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CLINICAL STUDY

ATLANTIC DIP: simplifying the follow-up of women with previous gestational diabetes

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Abstract

Objective: Previous gestational diabetes (GDM) is associated with a significant lifetime risk of type 2 diabetes. In this study, we assessed the performance of HbA1c and fasting plasma glucose (FPG) measurements against that of 75 g oral glucose tolerance testing (OGTT) for the follow-up screening of women with previous GDM.

Methods: Two hundred and sixty-six women with previous GDM underwent the follow-up testing (mean of 2.6 years (s.d. 1.0) post-index pregnancy) using HbA1c (100%), and 75 g OGTT (89%) or FPG (11%). American Diabetes Association (ADA) criteria for abnormal glucose tolerance were used.

Design, cohort study, and results: The ADA HbA1c high-risk cut-off of 39 mmol/mol yielded sensitivity of 45% (95% CI 32, 59), specificity of 84% (95% CI 78, 88), negative predictive value (NPV) of 87% (95% CI 82, 91) and positive predictive value (PPV) of 39% (95% CI 27, 52) for detecting abnormal glucose tolerance. ADA high-risk criterion for FPG of 5.6 mmol/l showed sensitivity of 80% (95% CI 66, 89), specificity of 100% (95% CI 98, 100), NPV of 96% (95% CI 92, 98) and PPV of 100% (95% CI 91, 100). Combining HbA1c $\geq$39 mmol/mol with FPG $\geq$5.6 mmol/l yielded sensitivity of 90% (95% CI 78, 96), specificity of 84% (95% CI 78, 88), NPV of 97% (95% CI 94, 99) and PPV of 56% (95% CI 45, 66).

Conclusions: Combining test cut-offs of 5.6 mmol/l and HbA1c 39 mmol/mol identifies 90% of women with abnormal glucose tolerance post-GDM (mean 2.6 years (s.d.1.0) post-index pregnancy). Applying this follow-up strategy will reduce the number of OGTT tests required by 70%, will be more convenient for women and their practitioners, and is likely to lead to increased uptake of long-term retesting by these women whose risk for type 2 diabetes is substantially increased.

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Introduction

Gestational diabetes mellitus (GDM) is associated with a significant lifetime risk of progression to type 2 diabetes. A recent meta-analysis carried out on the studies conducted over the last 40 years has shown a relative risk of 7.7 for the future development of type 2 diabetes in women with a history of GDM vs women with normal glucose tolerance (NGT) in pregnancy (1). Regular, effective follow-up is therefore essential. The benefits of this are twofold: firstly, retesting allows early detection of those women who have progressed to diabetes, or who have blood glucose concentrations in the pre-diabetic range. This enables the timely commencement of appropriate treatment to prevent diabetes-related complications, or ideally, intervention to prevent progression to overt diabetes. The potential for both intensive lifestyle intervention and metformin treatment to delay or prevent the onset of type 2 diabetes in these women has been previously demonstrated by the Diabetes Prevention Program study (2). Both interventions were shown to help prevent or delay the onset of type 2 diabetes in women with previous GDM (risk reduction of 53% for intensive lifestyle intervention and 50% for metformin treatment). Secondly, regular effective follow-up reduces the risk of undiagnosed type 2 diabetes predating a subsequent pregnancy, and the increased risk to mother and foetus associated with such an event (3).

Despite this, *post-partum* retesting is haphazard and uptake remains low (4, 5, 6, 7, 8, 9, 10, 11), with fasting plasma glucose (FPG) assay or oral glucose tolerance test (OGTT) performed in only 33–58% of women with previous GDM. Guidelines on how best to follow women with GDM in the *post-partum* period and beyond vary significantly. The American Diabetes Association (ADA) (12), American Congress of Obstetricians and Gynaecologists (ACOG) (13) and the Fifth International Workshop Conference on Gestational Diabetes (14) all recommend *post-partum* follow-up with a 75 g OGTT at 6–12 weeks, while the British National Institute for Clinical Excellence (NICE)

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guidelines (15) recommend follow-up with FPG measurement alone at 6–12 weeks *post-partum*. Beyond the immediate *post-partum* period, even more variation is evident. NICE guidelines recommend yearly FPG measurement, while ADA guidelines recommend a follow-up with either FPG, HbA1c, or OGTT on a 1–3 yearly basis after the initial *post-partum* OGTT. ACOG guidelines recommend a follow-up with either OGTT or FPG test at 3-yearly intervals. The 75 g OGTT is the current 'gold standard' for the diagnosis of abnormal glucose tolerance, and is the only method by which impaired glucose tolerance (IGT), which is associated with progression to type 2 diabetes (16), and, independently, increased risk of cardiovascular disease (17, 18) can be diagnosed. However, for the patient, a minimum 2-h time commitment is required, whereas for the healthcare provider, there are increased costs incurred due to the use of a glucose load, additional phlebotomy services, clinic time and laboratory analyses. An FPG measurement alone, however, misses up to 60% of women with abnormal 2-h glucose values (19). A previous study carried out by our research group has shown that the prevalence of GDM by the International Association of Diabetes in Pregnancy Study Groups (IADPSG) criteria during a period of universal screening was 12.4% (20). The total number of births for the region in which this study was carried out is ~10 000 per annum (21), meaning over 1200 women each year in this region alone would meet IADPSG criteria for GDM. Although not all of these will be new diagnoses, a yearly OGTT for each woman with a history of GDM, as is our current policy, clearly represents a significant clinical and economic burden. Given that retesting using the 75 g OGTT in clinical practice has been shown to be suboptimal (4, 5, 6, 7, 8, 9, 10, 11), we set out to design a pragmatic and cost-effective recall and retesting program using FPG and HbA1c assays, or a combination of both, to detect the progression to abnormal glucose tolerance in women with previous GDM.

Subjects and methods

We recruited women across four centres in the ATLANTIC DIP collaboration who had undergone a 75 g OGTT during pregnancy in the preceding 5 years (2006–2010), and who had values diagnostic of GDM, using the IADPSG criteria. This 5-year period included an 18-month period of universal screening for women attending for antenatal care. Otherwise, risk factor-based screening was employed. World Health Organization criteria for diagnosis of GDM were used before 2010. These women were identified using our clinical database (DIAMOND, Hicom, Woking) and were invited to attend their closest study centre for retesting. All women were sent a letter, with a follow-up telephone call to arrange an appointment. Of 468 women invited for testing, 342 accepted and 270 (78%) attended. Of these, four did not have valid HbA1c measurements, leaving a cohort of 266 women entered into this study. All participants gave informed consent for participation in this prospective cohort study, and institutional research ethics committee approval was obtained before the commencement of the study. Women who met IADPSG criteria only ($n=92$; 35%), but not WHO criteria, which were in use at the time of the index pregnancy, were informed that a change in diagnostic criteria and clinical practice had occurred since the index pregnancy. All women had clinical and laboratory parameters during their index pregnancy entered into our clinical database. Of these 266 women, 41 women (15%) were known to have abnormal glucose tolerance on 75 g OGTT at their first *post-partum* visit, 156 women (59%) were known to have NGT on a 12-week *post-partum* 75 g OGTT, while 69 (26%) had not undergone OGTT in the early *post-partum* period. A 75 g OGTT was performed in 89% ($n=237$), while FPG assay alone was performed on the remaining 11% ($n=29$). All women provided a sample for the determination of their HbA1c levels and participated in a structured standardised interview. Participants underwent an overnight fast, after which blood was drawn into a fluoride oxalate tube for FPG assay and into an EDTA tube for HbA1c assay. A 75 g glucose load was given (Polycal) and a 2-h post-load plasma glucose was determined. All assays were carried out in the same laboratory (University Hospital Galway) by the persons unaware of the participant's clinical history. Plasma glucose was measured using the hexokinase assay on the Roche Modular <P> Analytics system. The between run analytical coefficient of variation (CV_a%) at a mean plasma glucose of 2.97 mmol/l (53.5 mg/dl) and 18.88 mmol/l (340.2 mg/dl) was 1.9 and 1.5% respectively.

HbA1c was measured by reverse phase cation exchange chromatography using the Menarini HA8160 automated haemoglobin analyser. The method was calibrated according to International Federation of Clinical Chemistry (IFCC) standardisation (22). Diabetes Control and Complications Trial (DCCT) units (%) were derived from the IFCC (mmol/mol) measurement using the IFCC-DCCT/NGSP (National Glycohaemoglobin Standardisation Program) master equation. The between run CV_a% at a mean HbA1c of 41.6 mmol/mol (derived DCCT 6%) and 100.5 mmol/mol (derived DCCT 11.4%) was 2.0 and 1.3% respectively. ADA criteria were employed for the diagnosis of impaired fasting glucose (IFG), IGT and diabetes mellitus.

Statistical analysis was carried out using PASW Statistics (formerly known as SPSS) version 18 (IBM, New York, NY, USA) and Minitab 15 (Minitab, Inc., State College, PA, USA). Diagnostic accuracy was calculated using sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV).

Receiver–operator characteristic (ROC) curves were constructed for FPG and HbA1c, using the OGTT as the 'gold standard' for the diagnosis of abnormal glucose tolerance, and the area under the curve (AuROC) was calculated.

Differences between mean values of normally distributed continuous variables were compared using Student's *t*-test. Differences between the medians of non-parametrically distributed variables were compared using the Mann–Whitney *U* test (Fig. 1).

Results

Of 266 women attending for retesting, 89% ($n=237$) had a 75 g OGTT, while the remaining 11% ($n=29$: 19 of whom were known to have abnormal glucose tolerance at their first *post-partum* visit) had FPG test only. Baseline characteristics are shown in Table 1. Of the 266 women tested, 15.4% ($n=41$) were known to have abnormal glucose tolerance at their first *post-partum* visit (6.8% IFG, 2.6% IGT, 4.5% combined IFG/IGT, 1.5% diabetes mellitus). At retesting, 81.6% ($n=217$) had NGT, while 18.4% ($n=49$; 95% CI 14.2–23.5) had abnormal glucose tolerance (IFG, $n=30$; 11.3%; IGT, $n=8$; 3%, combined IFG/IGT, $n=5$, 1.9%; diabetes mellitus, $n=6$, 2.3%). Of those women meeting the IADPSG criteria, but not the WHO criteria ($n=95$), 12% ($n=11$) had abnormal glucose tolerance. Baseline characteristics and results at rescreening are summarised in Table 1.

HbA1c

Table 2 shows the test accuracy of HbA1c at defined thresholds for predicting abnormal glucose tolerance by ADA criteria. Using the recommended ADA, HbA1c cut-off for high-risk individuals of 39 mmol/mol (5.7%) yielded a sensitivity of 45% (95% CI 32–59), specificity of 84% (95% CI 78–88), NPV of 87% (95% CI 82–91) and PPV of 39% (95% CI 27–52). ROC curve analysis for HbA1c to predict any abnormal glucose tolerance gave an AuROC of 0.742 (95% CI 0.663–0.821). AuROC for 2-h glucose $\geq$7.8 mmol/l was 0.714 (95% CI 0.591–0.836).

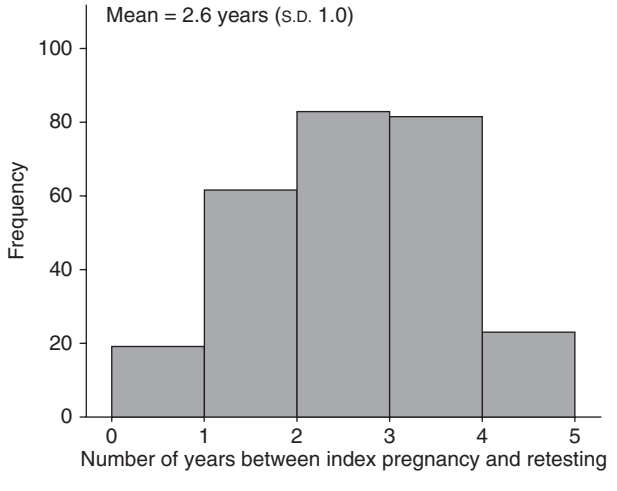

Figure 1 Histogram demonstrating the interval between the delivery date of the index pregnancy and retesting for the current study for all participants ($n=266$).

Fasting plasma glucose

Using the ADA high-risk criterion for FPG $\geq$5.6 mmol/l to identify any degree of abnormal glucose tolerance, sensitivity was 80% (95% CI 66–89), specificity was 100% (95% CI 98–100), NPV was 96% (95% CI 92–98) and PPV was 100% (95% CI 91–100). The characteristics for different cut-offs of FPG when used to screen for abnormal glucose tolerance are summarised in Table 3. ROC curve analysis examining the ability of FPG test alone to predict IGT (i.e. a 2-h plasma glucose of $\geq$7.8 mmol/l showed an AuROC of 0.609 (95% CI 0.438–0.779)).

HbA1c and FPG tests combined

The above results show suboptimal performance using HbA1c or FPG alone to detect abnormal glucose tolerance in this cohort. We therefore used defined cut-offs of a combination of HbA1c and FPG values to identify higher risk women who should proceed to confirmatory glucose testing with a 75 g OGTT. Women were classified as meeting the criteria if they met either the specified HbA1c or the FPG value. We calculated the NPV, PPV, sensitivity and specificity for each defined cut-off of a combination of HbA1c and FPG values. Results are shown in Table 4.

Discussion

The objective of this study was to evaluate the potential of a new follow-up testing regimen using a combination of FPG and HbA1c measurements to predict the progression to abnormal glucose tolerance *post-partum*, following initial *post-partum* assessment with a 75 g OGTT. Our data suggest that, by combining the decision threshold for HbA1c $\geq$39 mmol/mol (5.7%) and/or an FPG of $\geq$5.6 mmol/l, 90% (95% CI 78–96) of patients with any degree of glucose abnormality on a 75 g OGTT are identified, with a specificity of 84% (95% CI 78–88). Employing this new approach (requiring only a single blood draw) to identify those higher risk women who should proceed to a 75 g OGTT would reduce the number of OGTTs performed by almost 70%. At an estimated cost of Euro 35 200 per 1000 women tested (23) using 75 g OGTT, this new screening regime would reduce the cost of OGTT screening to Euro 10 560; however, this would of course offset the cost of measuring HbA1c and FPG in each patient.

Table 1 Baseline characteristics and summary of results. Values are mean (S.D.) unless stated otherwise.

Characteristic	Total GDM cohort $n=266$	NGT cohort $n=217$	Abnormal glucose tolerance cohort $n=49$	*P* value for difference	95% CI for difference
Age (years)	36.6 (5)	36.6 (5)	36.9 (5.1)	0.700	−1.3 to 1.9
Years since delivery	2.6 (1.0)	2.6 (1.1)	2.7 (1.0)	0.298	−0.2 to 0.5
BMI (kg/m^2)	29.7 (6.9)	29.1 (6.8)	32.4 (6.8)	0.002	1.2 to 5.5
Median HbA1c (range) (mmol/mol)	36 (61)	35 (19)	38 (54)	<0.001	1.5 to 4.5
Fasting glucose (mmol/l)	5.1 (1)	4.8 (0.4)	6.1 (1.7)	<0.001	0.9 to 1.9
2 h glucose (mmol/l)	5.6 (1.8)	5.2 (1)	8.0 (3)	<0.001	1.7 to 3.8
Waist circumference (cm)	93.3 (16.4)	91.8 (16.3)	100.1 (15.5)	0.001	3.2 to 13.4
Abnormal glucose tolerance at 12 weeks (%) (*n*)	16% (43)	NA	NA	NA	NA
Abnormal glucose tolerance at rescreening (%) (*n*)	19% (49)	NA	NA	NA	NA

In our cohort, employing this new screening approach (HbA1c $\geq$39 mmol/mol or FPG of $\geq$5.6 mmol/l) identified a total of 79 women who met the criteria, 44 of whom (56%) demonstrate abnormal glucose tolerance using either the OGTT or FPG test. In addition, we now identify a further subgroup of women (44%, $n=35$) who have NGT on OGTT, but meet our criteria by virtue of their HbA1c value alone. As the HbA1c cut-off of 39 mmol/mol is the ADA criterion value at which measures to delay or prevent progression to type 2 diabetes should be instituted (12), we would suggest that a 75 g OGTT adds little to the clinical course of these women.

Therefore, those women with a history of GDM, meeting either the HbA1c cut-off of 39 mmol/mol or FPG of 5.6 mmol/l, should undergo at least 3-yearly, and ideally annual (12, 13, 14, 15), follow-up for the assessment of progression to diabetes with HbA1c and FPG. At a minimum, individualised dietary and exercise advice should be offered to these high-risk women. However, given the proven efficacy of a structured lifestyle intervention program (2), this should be offered where possible, and a randomised controlled trial is underway at our centre to examine the clinical impact and cost-effectiveness of such a programme in women with previous GDM (24). Of course, if further pregnancy is desired, closer clinical follow-up is needed.

The results of this study, interestingly, are similar to those in recent papers by Megia *et al.* (25) and Picon *et al.* (26), who employed similar approaches to predict abnormal *post-partum* glucose tolerance, albeit describing a lower cut-off: HbA1c of 37 mmol/mol (5.5%, Megia *et al.*). There are several important differences between the studies, however. Our study shows a sensitivity of 90 vs 82% (Megia) and 83% (Picon), while we demonstrate a higher NPV (97%) vs Picon

Table 2 HbA1c performance using different cut-offs to identify abnormal glucose tolerance (ADA criteria).

HbA1c (mmol/mol)	No. of women meeting criteria[a] *n* (%)	Sensitivity %(95% CI)	Specificity %(95% CI)	PPV %(95% CI)	NPV %(95% CI)
32	247 (93)	98 (89, 100)	8 (5, 13)	19 (15, 25)	95 (75, 99)
33	232 (87)	96 (86, 99)	15 (11, 20)	20 (16, 26)	94 (81, 98)
34	205 (77)	94 (83, 98)	27 (21, 33)	22 (17, 29)	95 (86, 98)
35	176 (66)	86 (73, 93)	38 (32, 45)	24 (18, 31)	92 (85, 96)
36	140 (53)	80 (66, 89)	53 (47, 60)	28 (21, 36)	92 (86, 96)
37	108 (41)	71 (58, 82)	66 (60, 72)	32 (24, 42)	91 (85, 95)
38	79 (30)	55 (41, 68)	76 (70, 81)	34 (25, 45)	88 (83, 92)
39	57 (21)	45 (32, 59)	84 (78, 88)	39 (27, 52)	87 (82, 91)
40	36 (14)	37 (25, 51)	92 (87, 95)	50 (34, 66)	86 (81, 90)
41	26 (10)	31 (20, 45)	95 (91, 97)	58 (39, 74)	86 (81, 90)
42	17 (6)	27 (16, 40)	98 (95, 99)	76 (53, 90)	85 (80, 89)
43	12 (5)	22 (13, 36)	100 (97, 100)	92 (65, 99)	85 (80, 89)
44	9 (3)	18 (10, 31)	100 (98, 100)	100 (70, 100)	84 (79, 88)
45	8 (3)	16 (9, 29)	100 (98, 100)	100 (68, 100)	84 (79, 88)
46	7 (3)	11 (5, 23)	100 (98, 100)	100 (65, 100)	84 (79, 88)
47	6 (2)	12 (6, 24)	100 (98, 100)	100 (61, 100)	83 (78, 87)
48	6 (2)	12 (6, 24)	100 (98, 100)	100 (61, 100)	83 (78, 87)

[a]Number of participants who meet or exceed HbA1c cut-off value in adjacent column.

Table 3 FPG performance using different cut-offs to identify abnormal glucose tolerance (ADA criteria).

FPG (mmol/l)	No. of women meeting criteria[a] *n* (%)	Sensitivity %(95% CI)	Specificity %(95% CI)	PPV %(95% CI)	NPV %(95% CI)
5	126 (53)	84 (71, 91)	61 (54, 67)	33 (25, 42)	94 (89, 97)
5.1	110 (41)	82 (69, 90)	68 (61, 74)	37 (29, 46)	94 (89, 97)
5.2	93 (35)	82 (69, 90)	76 (69, 81)	44 (34, 54)	95 (90, 97)
5.3	70 (26)	82 (69, 90)	86 (81, 90)	58 (46, 69)	95 (92, 98)
5.4	61 (23)	80 (66, 89)	90 (85, 93)	65 (52, 76)	95 (91, 97)
5.5	49 (18)	80 (66, 89)	95 (92, 97)	81 (68, 90)	95 (92, 97)
5.6	39 (15)	80 (66, 89)	100 (98, 100)	100 (91, 100)	96 (92, 98)
5.7	36 (14)	73 (60, 84)	100 (98, 100)	100 (90, 100)	94 (91, 97)
5.8	32 (12)	65 (51, 77)	100 (98, 100)	100 (89, 100)	93 (89, 95)
5.9	28 (11)	57 (43, 70)	100 (98, 100)	100 (88, 100)	91 (87, 94)
6	26 (10)	53 (39, 66)	100 (98, 100)	100 (87, 100)	90 (86, 94)
6.1	25 (9)	51 (37, 64)	100 (98, 100)	100 (87, 100)	90 (86, 93)

[a]Number of participants who meet or exceed FPG cut-off value in adjacent column.

et al.'s (85%) study. This is a key difference when designing a pragmatic retesting programme for women with previous GDM. For these purposes, a higher sensitivity and NPV are desirable, and in this cohort, do not result in an unacceptable increase in confirmatory testing; the proportion of women meeting HbA1c/FPG criteria, and therefore requiring confirmatory testing, is 31% as compared with 29% in Megia *et al.*'s study and 47% in Picon *et al.*'s study. Both Megia *et al.*'s and Picon *et al.*'s studies involve higher risk cohorts, using the National Diabetes Data Group criteria for GDM as opposed to the newer, more stringent, IADPSG criteria, and accordingly, demonstrate a higher prevalence of abnormal glucose tolerance using OGTT; 45.9% in Picon *et al.*'s study and 27.8% in Megia *et al.*'s study. This is despite a shorter interval to *post-partum* retesting – 3 months (Megia) and 1 year (Picon) vs 2.6 years in our cohort. Other important differences include the ethnic composition of the cohorts – our cohort is 100% white European, compared with 8.5% of Megia *et al.*'s cohort comprising ethnic minorities (predominantly Arabic and Hispanic). Differences in HbA1c between ethnic groups have been well described previously (27), and our findings may therefore be only applicable to Caucasian women. Given the relatively low GDM prevalence of 12.4% in previous studies from our group (compared with the 17.8% across all HAPO centres (28)), the overall burden of follow-up testing, although significant, may be less than that in other centres. Also, the HbA1c assay used in the Megia and Picon studies is DCCT aligned, while our assay is fully metrologically traceable to the newer IFCC standard.

Another study by Kim *et al.* (29) in 54 women with a history of GDM further demonstrates the limitations of using HbA1c in isolation to predict abnormal glucose tolerance, showing an AuROC of 0.76 for abnormal glucose tolerance on OGTT, a sensitivity of 65% and specificity of 68% for predicting abnormal glucose tolerance when an HbA1c cut-off of greater than or equal to 5.7% (39 mmol/mol) is used.

One of the limitations in our study is that 11% of women ($n=29$) did not undergo a repeat OGTT for this

Table 4 Combined HbA1c/FPG cut-offs to identify abnormal glucose tolerance (ADA criteria).

FPG (mmol/l)	HbA1c (mmol/mol)	No. of women meeting criteria[a] *n* (%)	Sensitivity %(95% CI)	Specificity %(95% CI)	PPV %(95% CI)	NPV %(95% CI)
5.3	37	128 (48)	92 (81–97)	61 (55–68)	35 (27–44)	97 (93–99)
5.6	37	117 (44)	90 (78–96)	66 (59–72)	38 (29–47)	97 (92–99)
6.1	37	112 (42)	80 (66–86)	66 (60–72)	35 (27–44)	94 (88–96)
5.3	39	96 (36)	92 (81–97)	76 (70–81)	47 (37–57)	98 (94–99)
5.6	39	79 (30)	90 (78–96)	84 (78–88)	56 (45–66)	97 (94–99)
6.1	39	68 (26)	67 (53–79)	84 (78–88)	49 (37–60)	92 (87–95)
5.3	42	73 (27)	86 (73–93)	85 (80–89)	58 (46–68)	96 (93–98)
5.6	42	45 (17)	84 (71–91)	98 (95–99)	91 (79–97)	96 (93–98)
6.1	42	32 (12)	57 (43–70)	98 (95–99)	88 (72–95)	91 (87–94)
5.3	48	70 (27)	84 (71–91)	86 (81–90)	59 (47–69)	96 (92–98)
5.6	48	40 (15)	82 (69–90)	100 (98–100)	100 (91–100)	96 (93–98)
6.1	48	26 (10)	53 (39–66)	100 (98–100)	100 (87–100)	90 (86–94)

[a]Number of participants meeting either HbA1c or FPG value specified in adjacent columns.

study, but had fasting glucose levels only. On excluding these women from the analysis and taking the proposed cut-offs of HbA1c of 39 mmol/mol (5.7%) and fasting glucose of 5.6 mmol/l, the sensitivity dropped slightly to 85% (95% CI 70, 94), with a slightly increased specificity of 86% (95% CI 80, 90). PPV and NPV are similar at 50% (95% CI 38, 62) and 97% (95% CI 94, 99) respectively. However, given that those women who had fasting glucose levels only represent a higher risk group (69% of these 29 women were known to have abnormal glucose tolerance at their first *post-partum* visit), we feel that the best approach is to include these women in the analysis. This approach would also be similar to that taken in the clinical management of these women. Also, the majority of the women invited for retesting for this study (89%) underwent an OGTT. Offering the option of just a single blood draw for FPG and HbA1c assays (or even a single non-fasting sample for HbA1c alone) may well have a significant effect on the relatively low (58%) uptake of our offer of retesting. Although this study demonstrates that our approach is clinically feasible, a randomised controlled trial to compare uptake and effectiveness of the various testing modalities would be useful.

In summary, the combination of HbA1c and FPG measurements to predict abnormal glucose tolerance shows results superior to either one used alone. Ninety percent of women with abnormal glucose tolerance are identified using cut-offs of greater than or equal to 39 mmol/mol for HbA1c or 5.6 mmol/l for FPG, while reducing the number of OGTTs performed by over two-thirds. This proposed approach is likely to have a significant economic and social benefit from both a patient and healthcare provider perspective, although detailed economic evaluation will be necessary to provide an accurate cost–benefit analysis.

Declaration of interest

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

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Author contribution statement

E Noctor was involved in the study design, collected and analysed data and wrote the manuscript. C Crowe was involved in the study design, collected and analysed data and reviewed the manuscript. L A Carmody was involved in study design, collected data and reviewed the manuscript. G M Avalos was involved in study design, analysed data and reviewed the manuscript. B Kirwan collected data and reviewed the manuscript. J J Infanti was involved in study design, researched data and reviewed the manuscript. A O'Dea was involved in study design, researched data and reviewed the manuscript. J Newell, B McGuire and C O'Neill were involved in study design. P M O'Shea was involved in the study design, analysed data and reviewed the manuscript. F P Dunne is ATLANTIC DIP PI and was involved in study design, analysed data, edited the manuscript and made the decision to publish.

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References

1 Bellamy L, Casas JP, Hingorani AD & Williams D. Type 2 diabetes mellitus after gestational diabetes: a systematic review and meta-analysis. *Lancet* 2009 **373** 1773–1779. (doi:10.1016/S0140-6736(09)60731-5)

2 Ratner RE, Christophi CA, Metzger BE, Dabelea D, Bennett PH, Pi-Sunyer X, Fowler S & Kahn SE. Prevention of diabetes in women with a history of gestational diabetes: effects of metformin and lifestyle interventions. *Journal of Clinical Endocrinology and Metabolism* 2008 **93** 4774–4779. (doi:10.1210/jc.2008-0772)

3 Balsells M, Garcia-Patterson A, Gich I & Corcoy R. Maternal and fetal outcome in women with type 2 versus type 1 diabetes mellitus: a systematic review and metaanalysis. *Journal of Clinical Endocrinology and Metabolism* 2009 **94** 4284–4291. (doi:10.1210/jc.2009-1231)

4 Smirnakis KV, Chasan-Taber L, Wolf M, Markenson G, Ecker JL & Thadhani R. *Postpartum* diabetes screening in women with a history of gestational diabetes. *Obstetrics and Gynecology* 2005 **106** 1297–1303. (doi:10.1097/01.AOG.0000189081.46925.90)

5 Kim C, Tabaei BP, Burke R, McEwen LN, Lash RW, Johnson SL, Schwartz KL, Bernstein SJ & Herman WH. Missed opportunities for type 2 diabetes mellitus screening among women with a history of gestational diabetes mellitus. *American Journal of Public Health* 2006 **96** 1643–1648. (doi:10.2105/AJPH.2005.065722)

6 Russell MA, Phipps MG, Olson CL, Welch HG & Carpenter MW. Rates of *postpartum* glucose testing after gestational diabetes mellitus. *Obstetrics and Gynecology* 2006 **108** 1456–1462. (doi:10.1097/01.AOG.0000245446.85868.73)

7 Almario CV, Ecker T, Moroz LA, Bucovetsky L, Berghella V & Baxter JK. Obstetricians seldom provide *postpartum* diabetes screening for women with gestational diabetes. *American Journal of Obstetrics and Gynecology* 2008 **198** 528.e521–528.e525. (doi:10.1016/j.ajog.2007.11.001)

8 Dietz PM, Vesco KK, Callaghan WM, Bachman DJ, Bruce FC, Berg CJ, England LJ & Hornbrook MC. *Postpartum* screening for diabetes after a gestational diabetes mellitus-affected pregnancy. *Obstetrics and Gynecology* 2008 **112** 868–874. (doi:10.1097/AOG.0b013e318184db63)

9 Hunt KJ & Conway DL. Who returns for *postpartum* glucose screening following gestational diabetes mellitus? *American Journal of Obstetrics and Gynecology* 2008 **198** 404.e401–404.e406. (doi:10.1016/j.ajog.2007.09.015)

10 Ferrara A, Peng T & Kim C. Trends in *postpartum* diabetes screening and subsequent diabetes and impaired fasting glucose among women with histories of gestational diabetes mellitus: a report from the Translating Research Into Action for Diabetes (TRIAD) Study. *Diabetes Care* 2009 **32** 269–274. (doi:10.2337/dc08-1184)

11 Shah BR, Lipscombe LL, Feig DS & Lowe JM. Missed opportunities for type 2 diabetes testing following gestational diabetes: a population-based cohort study. *BJOG: an International Journal of Obstetrics and Gynaecology* 2011 **118** 1484–1490. (doi:10.1111/j.1471-0528.2011.03083.x)

12 American Diabetes Association. Standards of medical care in diabetes. *Diabetes Care* 2012 **35** S11–S63. (doi:10.2337/dc12-s011)

13 ACOG Committee. Opinion no. 435: *postpartum* screening for abnormal glucose tolerance in women who had gestational diabetes mellitus. *Obstetrics and Gynecology* 2009 **113** 1419–1421. (doi:10.1097/AOG.0b013e3181ac06b6)
14 Metzger BE, Buchanan TA, Coustan DR, de Leiva A, Dunger DB, Hadden DR, Hod M, Kitzmiller JL, Kjos SL, Oats JN *et al*. Summary and recommendations of the Fifth International Workshop-Conference on Gestational Diabetes Mellitus. *Diabetes Care* 2007 **30** (Suppl 2) S251–S260. (doi:10.2337/dc07-s225)
15 National Collaborating Centre for Women's and Children's Health (for National Institute for Clinical Excellence). Clinical Guideline 63: Management of diabetes and its complications from pre-conception to the postnatal period, 2008. London: National Institute for Health and Care Excellence.
16 Sartor G, Schersten B, Carlstrom S, Melander A, Norden A & Persson G. Ten-year follow-up of subjects with impaired glucose tolerance: prevention of diabetes by tolbutamide and diet regulation. *Diabetes* 1980 **29** 41–49. (doi:10.2337/diabetes.29.1.41)
17 Fuller JH, Shipley MJ, Rose G, Jarrett RJ & Keen H. Coronary-heart-disease risk and impaired glucose tolerance. The Whitehall study. *Lancet* 1980 **1** 1373–1376. (doi:10.1016/S0140-6736(80)92651-3)
18 Barr EL, Zimmet PZ, Welborn TA, Jolley D, Magliano DJ, Dunstan DW, Cameron AJ, Dwyer T, Taylor HR, Tonkin AM *et al*. Risk of cardiovascular and all-cause mortality in individuals with diabetes mellitus, impaired fasting glucose, and impaired glucose tolerance: the Australian Diabetes, Obesity, and Lifestyle Study (AusDiab). *Circulation* 2007 **116** 151–157. (doi:10.1161/CIRCULATIONAHA.106.685628)
19 Kousta E, Lawrence NJ, Penny A, Millauer BA, Robinson S, Dornhorst A, de Swiet M, Steer PJ, Grenfell A, Mather HM *et al*. Implications of new diagnostic criteria for abnormal glucose homeostasis in women with previous gestational diabetes. *Diabetes Care* 1999 **22** 933–937. (doi:10.2337/diacare.22.6.933)
20 O'Sullivan EP, Avalos G, O'Reilly M, Dennedy MC, Gaffney G & Dunne F. Atlantic Diabetes in Pregnancy (DIP): the prevalence and outcomes of gestational diabetes mellitus using new diagnostic criteria. *Diabetologia* 2011 **54** 1670–1675. (doi:10.1007/s00125-011-2150-4)
21 Vital Statistics Fourth Quarter and Yearly Summary. Dublin, Ireland: Central Statistics Office, 2012. Dublin, Ireland: The Stationery Office; 2012.58 p. Report No.: 592.
22 Sacks DB, Arnold M, Bakris GL, Bruns DE, Horvath AR, Kirkman MS, Lernmark A, Metzger BE & Nathan DM. Guidelines and recommendations for laboratory analysis in the diagnosis and management of diabetes mellitus. *Diabetes Care* 2011 **34** e61–e99. (doi:10.2337/dc11-9998)
23 Gillespie P, O'Neill C, Avalos G, O'Reilly M & Dunne F. The cost of universal screening for gestational diabetes mellitus in Ireland. *Diabetic Medicine* 2011 **28** 912–918. (doi:10.1111/j.1464-5491.2011.03293.x)
24 Infanti JJ, Dunne FP, O Dea A, Gillespie P, Gibson I, Glynn LG, Noctor E, Newell J & McGuire BE. An evaluation of Croi MyAction community lifestyle modification programme compared to standard care to reduce progression to diabetes/pre-diabetes in women with prior gestational diabetes mellitus (GDM): study protocol for a randomised controlled trial. *Trials* 2013 **14** 121. (doi:10.1186/1745-6215-14-121)
25 Megia A, Naf S, Herranz L, Serrat N, Yanez RE, Simon I & Vendrell J. The usefulness of HbA1c in *postpartum* reclassification of gestational diabetes. *BJOG: an International Journal of Obstetrics and Gynaecology* 2012 **119** 891–894. (doi:10.1111/j.1471-0528.2012.03325.x)
26 Picon MJ, Murri M, Munoz A, Fernandez-Garcia JC, Gomez-Huelgas R & Tinahones FJ. Hemoglobin A1c versus oral glucose tolerance test in *postpartum* diabetes screening. *Diabetes Care* 2012 **35** 1648–1653. (doi:10.2337/dc11-2111)
27 Herman WH, Ma Y, Uwaifo G, Haffner S, Kahn SE, Horton ES, Lachin JM, Montez MG, Brenneman T & Barrett-Connor E. Differences in A1C by race and ethnicity among patients with impaired glucose tolerance in the Diabetes Prevention Program. *Diabetes Care* 2007 **30** 2453–2457. (doi:10.2337/dc06-2003)
28 Sacks DA, Hadden DR, Maresh M, Deerochanawong C, Dyer AR, Metzger BE, Lowe LP, Coustan DR, Hod M, Oats JJ *et al*. Frequency of gestational diabetes mellitus at collaborating centers based on IADPSG consensus panel-recommended criteria: the Hyperglycemia and Adverse Pregnancy Outcome (HAPO) Study. *Diabetes Care* 2012 **35** 526–528. (doi:10.2337/dc11-1641)
29 Kim C, Herman WH, Cheung NW, Gunderson EP & Richardson C. Comparison of hemoglobin A1c with fasting plasma glucose and 2-h postchallenge glucose for risk stratification among women with recent gestational diabetes mellitus. *Diabetes Care* 2011 **34** 1949–1951. (doi:10.2337/dc11-0269)

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