New IADPSG recommendations: impact on care for gestational diabetes

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Practice Points

- The International Association of Diabetes and Pregnancy Study Group (IADPSG) consensus panel recommendations for gestational diabetes mellitus (GDM) are based on the hyperglycemia-related risk of adverse maternal and fetal outcomes.
- The IADPSG consensus panel recommends universal screening for GDM with a 2-h 75 g oral glucose tolerance test at 24 gestational weeks.
- A single abnormal glucose level on fasting, 1- or 2-h oral glucose tolerance test is sufficient to diagnose GDM.
- Screening high-risk women on presentation is recommended to diagnose 'overt diabetes'.
- These recommendations ensure the early referral of pregnant women to healthcare services for the management of cases of GDM.

SUMMARY If gestational diabetes mellitus (GDM) is not recognized and treated, it has a negative impact on maternal and fetal health. No general consensus on how best to screen for and diagnose this disease has been established to date. The Hyperglycemia and Adverse Pregnancy Outcomes (HAPO) study and two randomized trials on the treatment of mild GDM have confirmed the close relationship between maternal glycemia and perinatal outcome. In the light of these findings, new recommendations have recently been formulated by the International Association of Diabetes and Pregnancy Study Groups (IADPSG), also concerning the diagnosis of overt diabetes early in pregnancy and routine screening for GDM at 24 gestational weeks with a 75 g oral glucose tolerance test, considering even only one higher than normal value sufficient for a diagnosis of GDM. Here we discuss the possible impact of these new recommendations on the treatment of GDM.

Gestational diabetes mellitus (GDM), classically defined as a "carbohydrate intolerance with onset or first recognition during pregnancy" [1], is associated with an increased risk of maternal and fetal complications [2–4]. Although the impact of GDM on maternal and fetal health has been recognized, there is no general consensus on how best to screen for and diagnose this condition, or the glucose threshold to use.

As regards the screening procedures, while the WHO and other international professional organizations (e.g., American Conllege

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of Obstetricians and Gynecologists [ACOG], Australian Diabetes in Pregnancy Society [ADIPS], Società Italiana di Diabetologia-Associazione Medici Diabetologi [SID-AMD], Society of Obstetricians and Gynaecologists of Canada [SOGC], NICE) recommend screening all or high- and medium-risk pregnant women for GDM [5–16], the US Preventive Service Task Force has recently said there are insufficient data to warrant routine screening for GDM **(Tables 1 & 2)** [17].

Moving on to consider the diagnostic procedures used to date, we find much the same picture: there is no consensus on which glycemia conditions to measure (i.e., using fasting blood sugar levels, the oral glucose tolerance test [OGTT] with 100 g of glucose and measurements after 0, 60, 120 and 180 min, or the OGTT with 75 g of glucose and measurements after 0, 60 and 120 min); nor is there any agreement on which levels to consider diagnostic of GDM **(Tables 1 & 2)**.

GDM screening & diagnosis: the Hyperglycemia & Adverse Pregnancy Outcomes study

The original guidelines for diagnosing GDM are an extension of those developed for non-gestational diabetes and aimed to identify women at risk of diabetes after pregnancy [18]; they also reflected the lack of data relating to maternal hyperglycemia with poor maternal and fetal outcomes.

In this setting, the Hyperglycemia and Adverse Pregnancy Outcomes (HAPO) study was designed to clarify the risk of adverse fetal and maternal outcomes associated with maternal glucose levels not as high as those used to diagnose diabetes during pregnancy. The results of the HAPO study, which involved a multinational cohort of about 25,000 ethnically diverse pregnant women who underwent OGTT with 75 g of glucose between weeks 24 and 28 of pregnancy, show a continuous relationship between maternal glucose levels and primary outcomes (i.e., birth weight >90th percentile, primary Cesarean section, clinically defined neonatal hypoglycemia, and cord C-peptide >90th percentile) irrespective of any other risk factors; similar associations were also found for secondary outcomes (preeclampsia–eclampsia, preterm delivery, shoulder dystocia, birth injury, hyperbilirubinemia and need for neonatal intensive care) [19]. Because the correlations were continuous and no threshold was identified beyond which the risks of poor maternal and fetal outcome tended to increase, the investigators concluded that an international consensus was needed to translate the HAPO findings into information applicable to clinical practice.

The International Association of Diabetes and Pregnancy Study Groups (IADPSG) arranged an international workshop conference on the diagnosis and classification of GDM in Pasadena (CA, USA) in 2008: about 225 experts on diabetes in pregnancy from approximately 40 different countries reviewed the results of the HAPO study to translate the results into recommendations for clinical practice. During the conference, an IADPSG consensus panel (representing ten IADPSG member groups and other organizations interested in diabetes in pregnancy) further reviewed the HAPO study results and produced a consensus statement that was published in March 2010 in *Diabetes*

Table 1. Plasma glucose levels of the oral glucose tolerance test utilized in different countries to diagnose gestational diabetes mellitus.

Organization	OGTT glucose (g)	Values for diagnosis	FPG mmol/l (mg/dl)	1 h PG mmol/l (mg/dl)	2 h PG mmol/l (mg/dl)	3 h PG mmol/l (mg/dl)
NDDG	100	2	5.8 (105)	10.6 (195)	9.2 (165)	8.1 (145)
ADA	100	2	5.3 (95)	10 (180)	8.6 (155)	7.8 (140)
ADA	75	2	5.3 (95)	10 (180)	8.6 (155)	
ADIPS	75	1	5.5 (99)		8.0 (145)	
CDA	75	2	5.3 (95)	10.6 (195)	8.9 (160)	
CNOGF	100	1	5.3 (95)	10 (180)	8.6 (155)	7.8 (140)
EASD	75	1	6.0 (108)		9.0 (162)	
JDS	75	2	5.6 (101)	10 (180)	8.3 (149)	
WHO (1999)	75	1	7.0 (126)		7.8 (140)	

ADA: American Diabetes Association; ADIPS: Australian Diabetes in Pregnancy Society; FPG: Fasting plasma glucose; OGTT: Oral glucose tolerance test; PG: Plasma glucose.

Table 2. Procedures of screening and diagnosis of gestational diabetes mellitus adopted in different countries.

Organization	Screening	Gestational weeks of screening	GCT 50 g	OGTT	Step of procedure	Ref.
ADIPS (1998)	Universal/selected	26–30 weeks	Positive: ≥7.8 mmol/l (140 mg/dl)	ADIPS	2	[5]
WHO (1999)	Universal	24–28 weeks High risk 1st trimester	–	WHO	1	[6]
ACOG (2001)	Universal/selected Low-risk women could be excluded	24–28 weeks	Positive: ≥7.2 mmol/l (130 mg/dl) ≥7.8 mmol/l (140 mg/dl)	ADA (100) NDDG	2	[7]
SOCG (2002)	Universal/selected	24–28 weeks High risk earlier	Positive: ≥7.8 mmol/l (140 mg/dl)	ADA (100)	2	[8]
Committee of JDS (2002)	Universal	24–28 weeks	FPG ≥5.5 mmol/l (99 mg/dl) 1st visit 75 g 1 h	ADA (75)	2	[9]
Austrian (2004)	Universal	24–28 weeks High risk 1st trimester	–	ADA (75) 1 value	1	[10]
Joslin Diabetes Center (2005)	Universal	24–28 weeks	Positive: ≥7.8 mmol/l (140 mg/dl)	NDDG	2	[25]
AACE (2007)	Universal	24–28 weeks High risk 20 weeks		ADA (75)	1	[11]
5th IWC on GDM (2007)	Selected None for low-risk women	24–28 weeks High risk as soon as possible	Positive: ≥7.8 mmol/l (140 mg/dl)	ADA (75/100)	2	[12]
BSEM (2008)	Universal	At first antenatal visit: FPG >6.1 mmol/l (110 mg/dl) = GDM FPG >5.6 mmol/l (100 mg/dl) = positive screen FPG >4.7 mmol/l (85 mg/dl) after 24th gestational week = screen positive	Positive: ≥7.2 mmol/l (130 mg/dl) ≥7.8 mmol/l (140 mg/dl)	WHO	2	[13]
HKCOG (2008)		24–30 weeks Earlier in presence of risk factors	Positive: ≥7.8 mmol/l (140 mg/dl) ≥7.0 mmol/l (126 mg/dl) Local women	WHO	1	[14]
USPSTF (2008)	Selected Case by case decisions	24–28 weeks	Positive: ≥7.8 mmol/l (140 mg/dl)	ADA (100)	2	[17]
NICE UK (2008)	Selected Without risk factor screening could be offered	24–28 weeks Prior GDM 16–18 weeks SMBG and OGTT at 28 weeks		WHO		[15]
ADA (2010)	Selected None if low risk	24–28 weeks High risk at initial visit	Positive: ≥7.2 mmol/l (130 mg/dl) ≥7.8 mmol/l (140 mg/dl)	ADA (75/100)	1 high risk (OGTT 75 g) 2 for all others	[16]

AACE: American Association of Clinical Endocrinologists; ACOG: American Congress of Obstetricians and Gynecologists; ADA: American Diabetes Association; ADIPS: Australian Diabetes in Pregnancy Society; BSEM: Sociedad Brasileira de Endocrinologia e Metabologia; FPG: Fasting plasma glucose; GCT: Glucose challenge test; GDM: Gestational diabetes mellitus; HKCOG: Hong Kong College of Obstetricians and Gynaecologists; IWC: International Workshop Conference; JDS: Japan Diabetes Society; NDDG: National Diabetes Data Group; OGTT: Oral glucose tolerance test; SMBG: Self-monitored blood glucose; SOCG: Society of Obstetricians and Gynaecologists of Canada; USPSTF: US Preventive Services Task Force.

Care [20]. As stated in the paper, "it is expected that this report will be considered by diabetes, obstetric and other organizations and will serve as the basis for internationally endorsed criteria for the diagnosis and classification of diabetes in pregnancy".

To translate the results of the HAPO study (which showed a continuous association between maternal glycemic levels and adverse perinatal outcomes) into diagnostic thresholds, the panel considered the mean fasting plasma glucose values, and 1- and 2-h OGTT levels for the whole

study cohort, then set thresholds that are the average glucose values at which odds ratio for birth weight, cord C-peptide and percentage of body fat higher than the 90th percentile reached 1.75 times the estimated odds of these outcomes at mean glucose values, based on fully adjusted logistic regression models. At least one of these thresholds has to be equaled or exceeded to make the diagnosis of GDM **(Table 3)**. Since 11.1% of the women in the HAPO study had one high plasma glucose measurement, 3.9% had two, and 1.1% had all three, and given that 1.7% of the cohort was unblinded, applying these criteria meant that the total incidence of GDM was 17.8% **(Figure 1)**.

Given the rising frequency of Type 2 diabetes among young women in recent years [21–23], the panel then focused on the need for an early diagnosis of women who had already had diabetes before pregnancy but their condition was first noted during pregnancy (cases defined by the panel as 'overt diabetes'). The importance of detecting overt diabetes as soon as possible emerged from a number of studies showing an increased risk of diabetic complications during pregnancy and, importantly, an increased risk of congenital anomalies [24–27]. Therefore, these pregnancies need to be treated rapidly in order to ensure near-normal glycemia levels without delay and they necessitate close obstetric and metabolic follow-up. Assuming that this assessment would be included at the initial visit for prenatal care (the panel's recommendations are shown in **Figure 2**), the final decision was to recommend screening as soon as possible.

These new recommendations represent a real revolution in the diagnosis of GDM because they enable just one relatively simple test to be used to diagnose GDM, in other words, the OGTT with 75 g of glucose – the same test as is used outside pregnancy – avoiding the need for the two-step procedures (the glucose challenge test [GCT] and OGTT) used in most countries, and using diagnostic values that correlate with fetal outcome, not maternal outcome as before [18].

Table 3. Odds ratio for fetal outcome used to define the oral glucose tolerance test glucose cut-off in the Hyperglycemia and Adverse Pregnancy Outcomes study.

Glucose measured	OR 1.5	OR 1.75	OR 2.0
FPG mmol/l (mg/dl)	5 (90)	5.1 (92)	5.3 (95)
1 h PG mmol/l (mg/dl)	9.3 (167)	10 (180)	10.6 (191)
2 h PG mmol/l (mg/dl)	7.9 (142)	8.5 (153)	9 (162)

FPG: Fasting plasma glucose; OR: Odds ratio; PG: Plasma glucose.

Other studies have confirmed the continuum between maternal plasma glucose levels and fetal risk. In a Danish study, Jensen *et al.* found a linear relationship between pregnant women with 2-h 75 g glucose OGTT levels under 9 mmol/l and Cesarean section, shoulder dystocia and macrosomia [28]. In an Italian study on 758 women attending five diabetes centers for GDM screening at 24–28 gestational weeks, fasting plasma glucose levels after the GCT could predict fetal overgrowth, and a plasma glucose level higher than 85 mg/dl doubled the risk of delivering a large for gestational age (LGA) infant [29].

The recommendations of the consensus panel have been adopted by the American Diabetes Association (ADA) and American Association of Clinical Endocrinologists (AACE) in their own recently published recommendations [30,31].

Potential benefits of adopting the IADPSG recommendations

So what are the real benefits of following these new recommendations **(Box 1)**? First, using a single screening test will mean a reduction in the time elapsing between the screening test and the diagnosis, making it possible to diagnose GDM earlier. In turn, this will lead to an earlier treatment of the condition with a consequent reduction of the adverse maternal and fetal outcomes of real clinical importance as Cesarean section, shoulder dystocia, perinatal mortality and serious perinatal morbidity [32]. Finally, the chance to diagnose GDM on the strength of only one abnormal glucose value on OGTT will lead to the diagnosis of all cases with lower degrees of glucose tolerance. A number of clinical studies have demonstrated that such situations (previously considered less important) actually carry the same adverse maternal and fetal outcomes as in cases of GDM [33–35]. This is hardly surprising, given that this situation has been found characterized by physiopathological changes qualitatively indistinguishable from those seen in overt GDM, with similar patterns of insulin sensitivity and insulin secretion [35].

In an Italian population-based multicenter survey on 606 pregnant women with isolated gestational hyperglycemia (IGH) attending 31 Italian obstetrics or diabetes centers, macrosomia was significantly more frequent in IGH than in normal pregnant women (10.7 vs 7.4%; $p = 0.003$); stillbirth and neonatal mortality

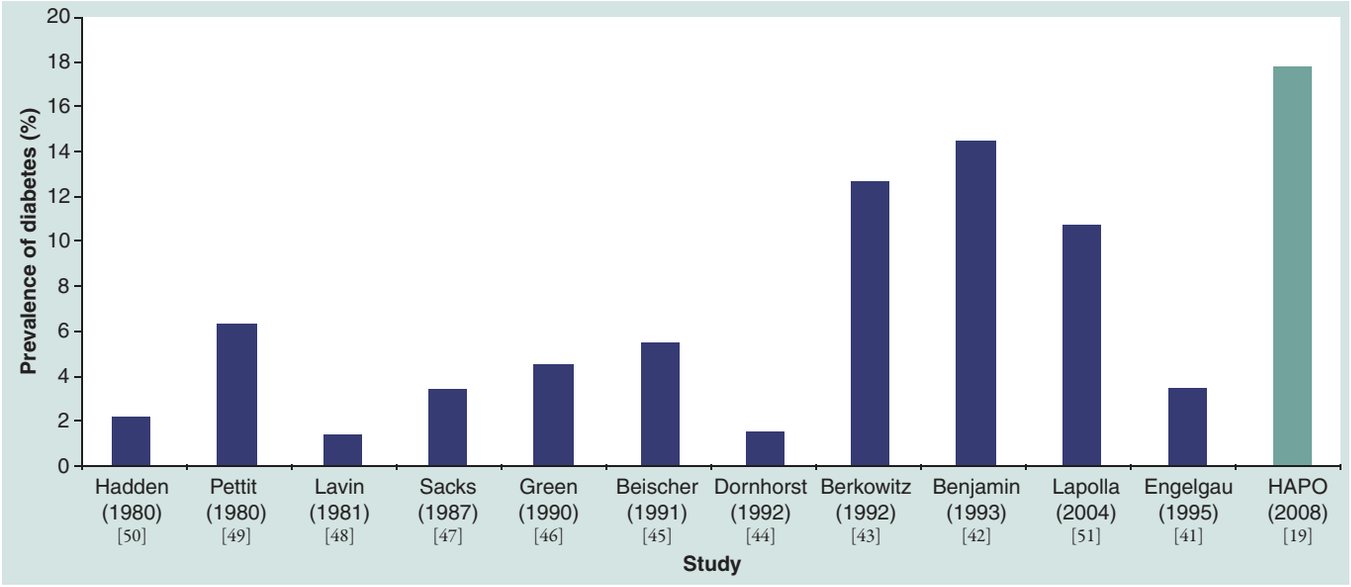

Figure 1. Prevalence of gestational diabetes mellitus in the world.

rates did not differ from those of normal pregnancies; however, the total frequency of malformations was higher among IGH babies, though not significantly so (1.48 vs 0.89%; $p < 0.11$), thus confirming the detrimental effect of even a minimally altered glucose tolerance on fetal outcome [35].

In the Australian Carbohydrate Intolerance Study in Pregnant Women (ACHOIS), the women in their 24–34th gestational weeks who did not meet the diagnostic criteria for GDM but had 75 g OGTT results between 140 and 199 mg/dl (consistent with mild hyperglycemia) were randomly assigned to usual prenatal care (control group) or dietary intervention, self-monitoring and insulin therapy as necessary (intervention group). The investigators found a significant reduction in the composite end points of perinatal death, shoulder dystocia, bone fracture and nerve palsy in the intervention group by comparison with the controls [36]. However, it should be noted that a number of deaths could not be attributed to the nontreatment of gestational diabetes, so the paper would benefit from an in-depth study into this topic. A subsequent randomized trial in the USA included women at 24–32 gestational weeks who did not meet the diagnostic threshold for GDM, but had abnormal results on 100 g OGTT, although their fasting glucose levels were below 95 mg/dl. The women were randomly assigned to usual prenatal care (control group) or dietary intervention, self-monitoring and insulin therapy as necessary (treatment group). Again, the group on intensive treatment had lower rates of macrosomia, shoulder dystocia, Cesarean delivery and hypertensive disorders than the group given conventional care [37]. However, it should be noted that the women included in these two trials were identified using a two-step testing procedure.

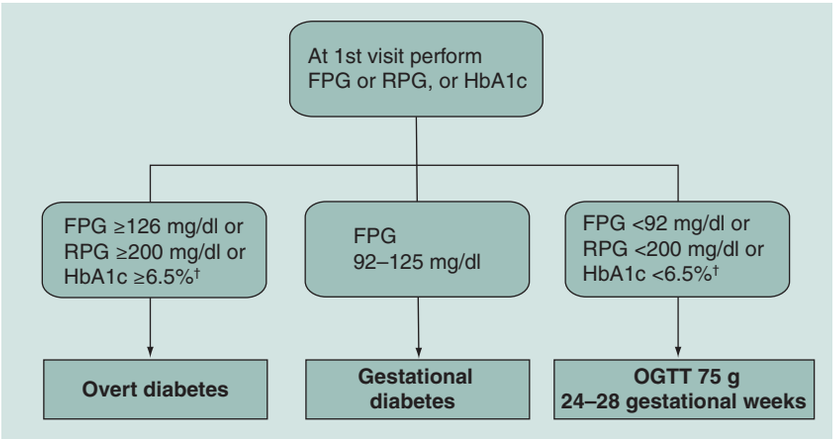

Figure 2. Procedure recommended by International Association of Diabetes and Pregnancy Study Groups for evaluation of hyperglycemia in pregnancy.
†HbA1c was standardized according to the International Federation of Clinical Chemistry (IFCC).
FPG: Fasting plasma glucose; OGTT: Oral glucose tolerance test; RPG: Random plasma glucose.

Box 1. International Association of Diabetes and Pregnancy Study Group recommendation: benefits and drawbacks.

- Benefits
  - Use of a single test (OGTT 75 g) to screen and diagnose GDM
  - Reduction in the time elapsing between the screening test and the diagnostic test
  - Reduction of the duration OGTT (2 vs 3 h, when the 3 h OGTT is adopted)
  - Reduction of glucose ingested (from 100 g to 75 g glucose, when 100 g glucose OGTT is adopted) and reduction of the frequent adverse effects of high glucose load (nausea, vomiting)
  - Earlier diagnosis of GDM and earlier treatment of the condition with a consequent reduction of adverse maternal and fetal outcomes
  - Diagnosis and treatment of all cases with lower degrees of glucose tolerance
  - Worldwide approach to GDM diagnosis
  - Possibility to compare the different country outcome if women were diagnosed with the same test
- Drawbacks
  - Increase of the number of women diagnosed as GDM
  - Increase of the costs for the follow-up programs of GDM women
  - Cost–effectiveness?
  - High workload for the health centers devoted to the care of GDM women
  - Reorganization at laboratory level of the procedures to screen and diagnose GDM

GDM: Gestational diabetes mellitus; OGTT: Oral glucose tolerance test.

The new recommendations also emphasize the importance of early screening for GDM. In 2001, the American College of Obstetricians and Gynecologists emphasized that, "the later in pregnancy the abnormality is diagnosed, the less time will be available for interventions" [7]. Schaefer-Graf reported that 20% of fetuses had macrosomia on ultrasound when GDM was diagnosed [38]. Bartha *et al.* screened 3986 women for GDM and reported that 5.9% had GDM; 28% of the latter were diagnosed early and they had a higher pregestational BMI and hypertension, and required more insulin treatment than those diagnosed with GDM later on [39]. Agarwal *et al.* reported that glucose screening in early pregnancy, using GCT instead of fasting plasma glucose, can diagnose most cases of GDM [40].

Potential drawbacks of adopting the IADPSG recommendations

The main difference arising from the application of these new recommendations is likely to be an increase in the frequency with which GDM is diagnosed **(Box 1 & Figure 1)**. As mentioned before, judging from the results of the HAPO study, the proportion of women with GDM will reach 17.8% [19,20], which is generally higher than the figures hitherto identified in many countries [41–51].

Agarwal *et al.* compared the impact of the IADPSG criteria and the old ADA criteria on GDM diagnoses in 10,283 pregnant women undergoing a 75 g OGTT in a routine GDM screening program [52]. The IADPSG and ADA criteria identified GDM in 3875 (37.7%) and 1328 (12.9%) of the women, respectively ($p < 0.005$), meaning a 2.9-fold higher rate using the IADPSG criteria.

In an Italian study, 3953 pregnancies were retrospectively analyzed and classified according to the new criteria: 1815 had a normal glucose tolerance and 2138 had GDM, and 112 (2.8%) of the latter would have been classified as normal according to the previous criteria (they were called new-GDM cases). These new-GDM women were younger and they had a lower pre-pregnancy BMI than the GDM women, as well as higher rates of Cesarean section and of ponderal indices beyond 2.85 g/cm^3 than in normal pregnancies. The new criteria for diagnosing GDM thus identified a group of GDM women classifiable as normal according to the Carpenter–Coustan criteria, but revealing metabolic characteristics and pregnancy outcomes resembling those of GDM women [53].

In a prospective, longitudinal, open study at five tertiary care centers in Austria, 1466 women underwent a 2-h 75 g OGTT at 24–28 gestational weeks and were treated if one or more values exceeded those of the Austrian recommendations; the impact of the IADPSG thresholds on maternal and fetal outcome was evaluated at the same time. A total of 49% of all

the women in the study cohort were diagnosed as having GDM according to Austrian guidelines, 46% according to the IADPSG criteria, but the IADPSG guidelines identified a higher rate of obstetrical complications (Cesarean section) and neonatal morbidity (LGA and macrosomic babies).

These preliminary data seem to support the use of the new, more stringent criteria proposed by the IADPSG because they can identify more women at risk of negative maternal outcomes as well as end points of real importance for fetal outcomes (e.g., Cesarean section, shoulder dystocia, perinatal mortality and serious perinatal morbidity) as well as surrogate measures as macrosomia, LGA and cord C-peptide [54].

Some doubts can arise by the use of HbA1c in the diagnosis of 'overt diabetes', considering ≥6.5% as a diagnostic value, as suggested for the diagnosis of diabetes outside of pregnancy [55]. However, this assay has yet to be standardized worldwide and it is also costly and has a number of methodological limits (i.e., the lower HbA1c value in pregnant women than in healthy women) [56–58].

What are the possible alternatives? Is there a validated screening test suitable for our purposes?

A Health Technology assessment report, published in 2002, concluded that selective screening, based on the risk factors, would leave approximately half the women with GDM undiagnosed [59]. A recent paper by Cosson *et al.* compared the outcome of screening all versus only selected pregnant women: GDM was diagnosed in 12.6% and 8.3% of cases, respectively [60].

Ideally, it will be useful to adopt risk factors that spare the low-risk population returning good test results in universal screening programs. The use of the GCT in screening for GDM carries a significant false negative rat [61], and the results depend on the time elapsing since the last meal [62]. Women with a positive GCT also have to return for a diagnostic test (OGTT), and this means a diagnostic delay and the loss of some women to follow-up (up to 23% of women with a positive GCT reportedly fail to undergo the OGTT [63]). A delayed diagnosis of GDM naturally means a delay in its treatment and a worse outcome [64].

A systematic review of the literature was conducted on the predictive power of the GCT (four observational studies, positive predictive value [PPV] between 0.6 and 1.3%), fasting plasma glucose (two observational studies, PPV 38–47%), glycosuria (two observational studies, PPV 12.8 and 21.1%), indicating that the diagnostic validity of these tests is limited [101].

In a randomized study, Griffin *et al.* compared screening based on risk factors with a universal approach in 4792 women: universal screening detected a prevalence of GDM of 2.7%, higher than after screening based on risk factors (1.45%). Universal screening also facilitated the early diagnosis of GDM and reduced the negative maternal and fetal outcomes of real clinical importance of Cesarean section, macrosomia, prematurity, preeclampsia and admission to the neonatal intensive care unit [65].

In a recent meta-analysis on randomized and quasi-randomized trials to assess the effects of different screening methods on maternal and fetal health in GDM, the authors concluded that, "There was insufficient evidence to determine whether screening for GDM, or what types of screening, can improve maternal and infant health outcomes" [66].

The predictive value of several different risk factors was evaluated in various studies, as shown in **Table 4**, showing here again that their predictive value is modest [67–69]. A secondary analysis at the Toronto TRI-Hospital Study demonstrated that applying a scoring system based on maternal age, BMI and race **(Table 5)** could achieve a sensitivity and specificity similar to those of universal screening, with a higher than 80% detection rate [70]. The weakness of this approach lies in that applying

Table 4. Power of different risk factors in the prediction of gestational diabetes mellitus.

Author (year)	Risk factors	OR (95% CI)	PPV (%)	Ref.
Ostlund *et al.* (2003)	Previous GDM	23.6 (11.6–48.0)	–	[69]
Scytte *et al.* (2004)	Glycosuria	9.04 (2.6–63.7)	–	[67]
Griffin *et al.* (2000)		–	50	[65]
Davey *et al.* (2001)	Family history of diabetes	7.1 (5.6–8.9)	–	[68]
Ostlund *et al.* (2003)		2.74 (1.47–5.11)	–	[69]
Griffin *et al.* (2000)	Family history 1st degree D2M	–	6.7	[65]
Griffin *et al.* (2000)	Family history 1st degree D1M	–	15	[65]
Ostlund *et al.* (2003)	Previous fetal macrosomia	5.59 (2.68–11.7)	–	[69]
Davey *et al.* (2001)	Age >25 years	1.9 (1.3–2.7)	–	[68]
Ostlund *et al.* (2003)		3.37 (1.45–7.85)	–	[69]

D1M: Type 1 diabetes mellitus; D2M: Type 2 diabetes mellitus; GDM: Gestational diabetes mellitus; OR: Odds ratio; PPV: Positive predictive value.

Table 5. Score for gestational diabetes mellitus screening taking into account clinical risk factors.

Risk factor	Score
Age (years)	
≤30	0
31–34	1
≥35	2
BMI (kg/m^2)	
≤22.0	0
22.1–25.0	2
≥25.1	3
Ethnicity	
Caucasian	0
Black	0
Asiatic	5
Others	2

Modified from [71].

the score adds to the healthcare provider's workload, meaning that it may result in a lower application rate.

Horvath *et al.* conducted a systematic review and meta-analysis of randomized controlled trials to assess the benefits and harms of treating women with GDM [71]. Five randomized studies met the inclusion criteria for specific versus usual treatment; these studies used a two-step approach (GCT or screening for risk factors, or both, followed by OGTT with 100 g or 75 g of glucose). Women treated specifically for GDM had a lower rate of shoulder dystocia (OR: 0.40, 95% CI: 0.21–0.75) and LGA infants (OR: 0.48), and one study also reported a reduction in preeclampsia (2.5 vs 5.5%; p = 0.02). In two studies, the treatment of GDM was associated with a reduction in birthweight, while it reduced the frequency of LGA babies in all five studies examined. Shoulder dystocia is another important clinical end point, which affects GDM-related pregnancies significantly more than those uncomplicated by GDM (OR: 2.74, 95% CI: 2.04–3.68) [72]. In the 13 randomized trials evaluating different treatment intensities, there was a significant reduction in shoulder dystocia among the women given more intensive treatment (OR: 0.31, 95% CI: 0.14–0.70). So treating GDM lowers the risk of certain maternal and fetal complications. Decisions regarding treatment should be made bearing in mind that the evidence of its benefits comes from trials selecting women by means of a two-step strategy.

However, a systematic review of 136 studies clearly showed that the recurrence rate of GDM falls between 30 and 84% [73]. It is also well known that Type 2 diabetes often develops after a pregnancy complicated by GDM [74], with a frequency in the range of 30 to 70% of GDM-related pregnancies [75]. These studies emphasize the importance of finding ways to identify as many women with GDM as possible in order to implement suitable prevention treatment programs, not only to reduce fetal and maternal complications, but also to prevent the future onset of diabetes.

GDM screening & diagnosis: cost–effectiveness analysis

Regarding the cost–effectiveness of screening, Round *et al.* evaluated this parameter for eight GDM screening strategies (including no screening) in terms of the individual patient's risk level, using the incremental cost per quality-adjusted life-year [76]. The results showed that the strategy with the highest cost–effectiveness depended on each woman's risk of developing GDM: for a risk <1.0% the no screening strategy is cost effective; for a risk between 1.0 and 4.2%, fasting plasma glucose followed by OGTT is the most cost effective; for a risk higher than 4.2%, universal OGTT is the most cost effective. The authors concluded that "If the individual risk of GDM in a woman can be accurately predicted, then healthcare resource allocation could be improved by providing an individual screening strategy."

The economic analysis of the ACHOIS study showed that intervention with more intensive dietary advice, blood glucose monitoring and insulin (when required) reduced serious perinatal complications and perinatal deaths. The incremental cost per additional serious perinatal complication prevented was $27,503 and per perinatal death prevented it was $60,606, while per discounted life-year gained it was $2,988 over the whole lifespan, so the incremental cost per extra life-year gained was highly favorable [77].

The NICE cost–effectiveness analysis found that two screening strategies were cost effective (i.e., selecting women according to the ADA criteria and then administering the 75 g OGTT, and selecting women by high-risk ethnicity then administering the 75 g OGTT) [102]. More recently, Meltzer *et al.*

assessed the (direct and indirect) costs of three methods for GDM screening and diagnosis, showing that the two-step methods (GCT then 75 g OGTT) cost less than 2-h OGTT alone [78]. The difference was not significant in the Asian group in their sample, however, because more women screened in this group were diagnosed as having GDM. The lower GCT value considered diagnostic in Canada (10.3 mmol/l) also makes it difficult to compare this study with others. Di Cianni *et al.* compared the costs of GDM screening and management in two different periods, reporting that universal screening is cost effective, while selective screening enabled a cost saving of only 5% per GDM diagnosis [79]. Although diagnosing and intensively treating GDM determine costs for the healthcare system, they result in a significant monetary saving due to the reduction in perinatal complications.

However, all these analyses were conducted before the HAPO results were published so it would now be useful to have an updated cost–effectiveness analysis based on the HAPO categories; such an analysis would surely provide a better basis for recommendations.

Finally, the criteria proposed by the panel were drawn from HAPO data collected at 24–28 gestational weeks, but the panel recommended using fasting glucose levels to diagnose GDM early in the pregnancy, before the related hormone changes have had an impact. The panel's claim that a single fasting plasma glucose suffices to diagnose GDM also raises concern, given that two above-normal values are generally needed to diagnose diabetes. More studies are needed to clarify this point. Another drawback can arise from basing the diagnosis on single blood glucose measurements. Generally speaking, postloading glucose measurements are known to have a coefficient of variation of 15–20% [80], but in pregnancy the coefficient of variation is less than 2% [81].

An increase in the number of GDM women could pose a problem due to the higher workload for the health centers devoted to their follow-up and, in principle, this may divert their attention from the management of women with more severe forms of diabetes in pregnancy. Issues could also arise from the higher costs deriving from the increased demand for care. However, judging from the results of recently published studies on mild GDM [32–34,36,37], many of these newly identified GDM women could be treated successfully simply with lifestyle changes. Management protocols involving other medical operators (i.e., nurses and dietitians) in the follow-up of GDM patients could prove useful. Educational programs providing structured information and proper nutritional recommendations are necessary too, in order to reduce the need for medical appointments [82,83]. Finally, in areas with a high prevalence of GDM, it may be more cost effective to provide such advice for all pregnant women.

Conclusion

Although the HAPO study and other trials [36,37] have enhanced our understanding regarding the diagnosis and management of GDM, some critical issues remain to be seen, some of which can be solved by further analyzing the HAPO data in terms of costs and benefits.

A risk assessment that also considers other risk factors responsible for adverse maternal outcomes (e.g., obesity, race and older maternal age) could be useful.

Given the rising rates of Type 2 diabetes and consequently of GDM too, there is a need for measures designed to prevent these diseases by means of an appropriate lifestyle, which means physical activity, a suitable diet and weight control.

Future perspective

Cost–effectiveness analyses to assess the economic impact of the IADPSG guidelines are needed. International studies to verify the real impact of the new criteria on the GDM rate and the outcome of women with GDM would also be useful. International studies to establish whether overt diabetes is diagnosed early enough to reduce its adverse effects on the intrauterine environment, based on the newborn's long-term outcome, should also be considered.

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