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Perinatal Outcomes of Two Screening Strategies for Gestational Diabetes Mellitus: A Randomized Controlled Trial

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Abstract

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Objective: To evaluate differences in short-term perinatal outcomes between the two prominent screening strategies for gestational diabetes mellitus (GDM), the International Association of Diabetes and Pregnancy Study Groups (IADPSG) and Carpenter-Coustan.

Methods: In this single-site, blinded, randomized, comparative effectiveness trial, participants received a non-fasting 50 g oral glucose tolerance test and if <200 mg/dL(<11.1mmol/L), were randomized to further screening with either IADPSG or Carpenter-Coustan criteria. Gestational diabetes treatment occurred per routine clinical care. The primary outcome was incidence of large-for-gestational age neonates. Prespecified secondary outcomes included small-for-gestational-age, cesarean birth and neonatal and maternal composites of adverse perinatal outcomes Assuming a 15% incidence of LGA neonates in the Carpenter-Coustan group, 782 participants provided more than 80% power to detect a 7% absolute risk reduction (RR) with the use of IADPSG; planned recruitment was 920 for anticipated attrition.

Results: From June 2015 to February 2019, 1,016 participants were enrolled and 921 were randomized to IADPSG (n = 461) or Carpenter-Coustan (n= 460) groups. Gestational diabetes incidence (14.4% vs. 4.5%, p<0.001) and diabetes medication use (9.3% vs. 2.4%; p<0.001) were more common in the IADPSG group; there were no differences in large-for-gestational age neonates, either overall (RR=0.90 [0.53, 1.52) or among women without gestational diabetes (RR=0.85 [0.49, 1.48). Those screened with IADPSG had higher rates of neonatal morbidity but fewer study-related adverse events. Rates of small-for-gestational age, cesarean birth, and maternal morbidity composite did not differ significantly between study groups.

Conclusions: The IADPSG screening criteria resulted in more women diagnosed and treated for gestational diabetes than Carpenter-Coustan without reducing the incidence of large-for-gestational age birth weight or maternal or neonatal morbidity.

Clinical Trial Registration: ClinicalTrials.gov, NCT02309138.

Precis

Compared to Carpenter-Coustan, the International Association of Diabetes and Pregnancy Study Groups criteria resulted in more women diagnosed and treated for gestational diabetes without reducing the incidence of large-for-gestational age neonates.

INTRODUCTION

In the United States, gestational diabetes mellitus (GDM) is commonly diagnosed by a two-step approach using the Carpenter-Coustan criteria based on two abnormal values during a 100-gm, 3-hour oral glucose tolerance test (OGTT).[87,9–11] The International Association of Diabetes and Pregnancy Study Group (IADPSG) proposed a one-step approach that defines GDM with one abnormal glucose value during a 75 gm, 2 hour OGTT based on the results of the Hyperglycemia and Adverse Pregnancy Outcomes (HAPO) study; this approach was intended to better identify women at risk for pregnancy-related maternal and neonatal complications with more mild hyperglycemia.[12] The National Institutes of Health Gestational Diabetes Consensus Development Conference Committee noted that the new IADPSG criteria compared to the Carpenter Coustan criteria could significantly increase the prevalence of GDM diagnoses and medical intervention without significant reduction in

adverse pregnancy outcomes; thus, experts recommended clinical trials to provide evidence to guide selection of the most appropriate diagnostic criteria.[13,14]

This pragmatic randomized controlled trial was designed to evaluate differences in perinatal outcomes between the IADPSG and Carpenter-Coustan screening approaches. Given that IADPSG is more sensitive for mild hyperglycemia, we hypothesized that: 1) women who undergo screening for GDM according to the IADPSG criteria will have lower rates of large-for-gestational age (LGA) neonates compared with those who undergo screening for GDM using the Carpenter-Coustan criteria; and 2) among the subset of women who are not diagnosed with GDM, those in the IADPSG group will have lower rates of LGA neonates compared with those in the Carpenter-Coustan group.

Methods

The Comparison of Two Screening Strategies for Gestational Diabetes (GDM2) trial was a single-center, parallel-group, comparative effectiveness trial. Pregnant women were recruited from 10 obstetric clinics affiliated with UPMC Magee Womens Hospital in Pittsburgh, PA, between June 2015 and February 2019. The trial design and study procedures were previously published[15] and were approved by the University of Pittsburgh's Institutional Review Board. Participants provided written informed consent before enrollment. An independent Data Safety Monitoring Board within the University of Pittsburgh Clinical and Translational Science Institute provided oversight.

Women between 18 and 45 years of age and between 18 weeks' and 28 weeks 6 days' pregnant were enrolled. Exclusion criteria were preexisting type 1 or 2 diabetes mellitus, diabetes diagnosed before 24 weeks' gestation, multifetal gestation, hypertension requiring medications, any corticosteroid use 30 days prior to enrollment, major congenital anomaly, anticipated preterm delivery before 28 weeks' gestation, inability to complete the glucose testing before 30 weeks' gestation, HIV infection, liver disease, and a history of gastric bypass surgery or other conditions that precluded OGTT consumption.

Baseline visits completed between 24 weeks 0 days' and 28 weeks 6 days' gestation included demographic and anthropometric assessments. All participants received a non-fasting 50 gm glucose challenge test (OGTT) and if the result was <200 mg/dL (<11.1mmol/L), were randomized to either the IADPSG or Carpenter-Coustan group. Women with 50 gm OGTT ≥ 200 mg/dL were presumed to have gestational diabetes and excluded from the study.

Participants presented to the second study visit, between 25 and 32 weeks' gestation, after an overnight fast. At visit 2, a fasting blood sample was collected for insulin, glucose, insulin resistance (HOMA-IR), and beta cell function (HOMA-β) to evaluate baseline metabolic profiles of the participants. Participants then received either the 2-hour 75 gm or 3-hour 100 gm OGTT. Participants were provided a snack and meal ticket after their OGTT, and all women with hypoglycemia noted on their OGTT were contacted by a member of the research team to assess for any ongoing symptoms of hypoglycemia.

GDM was diagnosed in the IADPSG group if the fasting 75 gm OGTT had at least one abnormal value (fasting ≥92 [5.11] | 1 hour ≥180 [9.99] | 2 hour ≥153 [8.49] mg/dL (mmol/L)); the 50 gm OGTT was ignored. GDM was diagnosed in the Carpenter-Coustan group if the 50 gm OGTT was ≥130 mg/dL (≥7.215 mmol/L) and the fasting 100 g OGTT test had ≥ 2 abnormal values (fasting ≥95 [5.27] | 1 hour ≥180 [9.99] | 2 hour ≥155 [8.60] | 3 hour ≥140 [7.77] mg/dL [mmol/L]).

Women included in this study received prenatal care in the maternal-fetal medicine and obstetric clinics in our integrated health system. After diagnosis of GDM, women underwent individualized nutritional counseling by certified diabetes educators in either a group (approximately 75%) or individualized (approximately 25%) setting. Women were advised to follow a carbohydrate-controlled diet with approximately 40–50% of energy from complex carbohydrates, 20–30% from protein, and 20–30% from fat. Self-monitoring of blood glucose four times daily was encouraged, and glucose targets included a fasting value less than 95 mg/dL, and one-hour post-prandial values less than 140 mg/dL.[16,17] Approximately 7 days after their diabetes education session, women were scheduled for a follow-up visit to discuss their GDM control and to obtain recommendations regarding therapy. In general, therapy was initiated or titrated when 30–50% of glucose values at any time point exceeded the recommended targets. However, final decisions regarding medical management of GDM were made pragmatically by the treating physician.

Stratified block randomization with varying block sizes was conducted by the statistician using STATA/SE 12.0 software (StataCorp, College Station, TX) to allocate participants to the screening groups in a 1:1 ratio. Stratification was based on clinic type (resident clinic, where care was provided by resident physicians supervised by attending physicians or by advanced practice professonals versus non-resident clinic, where patient care was provided by attending physicians or advanced practice professionals). We stratified by clinic type as the proportion of women with lower socioeconomic status was much higher in the resident clinics, which could affect the primary outcome if not considered during the enrollment process.., Participants were blinded to their randomized study group prior to arriving to their study visit. To minimize participant attrition due to a longer study visit, all participants were told that study visit 2 would last 4 hours. Obstetricians and nurse midwives were blinded to the screening criteria and glucose test values, and only notified that their patient did or did not have GDM. All study investigators, except the lead statistician, were blinded to the randomization schema and the study outcomes until completion unless the following occurred: (a) 50 gm OGTT ≥ 200 mg/dL (>11.1 mmol/L), (b) 50 gm OGTT <130 mg/dL (<7.22 mmol/L) and either a fasting glucose >105 mg/dL (>5.83 mmol/L) or a 2-hour ≥ 200 mg/dL (>11.1 mmol/L) on the 100 gm OGTT; or (c) a severe adverse event warranting immediate medical intervention. Women with a 50 gm OGTT ≥ 200 mg/dL (>11.1 mmol/L) were not randomized.

The primary outcome was LGA birth weight (≥90th percentile for sex and gestational age).[18] Secondary outcomes included: 1) small-for-gestational age birth weight (≤10th percentile for sex and gestational age)[18]; 2) macrosomia (birthweight ≥ 4000gm); 3) cesarean birth; 4) newborn length, weight, and head circumference; 5) a maternal morbidity composite (third- or fourth-degree perineal laceration, postpartum hemorrhage, or hypertensive disorder of

pregnancy including preeclampsia, eclampsia, HELLP and gestational hypertension);[19] and 6) a neonatal morbidity composite (clinical hypoglycemia as blood glucose <40 mg/dL [< 2.22 mmol/L] in the first 24 hours of life, clinical hyperbilirubinemia requiring phototherapy, stillbirth, and shoulder dystocia or brachial plexus injuries). Exploratory outcomes were neonatal hyperinsulinemia (cord blood C-peptide >90th percentile (1.70 ng/ml [0.567 nmol/L]),[7] and neonatal fat mass, lean mass and percent body fat assessed using validated skin fold measurements.[20] Additionally, use of glyburide, metformin, or insulin as well as healthcare utilization variables which included any obstetric ultrasound procedures, non-stress tests, neonatal intensive care unit admission and hospital length of stay, were exstracted from the electronic health record with the assistance of Center for Assistance in Research using eREcord (CARe) system.

Our co-primary hypotheses were: 1) women who undergo screening using the IADPSG criteria will have lower rates of LGA neonates compared with those who undergo screening using the Carpenter-Coustan criteria; and 2) among the subset of women who are not diagnosed with GDM, those in the IADPSG group will have lower rates of LGA neonates compared with those classified by Carpenter-Coustan criteria. For the first hypothesis, all participants were included in the analysis, while only the subset of participants without a diagnosis of GDM were considered for the second hypothesis.

Sample size calculations were based on a previous retrospective cohort study examining the association between different diagnostic criteria for GDM and adverse birth outcomes. [21] Assuming an incidence of LGA neonates of 15% in the Carpenter-Coustan group, 782 deliveries with complete ascertainment of the primary outcome provided more than 80% power to detect a 7% absolute risk reduction (RR) (small-to-moderate standardized effect size of approximately 0.22) for the first co-primary hypothesis. For the second co-primary hypothesis, 741 deliveries from the subset of women who were not diagnosed with GDM yielded approximately 86% power to see a similar reduction between-group reduction in LGA, assuming a 13% rate in the Carpenter-Coustan group. In terms of relative risk, these translate to a 47 and 54% relative reductions for the first and second co-primary hypothesis, respectively. In total, a sample size of 920 was planned to account for up to 15% attrition.

Within each study group, the primary and secondary outcomes were described using sample means or sample proportions along with 95% confidence intervals. Demographic and clinical characteristics were compared between groups at baseline using two-sample t-tests and chi-square tests. In the intention-to-treat analyses, logistic regression was used to quantify the probability of LGA as a function of the study group (IADPSG vs. Carpenter-Coustan) and clinic type (resident vs. non-resident). Relative risks and confidence intervals are presented as effect size estimates for LGA. As a sensitivity analysis, we conducted a per-protocol analysis that restricted our cohort to women who completed the screening method to which they were randomized. Additional sensitivity analyses included adjusting the primary analytic model for baseline marital status due to it’s association with study withdrawal.

Analyses of the secondary outcomes of cesarean birth, newborn size, and the maternal and neonatal composite outcome variables used logistic regression models with study group and

clinic type as covariates. Linear regression was used for newborn growth and body composition outcomes. Finally, we compared the proportion of women with serious adverse events between study groups using logistic regression. Similarly, relative risks and mean differences and confidence intervals are presented as measures of effect size.

To preserve an overall type I error of 5%, each of the co-primary hypotheses was based on a 2.5% significance level. Secondary outcomes were analyzed at the 5% significance level.

RESULTS

A total of 1,016 women completed the baseline visit; 921 were randomized to the IADPSG (n=461) or Carpenter-Coustan (n=460) groups (Figure 1). Following exclusion of those who withdrew from the study, were no longer eligible, or who did not have data regarding the primary outcome, 855 women were included in the intention-to-treat analysis.

Baseline demographic characteristics and risk factors for GDM were similar between screening groups (Table 1) overall, and within the subset who were not diagnosed with GDM (Appendix 1, available online at http://links.lww.com/xxx).

The overall incidence of GDM in this trial was 9.7% (n=80) and was significantly higher (14.5%, n=62) in the IADPSG group than in the Carpenter-Coustan group (4.5%, n =18); P<0.001). Among the total cohort, the incidence of GDM was similar in the non-resident clinics (10.2%, n=53) compared to the resident clinic (6.7%, n=27), P=0.062. However, among the 827 women who completed visit 2, the incidence of GDM was 11% among non-resident clinics vs 7.8% among resident clinics; P=0.152.

There were no significant differences in the incidence of LGA birth weight between the IADPSG and Carpenter-Coustan groups (Table 2). Similarly, the rate of LGA birth weight did not differ significantly among the subset of women without GDM. The per-protocol analyses of LGA incidences were also similar (data not shown). Additionally, after adjusting the co-primary analyses for marital status in a sensitivity analysis, we found negligible differences in the results (P=0.664 and P=0.571, respectively).

Rates of small-for-gestational age, newborn size, macrosomia, cesarean birth, and maternal morbidity did not differ significantly between study groups (Table 2). However, the relative risk of neonatal morbidity, defined by the neonatal composite outcome, was 40% higher in the IADPSG group compared with the Carpenter-Coustan group (Table 2).

Women in the IADPSG group were more likely to undergo fetal non-stress testing and receive medication (glyburide or insulin) for GDM compared with those in the Carpenter-Coustan group (Table 3). The proportion of women with at least 1 ultrasound performed was similar between the two groups.

A total of 284 adverse events occurred among 222 (24.1%) participants; the most common events including testing-related hypoglycemia, nausea, and vomiting (Appendix 2, available online at http://links.lww.com/xxx). Fewer women in the IADPSG group experienced at least one adverse event compared to those in the Carpenter-Coustan group. Serious adverse

events were rare and did not significantly differ by study group. Testing-related hypoglycemia (e.g. reactive hypoglycemia that occurred after the OGTT) was less common in the IADPSG group (4.3%) than in the Carpenter-Coustan (17.8%) group (p<0.0001). Nausea, vomiting, and dizziness were more frequent in the Carpenter-Coustan group.

We conducted a post hoc analysis to examine the frequency of LGA birth weight among the following subgroups GDM, no GDM by IADPSG; GDM, pre-GDM and no GDM by Carpenter Coustan (Appendix 3, available online at http://links.lww.com/xxx).

DISCUSSION

Use of the IADPSG screening criteria led to an increase in the number of women diagnosed with GDM and treated with medications. However, this did not result in significant differences in the rate of LGA neonates, cesarean birth, or maternal morbidity when compared withusing the Carpenter-Coustan criteria. Although the rate of neonatal morbidity was higher in women in the IADPSG group, there was no significant difference in the frequency of neonatal intensive care unit admissions, suggesting that the increased incidence of clinical hypoglycemia seen was mild in nature and possibly related to increased surveillance in the IADPSG group. Healthcare utilization was higher among women in the IADPSG group; these women were more likely to undergo fetal non-stress testing and receive medications, most commonly insulin, for GDM. These data indicate potential for increased medical interventions and costs to the healthcare system associated with adoption of the IADPSG criteria.

Treatment of GDM reduces adverse pregnancy outcomes.[21–29] Several cohort studies examined the association between using IADPSG criteria and clinical outcomes. These studies compared women who were screened for GDM in the period before the introduction of IADPSG, when Carpenter-Coustan criteria were used, with women who were screened in the time period afterward. The St. Carlos Study found that use of the IADPSG criteria increased the diagnosis of GDM 3.5-fold and was associated with a decrease in the rates of gestational hypertension, premature delivery, cesarean birth, small-for-gestational age, LGA, 1-minute Apgar scores <7, and neonatal intensive care unit admissions.[30] These findings, however, were not replicated by Pocobelli et al., who found that transition from Carpenter-Coustan to IADPSG criteria increased the diagnosis of GDM by 41%, as well as the use of insulin, labor induction, neonatal hypoglycemia, and outpatient non-stress testing while there was no association with other outcomes including cesarean birth or macrosomia.[31] Palatnik et al. found that use of the IADPSG criteria was associated with higher rates of GDM, cesarean birth, shoulder dystocia, and neonatal intensive care unit admission with no differences in rates of LGA birth weight.[32] None of these studies were RCTs comparing the use of IADPSG and Carpenter-Coustan criteria directly.

Hillier, et al. compared perinatal outcomes among 23,792 women randomized to either one-step or two-step screening for GDM as part of clinical care with all test results available to patients and healthcare practitioners. Similar to our findings, rates of GDM were higher in women screened using the one-step versus the two-step approach (16.5 vs 8.5%, RR 1.94 [1.79–2.11]) with no differences in LGA birth weight, perinatal composite morbidity,

hypertensive disorders of pregnancy, or primary cesarean birth.[33] Hillier, et al. also found that rates of neonatal hypoglycemia were higher in women screened with the one-step versus the two-step approach (9.2 vs 7.5%, RR 1.23 [1.12–1.34]). Our findings build on these results, as we were able to provide information on health care utilization (medications, fetal monitoring) between the two GDM testing strategies.

In the Carpenter-Coustan group, the higher rates of adverse events related to the glucose load were most likely due to differences between the trial protocol and usual care. In usual care, only those women with an elevated 50 g OGTT would undergo a 100 g OGTT, while in the trial everyone with a value <200 did either a 3-hour or 2-hour OGTT. If testing was performed per clinical care standards, only 4% of women in the Carpenter-Coustan group would have had adverse events because they would not have undergone testing, compared to the 13% of all women screened by IADPSG criteria.

A few study limitations deserve mention. First, our sample size was insufficient to compare outcomes among women who were diagnosed with GDM in each group. Approximately, 10,000 women would need to be randomized to the two study groups to have sufficient power to detect a difference in LGA among those diagnosed with GDM.Second, we estimated a higher rate of LGA (15%) in the Carpenter-Coustan group based on observed rates in our previous cohort study.[21] However, the actual rate of LGA in the Carpenter-Coustan group was 8.5%, which may have hampered our ability to detect a significant effect size similar to what was hypothesized a priori (i.e. 7% absolute reduction in LGA). Third, participant withdrawals before visit 2 were more common in the Carpenter-Coustan group than in the IADPSG group. Although this could have resulted in an underestimate of GDM incidence, demographic and clinical characteristics were similar between the 95 women who withdrew and those who remained, with the exception of marital status. In a sensitivity analysis adjusting for marital status, we found negligible differences in risk of LGA; thus, this differential attrition is unlikely to have affected the conclusions. Finally, all women received a 50 g OGTT, which would have been clinically unnecessary, if only the IADPSG criteria was used. Additionally, women with 50 g values ≥ 200 mg/dL (≥11.1 mmol/L) were not randomized and thus excluded, which slighted underestimated the incidence of GDM in the Carpenter Counstan group (4.5% without 50 g OGTT ≥200 mg/dL vs, 5.8% with the 50 g OGTT ≥200 mg/dL included). While we were unable to assess whether health team professionals remained completely blinded to the specific testing approach, performing the 50 g OGTT in both groups likely assisted with preserving blinding. In addition, healthcare practitioners did not have access to the numerical results.

Strengths of the GDM2 Trial include the randomized study design. The eligibility criteria were similar to women receiving GDM screening after 24 weeks' gestation in standard practice, and all participants were recruited and treated within a usual care setting. The results of the GDM2 Trial provide evidence that IADPSG criteria for diagnosing GDM increase the use of health care resources but do not reduce the risk for LGA birth weight or other pregnancy-related morbidities compared with Carpenter-Coustan.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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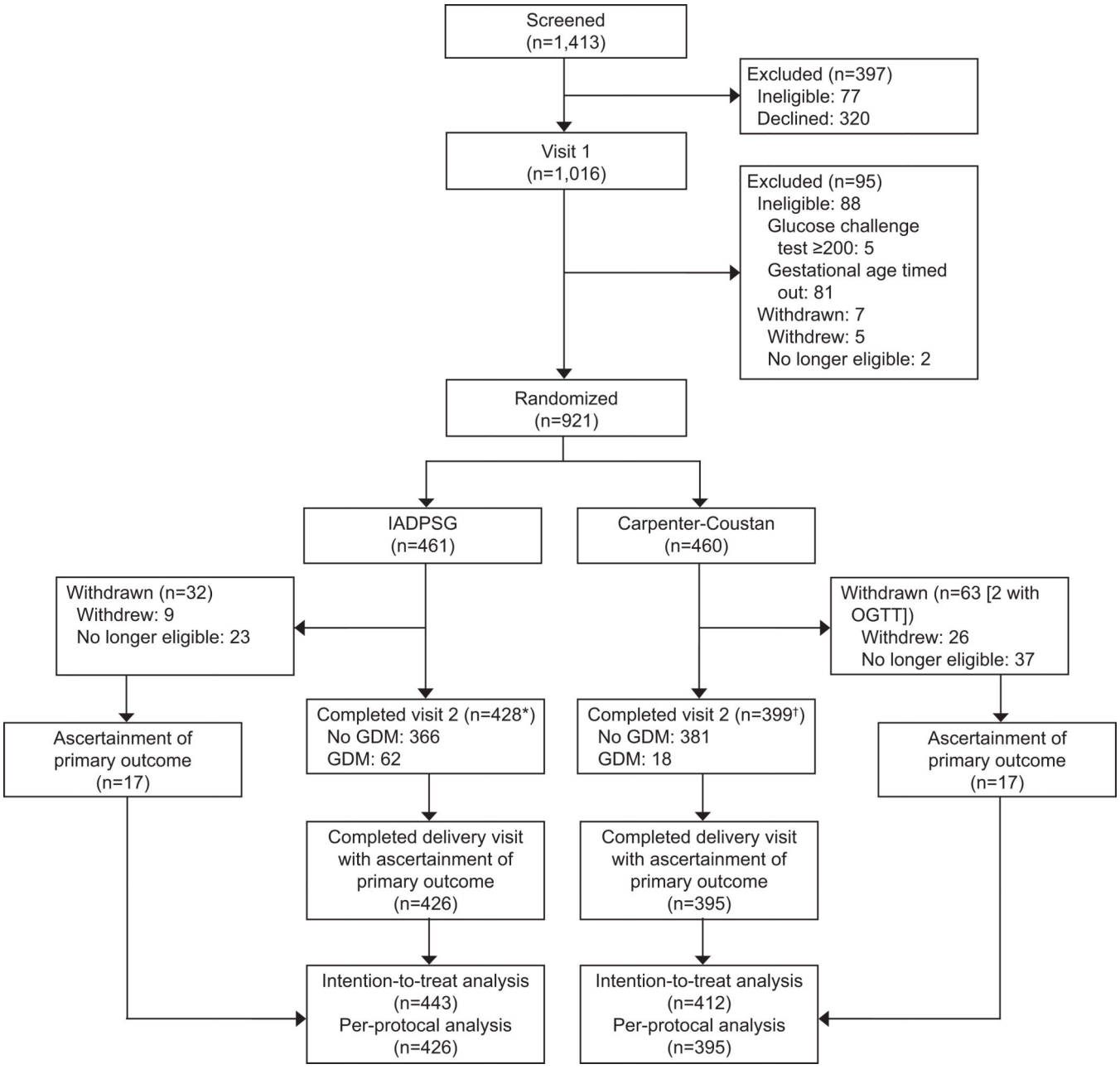

Figure 1:

Study participants screening, enrollment, randomization and follow-up. *One participant delivered before her visit 2 date and did not have a gestational diabetes classification. †Two participants withdrew at visit 2; however, they completed the oral glucose tolerance test (OGTT) and had a gestational diabetes mellitus (GDM) classification. IADPSG, The International Association of Diabetes and Pregnancy Study Groups.

Table 1.

Characteristics of randomized participants overall and by study group

Demographic and Clinical Characteristic	Overall (N=921)	IADPSG (n=461)	Carpenter-Coustan (n=460)
Measure	**Mean ± SD or n (%)**	**Mean ± SD or n (%)**	**Mean ± SD or n (%)**
Age, years	28.7 ± 5.2	28.6 ± 5.3	28.8 ± 5.1
Self-reported race *			
Asian	27 (2.9)	18 (3.9)	9 (2.0)
Black or African American	300 (32.7)	139 (30.2)	161 (35.2)
White	510 (55.6)	261 (56.7)	249 (54.4)
Other †	81 (8.8)	42 (9.1)	39 (8.5)
Ethnicity (Hispanic) *	30 (3.3)	15 (3.3)	15 (3.3)
Marital status (married)	429 (46.6)	215 (46.6)	214 (46.5)
Highest education			
Less than high school	46 (5.0)	24 (5.2)	22 (4.8)
High school diploma or GED	229 (24.9)	112 (24.3)	117 (25.4)
Some college (<4 years) or vocational	213 (23.1)	91 (19.7)	122 (26.5)
College degree	228 (24.8)	127 (27.5)	101 (22.0)
Master's degree	129 (14.0)	67 (14.5)	62 (13.5)
Doctoral, law, or medical degree or higher	76 (8.3)	40 (8.7)	36 (7.8)
Employment (working full-time or part-time)	621 (67.4)	310 (67.2)	311 (67.6)
Clinic type			
Demographic and Clinical Characteristic	**Overall (N=921)**	**IADPSG (n=461)**	**Carpenter-Coustan (n=460)**
Measure	**Mean ± SD or n (%)**	**Mean ± SD or n (%)**	**Mean ± SD or n (%)**
Resident	402 (43.6)	202 (43.8)	200 (43.5)
Non-resident	519 (56.4)	259 (56.2)	260 (56.5)
Pre-pregnancy BMI, kg/m^2 ‡	26.8 ± 7.0	26.9 ± 7.2	26.6 ± 6.8
BMI, kg/m^2 at OGTT	30.0 ± 7.0	30.0 ± 6.8	30.0 ± 7.2
Glucose Challenge 50 gm test, mg/dl §	106.2 ± 28.3	107.8 ± 28.9	104.7 ± 27.7
Fasting Insulin, ¼IU/mL §,¶	10.8 ± 9.6	11.2 ± 10.1	10.4 ± 8.9
Fasting Glucose, mg/dl §,¶	79.8 ± 9.1	79.8 ± 9.3	79.8 ± 8.8
HOMA-IR ¶	2.2 ± 2.3	2.3 ± 2.4	2.2 ± 2.2
HOMA-beta **	255.8 ± 319.7	277.4 ± 388.0	232.7 ± 222.6
Pre-pregnancy BMI category ‡			
Underweight (< 18.5)	36 (4.4)	17 (4.0)	19 (4.8)
Normal (18.5 to <25)	370 (44.7)	192 (44.9)	178 (44.6)
Overweight (25.0 to <30)	201 (24.3)	100 (23.4)	101 (25.3)
Obese (30.0 or higher)	220 (26.6)	119 (27.8)	101 (25.3)
Previous history of gestational diabetes ††	22 (2.7)	14 (3.3)	8 (2.0)

Demographic and Clinical Characteristic	Overall (N=921)	IADPSG (n=461)	Carpenter-Coustan (n=460)
Measure	**Mean ± SD or n (%)**	**Mean ± SD or n (%)**	**Mean ± SD or n (%)**
First-degree family history of diabetes ##	200 (24.8)	103 (24.8)	97 (24.7)

* Denotes 1 and 2 women missing this variable in the IADPSG and Carpenter-Coustan groups, respectively. Race was collected to evaluate if women of all races were adequately represented within the trial.

† includes American Indian, native Hawaiian, more than one race and other

‡ denotes 33 and 61 women missing this variable in the IADPSG and Carpenter-Coustan groups, respectively.

§ Conversion factor to SI Units for Glucose Challenge Test (mmol/L), Insulin (pmol/L), Glucose (mmol/L), and High Sensitivity C Reactive Protein (nmol/L) is 0.0555, 6.945, 0.0555, and 95.2381, respectively.

¶ denotes 32 and 60 women missing this variable in the IADPSG and Carpenter-Coustan groups, respectively.

** denotes 36 and 64 women missing this variable in the IADPSG and Carpenter-Coustan groups, respectively.

†† denotes 32 and 61 women missing this variable in the IADPSG and Carpenter-Coustan groups, respectively.

denotes 46 and 67 women missing this variable in the IADPSG and Carpenter-Coustan groups, respectively.

Table 2.

Delivery outcomes

		Overall (N=878) Mean ± SD or n (%)				Among participants without GDM (N=746) Mean ± SD or n (%)		
Type of Delivery Outcome	**N**	**IADPSG (n=451)**	**Carpenter-Coustan (n=427)**	**Relative Risk / Mean Difference (95% CI)**	**N**	**IADPSG w/ No GDM (n=366)**	**Carpenter-Coustan w/ No GDM (n=380)**	**Relative Risk/ Mean Difference (95% CI)**
Infant Female sex	872	222 (49.4)	184 (43.5)	-	742	177 (48.5)	169 (44.8)	
Gestational age (weeks)	863	38.7 ± 2.1	39.1 ± 1.8	-	746	38.8 ± 2.0	39.2 ± 1.8	
Primary outcome								
Large for gestational age (LGA) *	855	34 (7.7)	35 (8.5)	0.90 (0.53, 1.52) **	741	28 (7.7)	34 (9.0)	0.85 (0.49, 1.48) **
Secondary outcomes								
Small for gestational age (SGA) *	855	53 (12.0)	53 (12.9)	0.93 (0.65, 1.33)	741	42 (11.5)	47 (12.5)	0.93 (0.63, 1.37)
Macrosomia (weight ≥ 4000 gm)	873	29 (6.5)	29 (6.8)	0.94 (0.57, 1.55)	742	23 (6.3)	28 (7.4)	0.85 (0.50, 1.45)
Cesarean birth	872	131 (29.2)	118 (27.9)	1.05 (0.85, 1.29)	742	101 (27.7)	101 (26.8)	1.03 (0.82, 1.31)
Fetal Size								
Weight (gm)	873	3175.6 ± 580.7	3243.5 ± 535.1	−69.3 (−140.5, 1.8)	742	3179.5 ± 559.1	3261.3 ± 530.5	−73.5 (−148.0, 1.1)
Length (cm)	855	50.1 ± 3.2	50.4 ± 3.2	−0.3 (−0.7, 0.1)	730	50.1 ± 3.1	50.5 ± 2.8	−0.4 (−0.8, −0.01)
Head circumference (cm)	851	33.9 ± 1.9	34.0 ± 1.8	−0.1 (−0.4, 0.1)	727	33.9 ± 1.9	34.0 ± 1.7	−0.2 (−0.4, 0.1)
Maternal Composite	867	77 (17.4)	75 (17.6)	0.99 (0.74, 1.31)	744	62 (17.0)	63 (16.6)	1.02 (0.74, 1.41)
3rd or 4th degree vaginal laceration		7 (1.6)	10 (2.4)			5 (1.4)	10 (2.6)	
Postpartum hemorrhage		14 (3.2)	5 (1.2)			11 (3.0)	3 (0.8)	
Hypertensive disorders of pregnancy		58 (13.1)	64 (15.1)			48 (13.2)	52 (13.7)	
Neonatal Composite	867	83 (18.8)	57 (13.4)	1.40 (1.03, 1.91)	744	57 (15.6)	48 (12.7)	1.23 (0.86, 1.76)
Clinical Hypoglycemia #		56 (12.7)	39 (9.2)			35 (9.6)	33 (8.7)	
Clinical Hyperbilirubinemia #		20 (4.5)	16 (3.8)			16 (4.4)	14 (3.7)	
Stillbirth		4 (0.9)	2 (0.5)			3 (0.8)	1 (0.3)	
Birth trauma		8 (1.8)	4 (0.9)			7 (1.9)	4 (1.1)	
Exploratory Outcomes								
Fetal Adiposity	359				331			

		Overall (N=878) Mean ± SD or n (%)				Among participants without GDM (N=746) Mean ± SD or n (%)		
Type of Delivery Outcome	**N**	**IADPSG (n=451)**	**Carpenter-Coustan (n=427)**	**Relative Risk / Mean Difference (95% CI)**	**N**	**IADPSG w/ No GDM (n=366)**	**Carpenter-Coustan w/ No GDM (n=380)**	**Relative Risk/ Mean Difference (95% CI)**
Fat mass (g)		381.7 ± 175.0	392.2 ± 178.1	−11.1 (−47.4, 25.1)		386.4 ± 169.3	397.0 ± 177.1	−10.4 (−47.3, 26.6)
Lean mass (g)		2887.8 ± 345.4	2885.1 ± 326.3	0.6 (−66.8, 68.0)		2888.8 ± 342.2	2896.4 ± 323.6	−7.0 (−76.1, 62.2)
Percent body fat (%)		11.2 ± 4.1	11.5 ± 4.1	−0.3 (−1.2, 0.5)		11.4 ± 4.0	11.6 ± 4.0	−0.3 (−1.1, 0.6)
C-Peptide (ng/ml) ^	474	0.8 ± 0.5	0.8 ± 0.5	0.03 (−0.06, 0.11)	437	0.8 ± 0.5	0.8 ± 0.5	0.03 (−0.07, 0.12)
Hyperinsulinemia	474	16 (6.7)	13 (5.6)	1.22 (0.57, 2.60)	437	13 (6.1)	12 (5.4)	1.15 (0.51, 2.58)
NICU admission	811	62 (15.0)	47 (11.8)	1.31 (0.87, 1.97)	704	49 (14.3)	40 (11.0)	1.32 (0.84, 2.08)
Infant length of stay (days)	811	3.0 ± 1.6	2.9 ± 1.3	0.04 (−0.16, 0.24)	704	2.9 ± 1.1	2.9 ± 1.3	−0.03 (−0.21, 0.15)

GDM = gestational diabetes

* Accounts for gestational age and baby's sex (Talge)

** 2.5% CI

clinical hypoglycemia = blood glucose <40 mg/dL [< 2.22 mmol/L] in the first 24 hours of life, clinical hyperbilirubinemia defined requiring phototherapy

^ Conversion factor to SI Units (nmol/L): 0.333.

Note: Adjusted for treatment group and stratification group. Relative Risk for IADPSG group compared to Carpenter-Coustan group shown.

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Table 3.

Healthcare Utilization and Gestational Diabetes Medication Therapy

	Overall (N=921)							Among participants with no GDM (N=747)						
Type of Health Care and GDM Therapy Prescribed	**IADPSG (n=461)**			**Carpenter-Coustan (n=460)**				**IADPSG (n=366)**			**Carpenter-Coustan (n=381)**			
	# procedures	**# persons**	**% of randomized participants**	**# procedures**	**# persons**	**% of randomized participants**	**p-value**	**# procedures**	**# persons**	**% of randomized participants**	**# procedures**	**# persons**	**% of randomized participants**	**p-value**
Any ultrasound procedure*	504	256	55.5	413	234	50.9	0.16	364	193	52.7	377	215	56.4	0.31
Fetal non-stress test (CPT code 59025)	186	57	12.4	94	38	8.3	0.04	98	40	10.9	56	29	7.6	0.12
Any GDM medication prescribed	-	43	9.3	-	11	2.4	<.0001	-	0	0	-	0	0	-
Glyburide	-	7	1.5	-	1	0.2	0.07 (F)	-	0	0	-	0	0	-
Insulin	-	38	8.2	-	10	2.2	<.0001	-	0	0	-	0	0	-
Metformin	-	0	0	-	0	0	-	-	0	0	-	0	0	-

GDM = gestational diabetes

*Includes CPT codes 76805, 76811, 76815, 76816, 76818, 76819.