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Association between gestational diabetes mellitus diagnostic criteria and adverse pregnancy outcomes—a systematic review and meta-analysis of adjusted effect sizes from studies using current diagnostic criteria

Elhassan Mahmoud , Abdalla Moustafa Elsayed, Basant Elsayed, Yasmin Elsalakawi, Aswathy Gopinath, Tawanda Chivese

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Qatar University College of Medicine, Doha, Ad Dawhah, Qatar

Correspondence to
Tawanda Chivese;
tchivese@qu.edu.qa

ABSTRACT

Objectives To quantify the association between Gestational Diabetes Mellitus (GDM) and adverse pregnancy outcomes and primarily compare the associations between diagnostic criteria following the International Association of Diabetes and Pregnancy Study Groups (IADPSG) recommendations and non-IADPSG criteria, which use higher blood glucose cut-offs.

Design Systematic review and meta-analysis of observational studies using contemporary GDM diagnostic criteria.

Data sources PubMed, Scopus, Google Scholar, Cochrane Database of Systematic Reviews and the Cumulative Index to Nursing and Allied Health Literature (CINAHL) were searched for articles published between 2010 and 2023. The search was carried out on 15 May 2023.

Eligibility criteria Studies were included if they were observational studies that reported adjusted effect sizes for GDM-related adverse outcomes and compared outcomes between women with and without GDM, used contemporary diagnostic criteria and were conducted after 2010.

Data extraction and synthesis Two reviewers independently extracted data and assessed study quality using the MethodologicAl STandards for Epidemiological Research (MASTER) scale. Bias-adjusted inverse variance heterogeneity meta-analysis models were used to synthesise adjusted effect sizes. The same meta-analytic models were used to synthesise the overall OR and their 95% CIs for comparisons of the criteria which followed the IADPSG recommendations to other criteria, mostly with higher blood glucose cut-offs (non-IADPSG).

Results We included 30 studies involving 642 355 participants. GDM was associated with higher odds of maternal outcomes, namely; caesarean section (adjusted OR (aOR) 1.24, 95% CI 1.01 to 1.51) and pregnancy-induced hypertension (aOR 1.55, 95% CI 1.03 to 2.34). GDM was associated with higher odds of neonatal outcomes, specifically; macrosomia (aOR 1.38, 95% CI 1.13 to 1.69), large for gestational age (aOR 1.42, 95% CI 1.23 to 1.63), preterm birth (aOR 1.41, 95% CI 1.21 to 1.64), neonatal intensive care unit admission (aOR 1.42, 95% CI 1.12 to 1.78), neonatal hypoglycaemia (aOR 3.08, 95% CI 1.80 to 5.26) and jaundice (aOR 1.47, 95% CI 1.12 to 1.91). Further analyses showed no major differences in adverse pregnancy outcomes between IADPSG and non-IADPSG criteria.

Conclusions GDM is consistently associated with adverse pregnancy, maternal and foetal outcomes, regardless of the diagnostic criteria used. These findings suggest no significant difference in risk between lower and higher blood glucose cut-offs used in GDM diagnosis.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ Utilised contemporary studies with modern Gestational Diabetes Mellitus (GDM) diagnosis criteria, relevant to current debate on screening and diagnosis of GDM.
⇒ Included only adjusted effect sizes, minimising the influence of confounding on the relationship between GDM and outcomes.
⇒ Limitations include the use of data from observational studies, where confounding factors could not be fully eliminated.
⇒ Had a limited number of studies using non-International Association of Diabetes and Pregnancy Study Group criteria, potentially affecting the conclusiveness of the analysis.

INTRODUCTION

Gestational diabetes mellitus (GDM) is defined as any degree of glucose intolerance with onset or first recognition during pregnancy and it affects 14% of pregnancies globally.[1 2] After delivery, most women diagnosed with GDM revert to normal glycemic status, however, both the mother and their offspring are at a higher risk of developing type 2 diabetes and cardiovascular disease later

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in life.[3 4] The hyperglycaemia and pregnancy outcomes (HAPO) study showed that there was a linear increase in the risk of adverse pregnancy outcomes with increasing blood glucose, but there are no known cut-offs at which the risk of these outcomes becomes significantly elevated, unlike diabetes outside of pregnancy.[5 6] Although many guideline bodies have adopted the International Association of Diabetes and Pregnancy Study Groups (IADPSG) recommendations, debate is still ongoing about the appropriate GDM screening strategies, blood glucose cut-offs and timing of GDM testing.[7–9] Given the variation of the diagnostic criteria for GDM and screening approaches internationally, the prevalence of GDM varies widely.[10] It is still not clear how the heterogeneity in screening approaches and diagnostic criteria affects the association between GDM and adverse pregnancy outcomes.

There is now abundant evidence that GDM not only causes adverse pregnancy outcomes and future type 2 diabetes and cardiovascular disease, but also has impact on a woman's mental health and is associated with higher costs to the health system.[3 4 11–14] The landmark HAPO study findings showed that milder levels of hyperglycaemia can adversely affect pregnancy outcomes.[5] These findings resulted in changes and revisions to many international GDM diagnosis guidelines, based on the recommendations of the IADPSG published in 2010.[6] The WHO in 2013,[15] the American Diabetes Association (ADA),[16] the Australasian Diabetes in Pregnancy Society (ADIPS)[17] and the Society for Endocrinology, Metabolism and Diabetes of South Africa (SEMDSA)[18] are examples of guideline bodies which adapted their GDM diagnostic guidelines to align with the IADPSG recommendations. The IADPSG recommends universal screening for GDM of all pregnant women without pre-existing diabetes, between 24 and 28 weeks of gestation using a one-step 2 hour 75 g oral glucose tolerance test (OGTT) and to diagnose GDM if a woman has one abnormal test result based on the following cut-offs: fasting plasma glucose (FPG)≥5.1 mmol/L, 1 hour OGTT plasma glucose≥10.0 mmol/L or 2 hour OGTT plasma glucose≥8.5 mmol/L.[6]

Despite the consensus on the adverse effects of hyperglycaemia on pregnancy outcomes, there is still a lack of agreement on GDM screening, testing and diagnosis, evidenced by the existence of more than 30 different GDM dianostic guidelines in use in many regions and countries worldwide.[19] The differences in these criteria are not only in diagnostic maternal blood glucose levels, but also in the screening approaches, glucose testing methods and timing of GDM screening. Some of the heterogeneity also stems from differences in resource allocation for GDM care, while others arise from uncertainty in the evidence about the appropriate GDM screening and testing approaches. Some notable guideline bodies that have not adopted the IADPSG recommendations are the National Institute for Health and Care Excellence (NICE) which recommends risk factor-based GDM screening and has maintained a higher fasting glucose of ≥5.6 mmol/L for GDM diagnosis.[20] Another example is the Diabetes in Pregnancy Study Group India (DIPSI) which recommends testing in a non-fasting state and diagnosis of GDM only if the 2 hour plasma glucose is ≥7.8 mmol/L.[21] The heterogeneity in GDM screening and diagnostic criteria is likely one reason why there is variability in the observed effect magnitudes of the association between GDM and adverse pregnancy outcomes.

Findings on the estimates of the effect of GDM on adverse pregnancy outcomes are still not conclusive. A recent meta-analysis[22] evaluated the association between GDM and adverse pregnancy outcomes. However, this meta-analysis included studies based on older diagnostic criteria that are no longer in practice, potentially encompassing cohorts which include overt diabetes and pre-existing diabetes. This limitation may have led to overestimation of the impact of GDM by including undiagnosed pre-existing diabetes in the analysis. Further, some meta-analyses used unadjusted odds ratios (ORs), thereby reported associations that could be confounded.[23] To address these limitations, the current meta-analysis investigated the effect of GDM, diagnosed using contemporary criteria, on adverse pregnancy outcomes, and compared the effect sizes between criteria that conformed to the IADPSG recommendations and non-IADPSG criteria that generally used higher blood glucose cut-offs. By restricting our analysis to studies that report adjusted effect sizes, we aim to minimise the influence of confounders and provide a more accurate estimate of the true association between GDM and adverse pregnancy outcomes under current diagnostic practices.

RESEARCH QUESTIONS

What is the effect of GDM, diagnosed using contemporary criteria, on each adverse pregnancy outcome? Does the effect of GDM on adverse pregnancy outcomes differ between different GDM diagnostic criteria?

METHODS

Study design

A systematic review and meta-analysis of relevant studies was conducted. The study protocol is registered on the International Prospective Register of Systematic Reviews (PROSPERO) (CRD42020155061) and it follows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses protocol extension (PRISMA-P).[24]

Search strategy for identification of studies

Data sources and electronic searches

PubMed, Scopus, Google Scholar, Cochrane Central Register of Controlled Trials (CENTRAL), the Cumulative Index to Nursing and Allied Health Literature (CINAHL) were searched for articles published between 2010 and 2023. The search was carried out on 15 May 2023. Medical subject headings (MeSH words) and keyword searches for GDM and pregnancy outcomes were used in the search. Supplementary Tables 1-3

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contains the search strategy. Further, the reference lists of included papers were also searched. EndNote was used to remove duplicate, and studies were screened for inclusion using the Rayyan systematic review management website (www.rayyan.ai). Two reviewers (EM, AE) independently screened the studies for inclusion within Rayyan. Following the initial screening, four reviewers (EM, AE, BE, YE) evaluated the papers for inclusion using full text, according to the specified inclusion criteria.

Studies inclusion criteria

Inclusion criteria

Studies were included if they were observational cohort, cross-sectional and case–control comparing adverse pregnancy outcomes between women with and those without GDM. The studies were included if they were conducted between 2010, when the IADPSG recommendations were published, to the year 2023 and if they reported adjusted ORs for the association between GDM and adverse pregnancy outcomes. Experimental studies were included only if they compared GDM diagnostic criteria as intervention and comparators.

Exclusion criteria

Studies were excluded if they were conducted prior to 2010, review articles, included animal studies, did not report an effect size or any outcomes related to this study, did not report adjusted effect sizes or included participants with pre-existing diabetes.

Outcomes of interest

Maternal outcomes

Maternal outcomes included caesarean section, pregnancy-induced hypertension (PIH) and pre-eclampsia. Caesarean sections included both elective and emergency. PIH was defined as a systolic blood pressure≥140 mm Hg or diastolic blood pressure≥90 mm Hg diagnosed at ≥20 weeks gestation. Pre-eclampsia was defined as hypertension (≥140/90 mm Hg) and proteinuria.

Foetal outcomes

Foetal outcomes included large-for-gestational-age (LGA), small-for-gestational-age (SGA), macrosomia, preterm birth, shoulder dystocia, neonatal hypoglycaemia, neonatal intensive care unit admission (NICU), jaundice and respiratory distress syndrome (RDS). Macrosomia was defined as birth weight greater than 4000 g. LGA was defined as birth weight above the 90th percentile for gestational age. SGA was defined as birth weight of less than 10th percentile for gestational age. Preterm birth was defined as birth before 37 completed weeks of gestation.

Data extraction and management

For duplicate publications, we only included the article that contains the most information, and all others were excluded. The following data were extracted from the articles: study characteristics such as the publication year, duration of the study, region, country, study design, sample size, GDM diagnostic criteria used, numbers of participants with the outcomes of interest and the effect size with their corresponding CIs. Data were extracted into a predesigned and piloted Microsoft Office Excel spreadsheet. For each study, two reviewers independently extracted the data and compared thereafter. Disparity in data extracted was resolved via discussion between all the reviewers.

Assessment of risk of bias

The risk of bias and external validity of the included studies was assessed using the MethodologicAl STandards for Epidemiological Research (MASTER) scale.[25] Two reviewers independently assessed each study, and differences were resolved by discussion. If no consensus was reached, a third reviewer was consulted to resolve the conflict.

Data synthesis

Study characteristics and other data were narratively described and were presented as tables. Because the included studies were observational, of varying quality, a bias-adjusted inverse variance heterogeneity (quality effects) model was used as to synthesise overall effect sizes for the meta-analysis, with quality weights derived from the MASTER scale. Estimates from the random-effects model were also computed for comparison purposes, since this is the most widely used model in literature. The I^2 statistic and the Cochrane's Q p-values were both used to assess the heterogeneity. Doi plots and funnel plots were used for the assessment of publication bias. To explore the association between GDM diagnostic criteria and the odds of adverse outcomes, further analyses were carried out by comparing IADPSG to non-IADPSG. Non-IADPSG criteria in this study were Carpenter-Coustan (CC) (two studies[26 27]), 2008 Canadian Diabetes Association (CDA) (one study[28]), ADA 2014 (one study[29]), WHO 1999 (one study[30]) and the ADIPS (one study[31]). The studies using CC criteria employed universal OGTT screening. The cut-offs used in these studies varied. For CC and ADA 2014 criteria, fasting glucose≥5.3 mmol/L, 1-hour≥10.0 mmol/L and 2-hour≥8.6 mmol/L were used (n=7612). The WHO 1999 cut-offs included fasting glucose≥7.0 mmol/L or 2 hour glucose≥7.8 mmol/L (n=42 656). The 2008 CDA criteria used fasting glucose≥5.3 mmol/L, 1-hour≥10.6 mmol/L and 2-hour≥8.9 mmol/L (n=2 70 843). The ADIPS cut-offs used included fasting glucose≥5.5 mmol/L and 2-hour≥8.0 mmol/L (n=32 013). For analysis purposes, the non-IADPSG criteria were grouped together, since they used a higher FPG and are therefore expected to result in stronger associations with adverse pregnancy outcomes. The analysis was carried out using Stata V.17 software.

Patient and public involvement

No patients or members of the public were involved in this study.

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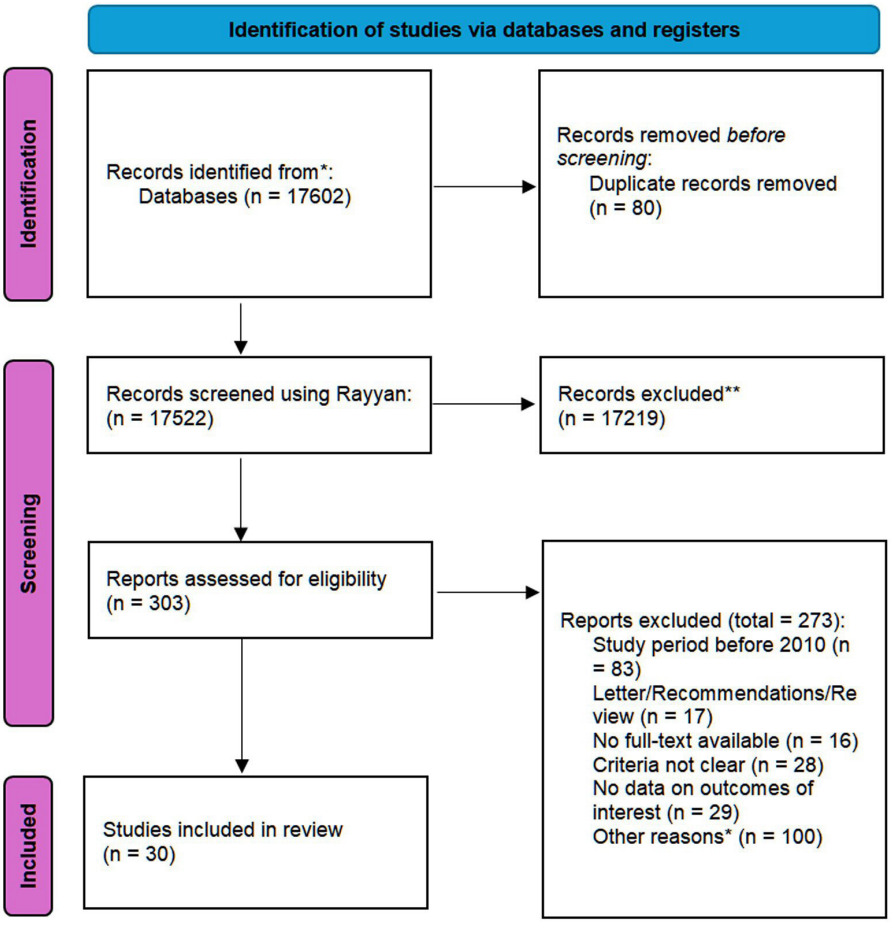

Figure 1 PRISMA flow chart showing the search. *Other reasons—did not exclude pre-existing diabetes, did not report relevant effect sizes (adjusted OR/RR). PRISMA, Preferred Reporting Items for Systematic reviews and Meta-Analyses.

RESULTS

Search results

A total of 17 513 records were identified. There were 80 duplicate records that were removed. Figure 1 shows the PRISMA flow chart for the search process. Out of 305 study records selected at the initial title and abstract screening, 273 were excluded as they did not meet the inclusion criteria. The reasons for the exclusions were as follows: studies conducted before 2010 (n=83), letters/recommendations/reviews (n=17), studies where full texts were not available (n=16), studies where the criteria used were not clear (n=28), studies with no outcomes of interest (n=29) and studies excluded for other reasons (n=100). The list of excluded studies and reasons for exclusion are in online supplemental table 4. A total of 30 studies[26–55] with 642 355 participants were finally included.

Characteristics of included studies

Table 1 shows the characteristics of the included studies. Of the 30 included studies, most (n=17) were from Asia,[26 27 29 37–39 41–44 47 48 51–55] four were from Europe,[30 34 36 49] three were from the Middle East,[32 33 50] two were from Australia,[31 40] two were from Africa,[45 46] one was from South America[35] and one was from North America[28] (table 1). The studies were from these countries: Australia,[31 40] Brazil,[35] Croatia,[30 36] India,[48] Iran,[26] Saudi Arabia,[32 50] Qatar,[33] Italy,[34 49] Canada,[28] Vietnam,[29 38 53] South Korea,[27] China[37 41–44 47 51 52 54 55] and Ethiopia.[45 46] All the studies employed either cross-sectional or cohort designs. Four of these studies contained two independent populations that were analysed separately in the meta-analysis. In table 1, these populations are labelled as 'Author, Year A' for the first population and 'Author, Year B' for the second population. While the total number of studies is 30, the inclusion of these separate populations increased the total number of assessed populations in the meta-analysis to 34. The years of data collection were from 2010 to 2023. All studies have employed universal screening.

Quality of included studies

Overall, most of the studies had relatively high scores in the quality assessment using the MASTER scale[56] (online supplemental figure 1). Four studies[33–35 55] scored 28/36, four studies[29 38 40 48] had a score of 27/36 and four studies[27 42 49 52] had a score of 26/36. The scores of the remaining studies ranged from 22/36 to 25/36. The main deficiencies were in equal retention, equal ascertainment, equal prognosis and sufficient analysis domains (online supplemental figure 1).

Maternal outcomes

Table 2 shows the results of the overall syntheses for the association between GDM and adverse pregnancy outcomes.

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Table 1 Characteristics of included studies

Study	Study duration	Country	Sample size	Region	Study design	Criteria	Screening
Alfadhli *et al*, 2015[32]	2011–2014	Saudi Arabia	954	Middle East	Cohort	IADPSG	Universal
Bashir *et al*, 2020[33]	2015–2016	Qatar	2221	Middle East	Cohort	IADPSG	Universal
Capula *et al*, 2013[34]	2010–2012	Italy	2448	Europe	Cohort	IADPSG	Universal
Carvalho *et al*, 2023[35]	2020–2020	Brazil	1618	South America	Cross-sectional	IADPSG	Universal
Darbandi *et al*, 2022[26]	2018–2018	Iran	3675	Asia	Cross-sectional	Non-IADPSG (CC)	Universal
Djelmis *et al*, 2016[36]	2012–2014	Croatia	4646	Europe	Cohort	IADPSG	Universal
Erjavec *et al*, 2016[30]	2010–2010	Croatia	42 656	Europe	Cross-sectional	Non-IADPSG (WHO-1999)	Universal
Erjavec *et al*, 2016[30]	2014–2014	Croatia	39 092	Europe	Cross-sectional	IADPSG	Universal
He *et al*, 2023[37]	2012–2021	China	115 097	Asia	Cohort	IADPSG	Universal
Hiersch *et al*, 2019[28]	2012–2016	Canada	266 942	North America	Cohort	Non-IADPSG (CDA)	Universal
Hiersch *et al*, 2019[28]	2012–2016	Canada	3901	North America	Cohort	Non-IADPSG (CDA)	Universal
Hirst *et al*, 2012[38]	2010–2011	Vietnam	2772	Asia	Cohort	IADPSG	Universal
Kawasaki *et al*, 2023[39]	2015–2019	Japan	1807	Asia	Cohort	IADPSG	Universal
Kim *et al*, 2019[27]	2014–2016	Korea	1907	Asia	Cohort	Non-IADPSG (CC)	Universal
Kim *et al*, 2019[27]	2014–2016	Korea	1969	Asia	Cohort	IADPSG	Universal
Laafira *et al*, 2016[40]	2011–2014	Australia	3105	Australia	Cohort	IADPSG	Universal
Li *et al*, 2014[41]	2011–2011	China	54 275	Asia	Cross-sectional	IADPSG	Universal
Lin *et al*, 2022[42]	2012–2020	China	2151	Asia	Cohort	IADPSG	Universal
Mak *et al*, 2019[43]	2015–2015	China	1901	Asia	Cohort	IADPSG	Universal
Mei *et al*, 2021[44]	2016–2018	China	333	Asia	Cohort	IADPSG	Universal
Muche *et al*, 2020[45]	2018–2019	Ethiopia	694	Africa	Cohort	IADPSG	Universal
Muche *et al*, 2020[46]	2018–2019	Ethiopia	684	Africa	Cohort	IADPSG	Universal
Nguyen *et al*, 2020[29]	2015–2016	Vietnam	2030	Asia	Cohort	Non-IADPSG (ADA-2014)	Universal
Pan *et al*, 2015[47]	2010–2012	China	17 808	Asia	Cohort	IADPSG	Universal
Punnose *et al*, 2022[48]	2011–2017	India	2638	Asia	Cohort	IADPSG	Universal
Ronco *et al*, 2023[49]	2010–2020	Italy	2364	Europe	Cohort	IADPSG	Universal
Wahabi *et al*, 2017[50]	2013–2015	Saudi Arabia	9723	Middle East	Cohort	IADPSG	Universal
Wan *et al*, 2019A[31]	2010–2013	Australia	3419	Australia	Cohort	Non-IADPSG (ADIPS)	Universal
Wan *et al*, 2019B[31]	2010–2013	Australia	28 594	Australia	Cohort	Non-IADPSG (ADIPS)	Universal
Wang *et al*, 2021[52]	2012–2013	China	8844	Asia	Cohort	IADPSG	Universal
Wang *et al*, 2023[51]	2018–2020	China	2031	Asia	Cohort	IADPSG	Universal
Yang *et al*, 2018[55]	2011–2015	China	1232	Asia	Cohort	IADPSG	Universal
Yue *et al*, 2022[53]	2016–2018	Vietnam	4703	Asia	Cohort	IADPSG	Universal
Zou *et al*, 2022[54]	2016–2018	China	4121	Asia	Cohort	IADPSG	Universal

ADA, American Diabetes Association; ADIPS, Australasian Diabetes in Pregnancy Society; CC, Carpenter-Coustan; CDA, Canadian Diabetes Association; IADPSG, International Association of Diabetes and Pregnancy Study Groups.

A total of 18 studies[26–28 30–33 35 36 40 42 43 45 48–50 52 53] reported data on total C-sections, with adjusted ORs (aORs) between 0.8[31 42] and 2.3.[36] The overall aOR of total C-section was 1.24 (95% CI 1.01 to 1.51) with high heterogeneity (I^2=85.9%) (online supplemental figure 2). GDM was associated with a 25% increase in the odds of pre-eclampsia, in overall synthesis (aOR 1.25, 95% CI 1.00 to 1.56, I^2=31.8%, n=8 studies[27 28 31 33–35 38 49]) (online

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Table 2 Results of overall syntheses for the association between GDM and each adverse pregnancy outcome

Outcome	Overall aOR (95% CI)	I^2 (%)	LFK*	Number of studies
Maternal outcomes				
Total C section	1.24 (1.01, 1.51)	85.9	1.7	18
Pre-eclampsia	1.25 (1.00, 1.56)	31.8	1.6	8
PIH	1.55 (1.03, 2.34)	69.4	−2.8	7
Birth size-related neonatal outcomes				
Macrosomia	1.38 (1.13, 1.69)	75.0	4.2	19
LGA	1.42 (1.23, 1.63)	60.1	2.8	19
SGA	0.91 (0.80, 1.04)	40.1	0.8	14
Shoulder dystocia	1.20 (0.86, 1.66)	0.0	−1.0	4
Other neonatal outcomes				
Preterm birth	1.41 (1.21, 1.64)	62.3	0.0	17
NICU admission	1.42 (1.12, 1.78)	78.7	0.0	14
Neonatal hypoglycaemia	3.08 (1.80, 5.26)	86.3	1.1	7
Jaundice	1.47 (1.12, 1.91)	65.0	−5.0	6
RDS	1.22 (1.01, 1.47)	40.1	2.7	6

*The LFK is a measure of symmetry of publication bias plots and reflects major asymmetry when its absolute value is greater than 2 (or −2).
aOR, adjsuted OR; GDM, Gestational Diabetes Mellitus; LGA, large-for-gestational-age; NICU, neonatal intensive care unit admission; PIH, pregnancy-induced hypertension; SGA, small-for-gestational-age.

supplemental figure 3). Finally, in overall synthesis of seven studies,[27 28 31 33–35 38 45 47–49] GDM showed an estimated 55% increase in the odds of PIH (aOR 1.55, 95% CI 1.03 to 2.34, I^2=69.4%; online supplemental figure 4). The analyses suggested minor evidence of publication bias for all maternal outcomes, except for PIH which showed major evidence (online supplemental figures 5–7). In further analyses, compared with the IADPSG, non-IADPSG criteria showed similar odds of pre-eclampsia, PIH and total C-section (table 3).

Birth size-related neonatal outcomes

Data from 19 studies were included in the analysis of macrosomia.[26 27 29 31–33 36 37 40 41 43 46–48 50 52–55] The overall aOR for macrosomia was 1.38 (95% CI 1.13 to 1.69) with moderate heterogeneity (I^2=75.0%) (online supplemental figure 8). Overall, GDM was associated with 1.42-fold higher odds of LGA (aOR 1.42, 95% CI 1.23 to 1.63, I^2=60.1%, n=19[27 29 31 33–38 42–44 46–49 52–54]) (online supplemental figure 9). However, the synthesis suggested no significant associations between GDM and the odds of SGA (aOR 0.91, 95% CI 0.80 to 1.04, I^2=40.1%, n=14;[27 31 33 34 38 39 42–44 46 49 52–54]online supplemental figure 10) or shoulder dystocia (aOR 1.20, 95% CI 0.86 to 1.66, I^2=0.0%, n=4;[27 31 32 50] online supplemental figure 11). The analyses suggested evidence of publication bias for macrosomia and LGA, minor evidence for shoulder dystocia and no evidence of publication bias for SGA (online supplemental figures 12–15). In further analyses, compared with the non-IADPSG, the IADPSG criteria showed similar odds of macrosomia, LGA and SGA (table 3).

Other neonatal outcomes

In an analysis of 17 studies,[26–28 31–34 38 39 43 46–48 50–53] GDM was associated with increased odds of preterm birth (online supplemental figure 16), with an overall aOR of 1.41 (95% CI 1.21 to 1.64) and moderate heterogeneity (I^2=62.3%). For NICU admission, data from 14 studies[27 28 31–35 38 39 42 43 48 50 53] showed that GDM was associated with a 1.42-fold increased odds (aOR 1.42, 95% CI 1.12 to 1.78) with high heterogeneity (I^2=78.7%) (online supplemental figure 17). The overall aOR for neonatal hypoglycaemia was 3.08 (95% CI 1.80 to 5.26, I^2=86.3%, n=7[27 28 31–33 38 42]) (online supplemental figure 18). GDM was associated with 1.47-fold higher odds of neonatal jaundice (aOR 1.47, 95% CI 1.12 to 1.91, I^2=65.0%, n=6;[27 28 31–34] online supplemental figure 19). Moreover, GDM was associated with a 1.22-fold increased odds of neonatal RDS (aOR 1.22, 95% CI 1.01 to 1.47, I^2=40.1%, n=6;[28 31–34 42] online supplemental figure 20). The analyses suggested evidence of publication bias for jaundice and RDS, minor evidence for neonatal hypoglycaemia and no evidence of publication bias for preterm birth and NICU admission (online supplemental figures 21–25). Analyses by diagnostic criteria showed that, compared with non-IADPSG, IADPSG criteria showed similar odds of jaundice, RDS, neonatal hypoglycaemia, preterm birth and NICU admission (table 3).

DISCUSSION

In this meta-analysis of 30 studies, we found strong associations between GDM diagnosed using contemporary

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Table 3 Results of analyses by criteria for the association between GDM and each adverse pregnancy outcome

Outcome	Criteria	Overall aOR (95% CI)	P for interaction
Maternal outcomes			
Total C-section	IADPSG	1.34 (1.12, 1.60)	0.398
	Non-IADPSG	1.20 (1.02, 1.43)	
Pre-eclampsia	IADPSG	1.08 (0.60, 1.94)	0.565
	Non-IADPSG	1.29 (1.11, 1.49)	
PIH	IADPSG	1.34 (0.82, 2.16)	0.636
	Non-IADPSG	1.57 (0.98, 2.54)	
Birth size-related neonatal outcomes			
Macrosomia	IADPSG	1.42 (1.24, 1.63)	0.577
	Non-IADPSG	1.04 (0.34, 3.13)	
LGA	IADPSG	1.41 (1.20, 1.66)	0.759
	Non-IADPSG	1.48 (1.14, 1.94)	
SGA	IADPSG	0.94 (0.80, 1.10)	0.298
	Non-IADPSG	0.81 (0.65, 1.01)	
Shoulder dystocia	IADPSG	1.36 (0.63, 2.95)	0.761
	Non-IADPSG	1.16 (0.60, 2.26)	
Other neonatal outcomes			
Preterm birth	IADPSG	1.44 (1.21, 1.71)	0.797
	Non-IADPSG	1.39 (1.15, 1.86)	
NICU admission	IADPSG	1.32 (1.11, 1.58)	0.723
	Non-IADPSG	1.41 (1.04, 1.92)	
Neonatal hypoglycaemia	IADPSG	3.09 (1.52, 6.29)	0.956
	Non-IADPSG	3.01 (1.64, 5.51)	
Jaundice	IADPSG	1.54 (1.24, 1.92)	0.816
	Non-IADPSG	1.46 (0.96, 2.22)	
RDS	IADPSG	1.32 (1.01, 1.74)	0.574
	Non-IADPSG	1.19 (0.92, 1.54)	

aOR, adjusted OR; GDM, Gestational Diabetes Mellitus; LGA, large-for-gestational-age; NICU, neonatal intensive care unit admission; PIH, pregnancy-induced hypertension; RDS, respiratory distress syndrome; SGA, small-for-gestational-age.

criteria and adverse pregnancy outcomes. The highest associations were observed for neonatal hypoglycaemia, PIH, jaundice, NICU admission, macrosomia, LGA and preterm birth. We found no major differences in the effect of GDM between IADPSG-based criteria and criteria that used higher glucose cut-offs.

We found no major differences between IADPSG and non-IADPSG criteria on the effect of GDM on adverse pregnancy, maternal and foetal outcomes. When comparing IADPSG to stricter GDM criteria, this meta-analysis showed that no outcome differed by criteria. Our findings are similar to those of older meta-analyses which have also found that the risk of adverse pregnancy outcomes was not largely different across the different diagnostic criteria.[23 57–59] A key difference between our synthesis and the older previously publishes studies is that we included contemporary studies, with adjusted effect magnitudes, that were conducted after 2010 when the IADPSG recommendations were published. Our findings and those of previously published studies raise the question about the benefits of using lower glucose cut-offs for the diagnosis GDM. It has been argued that the use of criteria with lower fasting glucose cut-offs combined with universal screening, like the IADPSG, leads to an increase in GDM prevalence, without a concurrent increase in benefit (ie, reduced pregnancy outcomes and postpartum type 2 diabetes).[10]

Our findings have several implications. For healthcare systems, adopting the IADSPG criteria, that is, universal screening and lower glycaemic thresholds compared with targeted screening and generally higher glycaemic diagnostic thresholds, may strain resources, as more women would require screening, monitoring and interventions. This could lead to an increase in healthcare costs,[60 61] which will lead to an increased burden, especially in settings where resources are already constrained. On the other hand, selective or targeted screening may result in some proportions of women progressing with

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undiagnosed hyperglycaemia in pregnancy, and the consequent higher risk of adverse pregnancy outcomes. The NICE, for example, has opted to keep their guidelines which use risk factor-based screening and higher glycaemic thresholds. It is crucial to balance the costs and benefits of adopting either the IADPSG recommendations or selective screening, higher glycaemic threshold approaches such as that used by the NICE. These considerations may be different for different health systems, depending on affordability and healthcare system capacity. For clinicians, these findings highlight the need for careful consideration when diagnosing and managing GDM, as they should be mindful of the potential for overdiagnosis and overtreatment, and they should tailor management strategies based on each patient's individual risk factors, ensuring that interventions are justified and beneficial. For women, the increased likelihood of a GDM diagnosis that comes with universal screening and lower glycaemic thresholds may result in increased anxiety and an increased likelihood of medical interventions, without a clear improvement of outcomes. GDM diagnosis has been associated with a higher occurrence of mental health problems in pregnant women.[62 63] It is therefore critical to provide women with clear and balanced information along with the implications, and to promote shared decision-making. More research is needed to identify appropriate blood glucose cut-offs where the benefit of GDM diagnosis outweighs the unintended negative consequences.

GDM was associated with around a 25% increase in the odds of pre-eclampsia and total C-section and 56% increase in the odds of PIH. A previous meta-analysis showed a 50% increase in pre-eclampsia and a 40% increase in C-sections in women with than in those without gestational diabetes mellitus.[22] The HAPO study found that the occurrence of pre-eclampsia was positively associated with blood glucose level even after adjusting for clinical centre, age, Body Mass Index, height, smoking status, alcohol consumption, family history of diabetes, gestational age at OGTT and urinary tract infection.[13 64] GDM causes increase in the insulin secretion by the foetal pancreas which itself is an anabolic hormone and leads to increase in the foetal weight. Fetuses with high birth size are usually delivered by caesarean sections as vaginal deliveries carry high risks to both mothers and babies.[65] The pathophysiology of pre-eclampsia is not well understood, and the association observed in these studies may be bidirectional. Irrespective of direction of association, the findings of this meta-analysis confirm the need to screen and monitor women with GDM for pre-eclampsia and PIH. Notably, pre-eclampsia and PIH are all associated with higher rates of both emergency and elective C-sections, and therefore may partly explain the higher risk of C-section in women with GDM.

The current meta-analysis showed that GDM was associated with higher the odds of neonatal hypoglycaemia, LGA, macrosomia, preterm birth, jaundice, NICU admission, RDS and shoulder dystocia. The higher odds of birth-size-related complications, LGA, macrosomia and shoulder dystocia, are likely because of maternal hyperglycaemia, which leads to a high glucose intrauterine environment which promotes foetal hyperglycaemia and hyperinsulinemia, which in turn induce excess fat deposition in the fetus.[66 67] Notably, the highest OR was observed for neonatal hypoglycaemia, with threefold higher odds for GDM exposed neonates compared with the non-GDM exposed neonates. However, it is important to consider that this risk could be exaggerated due to the possibility of allocation bias for this outcome. Neonates born to mothers with GDM are more likely to be routinely tested for blood glucose levels shortly after birth due to the known risks of hypoglycaemia, whereas neonates of non-GDM pregnancies do not typically undergo such testing unless clinically indicated. This difference in clinical practice likely increases the detection rate of hypoglycaemia in the GDM group, which could lead to an overestimation of the association between GDM and neonatal hypoglycaemia. Previous meta-analyses have generally found that GDM was associated with adverse pregnancy outcomes.[21 22] However, our findings differ from those of many of these previous meta-analyses in that our aORs, although still suggesting a higher risk of adverse pregnancy outcomes with GDM, are generally lower than those reported by the other meta-analyses.[23] This discrepancy is mostly due to the other meta-analyses having used unadjusted effect sizes. GDM is thought to cause RDS by interfering with the production of surfactant lipids and proteins.[68] Notably, some previous meta-analyses have reported contrasting findings in terms of the associations observed. Ye *et al*, using a meta-analysis of unadjusted ORs and studies with criteria that are no longer in use, found no association between shoulder dystocia and GDM was not significant.[22] Tehrani *et al* used a meta-analysis of unadjusted ORs and reported a 20% decrease in the odds SGA, contrary to our finding.[23]

A strength of this study is the use of contemporary studies using contemporary GDM diagnosis criteria, therefore contributing to the current debate about the appropriate screening tests and testing strategy for GDM. We only included adjusted effect sizes, thus minimising the effect of confounding on the relationship between GDM and the outcomes, which is the main limitation of existing meta-analyses. However, this study has some limitations. Since this study uses data from observational studies, the role of confounding cannot be fully eliminated. Our findings require confirmation by experimental randomised controlled trials which compare these criteria. Additionally, most of the included studies were conducted in Asia (54%), and relatively fewer studies from the other regions. This may limit the generalisability of our findings to non-Asian populations. Finally, the small number of studies using non-IADPSG criteria, most of which employed cut-offs relatively close to those recommended by IADPSG, limits the strength of the comparison between IADPSG and non-IADPSG criteria, as the non-IADPSG group may

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not fully represent the diversity of diagnostic approaches in use.

Conclusion

GDM showed consistent associations with pregnancy, maternal and foetal outcomes, with no major differences in the effects when different contemporary criteria were used.

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ORCID iD

Elhassan Mahmoud http://orcid.org/0000-0001-8528-0272

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