Racial/Ethnic Minority Youth With Recent-Onset Type 1 Diabetes Have Poor Prognostic Factors

*Maria Jose Redondo,[1] Ingrid Libman,[2] Peiyao Cheng,[3] Craig Kollman,[3] Mustafa Tosur,[1] Robin L. Gal,[3] Fida Bacha,[1] Georgeanna J. Klingensmith,[4] and Mark Clements,[5,6] for the Pediatric Diabetes Consortium**

Diabetes Care 2018;41:1017–1024 | https://doi.org/10.2337/dc17-2335

OBJECTIVE

To compare races/ethnicities for characteristics, at type 1 diabetes diagnosis and during the first 3 years postdiagnosis, known to influence long-term health outcomes.

RESEARCH DESIGN AND METHODS

We analyzed 927 Pediatric Diabetes Consortium (PDC) participants <19 years old (631 non-Hispanic white [NHW], 216 Hispanic, and 80 African American [AA]) diagnosed with type 1 diabetes and followed for a median of 3.0 years (interquartile range 2.2–3.6). Demographic and clinical data were collected from medical records and patient/parent interviews. Partial remission period or "honeymoon" was defined as insulin dose–adjusted hemoglobin A_{1c} (IDAA1c) ≤9.0%. We used logistic, linear, and multinomial regression models, as well as repeated-measures logistic and linear regression models. Models were adjusted for known confounders.

RESULTS

AA subjects, compared with NHW, at diagnosis, were in a higher age- and sex-adjusted BMI percentile (BMI%), had more advanced pubertal development, and had higher frequency of presentation in diabetic ketoacidosis, largely explained by socioeconomic factors. During the first 3 years, AA subjects were more likely to have hypertension and severe hypoglycemia events; had trajectories with higher hemoglobin A_{1c}, BMI%, insulin doses, and IDAA1c; and were less likely to enter the partial remission period. Hispanics, compared with NHWs, had higher BMI% at diagnosis and over the three subsequent years. During the 3 years postdiagnosis, Hispanics had higher prevalence of dyslipidemia and maintained trajectories of higher insulin doses and IDAA1c.

CONCLUSIONS

Youth of minority race/ethnicity have increased markers of poor prognosis of type 1 diabetes at diagnosis and 3 years postdiagnosis, possibly contributing to higher risk of long-term diabetes complications compared with NHWs.

Health disparities exist among individuals with type 1 diabetes of different races and ethnicities, with minorities having worse long-term diabetes outcomes than non-Hispanic whites (NHWs) in the U.S. (1). Characteristics at diagnosis, including initial hemoglobin A_{1c} (HbA_{1c}) levels and the presence of diabetic ketoacidosis (DKA), influence glucose control and the development of chronic complications many years later (2,3). Similarly, the first several years after diagnosis of type 1 diabetes, including

[1]*Baylor College of Medicine, Texas Children's Hospital, Houston, TX*
[2]*Division of Pediatric Endocrinology and Diabetes, Children's Hospital of Pittsburgh of University of Pittsburgh Medical Center, Pittsburgh, PA*
[3]*Jaeb Center for Health Research, Tampa, FL*
[4]*Barbara Davis Center for Childhood Diabetes, Department of Pediatrics, University of Colorado, Aurora, CO*
[5]*Children's Mercy Kansas City, Kansas City, MO*
[6]*University of Missouri-Kansas City, Kansas City, MO*

Corresponding author: Robin L. Gal, pdc@jaeb.org.

Received 7 November 2017 and accepted 6 February 2018.

This article contains Supplementary Data online at http://care.diabetesjournals.org/lookup/suppl/doi:10.2337/dc17-2335/-/DC1.

**A full list of members of the study groups can be found in the Supplementary Data online.*

the partial remission period or "honeymoon," also predict future blood glucose levels and other measures of later diabetes control. For instance, the Diabetes Control and Complications Trial (DCCT) linked persistent residual β-cell function after onset with decreased incidence of microvascular disease in the group on intensive therapy (4–6). In the same way, early intensive treatment conferred sustained protection from microalbuminuria (7) and overall diabetic nephropathy (8), as well as retinopathy (9). Furthermore, risk factors for cardiovascular disease, which is more frequent, presents earlier, and is more severe in individuals with type 1 diabetes (10–12), may already be present at diagnosis of type 1 diabetes or develop shortly afterward. Despite these known risks, few studies have compared races/ethnicities for all relevant risk factors present during the critical first years after diagnosis of type 1 diabetes (13–15). Defining markers that covary with race and ethnicity, that predict the clinical course of type 1 diabetes, or that represent early outcomes or targets for intervention is critical before strategies to address disparities in outcomes can be designed.

To begin to fill this gap in knowledge, we have evaluated the impact of race/ethnicity on factors present at diagnosis of type 1 diabetes and during the subsequent 3 years that are known to influence long-term health outcomes in persons with type 1 diabetes. The rising incidence of type 1 diabetes in minority youth (16), combined with the increasing prevalence of individuals of minority racial backgrounds in the U.S. (17), underscores the public health importance of understanding the basis of racial differences in type 1 diabetes outcomes. Furthering our knowledge of the influence of race and ethnicity in the natural history and clinical course of type 1 diabetes is critical for the design of strategies to address disparities in type 1 diabetes care and outcomes.

RESEARCH DESIGN AND METHODS

Participants

Between July 2009 and April 2011, the Pediatric Diabetes Consortium (PDC) enrolled 1,048 patients under 19 years of age with a clinical diagnosis of type 1 diabetes within the past 12 months and receiving care at one of the participating centers within 3 months of diagnosis. Individuals diagnosed with type 2 diabetes or other types of diabetes were excluded. The PDC aims to improve the care of children with diabetes through the analysis of shared data on health outcomes and practices, as well as evidence-based advocacy. At the time of this data collection, the PDC consisted of seven pediatric diabetes treatment centers in the U.S. Participants were followed until December 2013. There were no follow-up visits scheduled, and visits occurred as part of usual care. We excluded from the analysis registry participants from one of the seven PDC clinical centers that had no Hispanic participants and only one African American (AA) participant (N = 47). After exclusion of participants with unknown (N = 18) or other types of (N = 56) race/ethnicity, 927 PDC registry participants (631 NHW, 216 Hispanic, and 80 AA) were included in the analyses. Participants were followed for a median of 3.0 years (interquartile range [IQR] 2.2–3.6) after type 1 diabetes diagnosis. The protocol was approved by the institutional review board at each of the seven PDC centers in the U.S. Informed consent was obtained from participants >18 years of age; permission/assent was obtained for participants <18 years of age as required by local institutional review board regulations. A detailed description of PDC, the design of the study, and data collection methods have previously been published (18).

Data Collection

Demographic, socioeconomic, and clinical data were collected from medical records and from interviews with the participants and/or parents. Follow-up visits were completed per usual care, and all visits were entered in the standardized electronic case report forms for the study. Severe hypoglycemia events were defined as episodes of hypoglycemia that required the assistance of another person to treat with oral carbohydrate, intravenous glucose, or intramuscular glucagon, due to altered consciousness or seizure. DKA was defined by the DCCT criteria of pH <7.3 or HCO_3 <15 mEq/L with hyperglycemia and treatment in a health care facility. HbA_{1c} levels were measured by the DCA immunoassay method (Siemens Healthcare) at all of the centers. The insulin dose–adjusted HbA_{1c} (IDAA1c), calculated as HbA_{1c} % + [4 × insulin dose (units per kilogram per 24 h)], has been validated as an indicator of β-cell reserve in patients with type 1 diabetes, and IDAA1c values ≤9.0%, which correspond to a predicted stimulated C-peptide >300 pmol/L, have been used to define the partial remission period or "honeymoon" (18–20). Random C-peptide was measured by a two-site immunoenzymometeric assay using a Tosoh 2000 auto-analyzer (TOSOH Biosciences, Inc., South San Francisco, CA) at the Northwest Lipid Research Laboratory (University of Washington, Seattle, WA). Dyslipidemia was defined as having any of the following at any time: triglyceride level >150 mg/dL or HDL <40 mg/dL for males or HDL <50 mg/dL for females, or LDL >100 mg/dL, or noted as having dyslipidemia or elevated cholesterol in the medical chart. Hypertension was defined as, at least three times, ≥95th percentile for systolic or diastolic blood pressure with adjustment for age, sex, and height (for <18 years old) or having systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg (for ≥18 years old). Thyroid disease, celiac disease, other autoimmune diseases, and depression were assessed based on diagnosis in the medical record. Insulin delivery modality (i.e., insulin pump or injections) was obtained from the medical record. Family history of diabetes was collected along with information of the relationship of the individual with diabetes to the participant (parents, siblings, half-siblings, maternal and paternal grandparents), age of onset, and type of diabetes.

Statistical Analyses

Characteristics for participants of each race/ethnicity group were described using percentages, mean ± SD, or median (IQR). Logistic regression models were used to compare binary variables, and linear regression models were used to compare continuous and ordinal variables among Hispanics versus NHWs and AAs versus NHWs separately. Multinomial regression models were used to compare seasonality of presentation at type 1 diabetes onset. Demographic factors were treated as confounding variables and adjusted in the models in comparison of clinical variables. Potential confounding effects from socioeconomic status factors were also examined in comparison of racial differences in glycemic control outcomes. Since socioeconomic status factors are generally correlated with each other, only those with P values <0.10

were kept in the final model and reported accordingly. Change in HbA_{1c} levels from diagnosis to 6, 12, 24, and 36 months in each group was illustrated by box plots. Repeated-measures linear regression models with a spatial power covariance structure were conducted to assess the differences of BMI, HbA_{1c}, insulin doses, and IDAA1c between groups longitudinally. The difference between groups for proportion of participants in partial remission during follow-up was assessed by using repeated-measures logistic regression models. For continuous variables, linearity was tested; if a nonlinear trend was detected, either higher-order polynomials were added or the variable was discretized. Sensitivity analyses were conducted by excluding the sites with a minimal number of minorities. All reported *P* values are two sided, and all analyses were conducted using SAS, version 9.4 (SAS Institute, Cary, NC). Owing to multiple comparisons, only factors with *P* values $\leq$0.01 were considered statistically significant.

RESULTS

Table 1 illustrates the characteristics at diagnosis of type 1 diabetes of 927 pediatric participants in the PDC (631 NHWs, 216 Hispanics, and 80 AAs) who were included in this analysis. The mean (SD) ages at type 1 diabetes diagnosis were 9.2 (4.1), 9.1 (4.3), and 9.8 (4.4) years, respectively, among NHWs, Hispanics, and AA. The proportion of participants on an insulin pump and the percentage of total insulin delivered as basal (for pump users) or long-acting insulin (for injection users) are given in Supplementary Figs. 1 and 2, respectively.

Comparison of AAs and NHWs

At diagnosis of type 1 diabetes, AA, compared with NHW participants, had BMI in a higher percentile (BMI%) (median of 70% vs. 43%, *P* = 0.01), had more advanced Tanner stage of pubertal development ($P < 0.001$), and were more likely to present in DKA (48% vs. 32%, *P* = 0.004) after adjustment for age and sex. The difference in the prevalence of DKA at diagnosis between AA and NHW was largely removed by adjustment for health insurance (*P* = 0.08). AAs tended to be less likely to be positive for islet cell antibodies (62% vs. 74%, *P* = 0.05). At type 1 diabetes onset, HbA_{1c} levels, C-peptide levels, number of positive autoantibodies, and seasonality of presentation were not statistically different between AAs and NHWs.

During the 3 years of follow-up, compared with NHW, AA participants were more likely to have hypertension (15% vs. 7%, *P* = 0.009), severe hypoglycemia events (11% vs. 4%, *P* = 0.004), and DKA episodes (53% vs. 36%, *P* = 0.004) (Table 2) at or after diagnosis. The difference in proportion of participants with any DKA episode (at or after diagnosis) was largely explained by health insurance status (adjusted *P* = 0.09). After additional adjustment for parent education, severe hypoglycemia events were only borderline higher in AAs than in NHWs (*P* = 0.02). We observed no significant differences between NHWs and AAs in the presence of dyslipidemia, thyroid disease, celiac disease, or other autoimmune diseases.

In longitudinal analyses over the 3-year follow-up, AA, compared with NHW, had higher BMI% (Supplementary Fig. 3), HbA_{1c} (Fig. 1), and insulin doses (Supplementary Fig. 4) (all $P < 0.001$). With adjustment for age, sex, and type of health insurance, the difference in HbA_{1c} between NHW and AA youth was still statistically significant ($P < 0.001$). After adjustment for BMI, age, and sex, insulin doses were still different between AA and NHW ($P < 0.001$). Of note, Tanner stage of pubertal development was not statistically significant in the model. AAs had higher IDAA1c than NHWs throughout the follow-up ($P < 0.001$). The proportion of AA participants in partial remission or "honeymoon," as defined by IDAA1c $\leq$9.0%, was also significantly lower compared with NHWs ($P < 0.001$). As seen in Fig. 2, 28% of AA compared with 53% of NHW participants were in partial remission at 6 months, and the percentages decreased in both groups by 12 months (9% vs. 27%, respectively); then, the percentage remained stable among AAs, while it continued to decrease in NHWs, who reached levels similar to those in AAs by the end of the observation period.

Comparison of Hispanics and NHWs

As shown in Table 1, at diagnosis of type 1 diabetes, Hispanics had higher age- and sex-adjusted BMI (BMI%) compared with NHWs (median 64% vs. 43%, *P* = 0.002). They also tended to have more advanced Tanner stage of pubertal development (*P* = 0.06) and be positive for GAD65 (82% vs. 73%, *P* = 0.03) or insulin autoantibodies (59% vs. 51%, *P* = 0.04) (but not for islet cell autoantibodies), although the differences did not meet our criterion for statistical significance. There was borderline association between race and season for diagnosis of type 1 diabetes (*P* = 0.04), with Hispanics more likely to be diagnosed during the summer compared with NHWs (31% vs. 21%). Number of positive autoantibodies (among the three types tested), presentation in DKA, HbA_{1c}, and C-peptide levels, as well as family history of type 1 diabetes, were not different between NHWs and Hispanics at diagnosis.

For the median of 3.0 years' duration of the study (IQR 2.2–3.6), Hispanics were more likely to have a diagnosis of dyslipidemia (22% vs. 12%, $P < 0.001$) and tended to have more severe hypoglycemia (7% vs. 4%, *P* = 0.03) than NHWs (Table 2). However, the difference in the prevalence of severe hypoglycemia events was removed by additional adjustment for parent education (*P* = 0.36). We observed no differences between Hispanics and NHWs in the presence of other comorbidities (hypertension), thyroid disease, celiac disease, and other autoimmune diseases. Proportions of participants with any DKA event (at or after diagnosis) were not different between the two groups either.

Comparison of trajectories over the 3-year follow-up demonstrated that, compared with NHWs, Hispanics maintained higher BMI% ($P < 0.001$) (Supplementary Fig. 3). Similar longitudinal analyses indicated that Hispanics tended to have higher HbA_{1c} levels (*P* = 0.06) (Fig. 1) and were receiving higher insulin doses ($P < 0.001$) (Supplementary Fig. 4) than NHWs. With adjustment for age, sex, and type of health insurance, the difference in HbA_{1c} between NHWs and Hispanics was statistically nonsignificant (*P* = 0.75). After adjustment for BMI, age, and sex, insulin doses were still different between Hispanics and NHWs ($P < 0.001$). IDAA1c was higher in Hispanics than in NHWs throughout follow-up ($P < 0.001$) (Supplementary Fig. 5). The proportion of participants in partial remission or "honeymoon," as defined by IDAA1c $\leq$9.0%, tended to be lower in Hispanics than in NHWs (*P* = 0.02), as shown in Fig. 2, but the difference did not meet our criterion for statistical significance.

Table 1—Comparison of participant characteristics, by race/ethnicity, at diagnosis of type 1 diabetes (*N* = 927)

	NHW (*N* = 631)*	Hispanic (*N* = 216)*	AA (*N* = 80)*	$P_{AA\ vs.\ NHW}$	$P_{Hispanic\ vs.\ NHW}$
Age (years), mean ± SD	9.2 ± 4.1	9.1 ± 4.3	9.8 ± 4.4	0.20	0.87
<5	124 (20)	41 (19)	11 (14)		
5 to <12	340 (54)	114 (53)	43 (54)		
12 to <19	167 (26)	61 (28)	26 (33)		
Female sex	290 (46)	116 (54)	39 (49)	0.64	0.05
Health insurance					
Private	490 (79)	81 (38)	39 (49)	<0.001	<0.001
Children's health plan or other government insurance	102 (17)	120 (57)	39 (49)		
Military	10 (2)	5 (2)	1 (1)		
None	15 (2)	6 (3)	1 (1)		
Family income				<0.001	<0.001
<$25,000	26 (6)	49 (32)	15 (42)		
$25,000–$49,999	59 (14)	43 (28)	8 (22)		
$50,000–$74,999	72 (17)	27 (17)	4 (11)		
$75,000–$99,999	72 (17)	12 (8)	1 (3)		
≥$100,000	184 (45)	24 (15)	8 (22)		
Parent education				<0.001	<0.001
High school or less	116 (23)	120 (63)	25 (50)		
Associate degree	70 (14)	34 (18)	6 (12)		
BS/BA	166 (33)	28 (15)	11 (22)		
MS/MA/professional degree	155 (31)	10 (5)	8 (16)		
BMI%, median (IQR)†	43 (10–71)	64 (25–86)	70 (26–90)	0.01‡§	0.002‡§
<85%	323 (85)	108 (74)	27 (63)		
85 to <95%	33 (9)	18 (12)	11 (26)		
≥95%	24 (6)	20 (14)	5 (12)		
HbA_{1c}, % (mmol/mol), mean ± SD	11.4 ± 2.3 (101 ± 26)	11.4 ± 2.3 (101 ± 26)	11.9 ± 2.4 (107 ± 26)	0.13‡	0.60‡
<10.0 (<86)	165 (28)	56 (27)	18 (24)		
10.0 to <13.0 (86 to <119)	269 (45)	91 (44)	30 (39)		
≥13.0 (≥119)	163 (27)	59 (29)	28 (37)		
DKA	196 (32)	65 (31)	37 (48)	0.004‡	0.85‡
Family history of T1D	59 (9.4)	21 (9.7)	4 (5.0)	0.23‡	0.83‡
Number of positive autoantibodies‖				0.76‡	0.15‡
None	22 (6)	9 (6)	1 (2)		
1	83 (22)	26 (19)	10 (20)		
2	153 (40)	45 (32)	26 (53)		
3	123 (32)	60 (43)	12 (24)		
Positive IAA	241 (51)	101 (59)	27 (50)	0.86‡	0.04‡
Positive GAD	361 (73)	153 (82)	55 (80)	0.24‡	0.03‡
Positive ICA	329 (74)	124 (74)	41 (62)	0.05‡	0.96‡
Tanner stage¶				<0.001‡	0.06‡
1	204 (68)	81 (61)	25 (50)		
2	30 (10)	17 (13)	6 (12)		
3	26 (9)	7 (5)	2 (4)		
4	24 (8)	14 (11)	5 (10)		
5	16 (5)	14 (11)	12 (24)		
C-peptide (ng/mL), median (IQR)	0.5 (0.3–0.8)	0.5 (0.3–0.9)	0.4 (0.3–0.8)	0.11‡	0.63‡
Seasonality				0.33‡	0.04‡
Winter	181 (29)	60 (28)	29 (36)		
Spring	125 (20)	32 (15)	12 (15)		
Summer	135 (21)	66 (31)	20 (25)		
Fall	190 (30)	58 (27)	19 (24)		

Data are *n* (%) unless otherwise indicated. BA, Bachelor of Arts; BS, Bachelor of Science; IAA, insulin autoantibody; ICA, islet cell antibody; MA, Master of Arts; MS, Master of Science; T1D, type 1 diabetes. *Number of participants with missing or "unknown" data (NHW/Hispanic/AA): health insurance (14/4/0), family income (218/61/44), parent education (124/24/30), BMI% (251/70/37), HbA_{1c} (34/10/4), DKA (15/8/3), number of positive autoantibodies (250/76/31), positive insulin autoantibody (161/46/26), positive GAD (136/29/11), positive islet cell antibody (185/48/14), Tanner score (331/83/30), and C-peptide (399/106/34). †BMI% adjusted for age and sex based on 2000 Centers for Disease Control and Prevention growth charts with exclusion of those <2 years of age. ‡*P* value adjusted for age and sex. §BMI *z* score was used as dependent variable. ‖Limited to those tested for all three autoantibodies (*n* = 570). ¶Imputed as stage 1 for girls <8 years of age and boys <10 years of age.

Table 2—Comparison of comorbidities, by race/ethnicity, at diagnosis and over the first 3 years postdiagnosis

	NHW (*N* = 671)*	Hispanic (*N* = 216)*	AA (*N* = 81)*	$P_{AA\ vs.\ NHW}$	$P_{Hispanic\ vs.\ NHW}$
Dyslipidemia	75 (12)	48 (22)	12 (15)	0.57†	<0.001†
Hypertension‡	40 (7)	15 (8)	11 (15)	0.009§	0.77§
Thyroid disease	16 (3)	7 (3)	1 (1)	0.50§	0.59§
Celiac disease	34 (5)	9 (4)	1 (1)	0.16§	0.51§
Other autoimmune diseases	20 (3)	7 (3)	6 (8)	0.07†	0.92†
Depression	6 (1)	3 (1)	2 (3)	NA‖	NA‖
Severe hypoglycemia	25 (4)	16 (7)	9 (11)	0.004§	0.03§
DKA	228 (36)	77 (36)	42(53)	0.004†	0.84†

Data are *n* (%). NA, not applicable. *Number of participants with missing or "unknown" data (NHW/AA/Hispanic): hypertension (54/17/8). †*P* value adjusted for age and sex. ‡Limited to those tested at least three times (*n* = 848). §*P* value adjusted for age, sex, and diabetes duration. ‖No statistical comparison conducted owing to number of total cases <10.

CONCLUSIONS

We studied a large and racially/ethnically diverse cohort of 927 youth with type 1 diabetes, composing a sample geographically representative of the U.S. population. Overall, our results indicate that racial/ethnic minority youth have increased frequency of characteristics known to confer poor long-term prognosis in type 1 diabetes. In particular, as compared with NHW, AA and Hispanic youth appear to have lower residual β-cell function as reflected by IDAA1c, and AAs are less likely to enter the partial remission period. In addition, AAs have higher HbA_{1c} and frequencies of severe hypoglycemia and DKA events, largely due to socioeconomic status factors. Minorities also have higher BMI; require higher insulin doses per body weight, even after adjustment for BMI; and have higher frequency of cardiovascular risk factors (dyslipidemia in Hispanics and hypertension in AAs).

To our knowledge, this is the first study that directly compared biological factors during the first 3 years of type 1 diabetes between NHWs and the two largest racial/ethnic minority groups in the U.S. Our study is also unique in the analyses of trajectories for HbA_{1c}, BMI%, insulin dose, and IDAA1c during the observation period. By demonstrating racial/ethnic differences in factors known to influence long-term outcomes, this study adds to the limited data regarding the etiology of racial disparities in health-related outcomes among individuals with type 1 diabetes. Previous literature supports the notion that characteristics that present early in the course of the disease, such as higher HbA_{1c} and DKA at diagnosis (2,3), the absence of remission period, and the lack of residual β-cell function (4–6), are associated with worse long-term outcomes in individuals with type 1 diabetes. Epigenetic changes have been proposed as underlying the mechanism of this metabolic memory (21). Furthermore, dyslipidemia or hypertension will increase the risk of future cardiovascular disease (10–12). While it may not be immediately feasible to eliminate the biological (e.g., genetic) or social causes of these differential factors, by addressing them as therapeutic targets, we may contribute to diminishing long-term racial/ethnic health disparities.

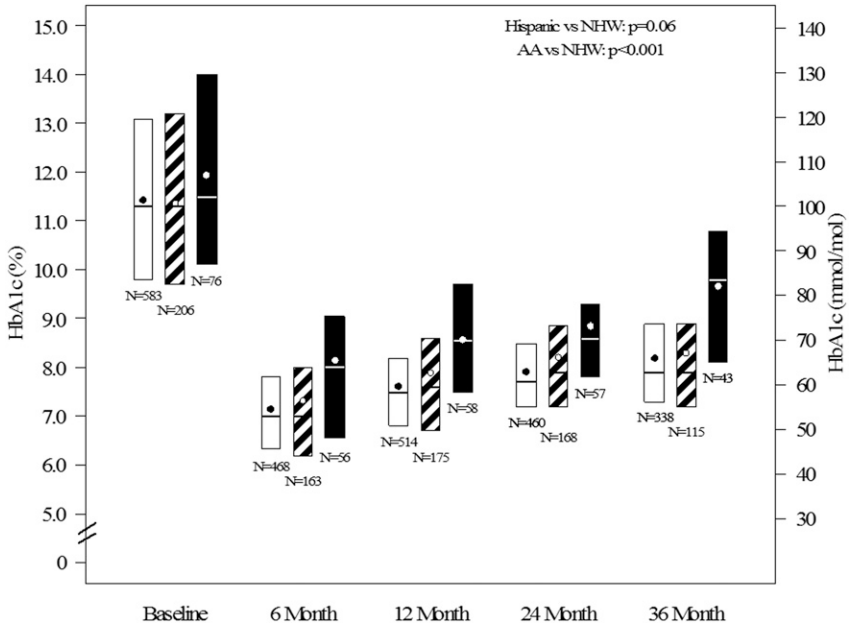

Figure 1—HbA_{1c} at diagnosis and on follow-up by race/ethnicity. Bottom and top of each box denote the 25th and 75th percentiles, respectively. Horizontal line inside each box denotes the median, and the dot denotes the mean. Solid white box represents the NHW group, black-and-white striped box represents the Hispanic group, and solid black box represents the AA group.

Analysis of HbA_{1c} trajectory over the first 3 years after diagnosis demonstrated higher overall HbA_{1c} levels in AAs than in NHWs, after adjustment for age, sex, BMI, type of health insurance, parent education, and family income. In contrast, HbA_{1c} trajectories were not statistically different between Hispanics and NHWs. Our observations during the first 3 years after diagnosis are consistent with those from the T1D Exchange in individuals with established diabetes, where AA youth, compared with other groups, had the highest age-centered HbA_{1c} (22), and with the observations in a study on the trajectory of HbA_{1c} during the first 6 months postdiagnosis in a cohort from the U.K. (23). The higher HbA_{1c} in black children with type 1 diabetes compared

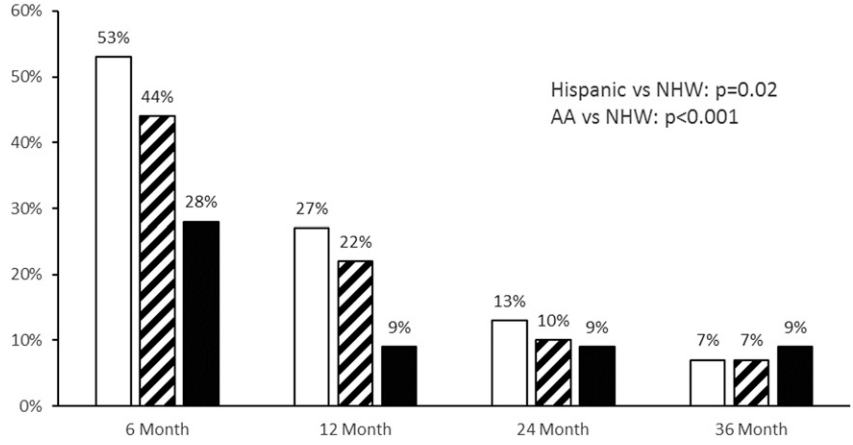

Figure 2—Proportion of participants with IDAA1c ≤9.0 (definition of partial remission or "honeymoon") during follow-up by race/ethnicity. Solid white box represents the NHW group, black-and-white striped box represents the Hispanic group, and solid black box represents the AA group.

with their white counterparts was reported to persist after adjustment for socioeconomic status, diabetes duration, and insulin dose (24,25). Similarly, the SEARCH for Diabetes in Youth study investigators observed that poor glucose control, as measured by HbA1c ≥9.5%, was present in 11.2% of NHW children aged 10–14 years and in 21.5% of those ≥15 years old (26), while it was 40.2% and 46%, respectively, for AA youth aged 10–14 and ≥15 years (27) and 30.9% and 36.2%, respectively, for Hispanic youth aged 10–14 and ≥15 years (28). The etiology of these racial differences in HbA_{1c} is not well understood. A recent study demonstrated that, although part of the HbA_{1c} difference between NHW and AA individuals may be related to HbA_{1c} overestimation of mean glucose concentration in AAs compared with NHWs, not all the difference was attributable to this effect (29). Nonwhite Caucasian race was also a factor of worse glycemic control in a multinational study from Europe and Japan (30).

Hispanic and AA youth had higher prevalence of acute diabetes complications. Specifically, the risk of severe hypoglycemia was higher in AA compared with NHW youth in the first 3 years after diagnosis, consistent with previous reports in individuals with established type 1 diabetes (25,31). Interestingly, after adjustment for parent education, the differences in frequency of severe hypoglycemia were only borderline significant (for AAs) or not significant (for Hispanics). It will be important to conduct studies to address parent education as a potential mechanism for the increased frequency of severe hypoglycemia among minority children with type 1 diabetes. DKA at diagnosis was not more frequent in Hispanic than in NHW youth, while the difference among AAs was largely explained by socioeconomic status factors, in particular health insurance, consistent with previous literature (32,33). Importantly, DKA at onset has been demonstrated to be a poor prognostic factor in type 1 diabetes, not only short-term but also long-term (2), which highlights the importance of efforts at preventing this acute diabetes complication.

Insulin dose per body weight (i.e., units per kilogram per day) throughout the first 3 years after diagnosis was higher in Hispanics and AAs than in NHWs even with adjustment for BMI%, sex, and age. This may be related to greater insulin resistance in AA compared with white children at similar total body adiposity (34). This is also consistent with prior reports that Hispanics have higher adiposity and adiposity-induced morbidity than NHWs after BMI is controlled for (35). These differences may underlie the higher frequency of hypertension in AAs and dyslipidemia in Hispanics. Since clinicians often factor weight-adjusted daily insulin dose in their clinical decisions, e.g., insulin dose adjustments, it may be necessary to consider race as a modifying characteristic. In addition, clinicians should be particularly aware of, and screen for, insulin resistance–induced comorbidities in their Hispanic or AA patients with type 1 diabetes.

The 3-year trajectory of β-cell function, as estimated by IDAA1c, was worse in Hispanic and AA youth than in NHW. Likely related to this, AA participants, compared with NHW, were less likely to be in partial remission or "honeymoon," as defined by IDAA1c ≤9.0%, within the initial 3 years postdiagnosis, while the difference between Hispanic and NHW youth did not reach the 0.01 level of significance. Since the presence of residual β-cell function has been linked to lower frequency of acute and chronic complications, this observation may contribute to the worse prognosis of type 1 diabetes in AAs. The reasons for these differences (e.g., genetic, environmental) warrant further investigation.

Compared with NHW, both Hispanic and AA youth had higher age- and sex-adjusted BMI at diagnosis and in longitudinal analyses for the first 36 months. Of note, the shape of BMI trajectory was similar in all three groups, with rapid increase quickly after diagnosis, which has been attributed to regaining the weight status attained prediagnosis (36). The higher BMI% in minority youth compared with NHW is consistent with previous reports in youth with (37,38) and without type 1 diabetes (39). Since sustained obesity and overweight accelerate the development of type 1 diabetes in individuals at risk (40), it is plausible that increased insulin resistance associated with an elevated BMI also worsens the severity of type 1 diabetes. Furthermore, as compared with NHW youth, in Hispanics dyslipidemia was more frequent, and hypertension was associated with AA race. Therefore, practitioners should bear in mind that minority children with type 1 diabetes have multiple risk factors for diabetic nephropathy and cardiovascular disease, in addition to the increased risk associated with type 1 diabetes (10), to guide their efforts in prevention, early diagnosis, and treatment of these conditions.

A limitation of this study is that, although it highlights racial discrepancies in prognostic factors and early outcomes, it does not provide an explanation for them. Further studies will be necessary to address this question. Although the proportion of participants in each racial/ethnic group under study differed, reflecting the current U.S. demographics, the relatively large sample size of the PDC allowed us to address the study questions. While the gold standard measure of β-cell function, e.g., mixed-meal stimulated C-peptide, was not available

to us, we were able to use IDAA1c as a biomarker in analyses. IDAA1c has been extensively and successfully used to estimate β-cell function and define the partial remission period based on clinically available measures (18–20).

In conclusion, these findings suggest that AA and Hispanic youth with type 1 diabetes have worse early outcomes and prognostic factors for complications than NHW youth during the critical first years after diagnosis of type 1 diabetes. The poorer early trajectory may contribute to the increased risk of long-term complications of diabetes in minority youth in the U.S. (1). Clinicians should be alerted to their higher risk of specific comorbidities so that appropriate screening and management are implemented. These data also underscore the importance of integrating race/ethnicity in predictive models for outcomes of interest to guide efforts to improve population health management. Furthermore, this study highlights the need for research that focuses on the gaps in knowledge on the etiology of racial differences in factors that predict poor diabetes outcomes and informs intervention trials that target vulnerable populations.

Acknowledgments. The authors thank Samantha Reese from the Jaeb Center for Health Research for editorial assistance.

Duality of Interest. The PDC and its activities are supported by the Jaeb Center for Health Research Foundation through unrestricted grants from Novo Nordisk, Inc.; Boehringer Ingelheim; and Takeda. P.C., C.K., and R.L.G. have grant funding from Novo Nordisk, Inc.; Boehringer Ingelheim; and Takeda. G.J.K. is a paid consultant for Novo Nordisk, Inc., and has grant funding from Novo Nordisk, Inc.; Boehringer Ingelheim; and Takeda. M.C. is a paid consultant for Medtronic and Novo Nordisk, Inc. No other potential conflicts of interest relevant to this article were reported.

Author Contributions. M.J.R. designed the study, interpreted data, and wrote the manuscript. I.L., M.T., R.L.G., F.B., and G.J.K. contributed to data interpretation and manuscript reviews and edits. P.C. and C.K. contributed to study design, analyzed data, contributed to data interpretation, and reviewed and edited the manuscript. M.C. contributed to study design, data interpretation, and manuscript review and edits. All authors except I.L. are members of the PDC. M.J.R. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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