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In This Issue of *Diabetes Care*

By Max Bingham, PhD

Severe Hypoglycemia Rates in Diabetes May Be Underestimated in the U.S.

Rates of severe hypoglycemia requiring medical attention in patients with diabetes may be higher than previous estimates from clinical trials, according to Pathak et al. (p. 363) who investigated the electronic medical records of nearly a million U.S. patients with diabetes between 2005 and 2011. They found that annual rates of severe hypoglycemia ranged from 1.4 to 1.6 per 100 person-years, whereas previous trial-derived data suggested that the rates were likely lower at 0.3–1 per 100 person-years. Of note, there was “no consistent improvement in trend during the study period” and there was “excess risk of hypoglycemia in high-risk subgroups, including those on insulin therapy, the elderly, and those with common comorbid conditions.” Commenting further on the study, Dr. Pathak stated: “Current diabetes guidelines are based on [data from] clinical trials in highly selected and closely monitored patients. Broad application of aggressive trial-based glucose treatment strategies to patients who are older, have more severe comorbidities, and are less closely monitored leads to higher risk for severe hypoglycemia than is often observed in clinical trial settings.” Dr. Pathak also elaborated on possible strategies for reducing the risk of hypoglycemic episodes: “More frequent interaction with providers, increased frequency of glucose testing, careful drug and dose selection, and less aggressive target HbA_{1c} levels and monitoring trends in HbA_{1c} for patients at high risk are strategies that can decrease the risk of severe hypoglycemia.” According to Dr. Pathak, the key may lie in personalization of treatment: “Instructions to patients to alter their glucose-lowering medication dose on their own for specific situations such as increased activity and variable carbohydrate intake should also be considered for a subset of well-informed patients. Health insurance companies may see a decrease in total cost of care for these high-risk patients if they support broad implementation of these strategies and accommodate the need for personalization of treatments and glycemic control goals in publicly reported diabetes quality-of-care measures.”

Pathak et al. Severe hypoglycemia requiring medical intervention in a large cohort of adults with diabetes receiving care in U.S. integrated health care delivery systems: 2005–2011. *Diabetes Care* 2016;39:363–370

Detection of Type 1 or Type 2 Diabetes in Young Adults Using Genetic Risk Factors

A genetic risk score, developed by Oram et al. (p. 337), based on known genetic variants associated with type 1 diabetes can discriminate between type 1 and type 2 diabetes and furthermore predict which individuals are likely to progress to severe insulin deficiency. According to the authors, rising obesity rates mean that successfully distinguishing between the two types of diabetes is becoming increasingly challenging, especially in young adults aged 20–45 years. The worry, of course, is that the two types of diabetes require different treatments and so getting the diagnosis right is important. Their approach, they report, could be a valuable addition to clinical diagnosis procedures, especially when the usual approaches result in equivocal outcomes. While genotyping has typically remained the reserve of research projects due to cost, prices have rapidly dropped in recent years with the introduction of new technologies. A notable point with targeting the genomic risk factors for type 1 diabetes is that diagnosis would not be time dependent—an individual’s genome does not change over time. This is in contrast to current diagnostic techniques where discriminative abilities change over time. Commenting more widely on the study, Prof. Hattersley stated: “Clinical diagnosis of diabetes subtype is becoming more difficult in young adults as the age of diagnosis falls in type 2 diabetes, BMI increases [are now common] in type 1 diabetes, and measuring islet autoantibodies does not always give clear answers. We hope that the type 1 diabetes genetic risk score will be an important addition to the tools available to health care professionals to help them to define a patient’s subtype of diabetes so they can be given appropriate education and treatment.” Getting the diagnosis right will, according to Prof. Hattersley, become increasingly needed: “Future development of specific immune modulation therapy in type 1 diabetes, which will have no effect in type 2 diabetes, will mean that making the correct diagnosis will be increasingly important.”

Oram et al. A type 1 diabetes genetic risk score can aid discrimination between type 1 and type 2 diabetes in young adults. *Diabetes Care* 2016;39:337–344

Diabetes Rates in Asia and the Pacific Are Growing Fast: Action Needed?

The sheer scale of issues related to diabetes in the Asia-Pacific region is highlighted in a review by Nanditha et al. (p. 472). They suggest that unless drastic steps are taken to curb the rise in diabetes in these countries, the challenges are likely to become “insurmountable.” Rates of diabetes have rocketed in recent years—a trend that looks set to continue in the coming decades, according to the authors. But huge variations in rates suggest a complex picture of causation with ethnicity, aging, urbanization, and lifestyle changes all likely contributing to increases. While sharing many risk factors with other regions of the world, certain ones may be more significant for Asian populations. Nanditha et al. highlight a range of issues that could be fuelling the increases including many relating to early development and suggest that fundamental change will be needed in national programs of prevention to curb the escalating trends. Commenting further, Prof. Zimmet stated: “Type 2 diabetes is likely to be one of the biggest epidemics in human history. The Asia-Pacific region represents over one-third of the global number of diabetes cases. Many of these countries lack the resources for treating the large number of people with diabetes making prevention the best option for reducing the burden. In this context, we also need a better appreciation of the extent to which early development factors in utero contribute to the epidemic and how to take this into consideration in prevention.” Prof. Zimmet also raises a notable point: “The methods used to estimate and monitor this epidemic in terms of trends in most nations in Asia and the Pacific fall far short of what is needed. An urgent need is to develop accurate and standardized monitoring methods, as health care planning for diabetes needs is dependent on these data.”

Nanditha et al. Diabetes in Asia and the Pacific: implications for the global epidemic. *Diabetes Care* 2016;39:472–485

CVD Risk Factors and Particularly BMI Linked to Marker of Atherosclerosis in Youth With Type 1 Diabetes

Shah et al. report in this issue of *Diabetes Care* (p. 418) on their longitudinal study (SEARCH CVD) and how the cardiovascular risk burden in youth with type 1 diabetes may already be significantly increased by the time they reach the end of teenage years. Moreover, they sought to determine how cardiovascular risk factors influenced future carotid intima-media thickness (IMT), a key early marker of atherosclerosis, and found that BMI was the only modifiable risk factor that was predictive of IMT. Examining nearly 300 youths with type 1 diabetes, the authors measured a range of risk factors including BMI, blood pressure, HbA_{1c}, and lipids at baseline around the age of 13 years and then followed up around 5 years later with IMT also assessed. Most of the risk factors worsened over time, and more than half of all study participants had two or more that were raised at follow-up 5 years later. Further analysis then revealed that older age at baseline, male sex, and higher BMI were predictive of increased IMT. Although the relationship between type 1 diabetes, cardiovascular disease risk, and particularly atherosclerosis is fairly well established in adults with childhood-onset type 1 diabetes, there is a surprising lack of data identifying the risk factors that contribute to early atherosclerosis. According to the authors, their study is the first to track the burden of risk factors overtime in U.S. teens with type 1 diabetes and highlights a “critical need to better understand the risk factors that influence carotid IMT early in the course of type 1 diabetes.” Commenting more widely on the implications of the study, Dr. Shah stated: “We know that having type 1 diabetes increases one’s risk of developing cardiovascular disease. It is important to continue work in this area to identify the risk factors that contribute to this process. Only then will we be able to develop therapies to decrease the cardiovascular disease burden in people with type 1 diabetes.”

Shah et al. Predictors of increased carotid intima-media thickness in youth with type 1 diabetes: the SEARCH CVD study. *Diabetes Care* 2016;39:418–425