REVIEW

Type 2 diabetes after gestational diabetes: The influence of changing diagnostic criteria

Eoin Noctor, Fidelma P Dunne

Eoin Noctor, Steno Diabetes Center, DK-2820 Gentofte, Denmark

Fidelma P Dunne, Galway Diabetes Research Centre, National University of Ireland, Dublin 2, Ireland

Correspondence to: Eoin Noctor, Chief Physician, Steno Diabetes Center, Niels Steensens Vej 2-8, DK-2820 Gentofte, Denmark. eoge@steno.dk
Telephone: +45-30-755033

Abstract

A previous diagnosis of gestational diabetes (GDM) carries a lifetime risk of progression to type 2 diabetes of up to 60%. Identification of those women at higher risk of progression to diabetes allows the timely introduction of measures to delay or prevent diabetes onset. However, there is a large degree of variability in the literature with regard to the proportion of women with a history of GDM who go on to develop diabetes. Heterogeneity between cohorts with regard to diagnostic criteria used, duration of follow-up, and the characteristics of the study population limit the ability to make meaningful comparisons across studies. As the new International Association for Diabetes in Pregnancy Study Group criteria are increasingly adopted worldwide, the prevalence of GDM is set to increase by two-to three-fold. Here, we review the literature to examine the evolution of diagnostic criteria for GDM, the implications of changing criteria on the proportion of women with previous GDM progressing to diabetes, and how the use of different diagnostic criteria may influence the development of appropriate follow-up strategies.

Key words: Gestational diabetes; Pregnancy; Type 2 diabetes; Impaired glucose tolerance; Diagnostic oral glucose tolerance test criteria

Core tip: Gestational diabetes (GDM) is associated with a greatly increased future risk of type 2 diabetes, but there are many different GDM diagnostic criteria in clinical use. Criteria with lower glucose thresholds increase GDM prevalence, and therefore the number of women requiring follow-up to detect progression to diabetes. However, lower diagnostic thresholds are also likely to decrease the proportion that progress to diabetes. Heterogeneity across studies with regard to diagnostic criteria, demographics, and duration of follow-up, limit direct comparison. As the International Association of Diabetes in Pregnancy Study Groups criteria enter widespread use, follow-up of these women will be an important issue.

Noctor E, Dunne FP. Type 2 diabetes after gestational diabetes:

INTRODUCTION

Background
Gestational diabetes (GDM) has long been recognised clinically. First described in pregnancy in 1824 in Germany[1], Joslin[2] described in 1916 a case of diabetes which presented in pregnancy, resolved with delivery, and recurred later in life. In the 1940s and 1950s, Hoet et al[3] recognised the association of this type of diabetes with adverse perinatal outcome, and characterised the relationship between glucose tolerance during pregnancy, and in the post-partum period. However, despite the long-recognised association, no standardised criteria for diagnosis were devised until 1964. In Boston City Hospital, O'Sullivan et al[4] carried out 3-h 100 g oral glucose tolerance tests on 752 patients at different stages of pregnancy. Women with 2 out of 4 values that were greater than 2 standard deviations (rounded to the nearest 5 mg/dL) above the mean glucose levels determined in this cohort were classified as having GDM. These criteria (with some modification) have continued in clinical use over the following four decades.

Evolution of diagnostic criteria for GDM
The major feature of these criteria was that they defined a cohort of women with a greatly increased future risk of progression to type 2 diabetes, demonstrating a lifetime risk of up to 60%[5]. The National Diabetes Data Group (NDDG) criteria, proposed in 1979[6] (Table 1), converted the O'Sullivan/Mahan criteria from whole blood to plasma values (see Figure 1 for timeline). The Carpenter-Coustan criteria[7], proposed in 1982, also converted the O'Sullivan/Mahan criteria to plasma values, but in addition, took a change in enzymatic methods into account. They soon entered widespread clinical use, and were subsequently validated for prediction of adverse perinatal outcome[8-12]. Essentially, therefore, all 3 sets of criteria were intended to define a similar population.

Studies directly comparing the prevalence of GDM by either NDDG or Carpenter-Coustan criteria show, however, significant differences, with an approximately 50% relative increase in GDM prevalence if the Carpenter-Coustan criteria are used[9,11-13]. In addition, in 2001, the American Diabetes Association (ADA), having previously endorsed the Carpenter-Coustan criteria, also allowed for the use of a 75 g, 2-h oral glucose tolerance test (OGTT) to make a diagnosis of GDM, using the same one- and two-hour cut-offs as the three-hour 100 g OGTT. The post-load glucose levels are estimated as being 0.9 mmol/L lower at one hour, and 0.5 mmol/L lower at two hours with the lower

glucose load[14], therefore these criteria will identify a different group of women. Indeed, only weak diagnostic agreement has been noted between the two glucose loads[15] (Cohen kappa index 0.18; although some this difference may also be attributable to day-to-day glycaemic variability).

The World Health Organisation (WHO) also recommended alternative criteria for the diagnosis of gestational diabetes beginning in 1980 (the 1965 WHO report did not comment on this issue). These thresholds were the same as those for non-pregnant adults. Initially, the WHO recommended a fasting glucose threshold of 8 mmol/L (see Table 1). These recommendations were revised again in 1985[16] (fasting glucose threshold lowered to 7.8 mmol/L, recommendation to treat impaired glucose tolerance added) and 1999[17] (fasting glucose threshold reduced to 7.0 mmol/L) (see Table 1). Although these thresholds were not chosen on the basis of predicting adverse pregnancy outcome, a subsequent large (n = 4998) prospective cohort study did show that these thresholds predicted increased risk for macrosomia (RR = 1.45, 95%CI: 1.06-1.95) and preeclampsia (1.94, 95%CI: 1.22-3.03), even when women with values diagnostic of diabetes in the nonpregnant adult[18].

The European Association for the Study of Diabetes also proposed new GDM criteria in 1996[19], using a fasting value of 6.0 mmol/L and a two-hour post 75 g glucose load value of 9.0 mmol/L, based on the distribution of glucose values on 75 g OGTTs on over 1000 European women. A subsequent retrospective cohort study supported this 2-h value in prediction of adverse perinatal outcome[20]. However, subsequent analysis of women in this cohort, with 2-h values below the 2-h threshold of 9.0 mmol/L (not treated for GDM), demonstrated a linear relationship between 2-h glucose and pregnancy outcome, with no clear threshold value[21].

In addition to these major criteria, multiple different diagnostic criteria are in use worldwide, some related to older criteria, some derived on the basis of local data. Therefore, the situation still exists where different centres in the same country, or even the same region, may employ different criteria for GDM diagnosis.

GDM criteria to predict adverse perinatal outcome
However, none of the available criteria had been designed specifically to predict adverse pregnancy outcome. To look at this issue, the International Association of Diabetes and Pregnancy Study Groups (IADPSG) convened a consensus conference in 2008 to review the Hyperglycaemia and Adverse Pregnancy Outcomes (HAPO) study findings (published and unpublished), along with other relevant studies. This consensus conference had two major outcomes[22]. Firstly, women meeting the cut-off values for diagnosis of diabetes in the non-pregnant adult (Table 1) would now fall into the new category of "overt diabetes" rather than GDM. The rationale for this was that

Table 1 Comparison of thresholds for criteria for gestational diabetes diagnosis

Criteria	Glucose load	Fasting glucose mmol/L (mg/dL)	1-h glucose mmol/L (mg/dL)	2-h glucose mmol/L (mg/dL)	3-h glucose mmol/L (mg/dL)	No. of criteria required
O'Sullivan *et al*[4]	100 g	5 (90)	9.2 (165)	8.1 (145)	6.9 (125)	≥ 2
NDDG	100 g	5.8 (105)	10.6 (190)	9.2 (165)	8.1 (145)	≥ 2
WHO 1980	75 g	8 (144)	N/A	8 (144)	N/A	≥ 1
Carpenter and Coustan	100 g	5.3 (95)	10 (180)	8.6 (155)	7.8 (140)	≥ 2
ADA	75 g or 100 g	5.3 (95)	10 (180)	8.6 (155)	7.8 (140)	≥ 2
WHO 1985	75 g	7.8 (140)	N/A	7.8 (140)	N/A	≥ 1
EASD	75 g	6 (108)	N/A	9 (162)	N/A	≥ 1
WHO 1999	75 g	7 (126)	N/A	7.8 (140)	N/A	≥ 1
IADPSG GDM	75 g	5.1 (92)	10 (180)	8.5 (153)	N/A	≥ 1
IADPSG overt diabetes	aNone/75 g	7 (126)	N/A	11.1 (200)	N/A	≥ 1

aThis diagnosis can also be made on a random glucose sample, a fasting glucose sample, or on an HbA1c value [if 6.5% (48 mmol/mol or over)]. NDDG: National Diabetes Data Group; WHO: World Health Organisation; EASD: European Association for the Study of Diabetes; ADA: American Diabetes Association; IADPSG: International Association of Diabetes and Pregnancy Study Groups; GDM: Gestational diabetes; N/A: Not applicable.
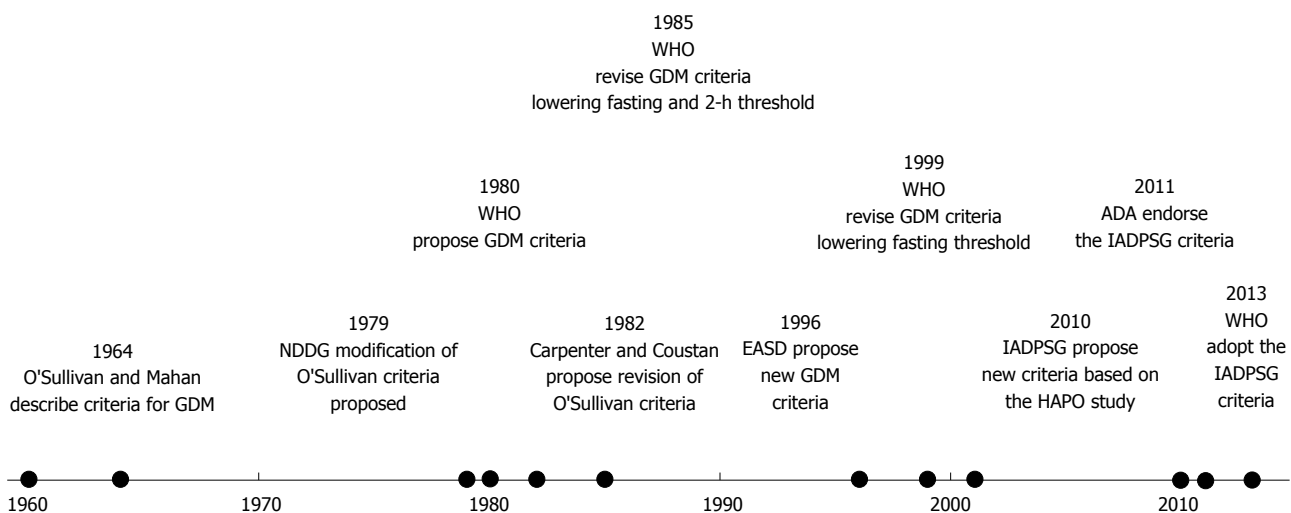

Figure 1 Timeline of evolution of criteria used to diagnose gestational diabetes from 1964-present. NDDG: National Diabetes Data Group; WHO: World Health Organisation; EASD: European Association for the Study of Diabetes; ADA: American Diabetes Association; IADPSG: International Association of Diabetes and Pregnancy Study Groups; GDM: Gestational diabetes; HAPO: Hyperglycemia and pregnancy outcomes study.

this group were felt to be distinct clinically and biochemically from women with milder degrees of hyperglycaemia. Secondly, the data from the 2008 HAPO study[23] was reviewed. This large (over 25000 participants screened), multicentre study showed that glucose levels at all time points on the 2-h 75 g OGTT were associated with adverse pregnancy outcomes (large for gestational age, macrosomia, cord c-peptide concentration greater than the 90th centile). In the absence of a clear threshold effect, and having considered various cutpoints, the IADPSG consensus committee ultimately decided to set new values for GDM diagnosis at the mean glucose values for which the odds ratio for adverse pregnancy outcome was 1.75. This lowered the fasting and 1-h values compared to previous values, while raising the 2-h value slightly. However, the major change was allowing a diagnosis to be made on just a single abnormal value, a change likely to greatly increase the prevalence of gestational diabetes. On applying these

criteria retrospectively to the HAPO cohort, 17.8% (range 9.3%-25.5%) met the criteria for diagnosis[24].

These consensus criteria were published in March 2010, and began to enter clinical use shortly afterwards. At the time of writing, in addition to the IADPSG endorsing the criteria, the ADA[25] and WHO[26] have also endorsed the criteria. However, the American College of Obstetricians and Gynaecologists (ACOG) have not adopted the new criteria, and still recommend a 100 g OGTT using the Carpenter-Coustan criteria, for diagnosis, a position endorsed by a National Institute of Health Consensus Conference in March 2013[27].

With this in mind, we will review the impact of changing criteria for GDM diagnosis with regard to the prevalence/cumulative incidence of abnormal glucose tolerance/diabetes post GDM, risk factors for progression to diabetes, and follow-up of women with previous GDM. This is a clinically relevant problem for 2 major reasons - firstly, prevention or delay of type 2 diabetes in women with previous GDM is a possibility,

as demonstrated by a subgroup analysis of the diabetes prevention program[28], and the Troglitazone In the Prevention Of Diabetes[29] and Pioglitazone In the Prevention Of Diabetes[30] studies. Secondly, undetected type 2 diabetes developing prior to a subsequent pregnancy carries the risk of congenital malformation and an increased risk of pregnancy complications.

HETEROGENEITY OF STUDIED COHORTS

Many studies have assessed the risk of progression to type 2 diabetes post gestational diabetes.

A major issue with all studies in this area however, is their marked heterogeneity. This is seen in several ways: (1) As discussed, the diagnostic criteria in clinical use for GDM diagnosis over the last four decades are numerous. This leads to the identification of cohorts who may not be directly comparable in terms of the severity of glucose intolerance; (2) Both the criteria and method used to diagnose diabetes and/or abnormal glucose tolerance in women who have previously had GDM varies significantly; (3) The ethnic mix of the cohorts is extremely heterogeneous with some composed entirely of a single ethnicity, and others showing very mixed composition; and (4) Duration of follow-up varies between studies, from 6 wk to almost 30 years[31].

In summary, meaningful comparison of the actual cumulative incidence or prevalence across studies is not possible. It is clear, however, that regardless of the criteria used, GDM signifies a high risk of future progression to type 2 diabetes.

RISK FACTORS FOR FUTURE PROGRESSION

Despite the heterogeneity of the cohorts, many studies identify similar factors predicting progression to diabetes/abnormal glucose tolerance. We will consider the most commonly associated risk factors here.

Pre-pregnancy factors

Given that most studies identify women with GDM at the time of diagnosis, most studies assess pre-pregnancy risk factors retrospectively. Therefore, information on this is limited. The exception to retrospective recall of pre-pregnancy factors is the large long-term longitudinal cohort population-based studies, such as the Nurse Health Study[32], which have detailed information preceding the index pregnancy. However, these also use self-reported GDM as an outcome measure. Although the diagnosis has been validated in a subset by medical record review, the precise criteria used by the healthcare provider are uncertain, and therefore lie outside the scope of this review. Of pre-pregnancy variables assessed, weight or BMI is the most common measure, and is commonly associated with increased risk of progression to abnormal glucose tolerance or diabetes[33-38], although the relationship is not particularly strong. Polycystic ovary syndrome has also been reported in a one retrospective study to be associated with later progression to abnormal glucose tolerance[39] on multivariable analysis, although this study used two different sets of criteria to diagnose GDM.

Index pregnancy-related factors

Pregnancy glucose values: Higher glucose values during pregnancy, as reflected by the index pregnancy OGTT, are consistently associated with increased later progression to diabetes. This is measured in various ways (number of abnormal values, area under the curve), but most commonly the values for plasma glucose at fasting, one hour, two hours (and three hours if applicable) are used. Fasting glucose shows the strongest association, being the most commonly identified risk factor associated with later abnormal glucose tolerance and diabetes[31,40-45]. Studies that have not identified fasting glucose as a factor associated with later progression to abnormal glucose tolerance tend to have either not measured it[46], not included it in the statistical models[47], or have excluded women with the highest fasting glucose levels from follow-up[48,49]. One large Australian study found fasting glucose was not associated with later abnormal glucose tolerance and diabetes despite its inclusion in the model[50]. One-hour[48,50,51] and two-hour glucose levels[37,40,51,52] are also associated with later glucose abnormalities, although less consistently, and to varying degrees. Also, higher haemoglobin (HbA1c) during pregnancy, although much less frequently studied, has been found to be associated with future risk of progression to diabetes[52,53].

More detailed characterisation of glycaemic response to a glucose load such as measures of insulin secretion[43], when undertaken, are also associated with later progression to abnormal glucose tolerance and diabetes. These measures, of course, are generally not available routinely clinically. Insulin use during pregnancy has also frequently been shown to be associated with increased risk of future progression to diabetes/abnormal glucose tolerance[36,46,54-56], presumably as a marker of higher glucose levels in pregnancy, even taking into account likely differences in prescribing practice between centres.

Body weight/body mass index: Body weight [or body mass index (BMI)] during the index pregnancy is commonly reported in studies of GDM cohorts, occasionally with waist circumference or body fat measurements. Studies are inconsistent as to whether weight or BMI persist as a risk factor when adjusted for other risk factors using multivariate analysis. Studies that have not found an association between pregnancy weight and BMI tend to examine women who have progressed to abnormal glucose tolerance in the early post-partum period. BMI during pregnancy may be

associated with abnormal glucose tolerance at this stage, but is not independently associated when antepartum glucose levels (indicating severity of hyperglycaemia) are included in the model[41]. Most studies that do show an association between pregnancy BMI and later abnormal glucose tolerance, independent of antepartum glucose measurements, involve longer-term follow-up post delivery[43,57,58], although this is not a universal finding[59].

Gestational age at diagnosis: Gestational age at diagnosis is another commonly reported association[37, 38,41,42,44,60,61]. However, many of the studies also specify a screening protocol that involves screening higher-risk women in early pregnancy, causing a significant bias. Women diagnosed with GDM in early pregnancy, before insulin resistance begins to rise[62,63], are likely to have a greater degree of hyperglycaemia, and therefore an increased likelihood of progression to abnormal glucose tolerance/diabetes. However, gestational age at diagnosis remains a risk factor, even when measures of glycaemia from the index pregnancy are included in the model, in many of these studies[41,42,44,60,61].

Ethnicity: There are few studies specifically examining the effects of ethnicity, although these that do have generally found an increased prevalence among those women of ethnicity other than white European origin[47,64-68]. Other studies have found no association[40,69]. The reasons for this are unclear. However, many studies have examined ethnically homogenous cohorts, who are often already at high risk of GDM. The prevalence of GDM is higher among ethnic groups who are not of white European origin, while the prevalence of GDM increases at a lower BMI[70] in the Asian populations studied. In addition, adoption of the IADPSG criteria may cause a disproportionate rise in GDM prevalence among Asian populations[71], which will be of relevance when determining the future risk of abnormal glucose tolerance or diabetes in these populations. In addition to the studies outlined above examining this question, comparison between studies does suggest a higher proportion of women of non-white European ethnicity progress to abnormal glucose tolerance[68]. However, meaningful comparison between studies is generally not possible due to the heterogeneity of the studies on the points listed above.

Family history of diabetes: This is uncommonly associated with progression to abnormal glucose tolerance/ diabetes among women with GDM after measures of glycaemia are taken into account. Several studies examining family history have found no effect[49,72,73]. Although some studies have shown an independent effect[39,47,59,74], it appears to be small, and the association is often not seen when analysed as part of a multivariate model[38,58,75,76]. Therefore, family history does not appear to play a major independent role in predicting future risk of diabetes or abnormal glucose tolerance.

Other factors: Age at diagnosis of GDM[44,52,54,76] has

been associated with future abnormal glucose tolerance or diabetes also, but is inconsistent, with other studies showing no association[57,77,78], and again, is rarely significant[54] when other variables are taken into account. Parity, most commonly classified as a binary variable (multiparous or nulliparous) has been identified[53,55,79] as potentially associated with higher risk of progression later, but this finding is inconsistent[41,78]. Potential gene associations have also been identified, but currently appear to add little to clinically assessing individual risk[80]. Autoantibody testing also been examined[81], and appears to be associated with risk of progression to type 1 rather than type 2 diabetes.

Risk factors post-pregnancy
Breastfeeding: Breastfeeding among women with GDM is associated with improved glycaemic indices in the early post-partum period[47,82]. Its role in prevention of later progression to abnormal glucose tolerance is at present unclear, although long-term follow-up of the Study of Women, Infant Feeding and type 2 diabetes mellitus after GDM (SWIFT) pregnancy cohort will address this issue.

Body weight/BMI: Weight (or associated measures) after the index pregnancy has been shown to be correlated in a number of studies[33,56,59,83-86] with progression to diabetes or abnormal glucose tolerance. This correlation appears more robust than that seen with pregnancy weight/BMI, which often loses significance in multivariable models (see above). Also, weight gain since the index pregnancy has been associated with metabolic deterioration[43]. Studies not demonstrating BMI as a predictive factor may take high-risk cohorts, for example, entirely composed of participants with postpartum impaired glucose tolerance[87], or are carried out in the early post-partum period[41,69,88]. Interestingly, Wang *et al*[84] showed that both waist circumference and body fat performed better than BMI in predicting type 2 diabetes in a Chinese cohort, while Jang demonstrated that waist circumference showed a stronger association than BMI in a Korean cohort[37]. This may help to explain why some Asian cohorts[38,87] have not demonstrated an association between BMI and future abnormal glucose tolerance or diabetes, despite longer-term follow-up.

Others: The type of contraceptive - specifically the progesterone-only oral contraceptive - is thought to confer a higher risk[89]. Subsequent GDM is also associated with greater risk of progression to diabetes/ abnormal glucose tolerance[83]. Age at follow-up is commonly reported. Although an association with later abnormal glucose tolerance has been noted[40,44,90-92], and despite the increasing prevalence of type 2 diabetes with advancing age in the general population, this is not a universal finding[38,93], particularly in multivariate analysis[94]. This may be due to the relatively small difference in ages within the cohorts of women involved in these studies, compared to the population as a whole.

Despite the heterogeneity of the studies for the reasons above, including diagnostic criteria used, there is consistency among most studies in the factors associated with a greater risk of diabetes after the index pregnancy in women with GDM. As can be seen, measures of glycaemia during the index pregnancy are not only the strongest predictor, but also frequently attenuate or remove the predictive ability of other traditional risk factors for type 2 diabetes. Thus, the most important risk factor for future abnormal glucose tolerance or diabetes in these women is simply a previous diagnosis of GDM, taking into account the degree of hyperglycaemia at diagnosis.

PREVALENCE OF DIABETES POST-GDM

The prevalence of progression from GDM to abnormal glucose or type 2 diabetes varies greatly. The lifetime cumulative incidence of diabetes among women with GDM is frequently cited at up to 60%, but this summary figure does not illustrate the many underlying different factors (*e.g.*, time since delivery, cohort demographics, and criteria for diagnosis of GDM and postpartum diabetes).

Duration of follow-up

With regard to timing, many studies have documented short-term follow-up only (*i.e.*, to the first post-partum test). Prevalence rates for diabetes at this time point differ, and are generally less than 10%, but depending on the cohort studied, and criteria used, may be significantly higher - Metzger *et al*[40] showed a prevalence of 38% up to one year post-partum in women meeting NDDG criteria[40]. These women are likely to be different from those developing diabetes at a later post-partum interval, and are more likely to have had pre-existing type 2 diabetes. It is therefore unlikely that any of the criteria in use for GDM diagnosis would fail to detect these women.

Beyond the post-partum period, prevalence or cumulative incidence figures continue to show great variation. Figures may be as low as 3% (up to 3 years post-partum from a Swedish cohort, using area under the glucose curve measures from the OGTT for diagnosis[85]), and as high as 62% (at up to 6.5 years in a cohort from Trinidad meeting the 1980 WHO criteria[64]). Follow-up of O'Sullivan's original cohort at 16 years showed a cumulative incidence by life-table analysis of 60%[85]. A systematic review from 2002[31] attempted to control for the marked heterogeneity in time among studies, by plotting actuarial projections of cumulative incidence of cohorts at up to 28 years follow-up, and concluded that most cohorts progressed to diabetes at a similar rate in the first 5 years post index pregnancy, and then levelled off by 10 years with few cases after this (however, this calculation included NDDG-diagnosed women only).

Cohort features

Cohort selection also plays a vital role in determining later progression to abnormal glucose tolerance/ diabetes, and makes comparison difficult. Selection of women who are known to have normal glucose tolerance in the early post-partum period[48], or restricting follow-up to those who did not require insulin for glycaemic control in pregnancy[34], would be expected to reduce the proportion progressing to abnormal glucose tolerance or diabetes, removing those women with the highest glucose levels during pregnancy. Ethnicity, as outlined above, appears also to be a risk factor for progression, with non-white populations demonstrating increased risk, although comparison across studies is difficult.

Criteria used

There is little evidence to directly compare future progression to diabetes or abnormal glucose tolerance among the different criteria in use. Studies directly comparing progression in women meeting the NDDG *vs* Carpenter-Coustan criteria[78] showed little difference in prevalence of diabetes at a median of 6 years post-partum (25.5% *vs* 25.3%) or at 3 mo post-partum (4.0% *vs* 3.2%)[95].

However, the WHO criteria (Table 1) would be expected to show a smaller proportion of women progressing to diabetes/abnormal glucose tolerance, given the increased number of women identified with GDM compared to the NDDG and Carpenter-Coustan criteria. However, again, direct comparison across studies is difficult. In any given population, therefore, lower diagnostic thresholds will lead to a greater prevalence of GDM. Conversely, criteria using higher thresholds to define GDM will identify fewer women with GDM, but these women will, on average, have higher glucose levels. Therefore, the proportion progressing to abnormal glucose tolerance/diabetes will be higher, despite the lower GDM prevalence.

Also, the criteria used to diagnose type 2 diabetes and abnormal glucose tolerance postpartum may differ - older cohorts in particular, using the NDDG or older WHO criteria would be expected to show a lower prevalence at follow-up due to higher thresholds for diagnosis of diabetes in the nonpregnant adult.

RELEVANCE OF IADPSG GDM CRITERIA

The new IADPSG criteria pose an important clinical question with regard to intensity of follow-up. With potentially up to one in four pregnancies in some centres meeting the new criteria for GDM diagnosis[24], lifelong follow-up of these women will have important clinical and resource implications. However, the optimal mode and timing of a follow-up strategy remains unclear. More women with milder degrees of hyperglycaemia are now classified as GDM. Accordingly, the proportion progressing to abnormal glucose tolerance should decrease. There are as of yet no prospective figures

on progression to type 2 diabetes or abnormal glucose tolerance post-partum in women with IADPSG-defined GDM. The ATLANTIC-DIP study retrospectively classified women using IADPSG criteria after a universal screening programme, and found that 19% had abnormal glucose tolerance at early post-partum follow-up[47]. Capula *et al*[39] looked at a mixed (approximately 60% diagnosed by IADPSG criteria) cohort, and found 4% had diabetes, and a further 32% abnormal glucose tolerance at 6-12 wk post-partum, although conclusions on the relative contribution of each set of criteria are not possible. Overall, it appears certain that more women will need to be tested to identify those women progressing to abnormal glucose tolerance and diabetes.

Some clues as to how women diagnosed with GDM by IADPSG criteria may behave on follow-up may be seen in several papers which follow women meeting just a single abnormal value on the pregnancy OGTT using the older criteria. Retnakaran *et al*[95,96], using NDDG criteria for GDM diagnosis, examined early post-partum outcomes among women along the spectrum of glucose tolerance: from normal glucose tolerance, to abnormal glucose challenge test (GCT) with normal OGTT, a single abnormal value on OGTT, and GDM. This demonstrated a graded relationship in abnormal glucose tolerance; from 3.2% in the normal glucose tolerance (NGT) group, 10.2% in the GCT abnormal, OGTT normal group, 16.5% in the GCT abnormal, single abnormal value on OGTT group, to 32.8% in the GDM group. Indeed, detailed characterisation of these groups[97] demonstrates the similarity between women with a single abnormal value at 1-h post glucose load (as opposed to later abnormal values) and women with GDM, as measured by AUC curve on OGTT and beta-cell dysfunction at 3 mo postpartum.

Thus we can see that a cohort of women with a single abnormal value only, albeit using higher cut-offs than the new IADPSG values, still have a clinically important increased risk of abnormal glucose tolerance. Other prospective studies examining similar cohorts, although at a longer follow-up interval, have drawn similar conclusions; Stuebe *et al*[98], using the stricter Carpenter-Coustan criteria, showed a higher HbA1c in women with a single abnormal value at 3-year follow-up, *vs* both women with GDM, and those with NGT in pregnancy. Vambergue *et al*[76] (using Carpenter-Coustan criteria) showed a similar graded relationship for progression to type 2 diabetes at almost 7 years follow-up, with 6% of women with a single abnormal value progressing to diabetes, as compared with 18% in the those meeting GDM criteria (less than 1% of those with no abnormal values had progressed to diabetes). Carr *et al*[99] (using Carpenter-Coustan criteria), in a large retrospective cohort study, found a HR of 2.0 for diabetes diagnosis among women with a single abnormal value on OGTT *vs* those who did not.

Therefore, all degrees of glucose abnormalities

in pregnancy, even those not meeting older GDM criteria, are associated with an increased risk of later glucose abnormalities. This may have important implications for those women with lesser degrees of hyperglycaemia who will now be classified as having GDM by IADPSG criteria.

RELEVANCE OF OVERT DIABETES

Women meeting criteria for diabetes diagnosis in the non-pregnant adult are now classified as separate category by the IADPSG criteria and represent the highest-risk GDM cohort, having an increased risk of congenital abnormalities and diabetes complications, and are likely to have had undiagnosed type 2 diabetes preceding the index pregnancy[22]. The future risk of these women is unclear at present. A retrospective audit of 254 women meeting criteria for overt diabetes demonstrated that 41% had normal glucose tolerance at 6-8 wk postpartum (although testing was carried out at 24-28 wk rather than at the booking visit, and diagnoses based on a 2-h value of $\geqslant$ 11.1 mmol/L were not confirmed with HbA1c or FPG measurements)[100]. Further prospective follow-up comparing women meeting both sets of IADPSG criteria will therefore be useful in further refining risk in this population.

POST-PARTUM FOLLOW-UP STRATEGIES

Current recommendations for follow-up of women with gestational diabetes vary from region to region. The ADA recommend an early post-partum OGTT (in line with ACOG guidelines) and follow-up with HbA1c, fasting plasma glucose (FPG) or 75 g OGTT thereafter, on a 1-3 yearly basis[101]. The International Diabetes Federation[102] recommend an early post-partum OGTT, and thereafter vary recommendations on whether a further pregnancy is planned, (OGTT prior to conception) and whether the woman is high-risk (annual OGTT) or low-risk (FPG every 2-3 years), the criteria for which are not defined. The British National Institute for Health and Care Excellence guidelines[103] recommend FPG alone in the early post-partum period, and an OGTT at follow-up only if a further pregnancy is planned. Several studies have examined the use of HbA1c and FPG[104-107] for both early and medium term follow-up in women with previous GDM, in order to avoid the inconvenience associated with the OGTT. Sensitivity for the detection of abnormal glucose tolerance after delivery varies widely according to the thresholds chosen, ranging from 23%-65% (specificity 68%-96%) for HbA1c values, increasing to a sensitivity of 82%-93% (specificity 84%-92%)when combined with FPG values. Further prospective study will be needed to examine the potential use of these approaches. This will be particularly important if IADPSG criteria are used, as the optimum frequency and mode of testing for such a large cohort of women with previous GDM is unknown.

CONCLUSION

Marked heterogeneity across studies of women with previous GDM with regard to the diagnostic criteria used, duration of follow-up, and cohort demographics limits the ability to compare findings across studies. However, regardless of which criteria are used, a history of GDM confers a large excess risk of progression to type 2 diabetes in later life, and the risk factors predicting progression remain similar across cohorts. The new IADPSG criteria increase the prevalence of GDM by 2-3 fold, and lifelong follow-up of these women has significant clinical and resource implications. Therefore, further prospective studies are necessary to determine the longer-term risk of progression to diabetes in those diagnosed using the new criteria, and also to determine the optimal method and frequency follow-up needed.

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