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

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BACKGROUND

- Gestational diabetes mellitus (GDM) and more subtle hyperglycemia in pregnancy, often associated with obesity, increase short and long-term health risks for both the pregnant individual and their offspring.[1]
- As the rate of obesity has increased, there is also rising awareness that even pregnant people who do not meet criteria for GDM may still have significant hyperglycemia or glucose intolerance earlier in their pregnancy.
- Interventions initiated during pregnancy that aim to mitigate risks associated with obesity, hyperglycemia, and GDM report mixed success.[2,3]
- Emerging evidence suggests developmental processes that occur in early pregnancy, including placental growth and organ development, may be particularly sensitive to maternal metabolic conditions in early pregnancy (i.e., ≤20 weeks gestation).[4–6]
- The objectives of our review were to identify and describe interventions conducted with pregnant individuals with risk factors for hyperglycemia, including overweight and/or obesity, history of type 2 diabetes, and history of GDM, that were initiated ≤20 weeks gestation and reported neonatal anthropometric outcomes.
- Healthcare providers can use our findings to identify and compare interventions to inform their care of pregnant individuals at risk for complications associated with excess adiposity and hyperglycemia, which currently affect more than 40% of pregnancies in the US.[7,8]

METHODS

In collaboration with a Health Sciences Research Librarian, we searched 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" in May 2023.

We included studies of randomized controlled trials, clinical trials, and of early pregnancy interventions initiated at or before 20 weeks gestation. 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.
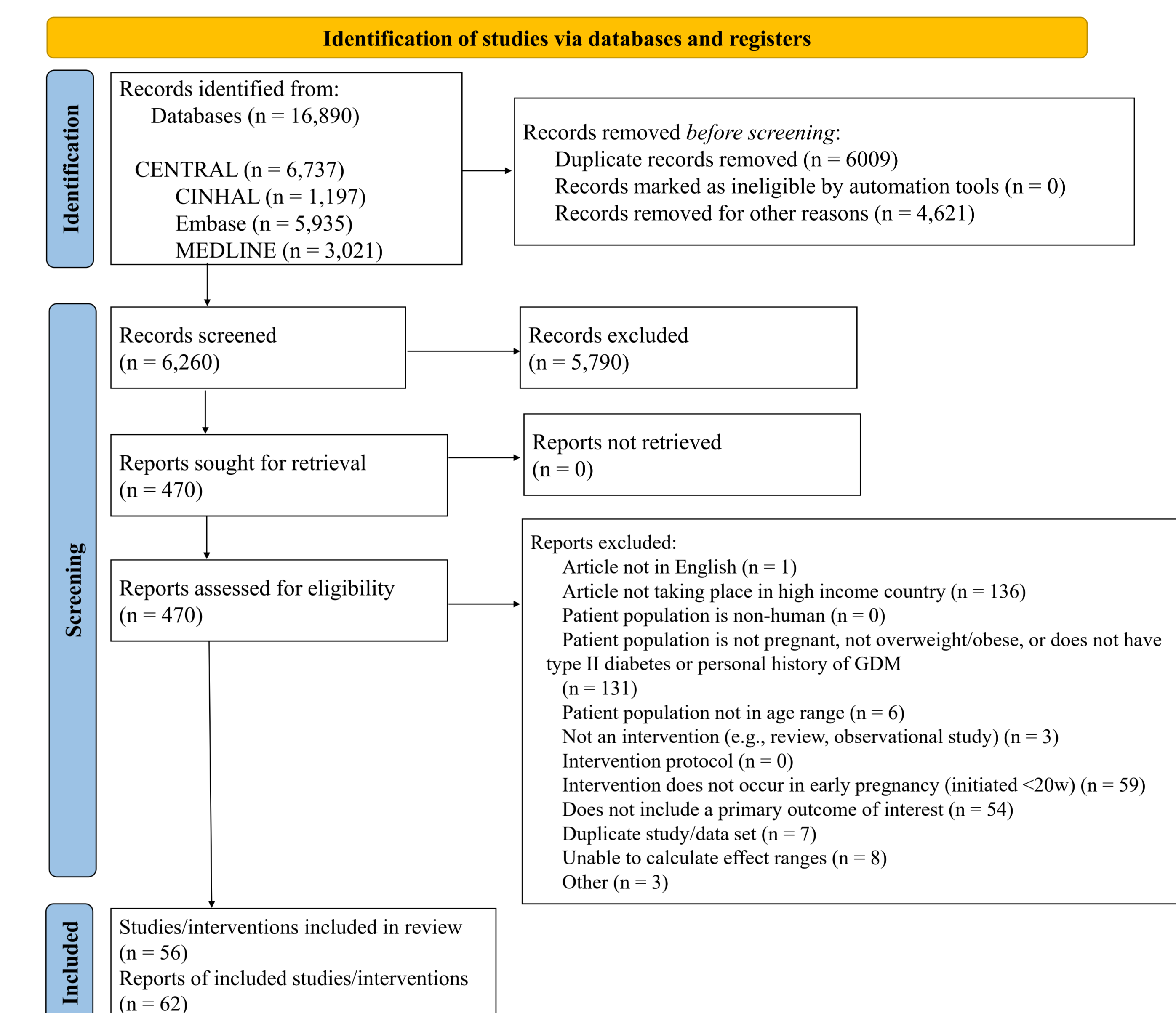
After study selection, four authors independently extracted data from 62 eligible studies. Quality control occurred during weekly meetings.

RESULTS

Table 1. Description of studies that reported statistically significant beneficial neonatal outcomes (LGA, SGA, neonatal adiposity (% fat mass), macrosomia (birth weight >4,000g)) that were identified in a systematic review of interventions initiated in early pregnancy (<20 weeks gestation) to promote healthy fetal growth conducted in June 2023 (n=8).

Author & year	Study design	Sample	Country	Intervention description	Intervention duration	Outcomes	Study quality
Diet only (n=2)							
Facchinetti, 2019	RCT	Overweight/obese (n=156)	Italy	A customized low glycemic index diet detailed by an RD (1800 kcal/day) and a one-hour counseling session encouraging a more active lifestyle (30 minutes walking 4 times/week)	9-12 weeks through 36 weeks gestation	LGA, n, %: intervention: 2, 2.5%, control: 9, 12%, p=0.020 Macrosomia, n, %: intervention: 0, 0%, control: 6, 8%, p=0.009	Fair
Menichini, 2020	RCT	Overweight/obese (n=82)	Italy	Caloric restriction that consisted of a low glycemic index, low saturated fat diet with a total intake of 1700 kcal/day	9-12 weeks gestation through delivery	LGA, n % intervention / control; p-value: 3, 8.3% / 12, 26.1%; p = 0.04	Fair
Diet and Exercise (n=1)							
Bruno, 2017	RCT	Overweight/obese (n=191)	Italy	An RD-prescribed a personalized dietary intervention of a hypocaloric, low-glycemic, low-saturated fat diet and physical activity tracking measured with a pedometer with follow-up by the RD every 4 weeks until 36 weeks.	9-12 weeks through 36 weeks gestation	LGA, intervention vs control, n (%): 1 (1.4%) vs 7 (11.3%); p=0.019	Good
Exercise Only (n=1)							
Ruiz, 2013	RCT	Overweight/obese (n=275)	Spain	Structured, supervised, light- to moderate-intensity 50- to 55-minute exercise intervention program 3 days a week	Gestational week 9 to weeks 38-39	Macrosomia (> 4000 g), overweight/obese subanalysis: Adjusted OR (95% CI): 0.141 (0.030-0.658); p = 0.01	Good
Lifestyle Counseling (n=2)							
Asbjornsdottir, 2019	Clinical Trial	Type II Diabetes (n=189)	Denmark	One-to-one sessions with a lifestyle coach (midwives) at each pregnancy visit, every 2 weeks. An individual action plan for improving dietary behavior was made during the first session and evaluated and tailored in subsequent sessions.	From first pregnancy visit to delivery	LGA (GROW curves), intervention vs control. n (%): 14 (14%) vs 24 (27%); p=0.04	Good
Dodd, 2014	RCT	Overweight/obese (n=2202)	Australia	Comprehensive dietary and lifestyle intervention delivered in-person or via telephone by an RD and trained research assistants that included a combination of dietary, exercise, and behavioral strategies like self-monitoring.	From randomization at <20 weeks to delivery	Birthweight above 4000g, Adjusted treatment effect (95% CI): 0.82 (0.68-0.99); p=0.04	Fair
Supplements (n=1)							
Callaway, 2019	RCT	Overweight/obese (n=411)	Australia	SPRING (Study of PRobiotics IN Gestation) administered probiotics (mixture of Lactobacillus rhamnosus (LGG) and Bifidobacterium animalis subspecies lactis (BB-12) at a dose of .1 3 109 colony forming units each per day) vs placebo (microcrystalline cellulose and dextrose anhydrate capsule) to be taken once daily from enrollment until birth	From enrollment until delivery	SGA (<10th percentile), Adjusted OR (95% CI): 0.33 (0.12-0.96); p=0.042	Good
Mixed (n=1)							
Haby, 2018	Clinical Trial	Overweight/obese (n=1,309)	Sweden	Counseling on food and physical activity delivered by midwives, RD-led group education, aqua aerobics, physiotherapist and midwife prescriptions for physical activity, pedometers for activity tracking	From first pregnancy visit to delivery	Macrosomia, intervention vs control, n (%): 22 (5.0%) vs 77 (8.8%); p=0.017	Good

Scan the QR code for a searchable database of all included study details and results

https://airtable.com/appQMKS1jmiJShkn7/shrPR1U9cidRRk4e4/tblBuhAiGEciZefcE/viwLyqytMqS3segPT?blocks=hide

RESULTS

Identification of studies via databases and registers

Identification
Records identified from:
Databases (n = 16,890)
CENTRAL (n = 6,737)
CINHAL (n = 1,197)
Embase (n = 5,935)
MEDLINE (n = 3,021)

Records removed before screening:
Duplicate records removed (n = 6009)
Records marked as ineligible by automation tools (n = 0)
Records removed for other reasons (n = 4,621)

Screening
Records screened (n = 6,260)

Records excluded (n = 5,790)

Reports sought for retrieval (n = 470)

Reports not retrieved (n = 0)

Reports assessed for eligibility (n = 470)

Reports excluded:
Article not in English (n = 1)
Article will take place in high income country (n = 136)
Patient population is non-human (n = 0)
Patient population is not pregnant, not overweight/obese, or does not have type II diabetes or personal history of GDM (n = 131)
Patient population not in age range (n = 6)
Not an intervention (e.g., review, observational study) (n = 3)
Intervention protocol (n = 0)
Intervention does not occur in early pregnancy (initiated <20w) (n = 59)
Does not include a primary outcome of interest (n = 54)
Duplicate study/data set (n = 7)
Unable to calculate effect ranges (n = 8)
Other (n = 3)

Included
Studies/interventions included in review (n = 56)
Reports of included studies/interventions (n = 62)

CONCLUSION

Trials that report promising results include lifestyle interventions that emphasize goal-setting and self-efficacy to improve diet and increase physical activity through individual and group sessions;[1] lifestyle coaching that included behavioral techniques designed to empower participants by fostering autonomy in a supportive environment;[2–4] group exercise classes three times per week;[5] and personalized dietary recommendations.[6]

Except for the GLOW study,[7] most studies reported 0 to <3% of participants identified as Asian, a racial group that has the highest rates of GDM in the US.[8]

Our findings provide healthcare providers with a comprehensive review of early pregnancy (<20 weeks) interventions that may improve maternal and neonatal outcomes among pregnant individuals with risk factors for hyperglycemia.

References & Acknowledgements
1. Trak-Fellermeier, M. A. et al. Diabetes, Metabolic Syndrome and Obesity 12, 225–238 (2019).
2. Asbjornsdottir, B. et al. BMJ Open Diabetes Res Care 7, e000733- (2019).
3. van Poppel, M. N. M. et al. Diabetologia 62, 915–925 (2019).
4. Gallagher, D. et al. Obesity 26, (2018).
5. Barakat, R. et al. Am J Obstet Gynecol 214, 649.e1–8 (2016).
6. Bruno, R. et al. Matern Child Nutr 13, 7 (2017).
7. Ferrara, A. et al. Lancet Diabetes Endocrinol 8, 490–500 (2020).
8. Gregory, E. C. W. & Ely, D. M. National Vital Statistics Reports 71, (2022).