



DIABETES IS PRIMARY

TIMELY NEWS AND NOTES FOR PRIMARY CARE PROVIDERS

from the American Diabetes Association

By Max Bingham, PhD

FROM THE JOURNALS.....

Self-Monitoring of Blood Glucose in Non-Insulin-Treated Type 2 Diabetes

Guidelines on the use of self-monitoring of blood glucose (SMBG) in people with non-insulin-treated type 2 diabetes are not uniform. For example, the American Diabetes Association and the International Diabetes Federation largely recommend it (although with certain caveats), whereas the Society of General Internal Medicine advises against it. Those advising against point to evidence suggesting that daily SMBG does not influence glycemic control (e.g., an article by Young et al. in *JAMA Internal Medicine*, doi.org/css3). Proponents argue that, despite such evidence, routine SMBG has the ability to promote lifestyle changes that are needed for glycemic control.

A good recent overview of the two sides of this debate, with some qualitative research, was recently published by Havele et al. (*Annals of Family Medicine*, doi.org/css4), who summarize 17 physicians' views on the matter. They found that the majority (14) were proponents of SMBG in the belief that the approach plays a positive role in education and lifestyle change, which then leads to improved glycemic control. Opponents, who voiced concern about a lack of efficacy in terms of A1C lowering, were more likely to cite evidence to back up their position.

Although the researchers grouped responses into four broad categories, a nuanced picture emerges of physicians taking a pragmatic approach toward patient care.

"Over and over again, I have noticed that people who check their blood sugar tend to be more engaged in the self-management of their diabetes," one physician is quoted as saying.

"I tend to see [that] patients who keep monitoring are the ones who are generally more engaged around their

self-care," another reportedly said. "In my experience, [SMBG] has been mostly correlated with their level of activation rather than the disease."

The article also touches on concerns about the cost of SMBG testing strips, patient safety, and considerations related to specific patient populations. Although their research is qualitative and has a number of limitations, the authors conclude on the side of opponents of the approach.

"Health care systems can look to SMBG as an opportunity to reduce spending with little to no harm to patients," they write. "Given that educational outreach alone has small benefits in changing behavior, targeting physicians' beliefs about the effectiveness of SMBG, along with policy-based interventions, could reduce this practice."

TREATMENTS + THERAPIES



Treatments Roundup

Empagliflozin Plus Insulin

Randomized controlled trials of a combination of the sodium-glucose cotransporter 2 (SGLT2) empagliflozin and insulin have met their primary end points according to trial sponsors Eli Lilly and Company and Boehringer Ingelheim (prn.to/2KsqQfv). Reportedly, three different doses of empagliflozin (2.5, 10, and 25 mg) combined with insulin therapy could reduce A1C over 26 weeks in patients with type 1 diabetes. Full results of the studies and the overall EASE phase 3 research program that includes them were due to be presented at the European Association for the Study of Diabetes annual meeting in Berlin, Germany, on 4 October 2018.

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ADA NEWS

Diabetes Is Primary: Free Webcasts Available With CME/CE Credits

The Diabetes Is Primary webcasts offer the latest diabetes treatment guidelines from nationally recognized experts. Learn about information and tools needed to improve patient outcomes through patient engagement. View the webcasts at professional.diabetes.org/ce.

Official Highlights of the American Diabetes Association's 78th Scientific Sessions

In collaboration with Infomedica, the American Diabetes Association (ADA) is pleased to announce the availability of the Official Highlights of the ADA's 78th Scientific Sessions. Visit the website to learn about key topics in diabetes and review clinical insights, clinical pearls, current research, and much more across multiple aspects of diabetes. The entire program is available in English, Spanish, Chinese, and Italian. Along with a review of research findings reported at the conference, the program will also have English and localized versions of interviews in multiple languages

for audiences in more than 30 countries worldwide. Go to www.adahighlights2018.com.

Mental Health Provider Referral Directory Available

Living with diabetes is exhausting, and your patients need support and empowerment to live their best life. ADA recommends that diabetes care providers routinely screen patients for psychosocial challenges and make referrals to mental health professionals who have experience with diabetes management and effective treatment strategies.

The ADA's new Mental Health Provider Referral Directory can help you locate mental health professionals with demonstrated expertise in your area. Check it out at professional.diabetes.org/mhdirectory.

This directory was made possible by generous support of The Leona M. and Harry B. Helmsley Charitable Trust.

Standards of Care App Available for Downloading

New from ADA, the *Standards of Medical Care in Diabetes* app puts the latest ADA practice recommendations at your fingertips. The app offers clinical tools, including interactive algorithms, and gives users the ability to take notes and bookmark important sections within the app.

The app can be downloaded for free from the Apple App Store (apple.co/2mJaFAV) or Google Play (goo.gl/7ABBEa). The full Standards of Care is also available for purchase online at www.shopdiabetes.org or in the bookstore at ADA conferences.

MARKETPLACE

Accuracy of Blood Glucose Meters Questioned

In a recent study by Klonoff et al. (*Diabetes Care*, doi.org/css5), only one-third of the blood glucose meters (BGMs) licensed in the United States (making up 90% of the total market) met predetermined accuracy standards similar to those required for regulatory clearance.

The study involved 1,035 subjects who had capillary blood glucose measured on six different commercial systems and additionally had a plasma sample measured in a reference laboratory. Three triple-blinded studies performed at three different locations resulted in 18 systems undergoing evaluation. Compliance was predefined as a blood glucose measurement being within 15% or 15 mg/dL of a reference plasma value depending on whether blood glucose was higher or lower than 100 mg/dL. Additional metrics were also calculated.

The researchers found that 6 of the 18 systems met the predefined accuracy standard in all three studies; 5 systems met the standard in two of the studies, and 3 met the standard in one of the studies. Four systems failed to meet the standard at all. The evaluated systems are named in the report, but the authors stress that these outcomes might not translate beyond their study because of various factors.

“Cleared BGMs do not always meet the level of analytical accuracy currently required for regulatory clearance,” they write. “This information could assist patients, professionals, and payers in choosing products and regulators in evaluating post-clearance performance.”

Eversense Implantable CGM Receives Approval for Up to 90 Days’ Usage

The U.S. Food and Drug Administration (FDA) has approved Senseonics’ implantable Eversense continuous glucose monitoring (CGM) device with a wear time of up to 90 days in adults ≥ 18 years of age (bit.ly/2vHy6yx). The system uses a

small sensor implanted just under the skin to transmit data to a skin-worn device, which then communicates with a smartphone app that displays data and alerts. The glucose sensor part of the system is inserted by a physician in a brief clinic procedure and will last for up to 3 months. Based on pivotal trial data from the company, the FDA’s advisory committee unanimously found the device to be safe and effective.

Senseonics is now eyeing the possibility of an even longer wear time for its sensor. Presenting data at the ADA’s 78th Scientific Sessions in June (https://bit.ly/2AM7yCb), Aronson et al. reported a trial involving 36 individuals with type 1 diabetes who wore the device for 180 days. They compared sensor readings with bench-marked laboratory glucose readings every 30 days and found that there was agreement between the two approaches for ~83% of readings. Further effectiveness measures (mean absolute relative difference [MARD] and Clarke error grid analysis) led them to conclude that the system was safe and accurate through 180 days of sensor wear.

“We were very pleased by the accuracy of the CGM system—it had a MARD comparable to other more established CGM systems,” lead author Ronnie Aronson said. “We were also impressed with the stability of the life span of the sensor, which showed no significant decline in accuracy from day 60 to days 90 and 180.”

Head-to-Head Accuracy Comparison Reported for Three CGM Devices

A three-way accuracy comparison of the Dexcom G5, Abbott Freestyle Libre Pro, and Senseonics’ Eversense CGM systems suggests that all performed well, with Eversense performing slightly better in terms of MARD and hyperglycemia control and the G5 system performing best for hypoglycemia control. The study was presented at the ADA’s 78th Scientific Sessions (bit.ly/2vmaRe0). A fuller report is available from bit.ly/2niqz5E.

CODING, REGULATIONS, + REIMBURSEMENTS

NEW ICD-11 CODES RELEASED—ALL 55,000 OF THEM

You read that right. The World Health Organization has released the 11th edition of its *International Classification of Diseases* (ICD-11) for pre-adoption review. The ICD-11 contains ~55,000 unique codes and has been in the making for 10 years. The previous edition, ICD-10, included 14,400 codes.

ICD-11 will be presented for adoption at the World Health Assembly in May 2019 and is expected to be implemented starting 1 January 2022. The June 2018 release was to allow countries time to plan how they will implement the updated coding system. The new version is available online from bit.ly/1m0RSdq. Many sections have received updates, including those covering diabetes, obesity, and cardiology.





CONFERENCE SPOTLIGHT

Risk of Autism Spectrum Disorders in Children of Mothers With Diabetes

Diabetes during pregnancy might increase the risk for autistic spectrum disorders (ASDs) in offspring, according to Xiang et al. (*JAMA*, doi.org/cstd). Compared to the children of mothers without diabetes, the risk appears higher in children of mothers with type 2 diabetes, gestational diabetes mellitus (GDM) before 26 weeks' gestation, or type 1 diabetes during pregnancy. Previously, a link between type 1 diabetes and ASD was suspected but not proven.

Discussing these findings at the American Diabetes Association's 78th Scientific Sessions in June (bit.ly/2nmiTzv), lead author Anny Ziang explained that the outcomes underline the importance of controlling blood glucose right from conception.

The retrospective cohort study included nearly 420,000 single births in a southern California hospital system between 1995 and 2012. Maternal diabetes was identified through electronic medical records, and children ≥ 1 year of age were then tracked through the record system through the end of 2017 for evidence of a clinical diagnosis of ASD.

The authors reported finding 621 children who were exposed to maternal type 1 diabetes, 9,453 exposed to maternal type 2 diabetes, 11,922 whose mothers had GDM diagnosed at < 26 weeks' gestation, and 24,505 whose mothers were diagnosed with GDM at > 26 weeks' gestation. Overall, 5,827 children were eventually diagnosed with ASD during a median follow-up of 6.9 years. Compared to no maternal diabetes, maternal type 1 diabetes had the highest adjusted hazard ratio (2.36, 95% CI 1.36–

4.12, $P = 0.03$), whereas type 2 diabetes and GDM diagnosed at < 26 weeks had lower, but still elevated, risks for ASD. GDM diagnosed at > 26 weeks had no elevated risks.

"These results suggest that the severity of maternal diabetes and the timing of exposure (early vs. late in pregnancy) may be associated with the risk of ASD in offspring of diabetic mothers," the authors conclude. "The potential role of maternal glycemia; other features of [type 1 diabetes] such as autoimmunity and genetic factors; prematurity; and neonatal hypoglycemia remains to be explored. Confounding due to paternal risk factors and other intrauterine and postnatal exposures could not be assessed."

Intensive Treatment of Type 2 Diabetes Is Cost-Effective

Intensive treatment of type 2 diabetes, involving multiple lifestyle and pharmacological interventions, is no more expensive than conventional treatment, according to an analysis by Gaerde et al. that was presented at the ADA Scientific Sessions (bit.ly/2nmiTzv). The findings come from the Steno-2 study, which previously showed that intensive treatment could reduce a number of complications and mortality in the longer term.

In the current analysis, researchers found that, over a period of ~ 21 years, there was no difference in total direct medical costs between the intensive and conventional approaches. The overall cost for intensive treatments in the 80 volunteers involved was $\sim \$13$ million, whereas the cost for 80 individuals receiving conventional treatment approach was $\$12.3$ million ($P = 0.19$). The

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Dulaglutide

Once-weekly dulaglutide, a glucagon-like peptide 1 (GLP-1) receptor agonist, is safe and effective and can replace insulin glargine in patients with type 2 diabetes and moderate to severe chronic kidney disease, according to Tuttle et al. (*Lancet Diabetes & Endocrinology*, doi.org/css6). The 52-week trial compared once-weekly injectable dulaglutide at 1.5 and 0.75 mg and daily insulin glargine, all in combination with insulin lispro. Both doses of dulaglutide were found to be noninferior to insulin glargine in terms of glycemic efficacy, and dulaglutide treatment showed an overall favorable safety profile along with possible therapeutic benefits, including lower rates of hypoglycemia, weight loss, reduced decline in estimated glomerular filtration rate, and greater reductions in albuminuria.

Insulin Glargine

Aggressive treatment with insulin glargine of type 2 diabetes in high-risk obese youth did not preserve β -cell function, according to the latest study from the RISE Consortium (*Diabetes Care*, doi.org/css7). The study included 91 youths who were randomized to either 3 months of insulin glargine followed by 9 months of metformin or 12 months of just metformin. β -Cell function declined in both groups and worsened after treatment ended.

"I am not entirely surprised with the outcome of RISE, not only because the disease appears to be more severe in youth, but [also] because its pathogenetic mechanisms . . . are worse even in the stage of prediabetes," Consortium member Sharon Edelstein said in a statement.

Oral Semaglutide

Results of numerous studies have been announced recently on the performance of semaglutide, Novo Nordisk's GLP-1 receptor agonist, against a range of potential competitors. The company announced in late June that, in head-to-head comparisons, oral semaglutide controlled

blood glucose at about the same rate as the oral dipeptidyl peptidase 4 inhibitor sitagliptin and the injectable GLP-1 receptor agonist liraglutide but was superior in terms of weight loss (reut.rs/2MIIAp2). Earlier, in May, the company also announced headline results of the PIONEER 2 trial, in which oral semaglutide achieved greater A1C reductions than the SGLT2 inhibitor empagliflozin (bit.ly/2ANaKO2). Results of the PIONEER 1 study were also released at the ADA's 78th Scientific Sessions (bit.ly/2ngKotY), showing that treatment with any of three doses of oral semaglutide achieved significantly greater A1C reductions than placebo. Finally, subcutaneous semaglutide was found to reduce A1C and body weight at rates comparable or superior to dulaglutide, according to post hoc outcomes from the SUSTAIN 7 trial (bit.ly/2M6RvmL).

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average cost per patient per year was slightly lower with the intensive approach than with conventional therapy (\$9,648 and \$10,681, respectively), but this was not significantly different ($P = 0.13$). Intensive treatment was found to be more expensive in terms of medication costs but had lower primary care and inpatient costs.

"We discovered that, while intensified, multifactorial treatment may lead to an initial increase in health care costs, this investment is recouped over time by the impressive health benefits and increased longevity the patients experienced," author Joachim Gaede said. "[I]nvesting in early intensified intervention of all known modifiable risk factors in high-risk individuals with [type 2 diabetes] will pay for itself over time due to a reduced cost of complications incurred by patients."

To learn more about ADA's continuing education opportunities, including Diabetes Is Primary events in your community, please visit professional.diabetes.org/ce.