

DECEMBER 2018

Diabetes Care®

In This Issue of *Diabetes Care*

By Max Bingham, PhD

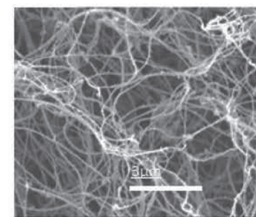
ADA and EASD Update Guidance on the Management of Hyperglycemia in Type 2 Diabetes

The American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) have updated their guidance on the management of type 2 diabetes and hyperglycemia. Authored by Davies et al. (p. 2669), the consensus report covers numerous aspects of diabetes care, including lifestyle management, therapeutics, technology, adherence to treatments, and nutrition. In particular, the report focuses on how drugs can influence cardiovascular outcomes and also the issue of obesity and overweight in people with type 2 diabetes. In a series of recommendations, the report highlights the need for patient-centered care, ongoing education, and support for diabetes self-management, and also the facilitation of adherence to treatments/interventions. The authors also step through the various stages of therapy that can be considered and explore a series of knowledge gaps that should be addressed with further research—and some gaps demand urgent attention. Commenting further on the report, author Melanie J. Davies told *Diabetes Care*: “Our update was informed by the wealth of evidence that has been generated in the last two years. We have given a greater focus to patient-related issues and self-management, which have a major impact on the success of any pharmacological interventions, and the preferred choices of glucose-lowering agents are driven by new evidence from the cardiovascular outcome trials, consideration of comorbidities such as chronic kidney disease and heart failure, but also a focus on areas of major clinical need including weight loss and reducing the risk of hypoglycemia. There is also an increased focus on the role of glucagon-like peptide 1 as a first-injectable therapy in the majority of patients with type 2 diabetes. There is an emphasis on the importance of weight loss and obesity management, including metabolic surgery. Our underlying principle emphasizes the importance of patient-centered care. We hope that this update is of help both to specialists and primary care doctors as they grapple with the increasing therapeutic options for glucose lowering.”

Prothrombotic Effects of Hypoglycemia Raised in Individuals With Type 2 Diabetes

Acute but moderate episodes of hypoglycemia result in prothrombotic effects that can last for up to seven days, according to Chow et al. (p. 2625). As a result, the authors suggest that while the precise clinical relevance remains to be fully established, clinicians should consider approaches that minimize hypoglycemia when addressing vascular health and optimizing glycemic control in patients with type 2 diabetes. The study involved 12 individuals with type 2 diabetes and no history of cardiovascular disease and 11 BMI and age-matched individuals without type 2 diabetes as control subjects. They took part in a series of clamp procedures to simulate two episodes of hypoglycemic or euglycemic conditions. A series of cardiovascular-related assays were then used on blood samples taken at baseline, immediately after the initial clamp test and then one and seven days later. The researchers found that hypoglycemia can result in acute and persistent prothrombotic effects that last for up to seven days and that these were enhanced in the case of individuals with type 2 diabetes. Specifically, they found that platelet reactivity and aggregation increased during hypoglycemia in both groups but the effects lasted less than 24 h. Hypoglycemia was also associated with early and late prothrombotic changes in the fibrin network in diabetes but less so in the healthy control individuals. Fibrinogen and C3 levels also increased, which the authors suggest may contribute to later prothrombotic changes in the fibrin network. Together, they say the data indicate that two episodes of moderate hypoglycemia can have acute prothrombotic effects and raise cardiovascular risk and that these are enhanced in individuals with type 2 diabetes. According to author Simon R. Heller: “Our study adds evidence that hypoglycemia could oppose the beneficial effects of intensive insulin therapy in people with established type 2 diabetes. Importantly, it shows that prothrombotic effects of hypoglycemia are present not only when blood glucose is low but for up to a week following the episode.”

Davies et al. Management of hyperglycemia in type 2 diabetes, 2018. A consensus report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). *Diabetes Care* 2018;41:2669–2701



Visualization of ex vivo fibrin clots from pooled plasma samples in participants with diabetes.

Chow et al. Prolonged prothrombotic effects of antecedent hypoglycemia in individuals with type 2 diabetes. *Diabetes Care* 2018;41:2625–2633

Mixed Results for Insulin Pump Therapy During Pregnancy and Type 1 Diabetes

Insulin pump therapy during pregnancy and in the context of type 1 diabetes may be suboptimal according to a prespecified analysis of the Continuous Glucose Monitoring in Women With Type 1 Diabetes in Pregnancy Trial (CONCEPTT) by Feig et al. (p. 2471). Specifically, users of multiple daily injections (MDI) of insulin had better glycemic control and less gestational hypertension, neonatal hypoglycemia, and intensive care admissions than users of pump therapy during pregnancy. The analysis involved 248 pregnant women with type 1 diabetes who were tracked over the course of pregnancy in relation to maternal glycemic control, obstetric and neonatal outcomes, and patient-related outcomes. Two groups were compared: insulin pump users and MDI users, and the primary outcome was glycemic control as assessed by change in HbA_{1c} from baseline to 34 weeks' gestation. They found that pump and MDI users had comparable HbA_{1c} levels in the first trimester of pregnancy but at 34 weeks, MDI users had a larger decrease in HbA_{1c} than pump users. At both 24 and 34 weeks, MDI users were more likely to hit HbA_{1c} targets than pump users. The decrease in HbA_{1c} levels achieved by MDI users was about 0.5% while pump users achieved a decrease of about 0.3% (the difference did achieve significance). Commenting more widely on the study, author Denice S. Feig said: "Our finding that pump users had less optimal glycemic control than women using multiple daily injections was surprising. Greater attention needs to be paid to pregnant women using pumps, with an emphasis on identifying potential reasons for suboptimal glucose control in the second and third trimesters. Possible reasons include overly cautious insulin dose adjustment, greater dietary freedom, and variations in day-to-day insulin absorption in late gestation. The flexibility of 0.05–0.1 units per hour dose increments may mean that patients and clinicians are insufficiently aggressive with insulin dose escalation. More research is needed to better understand how clinical teams can support and educate pregnant women to implement new technologies more effectively to optimize glycemic control and infant health outcomes."

Feig et al. Pumps or multiple daily injections in pregnancy involving type 1 diabetes: a prespecified analysis of the CONCEPTT randomized trial. *Diabetes Care* 2018;41:2471–2479

Economic Costs of Diabetes Vary Across U.S. States

The economic costs associated with diabetes in the U.S. are large but vary widely between states, according to an analysis by Shrestha et al. (p. 2526). As a result, the authors suggest the estimates can be used by policy makers to prioritize interventions according to needs and, specifically, economic burdens. They also point out that wide variations in costs between states suggest that any state-level estimates derived solely from national averages might be inaccurate with potential consequences for policy decisions and interventions. The analysis uses various data sources and methods to estimate direct and indirect costs due to diabetes. All cost estimates were adjusted to 2017 US\$ values and are presented as total as well as per-person costs at the state level. The analysis covers all 50 U.S. states and the District of Columbia. The researchers found that total economic costs at the state level ranged from \$694 million to \$55.5 billion, with the median cost being \$5.9 billion. Wyoming had the lowest costs while California had the highest costs. The total cost across the country was \$465.2 billion, where medical costs made up just under half the value, with the rest being costs due to morbidity and mortality. They also present costs according to payer with a breakdown according to Medicaid, Medicare, and other payers. Again, spending by state shows considerable variation. They go on to provide a detailed analysis of the costs per state and also the relative costs per person in each state—with the differences being considerable. According to author Sundar S. Shrestha, "In short, costs varied hugely across the states. Understanding detailed information on the economic costs of diabetes is important as it can be used to inform decision making for state policy makers and others who make decisions about costs passed on to the consumer. Our study provides the most comprehensive estimates using the most recent data available."

Shrestha et al. Economic costs attributable to diabetes in each U.S. state. *Diabetes Care* 2018;41:2526–2534

<https://doi.org/10.2337/dc18-ti12>