposures, particularly the measurement and reporting of BMI and GWG.

Despite these limitations, this study is the first meta-analysis on this topic and provides evidence from 18,965 pregnancies of the importance of BMI and GWG on pregnancy outcomes in type 1 diabetes. Overall, these findings are consistent with the results from studies and meta-analyses conducted in the general antenatal population (6,7,27), where it is well-established that higher maternal BMI and excessive GWG are associated with increased risk of gestational diabetes, hypertensive disorders of pregnancy (including preeclampsia), operative delivery, LGA, macrosomia, lowered APGAR score and NICU admission. Maintaining an optimal BMI before and after conception, mainly through improving health behaviours, is encouraged in the general antenatal population to improve perinatal outcomes (6,7,28). While higher BMI at the start of pregnancy and excessive GWG during pregnancy are common in the antenatal population, having a BMI<18.5 kg/m2 and/or insufficient GWG can also increase risk of some perinatal complications (6,27,28). However, in this systematic review we were unable to find enough studies assessing outcomes in women with BMI<18.5 kg/m2 or insufficient GWG in women with type 1 diabetes.

We identified that BMI and GWG are strongly associated with preeclampsia in women with type 1 diabetes. An increased periconception BMI was associated with the higher odds of preeclampsia by 27%; GWG above the IOM/NAM guidelines was associated with an increased odds of preeclampsia by 10%. The pathogenesis of preeclampsia is multifactorial, and although not fully understood, its main feature is generalized vasculopathy triggered by placental malfunction. It is likely that both maternal glucose and maternal insulin resistance contribute distinctly to the risk of preeclampsia. Maternal glucose is associated with the risk of preeclampsia (29), and may be responsible for toxic effects on vascular function (30). However, increased insulin resistance early in pregnancy can also affect placental function (31). Elevated maternal BMI and excessive GWG are linked to insulin resistance, dyslipidaemia and cardiometabolic complications which contribute to vascular changes, but may also exacerbate maternal hyperglycemia (32,33). Given that women with type 1 diabetes are at increased risk of preeclampsia, pre-pregnancy counselling and weight management strategies before and during pregnancy may support efforts to improve glycemia and may lessen the risk of preeclampsia. Further studies of the interaction between weight management, insulin resistance, glycemia and placental function concerning the risk of preeclampsia in women with type 1 diabetes are needed.

Our results show that Caesarean delivery was associated with excessive GWG but not with periconception BMI. This finding is not consistent with the existing literature. In the studies pooled for this association the results were inconsistent and mostly based on self-reported weight which is naturally prone to measurement bias.

This study identified that GWG is strongly associated with infant growth outcomes in women with type 1 diabetes. Excessive GWG, defined according to the IOM/NAM guidelines, increased odds of both LGA (by 80%) and macrosomia (by 92%). We did not find a significant association between BMI and fetal growth outcomes, but a substantial level of heterogeneity was observed among the effect sizes pooled for these outcomes. Despite advances in glycaemic control in mothers with type 1 diabetes, fetal overgrowth is still a significant problem (34). Similar associations have been documented in women with gestational diabetes or type 2 diabetes (35,36). It is unclear if associations between maternal GWG and fetal growth are mediated entirely through glucose, or whether other pathways are also involved. Recent work in the continuous glucose monitoring in women with type 1 diabetes in pregnancy trial (CONCEPTT) (34) identified that offspring growth was also significantly associated with maternal lipid metabolism, independently of maternal glucose, with evidence of increased lipogenesis, high levels of free fatty acids (FFAs) and triglycerides, resulting in excess weight in the baby (5), consistent with other contributions (17,37). These findings suggest that there may be a combination of factors involved in excessive fetal growth.

Since our search was completed in early 2024, this metanalysis covered a period of time before hybrid closed loop (HCL) systems were routinely used in women with type 1 diabetes in pregnancy. Our data are important for HCL implementation, since insulin dosing and delivery are important contributors to weight gain. For example, a study of commercially available automated insulin delivery systems (38) showed that despite achieving similar glycemic control, patients using HCL systems had more GWG and fetal overgrowth compared to patients on multiple daily insulin injections (MDI). Conversely, Lee and colleagues (39) demonstrated a reduction in GWG with the use of the CAM-APS XL HCL systems compared to standard care (MDI or pumps) suggesting that some HCL systems have the potential to improve outcomes, both through improved glycaemia but also through preventing excessive GWG.

In addition to the short-term effects for both the mother and the baby, excessive GWG is linked to postpartum weight retention, contributing to obesity and related complications for mothers in later life (40). Addressing BMI and GWG also has the potential to reduce fetal overgrowth, which has long-term metabolic implications that can adversely affect the health of the offspring in childhood and adolescence (37,40). While we consider that periconception BMI and GWG are both potentially modifiable, there have been limited intervention strategies in this population. Further studies are required to identify effective interventions, and to identify and quantify the benefits upon perinatal outcomes.

This systematic review and meta-analysis showed an increased risk of perinatal complications in association with higher BMI and GWG in women with type 1 diabetes. Our results suggest that in women with type 1 diabetes, tackling GWG might be more important compared to pre-pregnancy BMI. When women arrive in the antenatal clinic in early pregnancy, it is also more feasible to address GWG, as preconception BMI can no longer be changed. While there is little evidence of successful interventions to prevent excessive GWG in this population, increasing monitoring of weight gain, reiterating targets and providing nutrition and physical activity counselling may all be useful contributions.

Further work is also needed to identify optimal targets for GWG in pregnancies with type 1 diabetes. Despite providing a useful starting point for monitoring GWG, the IOM/NAM guidelines were not developed in this population and should be applied with caution, considering individual health factors, diabetes management needs and nutritional requirements. The IOM/NAM guidelines may be too strict, contributing to unrealistic expectations, patient burden, inadequate nutrition intake and diabetes distress (4), or not strict enough, especially in women with established pre-pregnancy obesity for whom gaining 5.0-9.1kg may be unhelpful.

In conclusion, maternal BMI and GWG are important, potentially-modifiable, determinants of perinatal complications in type 1 diabetes pregnancy showing particularly strong association with preeclampsia and fetal growth outcomes. Excessive GWG appears particularly detrimental. Addressing maternal BMI pre-pregnancy and preventing excessive GWG should be key clinical priorities in women with type 1 diabetes.

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**Conflict of Interest**

The authors have no conflicts relevant to this article to disclose**.**

**Author contributions**

CLM and NA conceptualized the study. NA designed the study and conducted the article search. NA, AE and CLM screened the titles and abstracts. NA, CJP and AE critically appraised the full texts against the inclusion criteria and extracted data. NA and CLM and CJP wrote the manuscript. LCK critically reviewed the manuscript. All authors reviewed and agreed to the final version of the manuscript. CLM and NA are the guarantors for study data.

**Prior presentation:**

An abstract of this study has been submitted to the American Diabetes Association (ADA) Scientific Sessions 2024 and is accepted for a poster presentation.

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**TABLES**

Table 1. Summary of the individual studies included in the systematic review and meta-analysis.

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **No** | **Author and publication year** | **Study period** | **Country** | **Study type** | **Total sample size\*** | **Inclusion criteria** | **Exclusion criteria** | **Exposure of interest** | **Perinatal outcomes** | **Glycaemic control variables in the study groups** |
| 1 | Weschenfelder, 2022 | 2000- 2019 | Germany | Retrospective cohort study | 118 | Singleton T1D pregnancies, with term deliveries (≥ 37 weeks of gestation) and trial of vaginal birth | Foetal death (n=3), preterm (37), missing data (10) elective C-S (27) | GWG (kg) according to IOM/NAM recommendation, pre pregnancy BMI (kg/m2)- classifications based on WHO criteria | Mode of delivery (successful vaginal delivery) | HbA1c was lower in women with vaginal delivery. |
| 2 | Oppermann, 2020 | 2005-2015 | Brazil | Retrospective cohort study | 78 | Pregnant women with T1D or T2D; study outcomes at or above 23 weeks of gestation | Women with less than 2 antenatal visits; multiple pregnancy, uncertain diagnosis of pregnancy, missing information on preeclampsia (n=7) | GWG (kg) according to the IOM/NAM recommendation, pre pregnancy BMI (kg/m2)- classifications based on WHO criteria | Preeclampsia | HbA1c was comparable between the groups of women with and without the outcome. |
| 3 | Stogianni, 2019 | 2009-2012 | Sweden | Retrospective population record review | 37 | All pregnant women with any type of diabetes; plus 135 pregnancies without diabetes matched for age, parity, date of delivery | No information | BMI at first visit (early pregnancy BMI), also dichotomized </≥ 25 kg/ m2, and 30 kg/m2; and gestational weight gain (GWG) (kg), dichotomized </≥8 kg. | C-S and LGA | No |
| 4 | McWhorter, 2018 | PPG 1978-1993 CSL 2002-2008 | USA | Multicentre study of two populating based cohorts | PPG= 333; CSL= 358 | TID and gestation at 23 completed weeks | Multiple gestation, foetal anomaly, stillbirth, and missing values for birth weight of the neonate, maternal pre-pregnancy and delivery weight and maternal height | GWG (kg) according to IOM/NAM recommendation, pre pregnancy BMI (kg/m2)- classifications based on WHO criteria | LGA | No |
| 5 | Abell, 2016 | 2010-2013 | Australia | Historical cohort study | 107 pregnancies in 94 women | Singleton births of at least 20 weeks | Women with type 2 diabetes and gestational diabetes mellitus (GDM) were excluded. | First trimester BMI (kg/m2)- classifications based on WHO criteria | LGA, SGA, C-S, Preterm birth, Hypertensive complications, Hypoglycemia, Jaundice, Shoulder dystocia, Congenital malformation, Perinatal death | HbA1c was comparable between the groups of women with and without the outcomes except for preterm birth and perinatal death (↑OR). |
| 6 | Morrens, 2016 | 1992-2014 | Belgium | Retrospective analysis of the medical files | 259 pregnancies in 180 women | Pregnant women with T1D (pregnant women with T1D with antepartum follow up <12 weeks) | pregnant T1DM women with antepartum follow-up < 12 weeks at UZ-Leuven were included in the study. Other exclusion criteria were women with GDM, T2DM, hereditary diabetes, secondary diabetes and use of a peritoneal insulin infusion pump. | GWG (kg) according to the IOM/NAM recommendation, pre pregnancy BMI (kg/m2)- classifications based on WHO criteria | LGA | HbA1c was higher in women with the outcome compared with those without the outcome. |
| 7 | Scifres, 2014 | 2009-2012 | USA | Retrospective cohort study | 175 | All women with T1D and singleton pregnancies | No information | GWG (kg) according to the IOM/NAM recommendation, pre pregnancy BMI (kg/m2)- classifications based on WHO criteria | LGA, SGA, macrosomia, C-S, NICU admission, preeclampsia, Hypoglycemia, Jaundice, Shoulder dystocia, congenital malformation, stillbirth | HbA1c was comparable in women with aGWG and those with eGWG; HbA1c was not different in women with LGA from those without LGA. |
| 8 | Kawakita, 2016 | 1978-1995 | USA | Secondary analysis of Diabetes in pregnancy Program project grant (PPG) Cohort | 338 | Elsewhere | elsewhere | Pre-pregnancy BMI: low BMI(<20 kg/m2), normal BMI(20to < 25 kg/m2), and high BMI ( 25 kg/m2) | Spontaneous abortion, gestational hypertension, preeclampsia, C-S, emergency delivery, preterm birth | HbA1c was comparable between the BMI groups. |
| 9 | Klemetti, 2012 | 1989-2008 | Finland | Secondary analysis of obstetric records of women with T1D | 881 | Singleton pregnancy of women having T1D | Only last pregnancy of each woman was included in this data analysis, the rest were excluded. | Pre pregnancy BMI (kg/m2)- classifications based on WHO criteria | C-S, Preterm birth, macrosomia, NICU admission, Hypoglycemia | HbA1c was different between of the outcome groups. |
| 10 | Lepercq, 2010 | 1997-2008 | France | Nested case control in a cohort study | 209 | All nulliparous women with T1D and a single pregnancy >22 weeks | Women were excluded if they were multiparous, had a foetus with major congenital malformation, or had intrauterine foetal death. | Pre pregnancy BMI (kg/m2)- classifications based on WHO criteria | C-S | HbA1c was comparable between the groups of women with and without the outcome. |
| 11 | Secher, 2014 | 2009-2011 | Denmark | Retrospective cohort study | 115 | Danish-speaking women with T1D before 14 completed gestational weeks and having a singleton pregnancy delivered at term (>37 weeks) | Women with preterm birth, presence of diabetic nephropathy and/or the development of preeclampsia | GWG (kg), according to local guidelines, women with BMI <30 kg/m2 were advised to gain 10–15 kg in pregnancy, whereas women with BMI >30 kg/m2 were advised to limit the total gestational weight gain to 5 kg. | Birth weight, NICU admission, Hypoglycemia, and Jaundice | HbA1c was comparable between the BMI and GWG groups. |
| 12 | Søholm, 2021 | 2015-2018 | Denmark | A secondary analysis of a prospective cohort study | 117 | Singleton pregnancies in women with pre-existing diabetes who followed ante- and perinatal care at the Center for Pregnant Women with Diabetes, Rigshospitalet, Denmark from September 2015 to February 2018. | Age less than 18 years, insufficient Danish language skills and a recurrent pregnancy during the study period. | GWG (kg) according to IOM/NAM guidelines, pre-pregnancy BMI | Preterm birth | HbA1c was comparable between the groups of women with and without the outcome. |
| 13 | Kawakita, 2016 | 1978-1995 | USA | Secondary data analysis of the Program Project Grant (PPG) of Diabetes in Pregnancy cohort | 293 | Pregnant women with T1D between 24 and 41 weeks of gestation | No information | GWG (kg) according to the IOM/NAM recommendation | Preeclampsia, C-S, preterm birth, LGA, macrosomia, 1 min APGAR<7, hypoglycemia, RDS, NICU admission, Hyperbilirubinemia, Polycythaemia | Post prandial glucose and HbA1c were comparable between the GWG groups. |
| 14 | Hauffe, 2019 | 2010-2017 | Germany | Retrospective cohort study | 339 pregnancies from 292 women | Pregnant women with preexisting T1D | women whose T1D condition is diagnosed in pregnancy | GWG (kg) according to the IOM/NAM recommendation, | LGA | HbA1c was higher in women with the outcome. |
| 15 | Persson, 2016 | 1997-2012 | Sweden | Population based cohort study (retrospective) | 7062 | Singleton births in Sweden with available data in the Swedish Medical Birth Registry (MBR) | Women with missing ID & information, multiple birth, and births with unknown gestational age | First trimester BMI (kg/m2)- classifications based on WHO criteria | Preeclampsia | No |
| 16 | Gutaj, 2017 | 2012- 2014 | Poland | Prospective nested case control study | 165 | Pregnant women with T1D | Having abortion, Having multiple pregnancy | GWG (kg) according to the IOM/NAM recommendation, pre pregnancy BMI (kg/m2)- classifications based on WHO criteria | Preeclampsia | HbA1c was higher in women with the outcome. |
| 17 | Ladfors, 2017 | 2006-2016 | Sweden | Retrospective chart review | 221 | Pregnant women (singleton) with pregestational diabetes who gave birth at Sakne University hospital at the study period, whose medical record of ANC was available | Multiple pregnancies, abortion, IUFD, having chromosomal disorders, major foetal anomalies, or syndromes | GWG (kg) according to the IOM/NAM recommendation, pre pregnancy BMI (kg/m2)- classifications based on WHO criteria | LGA | HbA1c was higher in women with the outcome. |
| 18 | Alexander, 2019 | 2009-2016 | Canada | Retrospective cohort study | 151 | Live singleton pregnancy of 28wks or more in women with preexisting diabetes who have medical records available | Multiple pregnancies, abortion, IUFD | GWG (kg) according to the IOM/NAM recommendation, pre pregnancy BMI (kg/m2)- classifications based on WHO criteria | LGA | HbA1c was comparable between the groups of women with and without the outcome. |
| 19 | Evers, 2002 | 1999-2000 | the Netherlands | Prospective cohort study | 289 | Pregnant women with T1D, no malformation, live singleton, delivery 28 gestational week or more | Not meeting the inclusion criteria | GWG (kg) according to the IOM/NAM recommendation, pre pregnancy BMI (kg/m2)- classifications based on WHO criteria | Macrosomia | HbA1c was higher in women with the outcome. |
| 20 | Castiglioni, 2013 | 1993-2008 | Italy | Prospective cohort study | 291 | Pregnant women with T1D | Women with pre-pregnancy overt nephropathy, multiple pregnancies | GWG (kg) according to the IOM/NAM recommendation | Preeclampsia | HbA1c was higher in women with the outcome. |
| 21 | Berk, 1989 | 1978-1986 | USA | Prospective cohort study | 72 | Pregnant women with preexisting insulin dependent diabetes | NR | GWG (kg) and third trimester weight gain | LGA | HbA1c (delivery) was higher in women with LGA. |
| 22 | Lepercq, 2002 | NR | France | Prospective cohort study | 65 | Pregnant women with T1D | Fetal congenital malformation (n=1) | GWG (kg), pre pregnancy BMI (kg/m2)- classifications based on WHO criteria | Macrosomia | HbA1c was comparable between the groups of women with and without the outcome. |
| 23 | Meek, 2023 | 2013-2016 | Canada, England, Scotland, Spain, Italy, Ireland and the USA | RCT | 174 | Women with T1D who were pregnant or planning pregnancy were recruited | Elsewhere | GWG (kg), pre pregnancy BMI (kg/m2)- classifications based on WHO criteria | Preeclampsia, pre-term birth, C-S, LGA, respiratory distress, neonatal hypoglycemia, NICU admission, hyperbilirubinemia | CGM%TIR and HbA1c |
| 24 | Persson, 2012 | 1998-2007 | Sweden | Population based cohort study (retrospective) | 3457 † | Women with type 1 with singleton pregnancy | Underweight women, and records with missed or extreme values | Pre pregnancy BMI (kg/m2)- classifications based on WHO criteria | pre-term birth, C-S, LGA, major malformation, perinatal death | No |
| 25 | Mackin, 2019 | 1998-2016 | Scotland | Retrospective cohort study (national registries) | 3778 | Women with singleton pregnancies recorded in the Scottish Morbidity Records 02 | Women with missing age, baby’s sex data or pregnancy loss, twin pregnancies | Pre pregnancy BMI | Stillbirth | HbA1c was higher in women with the outcome. |
| 26 | Cnattingius, 2017 | 1997-2011 | Sweden | Retrospective cohort study (national registries) | 5941 | Live singleton births | Babies with malformation | First trimester BMI (kg/m2) | APGAR score 5 min <7 | No |
| 27 | Aschwald, 2009 | 2000-2007 | USA | Medical chart review of a medical centre | 70 | Pregnancies in women with T1D | Women with missing data or late referral to the medical centre | GWG (Kg) and Pre pregnancy BMI (kg/m2)classifications based on WHO criteria | LGA | HbA1c was comparable in both outcome groups. |
| 28 | Cundy, 2002 | 1993-2000 | New Zealand | Cohort study | 100 | Singleton pregnancies with progression beyond 26 weeks | Twin pregnancies and women with uncertain type of diabetes | Pre pregnancy BMI (kg/m2) | Hypertensive disorders of pregnancy | HbA1c was comparable in both outcome groups. |
| 29 | Small, 1987 | 1980-1984 | Scotland | Nested case control in a cohort study | 40 | Singleton pregnancies  that proceeded beyond 28 weeks | mothers  attended only at term without prior prenatal care | First trimester BMI (kg/m2) | Macrosomia | HbA1c was comparable in both outcome groups. |

\*The total sample size represents all women with T1D who were eligible for inclusion in individual studies; † This cohort is also included in the article “Persson, 2016”; T1D: Type 1 diabetes; T2D: Type 2 diabetes; CSII: Continuous subcutaneous insulin infusion; PPG: Pregnancy Program Project cohort; CSL: Consortium on Safe Labour cohort; C-S: Caesarean section; LGA: Large for gestational age; SGA: Small for gestational age; aGWG: adequate gestational weight gain; eGWG: Excessive gestational weight gain; CGM%TIR: percentage of time in range in glycemia readings by continuous glucose monitoring

The complete reference list of the studies included in this systematic review is presented in the supplementary reference list.

**FIGURE LEGENDS**

A screenshot of a computer screen

Description automatically generated

Figure 1. Flowchart of the study selection for the systematic review and meta-analysis

Figure 2. Forest plots showing the effect size of the association between BMI and the perinatal outcomes. Most of the studies presented multiple perinatal outcomes which are pooled in the meta-analysis. In such cases, the same study is listed more the once in the forest plot.

\*:Hypertensive disorders include hypertensive problems in pregnancy except preeclampsia; **†**:Perinatal death of the baby including stillbirth; PPG: Pregnancy Program Project cohort; CSL: Consortium on Safe Labour cohort; LGA: Large for gestational age; NICU: Neonatal intensive care unit; SGA: Small for gestational age; RDS: Respiratory distress syndrome

A screenshot of a computer screen

Description automatically generated

Figure 3. Forest plots showing the effect size of the association between GWG and the perinatal outcomes. Most of the studies presented multiple perinatal outcomes which are pooled in the meta-analysis. In such cases, the same study is listed more the once in the forest plot.

PPG: Pregnancy Program Project cohort; CSL: Consortium on Safe Labour cohort; LGA: Large for gestational age; SGA: Small for gestational age; RDS: Respiratory distress syndrome; NICU: Neonatal intensive care unit