



# DIABETES IS PRIMARY

TIMELY NEWS AND NOTES FOR PRIMARY CARE PROVIDERS  
from the American Diabetes Association

By Max Bingham, PhD

## FROM THE JOURNALS.....

### **Screen Five Simple Markers to Detect Individuals at High Risk for Diabetes**

Screening five simple markers during clinic visits might help to identify high-risk adults who should make lifestyle changes to avoid cardiovascular disease and type 2 diabetes. This is according to updated clinical practice guidelines issued by The Endocrinology Society (*Journal of Clinical Endocrinology and Metabolism*, doi.org/ddm3) with co-sponsors the American Diabetes Association (ADA) and the European Society of Endocrinology.

The guidelines advise that health care providers (HCPs) assess blood pressure, waist circumference, fasting triglycerides, cholesterol, and A1C during clinic visits to screen individuals aged 40–75 years who might be at risk. They suggest that individuals with elevated values for at least three of these markers might be at risk and that HCPs should prioritize or even prescribe lifestyle and behavior interventions to reduce any further progression. Individuals with elevated values for only one or two of the markers should also be reevaluated every 3 years.

“Doctors haven’t been doing enough to measure waist circumference, but it’s essential to identifying patients at metabolic risk earlier and preventing more cases of heart disease and diabetes,” lead author James Rosenzweig said. “We emphasize the importance of lifestyle, dietary, and behavioral changes as the first-line treatment. However, treatment with medication is appropriate if goals are not met with lifestyle changes alone.”

### **Referrals to National Diabetes Prevention Program Remain Low**

A study at one U.S. clinic found that no patients with prediabetes were referred to the Centers for Disease Control and Prevention’s National Diabetes Prevention Program (National DPP) over a 3-year period. Using data from the electronic health record (EHR) and a survey of

clinicians, Keck et al. (*Journal of the American Board of Family Medicine*, doi.org/ddm9) described the screening, diagnosis, and treatment for prediabetes at the clinic, as well as the attitudes and knowledge of the clinicians providing care. The researchers found that the majority of clinicians surveyed believed that prediabetes was an important issue and that screening and diagnosis of the condition was important in terms of managing the care of individuals with it. However, only half were aware of the National DPP, despite the fact that a site offering the program was located in the same building as the clinic.

Based on national screening guidelines, 5,360 clinic patients were eligible for screening, and three-fourths of those had an A1C measured. Of those with an A1C test result, 1,437 had a result indicating prediabetes, and about half had prediabetes documented in the EHR. One hundred and forty-nine of those individuals were prescribed metformin, and none were referred to the National DPP. However, a majority of clinicians did counsel patients on physical activity and recommended nutrition counseling.

According to the authors, the survey was part of a broader initiative to improve diabetes prevention efforts and increase referrals to the National DPP. They concluded: “We will tailor implementation strategies to overcome identified barriers to [National] DPP referral, namely the lack of an EHR referral process, the underdocumentation of prediabetes, and the limited DPP awareness reported by clinicians, while reinforcing prediabetes care assets such as clinicians’ positive prediabetes attitudes and the use of [point-of-care] A1C testing.”



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## TREATMENTS + THERAPIES

### Type 2 Diabetes Affects Heart Structure and Increases Risks for Asians With Heart Failure

Asian individuals with type 2 diabetes and coexisting heart failure (HF) are likely to experience changes in heart structure, according to Yap et al. (*Journal of the American Heart Association*, doi.org/ddnd). Specifically, they report that such changes result in poorer quality of life and worse clinical outcomes such as rehospitalizations and mortality. In parallel, a second report from the same cohort by many of the same authors (Tromp et al., *Diabetes Care*, doi.org/ddnf) suggests that microvascular complications may be more common in Asian individuals with diabetes and HF with preserved ejection fraction compared to equivalent individuals with reduced ejection fraction.

In both cases, the conclusions come from work with the Asian Sudden Cardiac Death in Heart Failure registry, which includes ~6,500 HF patients, of which some have diabetes. In both studies, individuals were followed for ~3 years and had a primary outcome of a composite of 1-year all-cause mortality and HF hospitalization. Numerous other clinical measurements were included, along with echocardiography to assess heart structure.

The first study found that, irrespective of the type of HF experienced, diabetes conferred higher 1-year rates of the composite outcome compared to individuals without diabetes. They also found numerous alter-

ations in heart structure between groups with different types of HF and diabetes status and the control group.

“Primary prevention strategies and tailored treatment options are needed to tackle this twin scourge of diseases,” lead author Jonathon Yap said. “Our findings emphasize the need for preventive public health measures at the community and primary care level. For HF patients who have diabetes, physicians should closely monitor and optimize their management.”

In the second study, the researchers found that individuals with diabetes and any microvascular complication were more likely to have had preserved than reduced ejection fraction. In terms of the primary composite outcome, the presence of microvascular complications of diabetes was associated with a hazard ratio of 1.35 (95% CI 1.04–1.76,  $P = 0.024$ ) after adjusting for numerous factors including HF subtype.

“Our findings call into question the assumption that ‘diabetic heart disease’ refers only to macrovascular coronary artery disease and heart failure with reduced ejection fraction,” senior author Carolyn Lam told us. “In fact, heart failure with preserved ejection fraction may be a microvascular manifestation of diabetes. The clinical implication is that in screening for microvascular complications of diabetes, beyond checking the eyes, kidneys, and nerves for retinopathy, nephropathy, and neuropathy, we should consider the heart and [HF with preserved ejection fraction].”

### Federal Survey Data Illuminate Nonadherence Due to Diabetes Drug Costs

“Drugs don’t work in patients who don’t take them.” This widely quoted comment attributed to former U.S. Surgeon General C. Everett Koop cuts to the heart of one of the biggest health care issues in the U.S. today: medication nonadherence. Now the Centers for Disease Control and Prevention (CDC) have put some numbers to nonadherence in diabetes by looking at the percentage of U.S. adults with diabetes who use specific strate-

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## MARKETPLACE.....

### Random Plasma Glucose Tests May Detect Future Diabetes Risk

Random plasma glucose tests may be able to detect individuals at risk of developing diabetes over the next 5 years. According to Rhee et al. (*PLoS One*, doi.org/ddm5), glucose levels not high enough to indicate diabetes can indicate risk and predict the development of the disease. The authors suggest that plasma samples taken during regular clinic visits “could signal the need for further testing, allow preventive intervention in high-risk individuals before the onset of disease, and lead to earlier identification of diabetes.”

These conclusions come from an analysis of data from ~900,000 Veterans Affairs patients who were not diagnosed with diabetes at baseline. All patients had at least three random glucose tests over a single year, and most of those were obtained opportunistically during regular clinic visits. The authors found that 10% of the group went on to develop diabetes within 5 years. Individuals with at least two random glucose measurements >115 mg/dL within a 12-month period were highly likely to develop diabetes, and those with levels >130 mg/dL were even more likely to develop the disease. Conversely, among those with levels <110 mg/dL, there were few cases of incident diabetes in subsequent years.

“These findings have the potential to impact care in the VA and in the general U.S. population,” lead author Mary Rhee said, “because random plasma glucose levels—which are convenient, low-cost, and ‘opportunistic’—could appropriately prompt high-yield, focused diagnostic testing and improve recognition and treatment of prediabetes and early diabetes.”



## ADA NEWS

### “Know Diabetes by Heart” Webinar Available Online

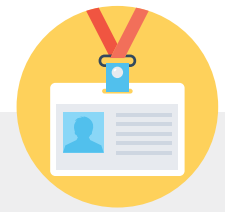
Last fall, the American Diabetes Association (ADA) and American Heart Association (AHA) held a live professional education webinar titled, “Managing Patients with Type 2 Diabetes: Approaches for Screening, Complication Management, and Treatment,” as part of their Know Diabetes by Heart joint initiative. During the webinar, expert panelists reviewed standard and novel approaches to assess for and reduce complications in patients with type 2 diabetes. A recording of the event can now be viewed at [knowdiabetesbyheart.org](http://knowdiabetesbyheart.org).

### Expert Programs for Patients Focus on Diabetes and Heart Disease

Patients can learn about their risk for heart disease and the connection between type 2 diabetes and heart health through the ADA’s Ask the Experts Q&A series. Participants ask questions of ADA’s diabetes experts and learn how their lifestyle habits affect their heart, blood vessels, and blood glucose. These live monthly events are available online or on the phone. They start at 2:00 p.m. Eastern Time and last for about 1 hour. Advance registration is free at [diabetes.org/experts4Pro](http://diabetes.org/experts4Pro), or patients can call 1-855-531-1065 at the time of the events to be directly connected.

Patients can also listen to “Ask the Experts: It’s Personal,” a Q&A podcast series featuring real questions from people with type 2 diabetes and answers from diabetes experts. Listeners will get practical tips on topics such as nutrition, medication management, and physical activity. Find the podcast on iTunes, on Spotify, or at [ateip.libsyn.com](http://ateip.libsyn.com).

The Ask the Experts Q&A Series and podcast are part of the “Know Diabetes by Heart” collaboration between the ADA and the AHA.



## CONFERENCE SPOTLIGHT

### ***Dapagliflozin: Benefits in Diabetes, but Is It About to Pivot to Global Heart Benefits?***

Evidence continues to build on the cardiovascular (CV) benefits of sodium–glucose cotransporter 2 (SGLT2) inhibitors in diabetes, with readouts from certain trials or entire research trial programs such as EMPA-REG OUTCOME (BI 10773 [Empagliflozin] Cardiovascular Outcome Event Trial in Type 2 Diabetes Mellitus Patients), the CANVAS (Canagliflozin Cardiovascular Assessment Study) Program, and DECLARE-TIMI 58 (Dapagliflozin Effect on Cardiovascular Events) pointing in a positive direction. For example, a systematic review and meta-analysis from January 2019 (*The Lancet*, doi.org/gfmx6s) summarized the state of play in relation to the CV benefits of three approved SGLT2 inhibitor agents. Likewise, in August 2019, a major Scandinavian registry (*The British Medical Journal*, doi.org/ddng) confirmed the cardioprotective effects of SGLT2 inhibitor use in people with type 2 diabetes compared to dipeptidyl peptidase 4 inhibitors based on real-world clinical data. Of note in this article, 83% of the patients who took an SGLT2 inhibitor took dapagliflozin. It is from this point that a pivot in thinking about the potential role of dapagliflozin in both diabetes and CV disease seems to be emerging.

In August 2019, AstraZeneca put out a press release (bit.ly/36CtCez) announcing top-line results of the DAPA-HF (Study to Evaluate the Effect of Dapagliflozin on the Incidence of Worsening Heart Failure or Cardiovascular Death in Patients With

Chronic Heart Failure With Reduced Ejection Fraction) trial showing that dapagliflozin significantly reduced CV death or worsening of heart failure (HF) compared to placebo. The statement added that the trial was conducted in patients both with and without type 2 diabetes who had HF with reduced ejection fraction.

In September 2019, the DAPA-HF results were announced at the European Society of Cardiology 2019 Congress in Paris, France (bit.ly/2WLbMS2). There, it was announced that dapagliflozin reduced the risk of a composite of worsening HF and CV mortality by a relative 26% compared to placebo. Notably, the effect sizes were nearly identical in the 45% of patients who had type 2 diabetes at baseline and the 55% who did not (HR 0.75, 95% CI 0.63–0.90, and HR 0.73, 95% CI 0.60–0.88, respectively).

DAPA-HF results were also presented in September 2019 at the 56th European Association for the Study of Diabetes (EASD 2019) annual meeting in Barcelona, Spain. There, even more details were announced from post hoc analyses showing that dapagliflozin offered similar benefits for patients regardless of whether they were taking an angiotensin receptor–neprilysin inhibitor at baseline and that dapagliflozin might also yield renal risk reduction. The full report was published simultaneously with EASD 2019 (*New England Journal of Medicine*, doi.org/gf9n3r).

### ***EASD 2019: Signs of Adult Type 2 Diabetes Seen in Children as Young as 8 Years of Age***

Signs of adult type 2 diabetes can be detected in children as young as 8 years of

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Conference Spotlight, *continued from p. 7*

age, according to Bell et al. (bioRxiv, doi.org/ddnk; EASD 2019 oral presentation 81, bit.ly/2qiQRJK). Specifically, they found that children with an elevated genetic risk score for diabetes had consistent alterations in certain metabolites that stretched from early childhood, through the teenage years, and into early adulthood. Some of the earliest signs included alterations in levels of different types of cholesterol, lipids, and amino acids and certain measures of inflammation. Many more alterations then occurred through the years.

The authors stressed that the individuals included in the study did not have diabetes but that the effects identified point toward a “liability” to develop the disease and offer a hint about how diabetes develops. They noted that their results were more preclinical than clinical at this stage, but that the insights they gained may point toward features of disease that could be targeted to prevent future progression.

“It’s remarkable that we can see signs of adult diabetes in the blood from such a young age; this is about 50 years before it is commonly diagnosed,” lead author Joshua Bell said. “If we want to prevent diabetes, we need to know how it starts. Genetics can help with that, but our aim here is to learn how diabetes develops, not to predict who will or will not develop it. Other methods may help with prediction but won’t necessarily tell us where to intervene.”

Treatments + Therapies, *continued from p. 5*

gies to cut costs associated with out-of-pocket expenses for prescription diabetes medicines.

Using data from the National Health Interview Survey 2017–2018 period, Robin Cohen and Amy Cha from the CDC’s National Center for Health Statistics (NCHS) found that about one-fourth of adults with diagnosed diabetes had asked their doctor for lower-priced diabetes medicines in the previous 12 months. Additionally, 13% reported that they did not take medication as prescribed primarily to reduce prescription drug costs. Specific strategies included skipping medication doses, taking less medication (i.e., splitting doses), delaying prescription fills, or asking doctors for a lower-cost medication. Women were statistically more likely than men to not take medications as prescribed to reduce the costs involved. The full report is available in an NCHS Data Brief No. 349 (bit.ly/2JRpeP0).

Comparing age-groups, the authors found that ~22% of older adults (>65 years of age) reported asking for a lower-cost medication, whereas ~26% of younger adults (18–64 years of age) reported the same behavior. The difference between the groups was statistically significant. Similarly, many more younger adults than older adults (~18 vs. ~7%) reported not taking medications as prescribed. Again, the difference was significant. Uninsured individuals reported the highest rates of both behaviors, with nearly 43% reporting they had asked their doctors for cheaper medications.

“In 2018, medications to treat diabetes ranked sixth out of the top 20 therapeutic classes of dispensed prescriptions, accounting for 214 million prescriptions,” the authors wrote. “In 2017, the annual per-capita expense for outpatient medication for those with diagnosed diabetes was almost \$5,000.” They continued, “Recently, there has been a shift toward lower-cost options as the first line of therapy for diabetes management. However, the burden associated with high prescription drug costs remains a public health concern for adults with diagnosed diabetes.”

To learn more about ADA’s continuing education opportunities, including Diabetes Is Primary events in your community, please visit [professional.diabetes.org/ce](http://professional.diabetes.org/ce).