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Review Article

Optimizing the diagnosis of gestational diabetes mellitus: Clinical pathways and obstetric complications

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Summary

The review critically synthesizes existing evidence on optimizing gestational diabetes mellitus (GDM) diagnostic procedures, focusing on best practices for early detection of at-risk mothers to address related obstetric complications. The review adopts the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines for systematic literature reviews and dissemination of study findings. The methodological framework follows three stages: planning, conducting the review, and reporting outcomes. The International Association of Diabetes and Pregnancy Study Group (IADPSG) screening criteria were more inclusive than those of other protocols, but no significant differences in maternal outcomes were reported between the protocols. One-step (75-g OGTT) performed relatively accurately compared with two-step screening (50-g GCT plus 75-g OGTT), even though no significant differences were reported, and the two-step screening was the more preferred diagnostic approach among participants. We found no statistically significant difference between early and routine Oral Glucose Tolerance Tests (OGTTs) in pregnancy outcomes. The review findings highlight the significant role of optimized diagnostic approaches in early detection of GDM to minimize the effects on pregnancy and related obstetric outcomes, as well as to reduce the incidence of diabetes mellitus later in life.

Key words: glucose challenge test, glucose tolerance test, hyperglycemia, insulin sensitivity, neonatal hypoglycemia

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Introduction

Gestational diabetes mellitus (GDM) is a common pregnancy complication characterized by glucose intolerance with onset or first recognition during pregnancy (Boyadzhieva et al. 2012; Moon and Jang 2022). Pregnancy-related hormonal and metabolic adaptations can reduce insulin sensitivity and contribute to pancreatic β-cell dysfunction, leading to hyperglycemia in susceptible women

(Mittal et al. 2025). Recent estimates suggest that GDM affects up to 14% of births worldwide and is associated with important maternal and neonatal complications, including preeclampsia, primary cesarean delivery, preterm birth, macrosomia, shoulder dystocia, and neonatal hypoglycemia (Kirovakov et al. 2025).

Despite its clinical relevance, screening and diagnostic pathways for GDM remain heterogeneous across guidelines and settings. The International Association of Diabetes and Pregnancy Study Group (IADPSG) thresholds are widely used and have been reported to increase the number of women classified with GDM, prompting ongoing debates about clinical utility and resource implications (Juan et al. 2022). In routine practice, diagnosis is commonly made using either a one-step 75-g oral glucose tolerance test (OGTT) after at least 8 hours of fasting, or a two-step approach consisting of a non-fasting 50-g glucose challenge test (GCT) followed by OGTT when the screen is positive (Frankel et al. 2024; Liu et al. 2025). Variation in diagnostic thresholds and the number of abnormal values required for diagnosis further contributes to differences in sensitivity and specificity (Moon et Jang 2022; Tehrani et al. 2023).

Beyond laboratory thresholds, optimizing diagnosis also requires attention to population-specific risk profiles, integration into antenatal care pathways, and downstream obstetric and longer-term metabolic outcomes. Placental hormones and pregnancy-associated proteins have been implicated in altered insulin sensitivity, underscoring the need for approaches that account for both clinical context and metabolic physiology (Kirovakov et al. 2025). Randomized evidence has compared screening strategies and criteria, with some studies reporting increased detection without consistent improvements in short-term perinatal outcomes (Davis et al. 2021; Hillier et al. 2021). Therefore, this review aims to synthesize contemporary evidence on GDM screening and diagnostic strategies, with a focus on clinical pathways for early identification of at-risk pregnancies and the implications for obstetric outcomes and complications.

Methodology

The present review focuses on a critical synthesis of the latest existing evidence on GDM-related diagnostic approaches. It focuses on clinical pathways and obstetric complications and adopts the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines for systematic literature reviews, as well as the Arksey and O'Malley approach to summarizing and disseminating study findings. The sequential methodological framework follows three stages: planning, conducting the review, and reporting outcomes. The detailed methodological framework is outlined in the subsequent sub-sections.

Search strategy and study selection

A comprehensive search was conducted across electronic databases, including PubMed, Embase, Scopus, Web of Science, MEDLINE/PubMed, PsycINFO, and the Cochrane Library, from their inception to June 2025. The search strategy included keywords and Medical Subject Headings (MeSH) terms, including Gestational Diabetes Mellitus (GDM), Glucose Intolerance, oral glucose tolerance test (OGTT), glucose challenge test (GCT), Maternal Health, and Fasting Blood Glucose. To broaden the search strategy and further refine the applicable

studies, all retrieved studies and other relevant reviews were manually filtered from their reference lists. The studies were selected based on strict inclusion and exclusion criteria that guaranteed methodological rigor and relevance.

Screening and selection criteria

Eligibility criteria were defined a priori across six domains: population, study design, diagnostic focus, outcomes, publication characteristics, and setting.

Inclusion criteria:

- pregnant women screened for or diagnosed with GDM, including both high-risk and general-population cohorts;
- study designs: randomized clinical trials, prospective or retrospective cohort studies, case-control studies, cross-sectional studies, and relevant clinical guidelines;
- diagnostic focus on GDM screening or diagnostic criteria/protocols and related clinical pathways;
- reported maternal outcomes (e.g., preeclampsia, gestational hypertension, cesarean section, preterm birth) and/or neonatal outcomes (e.g., macrosomia, hypoglycemia, neonatal intensive care admission, perinatal mortality);
- peer-reviewed publications in English;
- any geographic setting, with attention to evidence applicable to Bulgaria and Europe.

Exclusion criteria:

- studies not focused on GDM screening/diagnosis in pregnancy or not reporting relevant outcomes;
- case reports, editorials, and conference abstracts without full-text data;
- review articles (except when used to screen reference lists for potentially eligible primary studies).

Study selection was performed independently by two reviewers. Disagreements were resolved through discussion, with adjudication by a third clinical examiner when needed.

Data extraction, quality assessment, and reporting

Data were extracted using a standardized form to ensure consistency across studies. Extracted variables included study characteristics, participant population, diagnostic approach/clinical pathway, and reported outcomes.

Study quality and risk of bias were assessed independently by two reviewers using design-appropriate criteria. These criteria addressed selection and ascertainment, measurement of exposures and outcomes, control of confounding, and completeness of follow-up (and, for trials, randomization and allocation procedures). Any discrepancies were resolved by consensus, with third-reviewer adjudication when required.

Extracted evidence was synthesized narratively and summarized in Table 1.

Table 1. Selected articles and extracted data for the clinical pathways, pregnancy outcomes, and obstetric complications.

Author/Year	Research Design	Participants	GDM Diagnostic Approach/Clinical Pathways	Pregnancy Outcomes/ Obstetric Complications
Boyadzhieva et al. 2012	A prospective cohort study.	800 women at high risk for GDM in Bulgaria	IADPSG, American Diabetes Association (ADA), Australasian Diabetes in Pregnancy Society, Canadian Diabetes Association, European Association for the Study of Diabetes, New Zealand Society for the Study of Diabetes, WHO.	IADPSG criteria were the most inclusive, with the highest GDM prevalence. Only ADA and IADPSG criteria identified macrosomia and CS rate.
Davis et al. 2021	Single-site, blinded, randomized, comparative trial.	921 participants at high risk for GDM.	IADPSG, Carpenter-Coustan.	IADPSG screening criteria were more inclusive as compared with Carpenter-Coustan without a reduction in LGA birth weight or maternal or neonatal morbidity incidences.
Frankel et al. 2024	A population-based retrospective cohort study.	8,675 women who underwent GCT and were diagnosed with GDM	Glucose Challenge Test (GCT): a 100-g GTT following a previously conducted GCT test and a GCT result of ≥ 200 mg/dL for GDM diagnosed participants.	GCT results are strong predictors of GDM.
Hillier et al. 2021	A pragmatic, randomized trial.	Randomized 23,792 pregnant women	One-step screening (Glucose Tolerance Test) and Two-Step Screening (Glucose Challenge Test)	No significant between-group differences in the risks of the primary outcomes relating to perinatal and maternal complications between GTT and GCT.
Juan et al. 2022	A Systematic Review and Meta-Analysis.	61932 individuals (21978 women with GDM and 39954 controls)	IADPSG.	IADPSG provides an accurate prediction for the development of T2GDM and pre-diabetes in pregnant women.
Kirovakov et al. 2025	A Systematic Review	Women with GDM	Effect of Maternal Microbiota on GDM	Significant differences in gut microbiota for women with GDM as compared to healthy controls.
Khalifeh et al. 2018	A randomized controlled trial	284 pregnant women.	One-step (75-g OGTT) and two-step screening (50-g GCT plus 75-g OGTT).	There were no significant differences in incidence between the one-step and two-step approaches.
Liu et al. 2025	A non-randomized trial.	2265 pregnant women.	One-step (75-g OGTT) and two-step screening (50-g GCT plus 75-g OGTT).	One-step (75-g OGTT) performed relatively accurately compared with two-step screening (50-g GCT plus 75-g OGTT), even though no significant differences were reported.
Moon and Jang 2022	A systematic review.	Pregnant women at risk of GDM.	One-step (75-g OGTT) and two-step screening (50-g GCT plus 75-g OGTT).	One-step (75-g OGTT) has more than doubled the incidence of GDM.
Parsaei et al. 2024	A prospective cohort study.	1,565 pregnant women	Early pregnancy data, including maternal demographic and clinical characteristics	Elevated early-pregnancy fasting blood glucose and a history of preeclampsia are independent indicators of GDM.
Raets et al. 2021b	A prospective cohort study	1804 women	A glucose challenge test (GCT) and a 75 g oral glucose tolerance test (OGTT)	Two-step screening (50-g GCT plus 75-g OGTT) was the preferred diagnostic approach among participants.
Tehrani et al. 2022	A Cluster Randomized Noninferiority Field Trial	Pregnant women diagnosed with GDM	Two phases of GDM screening based on 5 different prespecified protocols	IADPSG screening criteria were more inclusive than those of other protocols, but no significant differences in maternal outcomes were reported across the protocols.
Tehrani et al. 2023	A randomized community trial.	28,771 pregnant women.	One-step screening approach [75-g 2-h oral glucose tolerance test (OGTT)] and Two-step method (the 50-g glucose challenge test followed by the 100-g OGTT).	The one-step (75-g OGTT) has more than doubled the incidence of GDM, but no statistically significant differences in maternal and neonatal outcomes have been reported.
Ye Y et al. 2021	A Retrospective Cohort Study	42406 women	Early Versus Routine Oral Glucose Tolerance Test (OGTT).	No statistically significant difference between early and routine Oral Glucose Tolerance Test (OGTT) in pregnancy outcomes.

Findings

The initial search strategy and study selection criteria yielded 239 articles from PubMed, Web of Science, Embase, PsycINFO, and the Cochrane Library. After removal of duplicates (n = 123), 116 articles were included based on initial title and abstract screening. After the removal of irrelevant studies (n = 56),

60 articles were reviewed in full-text. Another 47 articles were excluded based on the exclusion criteria, and 13 studies were included in the systematic review and fulfilled all inclusion criteria (PRISMA flowchart shown in Fig. 1).

Discussion

Key findings from this review indicate substantial heterogeneity in GDM diagnostic approaches across settings, with the International Association of Diabetes and Pregnancy Study Group (IADPSG) thresholds consistently identifying the greatest number of cases and reporting higher GDM prevalence compared with other protocols (Boyadzhieva et al. 2012; Davis et al. 2021; Juan et al. 2022; Tehrani et al. 2022). However, increased detection has not been consistently accompanied by improvements in short-term maternal or neonatal outcomes in comparative studies (Khalifeh et al. 2018; Davis et al. 2021; Hillier et al. 2021).

Across included studies, both one-step (75-g OGTT) and two-step (50-g GCT followed by OGTT) pathways remain clinically relevant. One-step testing generally increases case detection, whereas two-step strategies may reduce the number of diagnostic OGTTs performed and may be preferred by some patients and health systems (Raets et al. 2021b; Moon et Jang 2022; Brady et al. 2022; Liu et al. 2025). When meaningful differences do not align with differences in detection rates for obstetric outcomes, selection of a diagnostic strategy should explicitly balance sensitivity, feasibility, and the potential for overtreatment (Hillier et al. 2021; Tehrani et al. 2022).

The review further highlights related clinical pathways, history-based indicators, and preferred diagnostic approaches for GDM. According to the findings, two-step screening (50-g GCT plus 75-g OGTT) was the preferred diagnostic

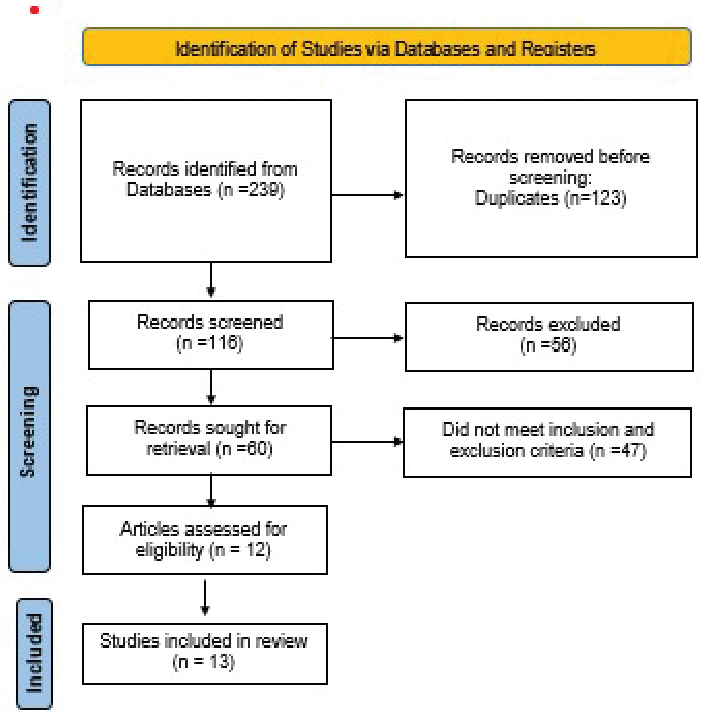

Figure 1. PRISMA flow diagram for the selection of articles included in this review.

approach among participants, especially those with improved metabolic profiles, whereas those with adverse metabolic profiles preferred one-step screening with OGTT (Raets et al. 2021b). These findings aligned with the recommended Flemish modified two-step screening method, which proposes a one-step screening strategy for high-risk GDM women and a two-step method for those at low risk (Raets et al. 2021b; Minschart et al. 2021). Furthermore, there is no statistically significant difference between early and routine OGTT in pregnancy outcomes, but it is highly recommended that pregnant women should constantly undergo screening for GDM for early interventions to prevent adverse pregnancy outcomes (Raets et al. 2021a; Sahu et al. 2021; Ye et al. 2022; Simmons et al. 2023; Ali 2025).

Clinical implications of these findings support a pragmatic, risk-informed approach. Early risk assessment based on clinical history and early pregnancy measures (including fasting glucose and history of preeclampsia) may help prioritize earlier testing and closer surveillance in higher-risk women (Parsaei et al. 2024). At the same time, routine mid-pregnancy screening remains important for women without early risk indicators, as early versus routine screening has not shown consistent differences in pregnancy outcomes (Ye et al. 2021). Standardization of protocols within healthcare systems may improve diagnostic consistency, referral pathways, and counseling, regardless of whether a one-step or two-step method is used.

Emerging evidence suggests that adjunct pathways such as maternal gut microbiota profiles may be associated with GDM, but current data are largely observational and do not yet support changes to diagnostic algorithms (Kirovakov et al. 2025). A key limitation across the literature is the scarcity of long-term follow-up assessing maternal cardiometabolic outcomes and offspring metabolic health, as well as comparative cost-effectiveness and patient-centered outcomes. Future studies should prioritize harmonized outcome reporting, longer follow-up, and implementation research evaluating how diagnostic strategy interacts with treatment intensity and health-system capacity.

Conclusion

Gestational diabetes mellitus (GDM) reflects pregnancy-related metabolic adaptations and is associated with significant maternal and neonatal morbidity. Across the included evidence, IADPSG thresholds and one-step testing increase detection, but higher detection has not been consistently associated with improved short-term pregnancy outcomes. Therefore, optimizing a diagnosis requires balancing sensitivity with clinical utility, feasibility, and integration into antenatal care pathways.

Future research should prioritize long-term maternal and offspring outcomes following different diagnostic thresholds and treatment pathways, as well as comparative cost-effectiveness and equity in diverse health systems. Prospective studies evaluating adjunct risk markers (early pregnancy clinical features, biomarkers, and microbiome signatures) and implementation-focused research on standardized care pathways are also needed to determine which diagnostic approaches deliver the greatest clinical benefit with the least unnecessary intervention.

Additional information

Conflict of interest

The authors have declared that no competing interests exist.

Ethical statements

The authors declared that no clinical trials were used in the present study.

The authors declared that no experiments on humans or human tissues were performed for the present study.

The authors declared that no informed consent was obtained from the humans, donors or donors' representatives participating in the study.

The authors declared that no experiments on animals were performed for the present study.

The authors declared that no commercially available immortalised human and animal cell lines were used in the present study.

Use of AI

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Author contributions

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Data availability

All of the data that support the findings of this study are available in the main text.

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