The Impact of Racial and Ethnic Health Disparities in Diabetes Management on Clinical Outcomes: A Reinforcement Learning Analysis of Health Inequity Among Youth and Young Adults in the SEARCH for Diabetes in Youth Study

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OBJECTIVE

To estimate difference in population-level glycemic control and the emergence of diabetes complications given a theoretical scenario in which non-White youth and young adults (YYA) with type 1 diabetes (T1D) receive and follow an equivalent distribution of diabetes treatment regimens as non-Hispanic White YYA.

RESEARCH DESIGN AND METHODS

Longitudinal data from YYA diagnosed 2002–2005 in the SEARCH for Diabetes in Youth Study were analyzed. Based on self-reported race/ethnicity, YYA were classified as non-White race or Hispanic ethnicity (non-White subgroup) versus non-Hispanic White race (White subgroup). In the White versus non-White subgroups, the propensity score models estimated treatment regimens, including patterns of insulin modality, self-monitored glucose frequency, and continuous glucose monitoring use. An analysis based on policy evaluation techniques in reinforcement learning estimated the effect of each treatment regimen on mean hemoglobin A_{1c} (HbA_{1c}) and the prevalence of diabetes complications for non-White YYA.

RESULTS

The study included 978 YYA. The sample was 47.5% female and 77.5% non-Hispanic White, with a mean age of 12.8 ± 2.4 years at diagnosis. The estimated population mean of longitudinal average HbA_{1c} over visits was 9.2% and 8.2% for the non-White and White subgroup, respectively (difference of 0.9%). Within the non-White subgroup, mean HbA_{1c} across visits was estimated to decrease by 0.33% (95% CI −0.45, −0.21) if these YYA received the distribution of diabetes treatment regimens of the White subgroup, explaining ~35% of the estimated difference between the two subgroups. The non-White subgroup was also estimated to have a lower risk of developing diabetic retinopathy, diabetic kidney disease, and peripheral neuropathy with the White youth treatment regimen distribution ($P < 0.05$), although the low proportion of YYA who developed complications limited statistical power for risk estimations.

CONCLUSIONS

Mathematically modeling an equalized distribution of T1D self-management tools and technology accounted for part of but not all disparities in glycemic control between non-White and White YYA, underscoring the complexity of race and ethnicity-based health inequity.

It is well-established that mean hemoglobin A_{1c} (HbA_{1c}) levels differ by racial and ethnic subgroups (1), in which non-Hispanic Black, American Indian, Hispanic, and Asian/Pacific Islander youth and young adults (YYA) with type 1 diabetes (T1D) are more likely to have higher HbA_{1c} levels compared with non-Hispanic White YYA, as well as a higher prevalence of early complications (2). It is also known that race- and ethnicity-based health inequity in T1D can and does manifest as disparities in diabetes management or self-management behaviors (3). Although the American Diabetes Association endorses the use of basal-bolus regimens, insulin pumps, and frequent glucose monitoring (4), the literature documents that non-White YYA do not typically receive the same treatment regimens as their White counterparts (5–8). Given trial and observational data documenting associations between diabetes treatment and HbA_{1c} (9–12), it may be reasonable to hypothesize that health disparities in diabetes treatment regimens contribute to disparate clinical outcomes across racial/ethnic subgroups.

Yet, relevant to health disparities research, a key component of Critical Race Theory calls on researchers to critically approach assumptions in knowledge generation and interpretation, particularly implicit or explicit tendencies toward reductionist thinking as it relates to studies of race, racism, and health outcomes (13). From a population perspective, it is not known the extent to which the observed differences in diabetes treatment regimens or technology use across subpopulations directly contribute to the racial disparities in outcomes among YYA with T1D. Further, there exists a broad range of additional factors, including multiple social determinants of health, that can contribute to poorer outcomes among non-White individuals with diabetes outside of diabetes regimen, such as differential access to care or diabetes education (14), lower diabetes care utilization (15) and quality of care (16,17), food insecurity (18), and poorer psychosocial outcomes or increased diabetes distress (19), among others. Of note, the social determinants of health, and especially their race- and ethnicity-based differences, have recently been emphasized as an integral aspect of diabetes care from both an individual and population health perspective (3).

Clarification of relationships among race/ethnicity, diabetes regimens, and clinical outcomes among YYA with T1D in the United States may provide forward movement from identification of patterns of race-related differences and racism, operating at interpersonal, institutional, or internalized levels toward interventions to address unmet needs. These data may also point to new directions to better understand the modifiable drivers of health inequity, especially as they relate to clinical care. Recent advances in statistical methods for precision medicine and off-policy policy evaluation methods in reinforcement learning allow for observational data to be leveraged to estimate outcomes across populations given the hypothetical receipt of different treatment regimens (20). Applying these novel statistical approaches, our aim was to estimate difference in population-level glycemic control and the emergence of diabetes complications, given a theoretical scenario in which non-White YYA with T1D receive and follow an equivalent distribution of diabetes treatment regimens as non-Hispanic White YYA. In this study, the combination of race and ethnicity was not considered as a biological construct, but instead as a proxy to identify subgroups of YYA in the United States who are more likely to experience complex social, economic, and political marginalization across the life course (21,47).

RESEARCH DESIGN AND METHODS

Study Sample

The SEARCH for Diabetes in Youth Study uses a population-based registry network at five sites in the United States to identify individuals diagnosed with diabetes (other than gestational diabetes) <20 years of age (22). The clinical sites include the state of South Carolina; Cincinnati, OH, and surrounding counties; the state of Colorado with southwestern U.S. American Indian sites; Seattle, WA, and surrounding counties; and Kaiser Permanente Southern California membership in seven counties, resulting in a catchment population of >5.5 million youth aged <20 years (23). Annual incidence of youth-onset diabetes in this population was continuously ascertained beginning in 2002 (24). Individuals diagnosed with T1D or type 2 diabetes in 2002–2006 and 2008 were invited to participate in an observational cohort research study on the natural history of youth-onset diabetes by completing baseline visits shortly after diagnosis (mean 9.6 [SD 6.4] months postdiagnosis). In 2011–2015 and 2015–2019, two follow-up cohort visits were conducted among those with ≥5 years' diabetes duration for assessment of health care quality, diabetes-related early complications, quality of life, and related characteristics (Supplementary Fig. 1*A*). The study was approved by the institutional review boards with jurisdiction in each study location. All participants provided consent or assent as age appropriate, and parents also provided consent for those aged <18 years. The distribution of demographic, metabolic, and socioeconomic characteristics of participants who completed the first follow-up visit was similar to that of the larger SEARCH registry population (25).

By design, approximately half of the participants with T1D who were non-Hispanic White were invited to complete in-person research visits (target n = ~700), while the rest were invited to complete web-based questionnaires without the in-person visit. Thus, participant characteristics for the second cohort visit (SEARCH 4) intentionally differed from that of the larger SEARCH registry population in terms of enriched representation of participants with T1D who were non-White

race or Hispanic ethnicity and participants with type 2 diabetes (all races/ethnicities) (Supplementary Fig. 1*B*). The SEARCH cohort has been described elsewhere in detail (26).

Research Visits

Trained research staff conducted the in-person baseline, follow-up, and cohort research visits. Participants (and/or parents, for younger participants) self-reported date of birth, sex, race, ethnicity, highest parental education, annual household income, and type of health insurance, including no insurance. For reporting of race and ethnicity, U.S. census methods (27) were used, which provided a series of fixed race and ethnicity categories as well as an "other" option for the self-report by parent or participant, depending on age. These were further categorized into "non-Hispanic White" and "non-White" racial/ethnic groups, including Hispanic (regardless of race), non-Hispanic Black, American Indian, Asian/Pacific Islander, and other/multiple races and ethnicities.

Diabetes type was based on provider documentation of diabetes type in the medical record. Date of diagnosis had been obtained previously from medical records during case ascertainment and was used to calculate age at diagnosis and diabetes duration at each research visit. Participants reported insulin delivery modality, classified as the use of an insulin pump, multiple daily injections (MDI) with long-acting insulin (i.e., glargine), or MDI with any combination of MDI but excluding long-acting insulin. Self-reported frequency of self-monitoring of glucose (SMG) was categorized as less than one time per day, one to two times per day, three times per day, and four or more times per day. Continuous glucose monitoring (CGM) use was defined as the home use of CGM within the past 12 months and was included as an additional level of the SMBG variable at the cohort visits only, which occurred later in time when CGM became available as a tool for diabetes self-management. Physical activity and screen time were assessed using questionnaires. High physical activity was characterized by the presence of self-reported vigorous activity 3–7 days weekly. High screen time was characterized by $\geq$2 hours of screen time per day. Smoking status was self-reported and classified as current/former smokers versus never smokers.

Laboratory Measures

A blood draw occurred after an 8-h overnight fast, and medications, including short-acting insulin, were withheld the morning of the visit. Blood samples were obtained and analyzed for HbA_{1c}, glucose, lipids, creatinine, and cystatin C at the central laboratory (Northwest Lipid Metabolism and Diabetes Research Laboratories, Seattle, WA).

Early Diabetes Complications

Early diabetes-specific complications were measured at the cohort visits. Definitions of outcomes complications were consistent with previous SEARCH studies (25,28,29). Diabetic retinopathy was assessed with 45° color digital fundus images taken with a nonmydriatic camera (Visucam Pro NM; Carl Zeiss Meditec) and centered on the disc and macula of both eyes. Photos masked to all clinical characteristics were graded by the Wisconsin Ocular Epidemiology Reading Center. Diabetic retinopathy was defined as mild, moderate, or proliferative retinopathy in at least one eye (30). Diabetic kidney disease (DKD) was defined as the presence of microalbuminuria (urinary albumin-to-creatinine ratio $\geq$30 μg/mg of creatinine) or low glomerular filtration rate ($<$60 mL/min/1.73 m^2 as estimated by the Chronic Kidney Disease Epidemiology Collaboration equation using serum creatinine and cystatin C) (31). Peripheral neuropathy was defined as a score $>$2 on the Michigan Neuropathy Screening Instrument (32). Cardiovascular autonomic neuropathy was assessed by heart rate variability using the SphygmoCor-Vx device (ATCOR Medical). Electrocardiographic R-R intervals measured in a supine position were used to estimate five heart rate variability indices: the SD of the intervals, root mean square differences of successive intervals, normalized high-frequency power, normalized low-frequency power, and the low-to-high frequency ratio. Cardiovascular autonomic neuropathy was defined as abnormalities in three or more of the five indices, based on $\leq$5th or $\geq$95th percentile (as appropriate) observed in age- and sex-matched control participants of the SEARCH CVD study (33).

Statistical Analysis

Inclusion criteria for the present analysis consisted of cases of T1D that were incident between 2002–2005. Youth who attended the SEARCH cohort visit in person as well as those who completed forms only without the visit were included. Youth who did not report their race/ethnicity or provided a response that could not be categorized were excluded. YYA were classified as non-White race or Hispanic ethnicity (non-White subgroup) versus non-Hispanic White race (White subgroup). The goal of the analysis was to use observational data to estimate the effect of the two different estimated T1D treatment regimens, referred to as treatment "regimes" in precision medicine literature (34), on the clinical outcomes over time. One regimen was modeled to represent that experienced by the non-White subgroup, and the other was modeled to represent that experienced by the White subgroup. There were two sequential steps for the statistical analysis, described below and in detail in the Supplementary Material: *1*) estimate the distribution of the diabetes treatment regimens used by non-White and non-Hispanic White subgroups; and *2*) estimate clinical outcomes for the non-White YYA in SEARCH assuming they received the treatment regimen distribution of the White subgroup. The diabetes treatment regimen was represented by three variables: insulin delivery modality, frequency of SMG (before cohort visits), and frequency of SMG including CGM usage (at the cohort visits).

Propensity Score Modeling to Estimate the Diabetes Treatment Regimen Distributions

The treatment regimen, or distribution of treatments, among the White subgroup was represented by π^{White}, while the treatment regimen observed among the non-White subgroup was represented by $\pi^{non\text{-}White}$. Data from the six possible SEARCH study visits were used to model a propensity score to estimate the treatment regimen distributions in both subgroups: π^{White} and $\pi^{non\text{-}White}$ controlling for age, sex, SEARCH study site, SEARCH visit, and T1D duration. Measures of socioeconomic status were

left out of propensity score modeling to avoid overadjustment or deconstruction of a lived experience by removing the contribution of race versus socioeconomic disadvantage or deprivation on the receipt of diabetes treatment regimen. The models were fit separately for racial/ethnic subgroups (i.e., the $\pi^{\text{non-White}}$ was fit on the non-White subpopulation and the π^{White} was fit on the White subpopulation). Multinomial logistic regression was used to fit the probability of treatment options given a linear combination of the aforementioned covariates, in which the outcome was the treatment regimen (insulin modality and glucose monitoring modality), including each possible participant response described above. Separate propensity score models were fit for insulin delivery modality, frequency of SMG (before cohort visits), and SMG with CGM use (cohort visits). Two separate models for frequency of glucose monitoring were fit for the visits (before the cohort visits vs. cohort visits) to incorporate the availability of CGM that became available over the duration of the study.

Estimation of the Effect of the Diabetes Treatment Regimens on Clinical Outcomes

The second step of analysis was to estimate the effect of each diabetes treatment regimen (i.e., $\pi^{non\text{-}White}$ and π^{White}, defined above) on the outcomes of non-White YYA over the duration of the SEARCH study. A modified version of reinforcement learning, regression-based Q-learning (34–36) (details given in Supplementary Material), was used to estimate HbA_{1c} outcomes across the SEARCH visits and the risk of early diabetes complications under the setting in which the non-White YYA receive the treatment regimen estimated in White subgroup. With this analytic design, differences in outcomes can be attributed to differences in the treatment regimen (i.e., White vs. non-White).

A series of regression models was constructed to estimate outcomes. Because regressions were based on data from two consecutive SEARCH study visits, participants were excluded in *each* regression, but not the overall analysis, if they had any missing data in the two visits for each regression. Using sequential data from the SEARCH study visits, we estimated mean HbA_{1c} averaged across visits under two different treatment regimens: $\pi^{non\text{-}White}$ and π^{White}. Secondary outcomes included early diabetes complications, including diabetic retinopathy, DKD, peripheral neuropathy, and cardiovascular autonomic neuropathy. We estimated the SEARCH study population-level mean risk of having these complications in the non-White subgroup under $\pi^{non\text{-}White}$ and π^{White} as well as the differences due to the receipt of different treatment regimens.

Because there were missing values of HbA_{1c} over the longitudinal study (i.e., not all individuals attended all visits), missing values were imputed using a multilevel multiple imputation technique (2 L.pan from the 'mice' R package [37,38]) and used to estimate longitudinal population means in both subgroups and their difference (as reported in Table 2, and see the Supplementary Material for more details).

To aid in interpretation of the magnitude of the estimated diabetes treatment regimen differences in the context of larger patterns of health inequity, the model-based differences were compared with the differences in clinical outcomes between the non-White and White subgroup in the data set and reported as a percentage of the observed difference. Note that given the nature of this comparison, it is possible that the risk difference due to the treatment regimen change from the non-White treatment regimen to the White treatment regimen, calculated within the non-White subgroup, may exceed the risk difference between the two subgroups with their respective treatment regimens.

All models were adjusted for: age at diagnosis, sex, SEARCH site, T1D duration, maximum parental education, health insurance type, smoking status, physical activity, and screen time. An indicator variable for non-Hispanic Black (vs. other non-White races/ethnicities) was added to account for differences between racial/ethnic subgroups that were aggregated in the non-White subgroup. As socioeconomic position (SEP) may confound association between treatment regimen and HbA_{1c} or the development of complications, education and health insurance type were included to quantify for differences in outcomes due to change in treatment regimen only. Each outcome model included YYA who had outcome measures and the aforementioned covariates available. Methods are described in greater detail in the Supplementary Material. Estimates produced with these methods are causally valid if the following assumptions are met: *1*) consistency; *2*) the stable unit treatment values assumption; *3*) sequential ignorability (i.e., no unmeasured confounders); and *4*) positivity (see Refs. 34,35 for details). In the current study, we believe that these assumptions are standard and reasonable based on the available variables and conceptual models. Sensitivity analyses examined models stratified by sex for evidence of modification.

RESULTS

Baseline participant characteristics are shown in Table 1. Of the 978 YYA with T1D with nonmissing baseline covariates used in the analysis and HbA_{1c}, 47.3% were female and 77.5% were non-Hispanic White, with a mean age of 12.8 ± 2.4 years at diagnosis. Compared with YYA in the White subgroup, YYA in in the non-White subgroup had a markedly lower prevalence of insulin pump use (1.8% vs. 11.5%; $P < 0.0001$), and a lower proportion reported testing glucose four or more times per day (76.8% vs. 84.6%; $P = 0.007$). Using multiple imputation to handle missing longitudinal values of HbA_{1c}, the estimated population mean of the longitudinal average HbA_{1c} over visits was 9.2% and 8.2% for the non-White and White subgroup, respectively (difference of 0.9%; $P < 0.0001$) (Table 2).

Multivariate Propensity Score Modeling to Estimate the Diabetes Treatment Regimens: $\pi^{\text{non-White}}$ and π^{White}

Propensity score modeling showed that YYA in the non-White subgroup received a different distribution of insulin regimens and had a different frequency of monitoring glucose levels, shown for insulin pump and SMG four or more times per day in Fig. 1 as illustrative examples. Shown in Fig. 2, individual propensity score ratios were consistent with trends in the population-level model, as each individual in the non-White population was estimated to be more likely to use an insulin pump or SMG four or more times per day under π^{White} than under $\pi^{non\text{-}White}$.

Table 1—SEARCH participant characteristics at the baseline visit

Characteristics	All YYA (*N* = 978)	Non-White subgroup[a] (*n* = 220)	White subgroup[a] (*n* = 758)	*P* value[b]
Demographic characteristics				
Race/ethnicity				
Non-Hispanic White	758 (77.5)	0 (0.0)	758 (100)	
Non-Hispanic Black	93 (9.5)	93 (42.3)	0 (0.0)	
Hispanic	101 (10.3)	101 (45.9)	0 (0.0)	
Asian Pacific Islander	15 (1.5)	15 (6.8)	0 (0.0)	
Native American	5 (0.5)	5 (2.3)	0 (0.0)	
Other/multiple race	6 (0.6)	6 (2.7)	0 (0.0)	
Female	463 (47.3)	122 (55.5)	341 (45.0)	0.007
Socioeconomic position				
Parental education of college graduate or higher	463 (47.3)	55 (25.0)	408 (53.8)	<0.001
Private health insurance	781 (79.9)	130 (59.1)	651 (85.9)	<0.001
Clinical characteristics and diabetes treatment regimen				
Diabetes duration (months)	10.0 (6.5)	10.7 (6.8)	9.8 (6.4)	0.061
Insulin delivery modality				<0.001
Pump	91 (9.3)	4 (1.8)	87 (11.5)	
MDI with long-acting insulin	402 (41.1)	72 (32.7)	330 (43.5)	
MDI with other combination of insulins without long-acting insulin	485 (49.6)	144 (65.5)	341 (45.0)	
Frequency of SMG				0.007
≥4 times/day	810 (82.8)	169 (76.8)	641 (84.6)	
3 times/day	97 (9.9)	25 (11.4)	72 (9.5)	
1 to 2 times/day	58 (5.9)	19 (8.6)	39 (5.2)	
Less than once/day	13 (13)	7 (3.2)	6 (0.8)	
Lifestyle factors				
Current or former smoker	142 (14.5)	28 (12.7)	114 (15.0)	0.39
Physically active[c]	615 (62.9)	132 (60.0)	483 (63.7)	0.315
High screen time[c]	533 (54.5)	143 (65.0)	390 (51.5)	<0.001

Data are mean (SD) or *n* (%). [a]The non-White subgroup includes all YYA who identified as non-Hispanic Black, Hispanic, Asian Pacific Islander, Native American, and other/multiple. The White subgroup includes all YYA who identified as non-Hispanic White. [b]Based on use of ANOVA, χ^2, or Fisher exact test as appropriate. [c]Physically active defined as exercise 3–7 days/week. High screen time defined as ≥2 hours of screen time/day.

Estimation of the Effect of the Diabetes Treatment Regimens $\pi^{non\text{-}White}$ and π^{White} on Clinical Outcomes

The total number of non-White SEARCH participants included in each modeling step is shown in Supplementary Table 1. Among YYA in the non-White subgroup, the estimated population mean of HbA_{1c} averaged across all SEARCH study visits decreased from 9.1 ± 0.1% under $\pi^{non\text{-}White}$ to 8.7 ± 0.1% under π^{White} diabetes treatment regimens. The estimated difference in mean HbA_{1c} among the non-White YYA with simulated receipt of the two racial/ethnic subgroup-specific treatment regimens was 0.33% (95% CI 0.21, 0.45; $P < 0.001$) (Table 2). Effects were not different by sex.

Among the YYA in the non-White subgroup, the risk of developing complications, including diabetic retinopathy, DKD, and peripheral neuropathy, at either cohort visit was estimated to be lower under π^{White} compared with $\pi^{non\text{-}White}$ diabetes treatment regimens (Table 2). The mean risk differences among non-White YYA for these outcomes were estimated to be 6.0% (95% CI 2.1, 9.9; $P = 0.002$) for diabetic retinopathy, 9.1% (95% CI 5.0, 13.2; $P < 0.001$) for DKD, and 5.9% (95% CI 2.4, 9.5; $P = 0.001$) for peripheral neuropathy. There was not a statistically significant reduction in the risk of developing cardiovascular autonomic neuropathy ($P = 0.72$) at the SEARCH cohort visits associated with applying $\pi^{non\text{-}White}$ versus π^{White}.

Comparison of Estimated Within-Subgroup Treatment Regimen Differences with the Across-Subgroup Differences in Clinical Outcomes

Based on the 0.9% difference in population level mean HbA_{1c} over the six SEARCH visits between the non-White and White youth, the estimated treatment regimen difference represents ∼35% of the difference in HbA_{1c} between subpopulations (i.e., 0.33% of the 0.95%). For some secondary outcomes, both the model-based estimates of the risk difference due to treatment regimen and the estimates of the risk difference between the two subpopulations from the observed data set had wide CIs, reflecting low sample size and statistical power. Calculations to place the estimated treatment regimen differences within the context of the observed differences across subgroups in the prevalence of complications at the SEARCH cohort visits suggested that the estimated treatment regimen difference is ∼269%, 71%, and 81% of the observed risk difference between non-White and White subgroups, respectively, for diabetic retinopathy, DKD, and peripheral neuropathy.

CONCLUSIONS

Using data from a longitudinal cohort study, we found that mathematically equalizing the essential components of T1D treatment was associated with a

Table 2—Observed and estimated clinical outcomes among non-White YYA according to diabetes treatment regimen

Outcomes	Non-White subgroup[a]	White subgroup[a]
Primary outcome: glycemic control		
HbA_{1c} (%), mean over all six SEARCH study visits (95% CI)		
Estimated[b] subgroup outcome	9.2 (8.9, 9.4)	8.2 (8.1, 8.3)
Estimated between-subgroup difference	0.9 (1.2, 0.7)	
Estimated outcome with non-White treatment regimen[c]	9.1 (8.8, 9.3)	—
Estimated outcome with White treatment regimen[c]	8.7 (8.5, 9.0)	—
Estimated within-subgroup treatment regimen difference[d]	0.3 (0.5, 0.2)	—
Secondary outcome: early diabetes complications		
Diabetic retinopathy, risk (%) of having complication at SEARCH cohort visits (95% CI)		
Estimated[b] subgroup outcome	19.5 (13.2, 27.7)	17.2 (13.0, 22.5)
Estimated between-subgroup difference	2.2 (11.0, −6.5)	
Estimated outcome with non-White treatment regimen[c]	23.9 (17.5, 30.3)	—
Estimated outcome with White treatment regimen[c]	17.9 (12.0, 23.7)	—
Estimated within-subgroup treatment regimen difference[d]	6.0 (9.9, 2.1)	—
DKD, risk (%) of having complication at SEARCH cohort visits (95% CI)		
Estimated[b] subgroup outcome	27.2 (19.1, 37.0)	14.3 (10.1, 19.8)
Estimated between-subgroup difference	12.9 (23.2, 2.6)	
Estimated outcome with non-White treatment regimen[c]	30.1 (22.8, 37.3)	—
Estimated outcome with White treatment regimen[c]	20.9 (14.0, 27.9)	—
Estimated within-subgroup treatment regimen difference[d]	9.1 (13.2, 5.0)	—
Cardiovascular autonomic neuropathy, risk (%) of having complication at SEARCH cohort visits (95% CI)		
Estimated[b] subgroup outcome	10.2 (5.6, 17.8)	17.5 (13.0, 23.1)
Estimated between-subgroup difference	−7.3 (0.5, −15.1)	
Estimated outcome with non-White treatment regimen[c]	13.4 (7.8, 19.0)	—
Estimated outcome with White treatment regimen[c]	12.7 (5.9, 19.4)	—
Estimated within-subgroup treatment regimen difference[d]	0.7 (4.6, −3.2)	—
Peripheral neuropathy, risk (%) of having complication at SEARCH cohort visits (95% CI)		
Estimated[b] subgroup outcome	21.1 (14.6, 29.4)	13.7 (10.0, 18.5)
Estimated between-subgroup difference	7.3 (16.0, 1.3)	
Estimated outcome with non-White treatment regimen[c]	21.7 (15.8, 27.6)	—
Estimated outcome with White treatment regimen[c]	15.7 (10.7, 20.8)	—
Estimated within-subgroup treatment regimen difference[d]	5.9 (9.5, 2.4)	—

[a]The non-White subgroup includes all YYA who identified as non-Hispanic Black, Hispanic, Asian Pacific Islander, Native American, and other/multiple. White YYA includes all individuals who identified as non-Hispanic White. [b]Estimated after multiple imputation to account for missing HbA_{1c} measures over the longitudinal study. [c]Multivariate propensity scores estimated the distinct treatment regimes, including insulin modality, SMG frequency, and CGM use in White vs. non-White youth. Estimated outcomes are adjusted for the following covariates at each SEARCH visit: age at diagnosis, sex, SEARCH site, T1D duration, maximum parental education, health insurance type, physical activity, screen time, and smoking status. [d]Calculated as the difference between estimated outcomes with non-White vs. White treatment regimens.

reduction in population level mean HbA_{1c} of 0.33%; this reduction was statistically significant and explained ∼35% of the differences in HbA_{1c} between the non-White and White subgroups at the population level. These data highlight the complex nature of health disparity in T1D, including its extensions beyond diabetes management regimen and technology use, and the opportunities for future interventions to address racially disparate outcomes in this population. The remaining differences in HbA_{1c} and in the prevalence of early diabetes complications may reflect unmeasured race- and ethnicity-related factors, including, at least in part, larger forms of institutional, interpersonal, or internalized racism or marginalization, such as different barriers or supports for the use of specific diabetes treatment regimens within the clinic as well as structural and environmental forces that may impact on adherence and health behaviors external to the clinic. These factors must be accounted for and addressed in order to improve health outcomes in non-White and Hispanic YYA in the future (3).

We hypothesized there would be significant differences in the distribution of diabetes regimens in the non-White subgroup compared with the White subgroup (5,8,12,39). Propensity score modeling revealed the most striking differences with regards to insulin pump use, in which each individual was more likely to use an insulin pump based on the treatment regimen received by White compared with non-White YYA. Except for cardiovascular autonomic neuropathy, the observed clinical outcomes we report provide further evidence for disparities in longitudinal glycemic control and diabetes complications that disproportionally affect Hispanic and non-White youth (8,25,29,40). Although HbA_{1c} itself may be affected by hemoglobinopathies that influence red blood cell turnover, including those which have a known higher prevalence among the non-White subpopulation (41), this or any other effect associated with a genetic etiology (42) is likely small when compared with the impact of structural and other forms of racism. Unfortunately, the current study did not directly measure these aspects and cannot elucidate their relative contributions.

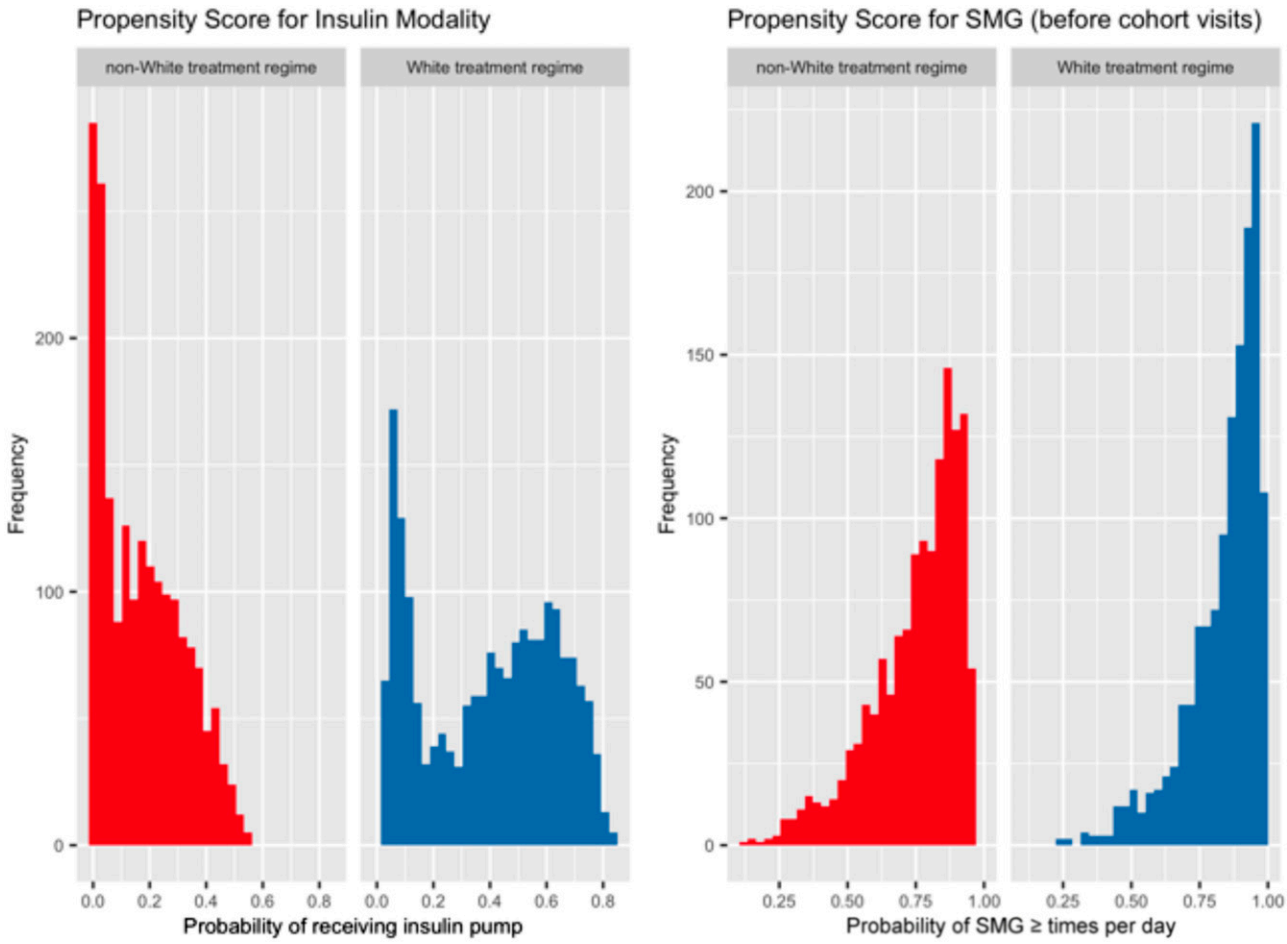

Figure 1—Selected propensity score model visualizations for diabetes treatment regimen, including insulin delivery modality and glucose monitoring. Results are shown for YYA in the non-White subgroup (i.e., non-White and Hispanic YYA) in the SEARCH study and presented as the probability of using an insulin pump or SMG four or more times per day, adjusting for age, sex, SEARCH site, and diabetes duration. Two treatment regimen distributions are shown: the red distribution represents the model fit in the non-White population ($\pi^{non\text{-}White}$), while the blue distribution represents the model fit in the White subgroup (π^{White}). A higher propensity score indicates a higher probability of using the given treatment.

Comparison of the estimated treatment regimen differences with observed differences is helpful to interpret the significance of the model-based differences, particularly for the primary outcomes HbA_{1c} over time and at the population level. Unfortunately, these calculations were limited by low statistical power for secondary outcomes. This is reflected in the wider CIs of the estimated treatment regimen differences. Despite these limitations, our data suggested that mathematically equalizing the essential components of T1D treatment explained more than half of the observed differences in the risk for developing the complications of DKD and peripheral neuropathy between the non-White and White subgroups at the population level. The instance in which estimated treatment regimen risk differences are >100% of the observed differences in diabetic retinopathy is likely a result of the lack of precision in the estimation of the secondary outcomes, and it is likely that the precision of this estimate would increase with greater statistical power lent by a larger data set. Alternatively, it is possible that the risk difference due to the change in treatment regimen within the non-White subgroup could exceed the risk difference between the two subgroups. Although the estimated effect of treatment regimens on cardiovascular autonomic neuropathy was not significant, it is worth noting that a higher prevalence of cardiovascular autonomic neuropathy among non-Hispanic White youth, compared with Hispanic and non-White youth, has been previously reported in the SEARCH study (25).

Race and ethnicity are markers for larger, lived experiences, all of which include intricately woven forces that may impact on diabetes management and outcomes. There are both modifiable and nonmodifiable factors at the individual, community, and societal level that may interact to shape a YYA's experience with managing diabetes as well as their outcomes. Further, specific challenges are heterogeneous across the population and likely vary for any given individual over time. A key limitation of the study is the lack of data to delve deeper into these factors and their dynamic roles underlying the observed racially disparate outcomes.

Although not designed to disentangle each of the multilevel factors that contribute to racial disparities, the study serves to delineate and frame several opportunities for future work. Our finding that disparities in treatment regimens contribute directly to disparate clinical

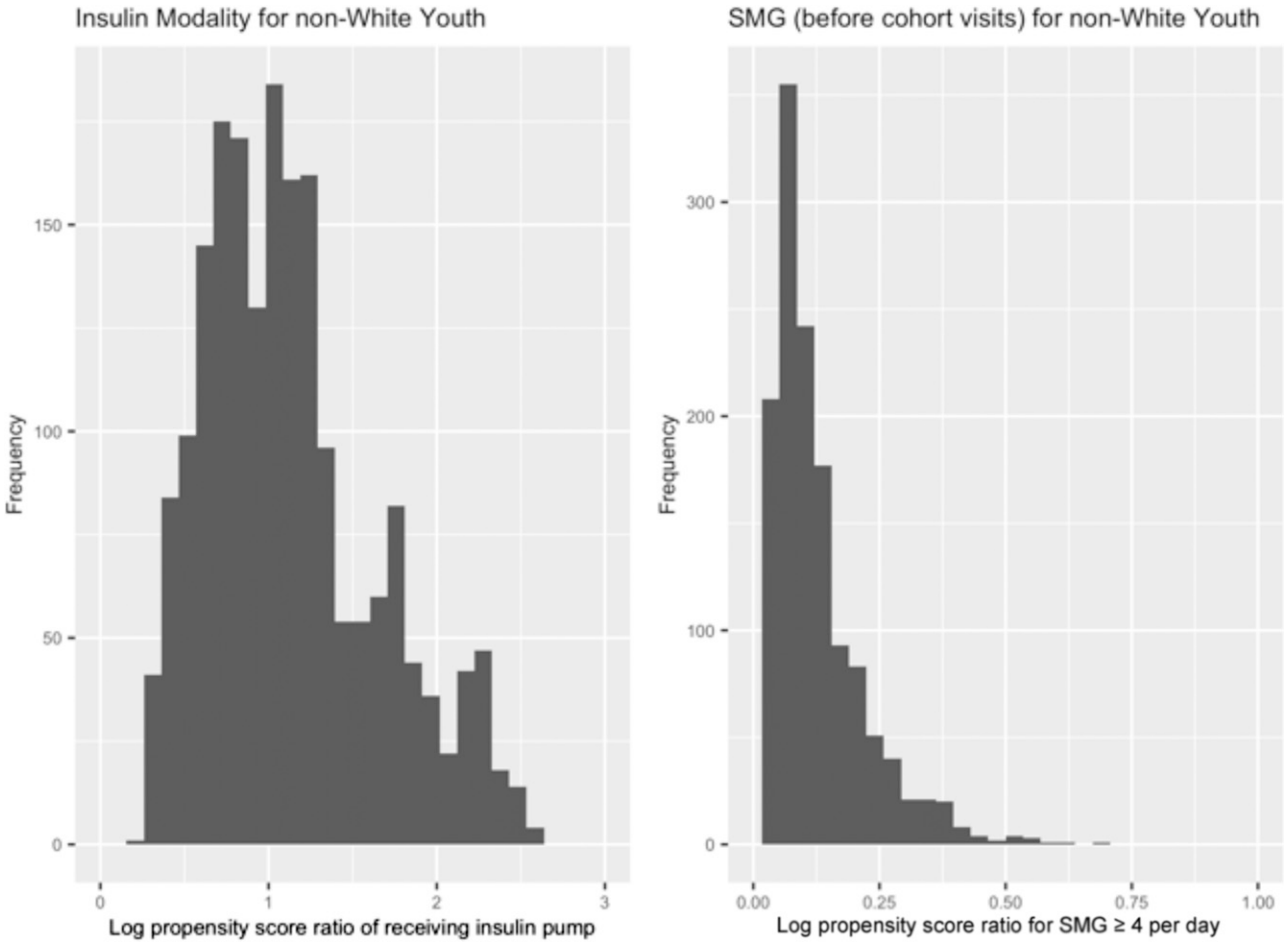

Figure 2—Selected individual propensity score ratios for diabetes treatment regimen, including insulin delivery modality and glucose monitoring. Results are shown for non-White YYA in the SEARCH study. The ratio of $\pi^{White}/\pi^{non\text{-}White}$ is calculated for each individual, adjusting for age, sex, SEARCH site, and diabetes duration. A ratio >1 or log ratio >0 indicates that each individual would be more likely to use both of those aspects of diabetes management under π^{White} than under $\pi^{non\text{-}White}$.

outcomes offers evidence for the importance of clinical care recommendations. From an interventional perspective, provider- or clinic-focused approaches represent an attractive target for interventions to promote health equity, particularly if it can be shown that inequity in prescription, education, support, and sustained patient use of diabetes regimens and management is a key, causal force of observed differences in glucose control as expressed by HbA_{1c} levels between racial and ethnic subgroups.

However, there are significant challenges that both patients and providers face as they relate to selecting and maintaining diabetes self-management regimens, such as health insurance coverage, navigation of the health care system, provision of adequate education and support for use of technology, access to care, preferences, and feasibility for adherence in the context of other lived experiences for a specific patient and family. A way forward to implement equitable access to technology will likely involve engagement from multiple stakeholders, particularly as new T1D treatment modalities continue to emerge (15). Critically, new technology offers the potential to revolutionize care and improve outcomes (43–45) but also carries the risk to further exacerbate existing disparities in technology use (i.e., the "digital divide" [12]), necessitating an integrated approach to consider social and biological influences both in the development and delivery of best care practices (46).

At the same time, the determinants of diabetes outcomes are recognized as much more complex than access to diabetes treatment and technology use alone (3,12). Despite multiple studies showing the interconnectedness of race/ethnicity, SEP, diabetes technology use, and HbA_{1c} (5,8,12,39), our finding that mathematically equalizing diabetes regimens explains less than half of the disparity in glycemic control is a sobering reminder that access to and utilization of such technology is only one of many forms of health inequity that may affect YYA with T1D. The substantial residual difference in outcomes underscores the individual, social, or environmental context that may affect the efficacy of a given intervention and points to additional, significant factors that appear to prevent non-White or Hispanic YYA from experiencing equitable clinical benefits even with the same treatment or technology. Multiple levels of racism could contribute to the outcome disparities for an individual, including structural forces such as access to health insurance, livable wages, safe neighborhoods for physical activity, access to healthful diets,

positive health behaviors, and psychosocial well-being. Non-White YYA may also be more likely to experience a higher number of daily stressors or experience more frequent and sustained stress responses, resulting in physiologic changes such as increased inflammatory markers and neuroendocrine or metabolic disruptions that can further complicate diabetes management (2). The remaining gap may also be driven, as least in part, by forms of interpersonal racism, ranging from implicit to explicit biases or discrimination, as well as internalized racism, which may manifest through diabetes self-management preferences or behaviors (21).

As such, these data underscore the importance of future work to increase our understanding of the other specific factors that may be contributing to disparate outcomes, including those operating outsides of the clinic walls. In the future, this understanding may reveal specific strategies to tailor support and resources to bolster a given intervention, at the individual level and subgroup level, to increase the likelihood of treatment satisfaction, the feasibility of adherence, and, ultimately, clinical efficacy. To this end, both quantitative and qualitative methods will be needed to capture a full picture of the care and support systems for YYA with T1D, including differences in preferences, constraints, and choices as they relate to diabetes self-management and technology use. Importantly, this work may reveal opportunities for health policy beyond efforts to facilitate equitable access to diabetes treatment regimens, including interventions to decrease the broader barriers to effective self-management behaviors over time that disproportionately affect non-White or Hispanic youth.

There are several limitations to the study. These data represent only diabetes regimens that YYA received and reported using, rather than treatment options that were discussed or offered. Understanding the former in context of the latter may illuminate ways for interventions to equalize key forces that shape the larger opportunities for YYA to choose and maintain a specific management strategy even when it is offered in an equitable fashion. We also did not have data on adherence to diabetes regimen or changes that may have occurred between research visits. Data that would facilitate geocoding for participants were not available for this analysis, so we did not have the opportunity to study the contribution of structural and environmental factors to racial and ethnic disparities in different settings or locations across the United States. From a statistical perspective, the small sample size of non-White YYA warranted combining YYA of different racial and ethnic backgrounds into a single group, which limited exploration of how different forms of socialized/structural racism affect different populations. An indicator variable for non-Hispanic Black was included in the outcome models to partially account for such variability; however, future work is needed to characterize the distinct nature and effects of health inequity across heterogenous individuals and communities. Further, the sample size prohibited further analyses to directly capture aspects of intersectionality; for example, how results may change when overlaying racial/ethnic inequity with other markers for marginalization, including sex, immigration status, or income, among others. Any causal assumptions, while reasonable, cannot be directly tested with the available data; in particular, the assumption of no unmeasured confounding is difficult to verify definitely in an observational study setting. Nevertheless, the approach taken is a significant advance over those approaches that do not consider causal validity and is more likely to give realistic results compared with other noncausal methods (35).

The study has several strengths. The application of reinforcement learning techniques to directly estimate outcomes in different hypothetical treatment scenarios allowed quantification of how disparities in diabetes management may contribute to the larger patterns of health inequity. This modeling technique allowed for sequential outcomes over multiple time points and accounted for potential delayed effect of treatments on outcomes, as well as adjusting the treatment regimen at each time point in a causally valid manner, given assumptions are met. Although the family of reinforcement learning methods has been largely applied to more fundamental precision medicine questions (20,35), this application of the method represents one of the most fundamental forms of precision health that exists, focused on how to equitably allocate use of resources to those who need them and can benefit most from them.

The goal of this work was to offer new insights from which to begin to disentangle the specific mechanisms of race- and ethnicity-based differences and racism in health outcomes. Mixed method approaches, integration of clinical and community drivers, and intentional efforts to engage stakeholders, including researchers, clinicians, individuals with diabetes, and their family members of diverse backgrounds, and particularly those who mirror the population under study, may reveal new ways to more effectively discover and capture race-based health inequity, as well as actionable pathways to address it.

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