Maternal and Neonatal Morbidity for Women Who Would Be Added to the Diagnosis of GDM Using IADPSG Criteria: A Secondary Analysis of the Hyperglycemia and Adverse Pregnancy Outcome Study

Thaddeus P. Waters,[1] Alan R. Dyer,[2] Denise M. Scholtens,[2] Sharon L. Dooley,[2] Elaine Herer,[3] Lynn P. Lowe,[2] Jeremy J.N. Oats,[4] Bengt Persson,[5] David A. Sacks,[6] Boyd E. Metzger,[2] and Patrick M. Catalano,[7] for the HAPO Cooperative Study Research Group

Diabetes Care 2016;39:2204–2210 | DOI: 10.2337/dc16-1194

OBJECTIVE

To assess the frequency of adverse outcomes for women who are diagnosed with gestational diabetes mellitus (GDM) by the International Association of the Diabetes and Pregnancy Study Groups (IADPSG) criteria using data from the Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study.

RESEARCH DESIGN AND METHODS

This is a secondary analysis from the North American HAPO study centers. Glucose measurements from a 75-g oral glucose tolerance test were used to group participants into three nonoverlapping categories: GDM based on Carpenter-Coustan (CC) criteria (also GDM based on IADPSG criteria), GDM diagnosed based on IADPSG criteria but not CC criteria, and no GDM. Newborn outcomes included birth weight, cord C-peptide, and newborn percentage fat above the 90th percentile; maternal outcomes included primary cesarean delivery and preeclampsia. Outcome frequencies were compared using multiple logistic regression, adjusting for predefined covariates.

RESULTS

Among 25,505 HAPO study participants, 6,159 blinded participants from North American centers were included. Of these, 81% had normal glucose testing, 4.2% had GDM based on CC criteria, and 14.3% had GDM based on IADPSG criteria but not CC criteria. Compared with women with no GDM, those diagnosed with GDM based on IADPSG criteria had adjusted odds ratios (95% CIs) for birth weight, cord C-peptide, and newborn percentage fat above the 90th percentile, as well as primary cesarean delivery and preeclampsia, of 1.87 (1.50–2.34), 2.00 (1.54–2.58), 1.73 (1.35–2.23), 1.31 (1.07–1.60), and 1.73 (1.32–2.27), respectively.

CONCLUSIONS

Women diagnosed with GDM based on IADPSG criteria had higher adverse outcome frequencies compared with women with no GDM. These data underscore the need for research to assess the effect of treatment to improve outcomes in such women.

[1]Department of Obstetrics and Gynecology, Loyola University Medical Center, Maywood, IL
[2]Northwestern University Feinberg School of Medicine, Chicago, IL
[3]Sunnybrook Health Sciences Centre, Toronto, Ontario, Canada
[4]Obstetric Medicine, Melbourne School of Population and Global Health, University of Melbourne, Carlton, Victoria, Australia
[5]Department of Pediatrics, Karolinska Institute, Stockholm, Sweden
[6]Department of Obstetrics and Gynecology, Kaiser Foundation Hospital, Bellflower, CA
[7]Department of Reproductive Biology, Case Western Reserve University at MetroHealth Medical Center, Cleveland, OH

Corresponding author: Thaddeus P. Waters, tedwatersmd@gmail.com.

Received 2 June 2016 and accepted 26 August 2016.

Gestational diabetes mellitus (GDM) is a common metabolic complication of pregnancy defined as glucose intolerance first identified during pregnancy (1). In the U.S., American Congress of Obstetricians and Gynecologists (ACOG) guidelines for diagnosis of GDM currently consist of a two-step process: screening with a random 50-g glucose load followed by a diagnostic 100-g, 3-h oral glucose tolerance test (OGTT) for those who equal or exceed a designated threshold on the initial screen (2).

Given the findings of the Hyperglycemia and Adverse Pregnancy Outcome study (HAPO) (3), the International Association of the Diabetes and Pregnancy Study Groups (IADPSG) proposed new criteria for the diagnosis of GDM (4). In brief, the IADPSG criteria for GDM were based on the average glucose value observed at the fasting time point and 1 or 2 h after a 75-g OGTT for women with at least 1.75 times the odds (relative to the HAPO cohort mean) for birth weight above the 90th percentile, cord C-peptide above the 90th percentile, and percentage body fat above the 90th percentile.

The utility of the IADPSG criteria for diagnosing GDM has generated much discussion regarding conflicting data about maternal and neonatal outcomes (5–8). An ongoing question is whether women diagnosed with GDM by IADPSG criteria who are classified as not having GDM based on Carpenter-Coustan (CC) criteria have clear risks of adverse perinatal outcomes. On the basis of these and other concerns, one-step GDM testing using IADPSG criteria has been endorsed by the World Health Organization and the International Diabetes Federation (9,10) but not by ACOG (2).

The purpose of this analysis was to evaluate whether women with IADPSG criteria for GDM, after excluding those who had GDM based on the CC criteria (11), are at increased risk for adverse outcomes when compared with women with no GDM based on the IADPSG criteria, using data from HAPO. Outcomes of interest included the frequency of large-for-gestational-age newborns (above the 90th percentile for the gestational age–specific threshold), newborn adiposity above the 90th percentile, newborn cord blood C-peptide above the 90th percentile, and other maternal morbidities such as maternal preeclampsia and primary cesarean delivery.

RESEARCH DESIGN AND METHODS

In brief, HAPO was a prospective, observational study of 25,505 pregnant women who underwent a 75-g OGTT between 24 to 32 weeks' gestation at one of 15 centers in 9 countries. The parent study protocol was approved by the institutional review board at all 15 field centers. All participants gave written informed consent. Medical caregivers and participants were "blinded" to glucose tolerance test results, unless glucose values exceeded predefined thresholds, meriting further follow-up (12). For this secondary analysis, we limited the data to the 6,159 participants who had blinded data and who participated only through one of the North American centers (members of the HAPO Study Cooperative Research Group North American Field Centers: Kaiser Foundation Hospital, Bellflower, CA; Prentice Women's Hospital of Northwestern Memorial Hospital–Northwestern University Feinberg School of Medicine, Chicago, IL; MetroHealth Medical Center–Case Western Reserve University, Cleveland, OH; Women and Infants' Hospital of Rhode Island–Brown University Medical School, Providence, RI; Sunnybrook and Women's College Health Sciences Centre–University of Toronto, Toronto, Ontario, Canada). Detailed study methods have been previously published (12). A brief overview is presented here.

Women were excluded from participation in HAPO if they were $<$18 years old, delivery was planned at another hospital, the date of the last menstrual period was not definitive and there was no ultrasound estimation from 6 to 24 weeks of gestational age available, they were unable to complete the OGTT within the designated window (24 to 32 weeks' gestation), it was a multiple pregnancy, conception was achieved using gonadotropin ovulation induction or in vitro fertilization, they underwent glucose testing before recruitment or received a diagnosis of diabetes during this pregnancy, they had glucose measurements outside HAPO after enrollment, they had diabetes antedating pregnancy requiring treatment with medication, they participated in another study that may interfere with HAPO, they were known to be HIV-positive or to have hepatitis B or C, they previously participated in HAPO, or they were unable to converse in the languages used on field center forms without the aid of an interpreter.

Participants in HAPO underwent a standard fasting 75-g OGTT between 24 and 32 weeks of gestation. Samples were collected at fasting and 1 and 2 h following the glucose load. To avoid confounding effects of center-to-center analytical variation, all OGTT specimens were analyzed at the HAPO Central Laboratory (Belfast, Northern Ireland, U.K.) using a chemical analyzer (Vitros 750; Ortho Clinical Diagnostics, Rochester, NY), and those results are used here.

For this study, the results of the 75-g OGTT were used to stratify participants into one of three unique (nonoverlapping) groups: *1*) women with no GDM per either the IADPSG or CC criteria; *2*) women with GDM based on CC criteria (diagnosed if a woman has $\geq$2 abnormal values using the following OGTT thresholds: fasting $\geq$95 mg/dL; 1 h $\geq$180 mg/dL ; 2 h $\geq$155 mg/dL); or *3*) women meeting IADPSG criteria for GDM (one or more abnormal values using the following OGTT thresholds: fasting $\geq$92 mg/dL; 1 h $\geq$180 mg/dL; 2 h $\geq$153 mg/dL), excluding those meeting CC criteria. Of note, a 3-h result was not used as part of the criteria for CC-based GDM in this study because no such value was available for HAPO participants. Also, while CC criteria were used to identify which subjects would be diagnosed with GDM based on IADPSG criteria for the purposes of this analysis, subjects categorized either as GDM diagnosed based on IADPSG or GDM based on CC criteria would both qualify for GDM per IADPSG criteria. Outcomes of interest were compared among study groups, with women having no GDM based on IADPSG criteria serving as the referent group.

HAPO outcomes examined in this report include birth weight above the 90th percentile, cord C-peptide above the 90th percentile, newborn percentage body fat above the 90th percentile, primary cesarean delivery, neonatal hypoglycemia, sum of skin folds above the 90th percentile, preeclampsia, premature delivery (defined as delivery before 37 weeks' gestation), shoulder dystocia or birth injury, newborn admission to the neonatal intensive care unit (NICU), and hyperbilirubinemia. Ninetieth percentiles for birth weight for gestational age (30–44 weeks only) were

determined using quantile regression analyses for each of eight newborn sex-ethnic groups (Caucasian or other, black, Hispanic, Asian), with adjustment for gestational age, field center, and parity. A newborn was considered to have a birth weight above the 90th percentile if the birth weight was greater than the estimated 90th percentile for the baby's sex, gestational age, and ethnicity; field center; and maternal parity. Otherwise, the newborn was considered to have a birth weight below the 90th percentile. Newborn cord blood C-peptide was derived from specimens obtained at the time of delivery; the 90th percentile was derived from the values for the total HAPO sample. Newborn percentage body fat above the 90th percentile was defined based on sex, ethnicity, field center, gestational age (≥36 weeks only), and maternal parity using quantile regression analysis. Clinical neonatal hypoglycemia was defined as present if there was notation of neonatal hypoglycemia in the medical record and there were symptoms and/or treatment with a glucose infusion or a local laboratory report of a glucose value <1.7 mmol/L (30.6 mg/dL) in the first 24 h and/or <2.5 mmol/L (45 mg/dL) after the first 24 h after birth. Preeclampsia was defined as systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg on two or more occasions a minimum of 6 h apart and proteinuria of 1+ or more on a dipstick test or a protein level in the urine ≥300 mg for a 24-h period. If the criteria for elevated blood pressure were met but those for proteinuria were not, the hypertension was classified as gestational hypertension. Intensive neonatal care was defined by admission to any type of unit for care more intensive than normal newborn care and lasting more than 24 h, or by the death of the baby or transfer to another hospital. Data were excluded for admissions that were only for possible sepsis or sepsis, observation, or feeding problems. Hyperbilirubinemia was defined by treatment with phototherapy after birth, at least one laboratory report of a bilirubin concentration ≥20 mg/dL (342 μmol/L), or readmission for hyperbilirubinemia.

Maternal and newborn characteristics not used for defining GDM categories or outcomes were compared across the three GDM categories (no GDM, IADPSG GDM [not CC], CC GDM) using ANOVA for continuous variables and χ^2 tests for categorical variables. Multiple logistic regression was used to estimate odds ratios and 95% CIs for dichotomous outcomes for both IADPSG GDM (not CC) and CC GDM groups versus the referent group with no GDM. Model adjustments depended on the outcome and are consistent with HAPO analyses using the full cohort (3,13). For newborn birth weight, percentage body fat, and sum of skinfolds above the 90th percentile, model I adjusted for variables used in estimated 90th percentiles, and model II additionally adjusted for age, height, BMI, and gestational age at OGTT; smoking; alcohol use; hospitalization before delivery; family history of diabetes; and mean arterial pressure. For cord C-peptide above the 90th percentile, model I adjusted for field center and model II additionally adjusted for age, height, BMI, and gestational age at the OGTT; smoking; alcohol use; hospitalization before delivery; family history of diabetes; parity; baby's sex; mean arterial pressure at the OGTT; and cord glucose. For primary cesarean delivery, model I adjusted for field center and model II additionally adjusted for age, height, BMI, and gestational age at the OGTT; smoking; alcohol use; hospitalization before delivery; family history of diabetes; baby's sex; and mean arterial pressure. For preeclampsia, model I adjusted for field center and model II additionally adjusted for age, height, BMI, and gestational age at the OGTT; smoking; alcohol use; family history of diabetes; family history of high blood pressure; parity; baby's sex; and maternal urinary tract infection. Model adjustments for all other outcomes were the same as for cord C-peptide above the 90th percentile, except that cord glucose was not included in model II adjustments. All analyses were performed using Stata 11. A P value <0.05 was considered significant.

RESULTS

Table 1 presents the maternal and demographic characteristics of the North American cohort by the classification of GDM used for this analysis. Overall, 261 subjects (4.2%) met criteria for GDM based on the CC criteria (GDM by CC), 878 (14.3%) were diagnosed with GDM based on IADPSG criteria but not CC criteria (GDM diagnosed based on IADPSG), and 5,020 (81.5%) had no GDM. Significant differences across groups were noted in this analysis, including maternal age, history of pregnancy, prepregnancy BMI, height, BMI at OGTT, and mean arterial blood pressure; women in the no GDM group were younger, taller, and more often nulliparous and had a lower blood pressure and BMI. Women without GDM were more often Caucasian or African American and less often Hispanic, less often had a family history of diabetes, and had a lower frequency of tobacco use when compared with those in either GDM group. Gestational age at the time of OGTT and newborn sex were not different between groups.

Table 2 presents the relevant maternal and neonatal outcomes according to our study groups. Higher frequencies were noted for birth weight above the 90th percentile (15.3% vs. 7.9%), cord blood C-peptide above the 90th percentile (14.5% vs. 6.0%), and newborn percentage body fat above the 90th percentile (15.3% vs. 8.1%) for women diagnosed with GDM based on IADPSG criteria compared with women with no GDM. In addition, the frequencies of primary cesarean delivery (23.9% vs. 17.2%), neonatal hypoglycemia (2.9% vs. 1.3%), newborn sum of skinfolds above the 90th percentile (16.2% vs. 7.6%), and preeclampsia (14.9% vs. 6.4%) were higher for women diagnosed with GDM based on IADPSG criteria compared with those without GDM. These findings were significant in both the model I and model II adjusted analyses. Delivery before 37 weeks was more common for those in the GDM diagnosed based on IADPSG group when compared with those with no GDM (7.7% vs. 6.0%), as was shoulder dystocia (3.0% vs. 1.8%) and NICU admission (8.1% vs. 6.3%). However, these differences were not significant in the adjusted model I and model II analyses. Results for those participants fulfilling criteria for CC-based GDM (also GDM based on IADPSG criteria) had outcome frequencies that were, in general, similar to or higher than those diagnosed with GDM based on the IADPSG criteria.

CONCLUSIONS

Using data from HAPO, we examined the frequencies of adverse neonatal and

Table 1—Descriptive statistics for the HAPO North American cohort

	All (*N* = 6,159)	No GDM (*n* = 5,020)	GDM based on IADPSG criteria (*n* = 878)	GDM based on CC criteria (*n* = 261)	*P* value*
Maternal characteristics					
Age at OGTT, years	30.3 (5.7)	30.1 (5.8)	31.0 (5.6)	32.3 (5.3)	<0.001
BMI at OGTT, kg/m^2	28.8 (5.4)	28.2 (4.9)	31.5 (6.4)	31.6 (5.8)	<0.001
Height at OGTT, cm	162.5 (6.8)	162.7 (6.8)	161.9 (6.7)	160.9 (6.7)	<0.001
Mean arterial pressure at OGTT, mmHg	83.2 (8.0)	82.7 (7.9)	85.4 (8.5)	86.0 (8.3)	<0.001
Prepregnancy BMI, kg/m^2	25.0 (5.3)	24.4 (4.9)	27.5 (6.4)	27.7 (5.9)	<0.001
Fasting plasma glucose, mg/dL	82.6 (6.9)	80.6 (5.2)	90.8 (6.3)	93.0 (7.8)	—
1-h plasma glucose, mg/dL	133.0 (30.7)	125.1 (22.8)	160.0 (28.1)	195.3 (15.2)	—
2-h plasma glucose, mg/dL	110.1 (23.3)	104.8 (18.8)	125.9 (22.6)	159.0 (23.4)	—
Field center, *n* (%)					<0.001
Bellflower, CA	1,903 (30.9)	1,468 (29.2)	340 (38.7)	95 (36.4)	
Chicago, IL	738 (12.0)	616 (12.3)	97 (11.1)	25 (9.6)	
Cleveland, OH	784 (12.7)	598 (11.9)	142 (16.2)	44 (16.9)	
Providence, RI	746 (12.1)	640 (12.8)	82 (9.3)	24 (9.2)	
Toronto, ON, Canada	1,988 (32.2)	1,698 (33.8)	217 (24.7)	73 (28.0)	
Race/ethnicity, *n* (%)					<0.001
White	3,099 (50.3)	2,620 (52.2)	371 (42.3)	108 (41.4)	
Black	525 (8.5)	438 (8.7)	67 (7.6)	20 (7.7)	
Hispanic	1,984 (32.2)	1,547 (30.8)	343 (39.1)	94 (36.0)	
Asian	397 (6.5)	290 (5.8)	76 (8.7)	31 (11.9)	
Other	154 (2.5)	125 (2.5)	21 (2.4)	8 (3.1)	
Parity, *n* (%)					<0.001
0	2,939 (47.7)	2,465 (49.1)	359 (40.9)	115 (44.1)	
1	1,949 (31.6)	1,587 (31.6)	288 (32.8)	74 (28.4)	
≥2	1,271 (20.6)	968 (19.3)	231 (26.3)	72 (27.6)	
Alcohol use during pregnancy (any), *n* (%)	203 (3.3)	172 (3.4)	24 (2.7)	7 (2.7)	0.49
Smoking during pregnancy (any), *n* (%)	301 (4.9)	226 (4.5)	56 (6.4)	19 (7.3)	0.011
Family history of diabetes, *n* (%)	1,386 (22.5)	1,031 (20.5)	261 (29.7)	94 36.0)	<0.001
Family history of hypertension, *n* (%)	2,650 (43.0)	2,134 (42.5)	389 (44.3)	127 (48.7)	0.11
Hospitalization before delivery, *n* (%)	240 (3.9)	179 (3.6)	48 (5.5)	13 (5.0)	0.018
Maternal UTI, *n* (%)	729 (11.8)	575 (11.5)	125 (14.2)	29 (11.1)	0.058
Newborn characteristics					
Birth weight, g	3,408 (516)	3,386 (505)	3,505 (539)	3,510 (599)	—
Body fat, %	12.3 (3.5)	12.1 (3.5)	13.2 (3.7)	13.3 (3.8)	—
Sum of skin folds, mm	12.3 (2.6)	12.1 (2.5)	13.1 (2.8)	13.4 (3.1)	—
Cord blood C-peptide, ug/L	0.98 (0.57)	0.93 (0.53)	1.17 (0.84)	1.36 (0.78)	—
Cord blood glucose, mg/dL	76.9 (15.9)	76.4 (15.4)	78.3 (16.8)	80.7 (20.0)	<0.001
Gestational age, weeks					
At OGTT	27.6 (1.7)	27.6 (1.7)	27.5 (1.8)	27.7 (1.7)	0.30
At delivery	39.6 (1.3)	39.6 (1.2)	39.5 (1.3)	39.2 (1.3)	—
Sex, *n* (%)					0.84
Male	3,191 (51.8)	2,593 (51.7)	463 (52.7)	135 (51.7)	
Female	2,968 (48.2)	2,427 (48.3)	415 (47.3)	126 (48.3)	

Data are mean (SD), unless otherwise stated. *Characteristics were compared across the categories of no GDM, GDM diagnosed based on IADPSG criteria, and GDM based on CC criteria (also GDM based on IADPSG criteria) using ANOVA for continuous variables and χ^2 tests for categorical variables. Maternal glucose values were not compared across groups because they were used to define the IADPSG and CC categories. Newborn birth weight, body fat, sum of skinfolds, cord blood C-peptide, and gestational age at delivery were not compared across groups because these variables were dichotomized and treated as formal outcomes in adjusted logistic regression analyses. UTI, urinary tract infection.

maternal outcomes for women who would be diagnosed with GDM using IADPSG criteria. For birth weight above the 90th percentile, we observed that infants of women diagnosed with GDM based on IADPSG criteria had a significantly higher frequency of this outcome compared with those with no GDM. Those who would be diagnosed with GDM based on IADPSG criteria also had higher frequencies of newborn percentage body fat above the 90th percentile, cord blood C-peptide above the 90th percentile, primary cesarean delivery, neonatal hypoglycemia, newborn sum of skinfolds above the 90th percentile, and preeclampsia compared with those with no GDM.

The initial HAPO data clearly demonstrated that adverse perinatal outcomes occurred on a linear incremental spectrum of maternal hyperglycemia and not just for those with the highest maternal glucose values. On the basis of these observations, revised criteria were proposed for the diagnosis of GDM—the IADPSG criteria. One of the key strengths of the IADPSG criteria was the use of the HAPO data and others to derive where maternal hyperglycemia could be clearly correlated to preset thresholds of adverse neonatal outcomes in a large, blinded, prospectively screened, and non-treated cohort (3,13). This approach did not have the limitations of traditional criteria for GDM, which are based on identifying women at high risk for the development of diabetes after pregnancy (14,15), nor were they

Table 2—Relationship between maternal GDM status (no GDM, GDM diagnosed based on IADPSG criteria, and GDM based on CC criteria) and outcomes in the HAPO North American cohort

Outcome	Participants in category, *n*	Participants in category with the outcome		Model I		Model II	
		n	%	OR	95% CI	OR	95% CI
Birth weight >90th percentile*							
No GDM	5,303	394	(7.9)	1.00		1.00	
GDM diagnosed based on IADPSG criteria	877	134	(15.3)	2.11	1.71–2.60	1.87	1.50–2.34
GDM based on CC	260	50	(19.2)	2.79	2.01–3.86	2.56	1.82–3.61
Total	6,140	578	(9.4)				
Cord C-peptide >90th percentile†							
No GDM	4,204	252	(6.0)	1.00		1.00	
GDM diagnosed based on IADPSG	758	110	(14.5)	2.57	2.02–3.27	2.00	1.54–2.58
GDM based on CC	221	48	(11.0)	4.30	3.04–6.07	2.93	2.01–4.27
Total	5,183	410	(21.7)				
Newborn percentage body fat >90th percentile‡							
No GDM	3,775	306	(8.1)	1.00			
GDM diagnosed based on IADPSG	659	101	(15.3)	2.05	1.61–2.60	1.73	1.35–2.23
GDM based on CC	189	34	(18.0)	2.49	1.69–3.67	2.08	1.39–3.12
Total	4,623	441	(9.5)				
Primary cesarean delivery§							
No GDM	4,441	764	(17.2)	1.00		1.00	
GDM diagnosed based on IADPSG	728	174	(23.9)	1.65	1.36–1.99	1.31	1.07–1.60
GDM based on CC	224	68	(30.4)	2.21	1.64–2.98	1.59	1.17–2.18
Total	5,393	1,006	(18.7)				
Neonatal hypoglycemia‖							
No GDM	5,006	67	(1.3)	1.00		1.00	
GDM diagnosed based on IADPSG	875	25	(2.9)	2.66	1.66–4.27	2.11	1.28–3.49
GDM based on CC	260	8	(3.1)	2.81	1.32–5.99	1.90	0.86–4.19
Total	6,141	100	(1.6)				
Newborn sum of skinfolds >90th percentile‡							
No GDM	3,832	291	(7.6)	1.00			
GDM diagnosed based on IADPSG	673	109	(16.2)	2.35	1.85–2.98	2.00	1.56–2.57
GDM based on CC	193	38	(19.7)	2.98	2.05–4.34	2.53	1.71–3.74
Total	4,698	438	(9.3)				
Preeclampsia¶							
No GDM	4,420	285	(6.4)	1.00			
GDM diagnosed based on IADPSG	732	109	(14.9)	2.24	1.75–2.86	1.73	1.32–2.27
GDM based on CC	200	28	(14.0)	2.27	1.47–3.49	1.79	1.12–2.87
Total	5,352	422	(7.9)				
Preterm delivery (<37 weeks)#							
No GDM	5,020	301	(6.0)	1.00			
GDM diagnosed based on IADPSG	878	68	(7.7)	1.32	1.00–1.74	1.22	0.91–1.64
GDM based on CC	261	36	(13.8)	2.51	1.73–3.65	2.37	1.60–3.52
Total	6,159	405	(6.6)				
Shoulder dystocia or birth injury#							
No GDM	5,006	92	(1.8)	1.00		1.00	
GDM diagnosed based on IADPSG	875	26	(3.0)	1.50	0.96–2.34	1.38	0.87–2.19
GDM based on CC	260	6	(2.3)	1.19	0.52–2.76	1.15	0.49–2.70
Total	6,141	124	(2.0)				
NICU admission**							
No GDM	5,006	313	(6.3)	1.00			
GDM diagnosed based on IADPSG	875	71	(8.1)	1.22	0.93–1.60	1.07	0.81–1.43
GDM based on CC	260	25	(9.6)	1.49	0.97–2.29	1.32	0.84–2.06
Total	6,141	409	(6.7)				
Hyperbilirubinemia††							
No GDM	5,006	249	(5.0)	1.00			
GDM diagnosed based on IADPSG	875	57	(6.5)	1.47	1.09–1.98	1.31	0.95–1.79
GDM based on CC	260	22	(8.5)	1.88	1.19–2.98	1.67	1.03–2.69
Total	6,141	328	(5.3)				

Continued on p. 2209

derived from criteria used for nonpregnant individuals (16).

After the publication of the IADPSG criteria, several investigations attempted to clarify the additional benefit of the IADPSG criteria compared with traditional testing in identifying patients at risk for adverse pregnancy outcomes. In a prospective evaluation of subsequent IADPSG screening compared with traditional CC screening, Duran et al. (8) showed significant improvement in several perinatal outcomes when comparing the frequency of maternal hypertensive disorders, cesarean delivery, and NICU admission among all subjects before and after the introduction of IADPSG criteria. In addition, the authors noted a reduction in cesarean delivery and NICU admission when specifically comparing women categorized based on CC criteria versus IADPSG criteria. While IADPSG screening increased the frequency of women diagnosed with GDM, this approach was still noted to be cost-effective. A retrospective analysis by Ethridge et al. (5) also suggested women who would be diagnosed with GDM based on IADPSG criteria have significant increases in adverse pregnancy outcomes compared with women undergoing normal GDM screening. These findings contrast with other data, including a recent publication by Feldman et al. (7), which cited an increased number of women diagnosed with GDM when using IADPSG criteria, but no difference among large-for-gestational-age newborns or those with macrosomia when either the CC or IADPSG criteria were used. Because of the lack of clarity regarding the additional benefit of universal one-step testing with IADPSG criteria, ACOG continues to recommend traditional testing with a 50-g screen and a diagnostic 100-g OGTT (2).

In this analysis of adverse neonatal and maternal outcomes for women in North America who do not meet CC criteria for GDM but would be diagnosed with GDM using IADPSG criteria, we sought to address the perceived lack of clear outcome data in these pregnancies. We observed that excessive fetal growth and adiposity are more common among North American women diagnosed with GDM based on IADPSG criteria than those with no GDM. These findings add to the present body of knowledge on this subject in several ways. First, it corroborates the findings of others, without the limitations of retrospective data from small, single centers or inconsistently measured clinical outcomes. These data also are directly applicable to women in North America, since only HAPO centers from the U.S. and Canada were included. Also, because investigators and women in HAPO were masked to the diagnosis of GDM, the outcomes we observed (such as primary cesarean delivery) for those diagnosed with GDM based on IADPSG criteria do not have confounding issues created by antenatally labeling a pregnant woman as having GDM. As another large observational study similar to HAPO is unlikely; the data presented here compose probably the largest, most complete information on risks for women who have GDM based on IADPSG criteria without evidence of traditional GDM based on CC criteria.

We acknowledge the limitations of our study. First, women in HAPO underwent a 75-g, 2-h OGTT and not a 100-g, 3-h OGTT. Therefore the number of additional women who would have fulfilled CC criteria for GDM with an elevated 3-h value is unknown, and we accept that some of these women may have been included in our IADPSG GDM group and could have biased our results by increasing the observed risks of adverse perinatal outcomes. However, while the proportion of women who qualify for GDM with the inclusion of the 3-h result is unknown in a North American population, an investigation of the utility of the 3-h result from Peking Hospital noted that 1.9% of all women evaluated with an OGTT would have been misclassified (17).

Second, since HAPO participants had a 75-g glucose load, there is also the chance that the observed glucose values within the HAPO data are lower than what might have occurred with a 100-g load (18–20). However, the difference in mean glucose values after a 75- or 100-g OGTT are unclear and have been reported to be no different at the

*The 90th percentile for gestational age (30–44 weeks only) was determined using quantile regression analyses for each of eight newborn sex-ethnic groups (Caucasian or other, black, Hispanic, Asian), with adjustment for gestational age, field center, and parity (0, 1, ≥2). A newborn was considered to have a birth weight above the 90th percentile if the birth weight was greater than the estimated 90th percentile for the baby's sex, gestational age, ethnicity, field center, and maternal parity. Otherwise the newborn was considered to have a birth weight at or below the 90th percentile. Model I: Adjusted for the variables used in estimating 90th percentiles. Model II: Model I adjustment plus age, height, BMI, and gestational age at the OGTT; smoking; alcohol use; hospitalization before delivery; family history of diabetes; and mean arterial pressure. †The 90th percentile of the values for the total HAPO sample. Model I: Adjusted for field center. Model II: Model I adjustment plus age, height, BMI, and gestational age at OGTT; smoking; alcohol use; hospitalization before delivery; family history of diabetes; parity; and baby's sex, mean arterial pressure, and cord glucose. ‡Defined based on sex, ethnicity, field center, gestational age (36–44 weeks), and parity using quantile regression analysis. Model I: Adjusted for the variables used in estimating 90th percentiles. Model II: Model I adjustment plus age, height, BMI, and gestational age at OGTT; smoking; alcohol use; hospitalization before delivery; family history of diabetes; and mean arterial pressure. §Model I: Adjusted for field center. Model II: Model I adjustment plus age, height, BMI, and gestational age at the OGTT; smoking; alcohol use; hospitalization before delivery; family history of diabetes; baby's sex, and mean arterial pressure. ‖Clinical neonatal hypoglycemia was defined as present if there was a notation of neonatal hypoglycemia in the medical record and there were symptoms and/or treatment with a glucose infusion or a local laboratory report of a glucose value ≤1.7 mmol/L in the first 24 h and/or ≤2.5 mmol/L after the first 24 h after birth. Models I and II adjusted for the same variables as cord C-peptide >90th percentile, except for cord glucose in Model II. ¶Preeclampsia was defined as systolic blood pressure ≥140 mmHG or diastolic blood pressure ≥90 mmHG on two or more occasions a minimum of 6 h apart and proteinuria of ≥1+ on a dipstick test or a protein level in the urine ≥300 mg within a 24-h period. If the criteria for elevated blood pressure were met but those for proteinuria were not, the hypertension was classified as gestational hypertension. Model I: Adjusted for field center. Model II: Model I adjustment plus age, height, BMI, and gestational age at the OGTT; smoking; alcohol use; family history of diabetes; family history of high blood pressure; parity; baby's sex; and maternal urinary tract infection. #Models I and II adjusted for the same variables as the models for neonatal hypoglycemia. **Intensive neonatal care was defined by admission to any type of unit for care more intensive than normal newborn care and lasting more than 24 h or by death of the baby or transfer to another hospital. Data were excluded for admissions that were only for possible sepsis or sepsis, observation, or feeding problems. Models I and II adjusted for the same variables as neonatal hypoglycemia. ††Hyperbilirubinemia was defined by treatment with phototherapy after birth, at least one laboratory report of a bilirubin level ≥20 mg/dL (342 μmol/L), or readmission for hyperbilirubinemia. Models I and II adjusted for the same variables as neonatal hypoglycemia. OR, odds ratio.

fasting and 1-h time points, with a minimal difference at the 2-h time point (18). Furthermore, the observed frequency of GDM based on CC criteria in our data are consistent with the reported incidence of GDM in the U.S. (21), and our observed outcomes for the IADPSG-based (non-CC-based) GDM are similar to those in a retrospective trial by Ethridge et al. (5), where a 100-g OGTT was used to classify patients as CC-based GDM and IADPSG-based GDM (non-CC). Finally, within the entire HAPO cohort, the majority of subjects qualify for GDM based on IADPSG criteria with the fasting or 1-h result; only an additional 2.1% achieved the diagnosis with the 2-h result (4).

In conclusion, these results offer robust evidence of adverse neonatal and maternal outcomes for women who have GDM based on IADPSG criteria but not GDM based on the traditional CC criteria compared with women with no GDM based on both IADPSG and CC criteria. Therefore these data provide a rationale to examine whether women with GDM defined by IADPSG but not CC criteria would benefit from treatment relative to a no-treatment group.

Duality of Interest. No potential conflicts of interest relevant to this article were reported.

Author Contributions. T.P.W., A.R.D., D.M.S., B.E.M., and P.M.C. designed the study, analyzed data, and prepared the manuscript. A.R.D., D.M.S., and B.E.M. performed statistical analysis. S.L.D., E.H., L.P.L., J.J.N.O., B.P., and D.A.S. designed the study and prepared the manuscript. T.P.W., A.R.D., D.M.S., B.E.M., and P.M.C. are the guarantors of this work and, as such, had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

References

1. American Diabetes Association. Sec. 2. Classification and diagnosis of diabetes. In *Standards of Medical Care in Diabetes—2016*. Diabetes Care 2016;39(Suppl. 1):S13–S22
2. Committee on Practice Bulletins–Obstetrics. Practice bulletin no. 137: gestational diabetes mellitus. Obstet Gynecol 2013;122:406–416
3. Metzger BE, Lowe LP, Dyer AR, et al.; HAPO Study Cooperative Research Group. Hyperglycemia and adverse pregnancy outcomes. N Engl J Med 2008;358:1991–2002
4. Metzger BE, Gabbe SG, Persson B, et al.; International Association of Diabetes and Pregnancy Study Groups Consensus Panel. International association of diabetes and pregnancy study groups recommendations on the diagnosis and classification of hyperglycemia in pregnancy. Diabetes Care 2010;33:676–682
5. Ethridge JK Jr, Catalano PM, Waters TP. Perinatal outcomes associated with the diagnosis of gestational diabetes made by the international association of the diabetes and pregnancy study groups criteria. Obstet Gynecol 2014;124:571–578
6. Bodmer-Roy S, Morin L, Cousineau J, Rey E. Pregnancy outcomes in women with and without gestational diabetes mellitus according to the International Association of the Diabetes and Pregnancy Study Groups criteria. Obstet Gynecol 2012;120:746–752
7. Feldman RK, Tieu RS, Yasumura L. Gestational diabetes screening: the International Association of the Diabetes and Pregnancy Study Groups compared with Carpenter-Coustan screening [published correction appears in Obstet Gynecol 2016;127:806]. Obstet Gynecol 2016;127:10–17
8. Duran A, Sáenz S, Torrejón MJ, et al. Introduction of IADPSG criteria for the screening and diagnosis of gestational diabetes mellitus results in improved pregnancy outcomes at a lower cost in a large cohort of pregnant women: the St. Carlos Gestational Diabetes Study. Diabetes Care 2014;37:2442–2450
9. World Health Organization. *Diagnostic Criteria and Classification of Hyperglyacemia First Detected in Pregnancy*. Geneva, World Health Organization, 2013
10. IDF Clinical Guidelines Task Force. *Global Guidelines on Pregnancy and Diabetes*. Brussels, International Diabetes Federation, 2009
11. Carpenter MW, Coustan DR. Criteria for screening tests for gestational diabetes. Am J Obstet Gynecol 1982;144:768–773
12. HAPO Study Cooperative Research Group. The Hyperglycemia and Adverse Pregnancy Outcome (HAPO) Study. Int J Gynaecol Obstet 2002;78:69–77
13. HAPO Study Cooperative Research Group. Hyperglycemia and Adverse Pregnancy Outcome (HAPO) Study: associations with neonatal anthropometrics. Diabetes 2009;58:453–459
14. Metzger BE, Buchanan TA, Coustan DR, et al. Summary and recommendations of the Fifth International Workshop-Conference on Gestational Diabetes Mellitus. Diabetes Care 2007;30(Suppl. 2):S251–S260
15. O'Sullivan JB, Mahan CM. Criteria for the oral glucose tolerance test in pregnancy. Diabetes 1964;13:278–285
16. WHO Expert Committee on Diabetes Mellitus: second report. World Health Organ Tech Rep Ser 1980;646:1–80
17. Gao XL, Wei YM, Yang HX, et al. Difference between 2 h and 3 h 75 g glucose tolerance test in the diagnosis of gestational diabetes mellitus (GDM): results from a national survey on prevalence of GDM. Front Med China 2010;4:303–307
18. Mello G, Elena P, Ognibene A, et al. Lack of concordance between the 75-g and 100-g glucose load tests for the diagnosis of gestational diabetes mellitus. Clin Chem 2006;52:1679–1684
19. Weiss PAM, Haeusler M, Kainer F, Pürstner P, Haas J. Toward universal criteria for gestational diabetes: relationships between seventy-five and one hundred gram glucose loads and between capillary and venous glucose concentrations. Am J Obstet Gynecol 1998;178:830–835
20. Soonthornpun S, Soonthornpun K, Aksonteing J, Thamprasit A. A comparison between a 75-g and 100-g oral glucose tolerance test in pregnant women. Int J Gynaecol Obstet 2003;81:169–173
21. American Diabetes Association. Gestational diabetes mellitus. Diabetes Care 2003;26(Suppl. 1):S103–S105