Elevated Cardiometabolic Risk Profile Among Young Adults With Diabetes: Need for Action

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In this issue of *Diabetes Care*, Saydah et al. (1) from the Division of Diabetes Translation, Centers for Disease Control and Prevention, explore differences in demographic and cardiovascular disease risk factors in younger adults (18–44 years of age) and older adults (≥45 years) with diabetes compared with persons without diabetes. This is an important area for research, since, as documented recently by the SEARCH for Diabetes in Youth (SEARCH) study, prevalence (2) and incidence (3) trends are rising among youth for both type 1 diabetes (T1D) and especially type 2 diabetes (T2D), yet little work on the characteristics of younger adults with diabetes has been published.

Saydah et al. analyzed the U.S. National Health and Nutrition Examination Survey (NHANES) from 2007 to 2016, which included a representative sample of U.S. adults aged 18 years and older (*n* = 23,798). Among younger persons with diabetes (mean age 36.4 years), with an average of 7.7 years of clinical diabetes duration, 29% had no health insurance, 22% had Medicaid-like plans, and only 65% reported having a usual place to receive care—all higher proportions than among persons without diabetes. They were also more likely to report living below the poverty line and being of minority race/ethnicity. Not surprisingly, persons with diabetes in both

age-groups had higher adiposity, hypertension, and lipids and a poorer diet and less leisure-time physical activity than persons without diabetes in both age-groups. Perhaps more surprising, young adults with diabetes had significantly elevated lipids and adiposity, as well as nonsignificantly poorer diet and less physical activity, than older adults with diabetes after adjustment for demographics and insurance status. They were also less likely to be treated for high cholesterol or hypertension than older counterparts, and over 25% had A1C levels higher than 9% (75 mmol/mol), indicating very poor glycemic control. Moreover, chronic kidney disease (estimated glomerular filtration rate <60 mL/min/1.73 m^2 or urinary albumin/creatinine ratio ≥30 mg/g) was detected in almost 30% of younger persons with diabetes, a figure almost as high as among older persons with diabetes (35%).

The strengths of the report by Saydah et al. lie in its use of a population that represents both younger and older adults with and without diabetes in the U.S., in the large sample size, and in the use of standardized cardiometabolic measures. It highlights the excess of cardiovascular disease risk and early chronic kidney disease that besets persons with younger-onset diabetes.

The "difference-in-difference" analysis approach used by the authors requires

some care in interpretation. This approach provides a picture of whether younger adults have a larger excess prevalence than older persons do when compared with those without diabetes. The concern with this approach, as in any difference or ratio approach, is that the excess can be due to either higher prevalence in the group with diabetes or an unexpectedly lower prevalence in the comparison group, or both. Comparing across ages requires careful interpretation because many of the factors examined change substantially with age. A design that reduces these problems is a longitudinal observational cohort study, crossing relevant life stages from diabetes onset. This strategy was used successfully by the Pittsburgh Epidemiology of Diabetes Complications (EDC) study to explore the life course evolution among patients with youth-onset T1D (4,5). However, given the recent changing health care environment and advances in therapies, as well as the changing landscape of youth-onset diabetes, more contemporary cohorts and ones including both people with T1D and those with T2D are required. The SEARCH study is an example of such a cohort (6), and because of the early onset of diabetes and the longitudinal follow-up, it is possible to study prospectively the role of socioeconomic factors, medical care access, and metabolic and behavioral risk

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factors in relation to diabetes-related morbidity and mortality as youth transition to young adulthood and beyond. In addition, the SEARCH cohort study includes several inception cohorts recruited over more than a decade, thus also allowing study of the changing health care environment (3).

Saydah et al. (1) note several limitations in their article, especially the inability to identify the type of diabetes. While 90% or more of the diabetes among people with older onset is likely T2D, in the younger age-group the assumption that most are T2D may not be completely valid (2). Thus, it remains unclear from this article whether the excesses seen are being concentrated in one "type" of diabetes or another or are present in both.

Data are now available showing that youth-onset T2D has a higher burden of cardiometabolic risk factors (6), comorbidities, complications, and mortality than either youth-onset T1D (7,8) or adult-onset T2D of similar duration (9). These excesses were initially described in indigenous peoples (9–11) and recently have been highlighted by the population-based SEARCH study, where an excess burden of early diabetes-related complications and comorbidities (diabetic kidney disease, retinopathy, peripheral neuropathy, arterial stiffness, and hypertension) was observed among youth with T2D and minority youth with T1D (7). Overall, 72% of adolescents and young adults with T2D and 32% of those with T1D had a least one diabetes-related complication or comorbidity. Similar findings from the Treatment Options for Type 2 Diabetes in Adolescents and Youth (TODAY) clinical trial showed rapid development of albuminuria, hypertension, hyperlipidemia (12), and arterial stiffness (13) among youth with T2D enrolled at a mean age of 20.8 years and a mean diabetes duration of only 7.6 years, similar to the SEARCH results. Thus, it is becoming clear that risk factor and early complications patterns among individuals diagnosed with diabetes early in life, especially those with T2D and those with T1D of minority racial/ ethnic background, arise at an accelerated rate. These results serve to highlight the importance of the article by Saydah et al. (1). There are large numbers of people with diabetes in young adulthood, they have been poorly studied, and they likely are not receiving care that could protect them into later life.

The reasons for the differences reported by Saydah et al. remain complex. It is not clear whether they result from a different disease process among people with a younger age at onset of diabetes, for which increasing data are available, at least with respect to youth-onset T2D (14), or whether a combination of socioeconomic, health care access, transition from pediatric to adult care (15), limited health insurance, and other factors underlie the differences (16). This is clearly an area for further research since, without appropriate intervention, youth and young adults with diabetes face a longer lifetime exposure to hyperglycemia, hypertension, obesity, and inflammation, which will likely result in increased risks of end-stage kidney disease, heart attack, stroke, and congestive heart failure at an earlier age than among prior generations of patients with diabetes.

In summary, the work by Saydah et al. presents both a thorough descriptive analysis and a call to action for clinicians to identify and treat obesity, diabetes, and cardiovascular disease risk factors in young adults, and likely much earlier during the life course.

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