Innovative Approaches to Understanding and Addressing Health Disparities in Diabetes Care and Research

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With the recent published update on the management of hyperglycemia in patients with type 2 diabetes (T2D) as outlined from the American Diabetes Association and the European Association for the Study of Diabetes 2012 position statement, treatment strategies continue to evolve (1). The update is very timely when one considers the growing number of new agents and, as stated by the authors, the "growing uncertainty regarding their proper selection and sequence" (1). The approach to the patient from the position statement clarified the separation of those factors felt to be "modifiable" (i.e., patient attitude, resources, support system, etc.) as opposed to those that usually are not (i.e., disease duration, life expectancy, comorbidities, etc.). However, as timely and up-to-date as the recommendations seem to be, and that the focus continues to be on personalizing treatment strategies, there are other important factors not considered or addressed by the update that greatly affect our treatment decisions.

Specifically, we recognize that among the world's population there are observable differences in diabetes prevalence, incidence, mortality, and disease burden that clearly impact our approach to treatment (2). While these factors contribute to disparities in diabetes presentation, diagnosis, and treatment, they are not easily measured, adequately studied, or routinely considered in daily management. Given the importance of the topic of health disparities in diabetes, our editorial team has featured six articles in this issue of *Diabetes Care* that report on research related to understanding health disparities. The topics range from discussing the impact of interventions led by community health workers (CHWs) to understanding the role of language barriers on diabetes complications, evaluating cerebral structural changes in diabetic kidney disease in African Americans (AAs), and understanding racial differences in underlying biological factors (3–8).

It is reported that minority groups in the U.S. may have less access to health care services, including preventive care, specific treatment, or surgery, and, as such, may experience a delay in diagnosis (2,9). Given these observations, it is not surprising that certain ethnic groups present with more comorbidities at diabetes diagnosis (2). The statistics on health disparities are striking, and a few examples follow. The prevalence of diagnosed diabetes in adults is highest among non-Hispanic blacks (NHBs), Mexican Americans, and American Indians compared with non-Hispanic whites (NHWs) (2). There is racial/ethnic bias in diabetes diagnosis based on fasting glucose versus physician diagnosis. The age-adjusted prevalence of obesity, the strongest diabetes risk factor, is highest among NHB adults, followed by Mexican American and then NHW adults (2). Ethnic minority populations experience microvascular complications at a greater rate. For example, the presence of diabetic retinopathy is 46% higher in NHBs and 84% higher in Mexican Americans than in NHWs (2). Interestingly, Hispanic Americans have a lower prevalence of cardiovascular disease (CVD) when compared with NHWs, and while NHBs have a lower incidence of CVD in the setting of diabetes compared with NHWs, NHBs are more likely to die of CVD, implicating issues of treatment and access to care. It was also reported that "NHBs, Native Americans and Alaska Natives, and Hispanic-Americans are 2.3, 1.9, and 1.5 times more likely to die from diabetes than NHWs" (2). Thus, there is still so much to learn about the differences in disease presentation, treatment, and prevention of complications among minority groups with diabetes.

There is no question that Latinos are the fastest-growing minority group in the U.S. and that they experience a high diabetes disease burden and

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See accompanying articles, pp. 189, 197, 206, 213, 220, and 228.

related complications. It is important that we devise culturally appropriate regimens to address this high-risk group. In this issue of *Diabetes Care*, Pérez-Escamilla et al. (3) reported on a CHW-led structured intervention with the aim to improve glycemic control among Latinos with T2D. The study was called the Diabetes Among Latinos Best Practices Trial (DIALBEST). In this study, they evaluated 211 adult Latinos with poorly controlled T2D and randomly assigned one group to the standard of care and the other to the CHW intervention. The CHW intervention, as reported, consisted of 17 individual sessions delivered at home over a 12-month period. The specific sessions covered topics such as diabetes complications, healthy lifestyles, nutrition, healthy food choices and diet for diabetes, blood glucose self-monitoring, and medication adherence. Parameters were assessed at baseline and 3, 6, 12, and 18 months (6 months postintervention). As described, participants had poorly controlled diabetes at baseline (mean A1C 9.6% [81 mmol/mol]). It was apparent that the CHW intervention had a significant effect given the reductions in A1C at 3 months (−0.42%), 6 months (−0.47%), 12 months (−0.57%), and 18 months (−0.55%). The intervention also had a significant effect on fasting glucose, whereas there was no significant effect on blood lipids, hypertension, and weight. Despite the lack of effect on some CVD risk factors, DIALBEST did show efficacy to improve glycemic control among Latinos with T2D.

Also in this issue is a report evaluating the impact of language barriers among immigrants on disease outcomes. As stated by Okrainec et al. (4), language barriers are reported to decrease access to health care and effect adherence to treatment regimen and may increase mortality. Thus, the study's objective was to examine the impact of language barriers on the risk of acute and chronic diabetes complications and mortality among immigrants (4). The authors used linked health and immigration databases of 87,707 adults with diabetes who immigrated to Ontario, Canada, between 1985 and 2005. They stratified the cohort by language ability at the time of immigration application. The end points evaluated included emergency department visits or hospitalization for hypo- or hyperglycemia, skin and soft tissue infection, or foot ulcer. They also evaluated cardiovascular events or mortality. Immigrants had less education and a higher use of health care. However, and of great interest, immigrants with language barriers did not have higher adjusted rates of diabetes complications, cardiovascular events, or mortality. Thus, the authors concluded that language barriers did not increase the risk of diabetes complications, but "their effect may vary based on age at time of landing, education level, marital status, and neighborhood of settlement" (4).

One factor that is understudied in evaluating the etiologies of health care disparities is differences in biological factors. Thus, it is also of great interest that two of the featured studies comment on metabolic markers between ethnic groups. In the first study, Healy et al. (5) evaluated whether modestly severe obesity modifies glucose homeostasis, cardiometabolic markers, and HDL function in AAs and white Americans (WAs) with prediabetes. They studied 145 subjects (*N* = 61 WAs, 84 AAs) and measured fasting lipids, lipoproteins, inflammatory markers (C-reactive protein), HDL functionality (paraoxonase 1 [PON1]), oxidized LDL, and adiponectin and interleukin levels. They assessed carbohydrate tolerance with serum glucose, insulin, and C-peptide during oral glucose tolerance test. The insulin sensitivity index (Si), glucose effectiveness (Sg), glucose effectiveness at zero insulin (GEZI), and acute insulin release (AIRg) were derived using frequently sampled intravenous glucose tolerance test (minimal model) (5). The data suggested that mean fasting and incremental serum glucose, insulin, and C-peptide levels tended to be higher in WAs versus AAs and mean AIRg and disposition index (DI) as well as Sg and GEZI were lower in WAs than in AAs. WAs had higher serum triglycerides than AAs. They concluded that "modestly severe obesity has differential effects on the pathogenic mechanisms underlying glucose homeostasis and atherogenesis in obese AAs and WAs with prediabetes" (5).

In the second study evaluating biomarkers, Zhao et al. (6) had an objective to identify novel metabolic markers for diabetes development in American Indians as part of the Strong Heart Family Study. They conducted metabolomics analysis of study participants who developed incident T2D (*n* = 133) and those who did not (*n* = 298) from 2,117 normoglycemic American Indians followed for an average of 5.5 years. The data suggested that seven metabolites (five known, two unknown) significantly predicted the risk of T2D, and their findings suggested "that these newly detected metabolites may represent novel prognostic markers of T2D in American Indians, a group suffering from a disproportionately high rate of T2D" (6).

In trying to understand additional biological factors explaining disparities, Sink et al. (7) reported findings that try to provide further understanding of the relationship of albuminuria and reduced kidney function to cognitive impairments. Specifically, they examined the cross-sectional relationship between renal parameters (i.e., urine albumin-to-creatinine ratio [UACR] and estimated glomerular filtration rate [eGFR]) and cerebral MRI volumes (white matter, gray matter, hippocampal, and white matter lesion volumes) in 263 AAs with T2D. They found that those with chronic kidney disease (CKD) (eGFR <60 mL/min/1.73 m^2 or UACR >30 mg/g) had smaller gray matter and higher white matter lesion volumes and that higher UACR was associated with significantly higher white matter lesion volume and greater atrophy (larger cerebrospinal fluid volumes) and smaller gray matter and hippocampal white matter volumes. They concluded that albuminuria was a better marker of cerebral structural changes than the eGFR in AAs with T2D. They also suggested that the relationship "between albuminuria and brain pathology may contribute to poorer cognitive performance in patients with mild CKD" (7).

As stated above, certain minority groups may have a delay in diabetes diagnosis, so it is important that our diagnostic and screening strategies are validated in each group. In this regard, it is important that we fully understand the effect of hemoglobin variants on A1C values in certain minority groups.

Sumner et al. (8) stated that sickle cell trait may occur in 6–8% of AAs and that hemoglobin C trait occurs in 2% of AAs. The diagnostic ability of A1C in Africans

with heterozygous variant hemoglobin, such as sickle cell trait or hemoglobin C trait, has not been rigorously evaluated. Thus, Sumner et al. (8) determined the sensitivities of fasting plasma glucose, A1C, and combined fasting glucose and A1C for the detection of abnormal glucose tolerance in 216 U.S.-based African immigrants with and without variant hemoglobin. Variant hemoglobin was identified in 21%. The results showed no difference in sensitivity of A1C to detect abnormal glucose tolerance by variant hemoglobin status. They concluded that "for the diagnosis of abnormal glucose tolerance in Africans, the sensitivity of A1C combined with FPG is significantly superior to either test alone" (8).

Based on progress to date and knowledge gained in understanding the basis for health disparities, translating these findings into clinical medicine should be a major priority. By featuring a few selected articles on health disparities in this issue of *Diabetes Care,* it was our desire as an editorial team to heighten the awareness of this topic. Understanding the basis for the differences in disease presentation, disease progression, and disease management approaches for various racial/ethnic groups is an important goal. The most effective interventions to reduce racial/ethnic disparities in diabetes care are those that are culturally adapted and multilevel, targeting the patient, provider, health care system, and the interface of the health care system with surrounding community-based resources. Novel approaches to health care delivery to underserved minority populations using CHWs, nurse case managers, and patient navigators will be critical to serve as a bridge between the patient's community and health care environments and to reduce health care disparities in the era of accountable care.

Finally, we should continue to pursue novel biomarkers that may predict diabetes and its complications, predict responses to treatment, and provide insight into physiological differences contributing to diabetes disparities. Achieving these goals will require an interdisciplinary approach that includes basic, clinical, translational, population-based, and implementation science research approaches. Our contributions as researchers and clinicians will be critical in raising awareness of the need to fund research, design and implement disease management programs, and develop health policies to reduce and eliminate diabetes disparities and improve our nation's health.

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