

# INPLASY

## A Systematic Review of Interventions in Early Pregnancy Among Pregnant Individuals at Risk for Hyperglycemia

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### ADMINISTRATIVE INFORMATION

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**Review Stage at time of this submission** - Completed but not published.

**Conflicts of interest** - None declared.

**INPLASY registration number:** INPLASY202450137

**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 30 May 2024 and was last updated on 30 May 2024.

### INTRODUCTION

**Review question / Objective** Identify and describe interventions initiated in early pregnancy (before 20 weeks gestation) and their effects on primary (neonatal adiposity, small for gestational age, large for gestational age, macrosomia) and secondary outcomes (gestational weight gain, maternal hypertensive disorder, birth injury, NICU admission, preterm delivery, emergency Cesarean section) among pregnant individuals who enter pregnancy at risk for hyperglycemia.

**Rationale** Fetal growth trajectories are particularly sensitive to the maternal metabolic environment in early pregnancy. Healthcare providers need a comprehensive view of options for early pregnancy intervention to determine the best care plans for their patients.

**Condition being studied** Pregnancies at risk for hyperglycemia (i.e., enter pregnancy with overweight or obesity, history of gestational diabetes mellitus, and/or a history of type II diabetes).

### METHODS

**Search strategy** In collaboration with a health sciences research librarian, we searched the Cochrane Central database (May 19, 2023) as well as Medline, Embase, and CINAHL databases (June 12, 2023) for clinical trials published in the last ten years. Search terms included the key words “early OR during” OR “first trimester OR second trimester” AND “gestation OR pregnancy” OR “prenatal care” AND “insulin resistance” OR “metabolic health” OR “diabet\*” OR “body composition” OR “obes\*” OR “weight gain” OR “gestational diabetes” AND “clinical trial.”

**Participant or population** Pregnant individuals with risk factors for hyperglycemia, including overweight and/or obesity, history of type 2 diabetes, and history of GDM.

**Intervention** Interventions initiated before 20 weeks gestation aimed at reducing risks associated with hyperglycemia in pregnancy.

**Comparator** Not applicable.

**Study designs to be included** Randomized controlled trials, clinical trials, and trials.

**Eligibility criteria** Trials of early pregnancy interventions initiated at or before 20 weeks gestation published between 2013 - 2023. Studies were conducted in high-income countries, included people with singleton pregnancies who were either overweight or obese, had a history of gestational diabetes mellitus, and/or a history of type II diabetes and reported at least one primary outcome of interest: neonatal adiposity, LGA, SGA, and macrosomia.

**Information sources** In collaboration with a health sciences research librarian, we searched the Cochrane Central database (May 19, 2023) as well as Medline, Embase, and CINAHL databases (June 12, 2023) for clinical trials published in the last ten years.

**Main outcome(s)** Neonatal adiposity, large-for-gestational age (LGA), small-for-gestational age (SGA), and macrosomia.

**Additional outcome(s)** Secondary outcomes for neonates: preterm birth, neonatal hypoglycemia, NICU admission, and birth injuries (shoulder dystocia, brachial plexus palsy, etc.), and, for pregnant individuals: total gestational weight gain, pre-eclampsia or pregnancy-induced hypertension, and emergency cesarean section.

**Data management** The web application Covidence was used to manage collected articles during the two screening phases of this study. Extracted data was recorded in a sharable spreadsheet.

**Quality assessment / Risk of bias analysis** We used the Downs and Black checklist to evaluate the methodological quality and risk of bias of studies included in our systematic review. The checklist consists of 27 items across five domains: 1) reporting (ten items); 2) external validity (three items); 3) internal validity- bias (seven items); 4) internal validity- confounding or selection bias (six

items); and 5) power (one item). 26 items were rated as either “yes” (1 point) or “no/unable to determine” (0 points), and one item related to the reporting of confounders was rated on a three-point scale (yes=2 points, partially=1 point, no=0 points). As done in previous reviews, we revised the item regarding power calculations to be rated as either “yes” (1 point) or “no/unable to determine” (0 points). This resulted in a maximum total score of 28 points with higher scores indicating stronger methodological quality. There were several questions that specifically pertained to randomization procedures, however, because our systematic review included non-randomized trials, we did not count non-applicable items in the total score. Two authors each assessed half of the studies and resolved any concerns with the other study team members. Psychometric properties (e.g., internal consistency, test-retest reliability, and interrater reliability) of the Downs and Black checklist have previously been reported as appropriate, and the checklist is ranked among the top six quality-assessment tools for use in systematic reviews.

**Strategy of data synthesis** After study selection, four authors independently extracted data from eligible studies. Microsoft Excel was utilized for data collection, extraction, and study comparison. Main data items sought in this stage were information on study design, population, risk factors, length of intervention, time of measurement, primary and secondary outcomes, and relevant summary measures of results (i.e.,  $\beta$  coefficients, odds ratios, mean differences, etc.). Any conflicts or discrepancies in the data were discussed and resolved among the research team.

**Subgroup analysis** Not applicable.

**Sensitivity analysis** Not applicable.

**Language restriction** English.

**Country(ies) involved** United States.

**Keywords** pregnancy; gestation; gestational diabetes mellitus; intervention; behaviors; nutrition; diet; physical activity; exercise; pharmaceutical; review; clinical; glucose intolerance; hyperglycemia; counselling; lifestyle.

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