



# DIABETES IS PRIMARY

TIMELY NEWS AND NOTES FOR PRIMARY CARE PROVIDERS

from the American Diabetes Association

By Max Bingham, PhD

## FROM THE JOURNALS.....

### **Equitable Access to Vaccines: Pressure Grows on CDC to Prioritize Both Types of Diabetes**

With vaccines coming online and promising us more control over coronavirus disease 2019 (COVID-19), we learn from numerous reports about issues facing individuals with diabetes if they catch the SARS-CoV-2 virus that causes COVID-19. The Centers for Disease Control and Prevention (CDC) ([bit.ly/2Yw5uY9](https://bit.ly/2Yw5uY9)) currently lists type 2 diabetes along with 11 other conditions that put adults at "increased risk of severe illness" from the virus, placing them in a high-priority group for vaccination. However, type 1 diabetes is on a separate list of 12 conditions that "might" cause an increased risk for severe illness, resulting in a lower vaccination priority. Now, pressure is building for the CDC to classify both types of diabetes as having the same level of risk and thus to assign any adult with diabetes the same priority ([wb.md/3cDILT4](https://www.medicinesdivision.org/3cDILT4)).

This move began after the publication of an article by Gregory et al. (*Diabetes Care*, [doi.org/fszn](https://doi.org/fszn)) showing that individuals with type 1 diabetes were about four times more likely to be hospitalized with COVID-19 and about three times more likely to have greater illness severity, placing them at about the same level of risk as individuals with type 2 diabetes. An earlier population study from Scotland by Barone et al. (*The Lancet Diabetes and Endocrinology*, [doi.org/fszp](https://doi.org/fszp)) had also concluded that both types of diabetes were independently associated with significant increased odds of in-hospital death with COVID-19.

In mid-January, the American Diabetes Association (ADA) and 18 other organizations sent an open letter to the CDC committee responsible for making vaccine use recommendations in the United States ([bit.ly/2L7dn2X](https://bit.ly/2L7dn2X)). The letter highlighted the new evidence and urged the committee to update guidance to reflect equal risk from

COVID-19 in all types of diabetes. The signatories pointed out that the issue is time sensitive, as states are now rolling out vaccine delivery.

"As the data make clear, differentiating between [type 1 and type 2 diabetes] for purposes of assessing COVID-19 risk is an error that could cost even more lives, and we urge CDC to correct this immediately," Dr. Robert A. Gabbay, ADA's Chief Scientific and Medical Officer, said in a statement ([bit.ly/2MnDsvm](https://bit.ly/2MnDsvm)).

Although the CDC issues national guidelines, individual states are responsible for the practicalities of vaccine roll-out. While many will follow national guidelines, each is free to set its own vaccination priorities. In Tennessee, for example, both types of diabetes are already prioritized together ([bit.ly/3pCRwzC](https://bit.ly/3pCRwzC)). A thorough overview of states' priorities is available in a report from the Kaiser Family Foundation ([bit.ly/39CQRZn](https://bit.ly/39CQRZn)).

### **Telehealth: Racial and Geographic Disparities in Internet Access Raise Concerns**

The sustained growth in telehealth and telemedicine seen over the past year is perhaps one bright spot amid the COVID-19 pandemic that will persist into the future. Shopping, education, and work have all moved online, and routine health care has followed suit. All of these activities share one fundamental requirement: access to a reliable Internet connection. However, such access is not a given in the United States, according to an article by Jain et al. (*Diabetes Care*, [doi.org/ghszzd](https://doi.org/ghszzd)), especially for individuals with hypertension or diabetes, and even more so for those who are Hispanic or Black.

Using data from the 2016–2017 Behavior Risk Factor Surveillance System, the authors identified just under 1 million U.S. adults who reported having hypertension or diabetes and looked at how they answered the question, "Have you used the Internet in the past 30 days?" Although Internet use in the overall population stood at 84%, the authors found it was 72% among individuals with either self-reported hypertension or diabetes. Seventy-four percent of those with hypertension reported Internet use compared to 89% of those without hypertension.

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For diabetes, the proportions reporting Internet use were 65 and 86% for those with and without the disease, respectively.

**"Efforts are needed to mitigate these disparities, especially since Black and Hispanic populations have higher rates of hypertension and diabetes."**

**—SALIM VIRANI**

Internet use among White individuals with hypertension or diabetes was 77%, whereas it was 62% in Blacks and 56% in Hispanics with either disease. These differences translated into adjusted odds ratios (ORs) for the association between Internet use and race of 0.49 (95% CI 0.44–0.53) for Blacks and 0.58 (0.51–0.66) for Hispanics compared to Whites. Although median Internet use overall was ~15–16% lower for Hispanic and Black individuals compared to Whites, the authors reported considerable disparities across the country, with some states having Internet usage rates as much as 30–40% lower among minority groups compared to Whites.

"Efforts are needed to mitigate these disparities, especially since Black and Hispanic populations have higher rates of hypertension and diabetes," senior author Salim Virani said in a statement ([bit.ly/2MMK5XL](https://bit.ly/2MMK5XL)). "Given that morbidity and mortality from COVID-19 is much higher in patients with diabetes or hypertension, and that these patients require chronic care that is now delivered using telehealth, efforts are urgently needed to ensure that the racial and ethnic disparities in outcomes seen in COVID-19 do not spill over into chronic disease care as we shift to a telehealth model of care delivery."

## TREATMENTS + THERAPIES



### Tirzepatide Significantly Lowers A1C and Weight in Type 2 Diabetes and Obesity

Topline results from the SURPASS-1 trial suggest that tirzepatide can significantly reduce blood glucose and body weight in individuals with type 2 diabetes. Trial results suggest that the dual glucose-dependent insulinotropic polypeptide/glucagon-like peptide-1 receptor agonist can reduce A1C by ~2.0%; it reduced A1C from 7.9% at baseline to as low as 5.7% in about half of the trial participants. Reported weight changes included an average reduction of 9.5 kg with the highest dose tested.

The 40-week phase 3 study, which included 478 adults with type 2 diabetes, compared the effects of different doses of tirzepatide on glucose control (A1C) and weight changes compared to placebo. Participants tended to be early in the disease course and had only slightly elevated glucose levels and few comorbidities. Doses of the once-weekly injectable drug were 5, 10, and 15 mg.

According to a press release from Lilly ([bit.ly/2YB4wKc](https://bit.ly/2YB4wKc)), the trial assessed the effects of tirzepatide according to efficacy and treatment-regimen estimands. In both estimands, the three doses reportedly reached statistical significance for A1C and body weight reductions from baseline. In the efficacy estimand, A1C reduction from a baseline of 7.9% ranged from 1.87 to 2.07%, whereas weight reduction from a baseline of 85.9 kg ranged from 7.0 to 9.5 kg, depending on dose. Generally larger effects were reported with higher doses.

The percentage of participants achieving an A1C <7.0% was ~90% for all doses compared to ~20% for placebo. Approximately 30% of participants achieved the stricter A1C target of <5.7%, with the 5- and 10-mg doses, whereas just over 50% reached that target with the 15-mg dose. Fewer than 1% achieved the stricter target in the placebo group.

Similar patterns were observed in the treatment-regimen estimand. The most commonly reported adverse events were gastrointestinal in nature, with noticeably higher levels of nausea, diarrhea, vomiting, and constipation in the treatment groups.

Full results of this trial are expected to be presented at the American Diabetes Association's virtual 81st Scientific Sessions, scheduled for 25–29 June 2021, and published thereafter.

## ADA NEWS

### Nationwide Survey Reveals Financial and Economic Toll of COVID-19 on Diabetes Community

Insights from survey data from the American Diabetes Association (ADA) and Thrivable ([bit.ly/2YCXTa](https://bit.ly/2YCXTa)) suggest that millions of individuals with diabetes in the United States are facing serious challenges in the wake of the coronavirus 2019 (COVID-19) pandemic. The survey, conducted at the end of 2020, found that nearly half of ~2,500 respondents had delayed seeking routine medical care during the pandemic. Of those, more than half cited fear of exposure to the virus, and nearly 10% said they simply could not afford health care during the pandemic. Other trends included problems accessing diabetes technologies such as insulin pumps and continuous glucose monitoring devices and related supplies, often because of financial constraints. A minority of respondents reported disruption to health insurance, often because of job loss.

The pandemic was also found to affect access to healthful food, with more than one-fourth of respondents experiencing food insecurity and a slightly smaller proportion relying on food assistance such as food banks. Respondents also reported that the quality of food received was not good for effectively managing their diabetes, and 20% said they had to choose between buying food and buying necessary medications and supplies. One positive finding was an apparent large increase in telehealth use (73 vs. 11% before the pandemic). Notably, 40% of those who used telehealth services found that it made managing their diabetes easier.

"As many as 40% of the COVID fatalities—120,000 Americans—have been people with diabetes, and more in our community may be at risk of the worst of the virus' effects because so many are now unable to manage their diabetes effectively," said Tracey D. Brown, ADA's Chief Executive Officer. "We must be even more mindful that our community, which includes an outsized portion of people of color and those of lesser means, must be a priority for relief efforts, including prioritized access to the COVID vaccine."

### ADA Review Examines Social Determinants of Health in Diabetes

A major review of social determinants of health (SDOH) in diabetes suggests that a multitude of solutions are still needed to address racial, ethnic, and socioeconomic disparities in the incidence and outcomes of diabetes. According to Hill-Briggs et al. (*Diabetes Care*, doi.org/ghjtcq), there is potential for progress, but a considerable amount of research and cooperation will be needed across sectors to develop effective interventions.

Covering issues such as socioeconomic status, the physical environment, and access to food and health care, the review centers on two themes: how these factors affect the incidence and outcomes of diabetes and whether any past interventions have had an impact on outcomes. It paints a picture of extremes, in which poverty, social deprivation, years of underinvestment, and outright racism converge to drive the worst health outcomes in diabetes.

The authors focus particularly on socioeconomic status as a key predictor of disease onset and progression, highlighting that the construct, which comprises economic, educational, and occupational status, can be linked to nearly



all SDOH in diabetes. Lower income and lower educational levels both correlate with increased diabetes incidence and prevalence, and certain jobs, job insecurity, unemployment, and long working hours are all associated with high risk for diabetes. The report also highlights a near total lack of evidence for interventions that have attempted to change socioeconomic status in a bid to reduce diabetes risk.

The report also addresses additional SDOH, including neighborhood and physical environment,

toxic environmental exposures and air pollution, the food environment, and various aspects of health care and social support. The authors offer recommendations for future research, including the need to reach a consensus on definitions and metrics, as well as the need to study SDOH and diabetes in different populations and to form partnerships to design and execute studies to determine whether and how SDOH might be a root cause of diabetes.

## MARKETPLACE.....

### Wholesale Prices for Diabetes Drugs Increased Steadily Between 2015 and 2020

Prices of brand-name pharmacological agents in five major drug classes, including three for the treatment of diabetes, increased “in lock-step” every year from 2015 to 2020, according to Liu et al. (*JAMA Network Open*, doi.org/fs2g). Increases ranged from an annual average of 6.6% for branded dipeptidyl peptidase 4 (DPP4) inhibitors, 8.0% for glucagon-like peptide 1 (GLP-1) receptor agonists, and 8.6% for sodium–glucose cotransporter 2 (SGLT2) inhibitors. The analysis also included direct oral anticoagulants and P2Y12 anti-platelet agents.

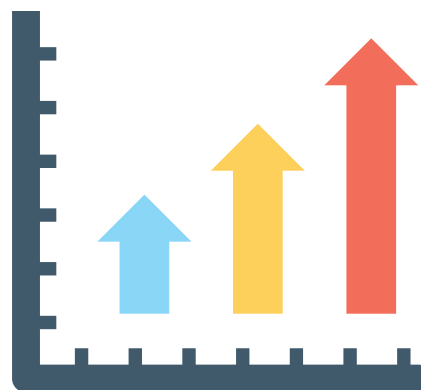
In all cases, price increases far out-paced general inflation and the average price inflation for all prescription drugs (2.1% during the same period). For the diabetes drug classes, correlation coefficients over the 5-year period were 0.98 for SGLT2 inhibitors, 0.96 for DPP4 inhibitors, and 0.92 for GLP-1 receptor agonists.

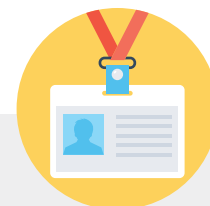
The study was based on publicly available data obtained from the Micromedex Red Book (IBM).

Brands in the SGLT2 inhibitor class included Farxiga (dapagliflozin), Invokana (canagliflozin), Jardiance (empagliflozin), and Steglatro (ertugliflozin). Select other brands in the DPP4 inhibitor and GLP-1 receptor agonist classes included Januvia (sitagliptin), Tradjenta (linagliptin), Trulicity (dulaglutide), Byetta (exenatide), and Victoza (liraglutide).

The authors noted a number of limitations to their analysis, not least that rebates and discounts were not accounted for, but said patients were nevertheless likely to suffer in that rebate growth is positively correlated with list price increases.

“The lock-step price increases of brand-name medications, without evidence of price competition, raise concerns and would be expected to adversely affect patient adherence to medications and thus clinical outcomes,” the authors noted. They suggested that policies that limit such price increases, as well as shorter patent periods and the encouragement of generic equivalents of these drugs might help to limit cost burdens for patients.





## CONFERENCE SPOTLIGHT

### ***Sotagliflozin Reduces Cardiovascular Risks in Type 2 Diabetes***

Sotagliflozin, a novel inhibitor of sodium–glucose cotransporter (SGLT) 1 and 2, reduces cardiovascular events in high-risk patients with type 2 diabetes and heart failure (HF) or chronic kidney disease (CKD), according to two trials presented at the virtual American Heart Association annual meeting in November 2020 and published simultaneously.

According to Bhatt et al. (*New England Journal of Medicine*, doi.org/fs2d), the SCORED trial demonstrated that sotagliflozin reduced a composite outcome of cardiovascular death and hospitalizations/urgent visits for HF by a relative 26% compared to placebo (5.6 vs. 7.5 events per 100 patient-years in the sotagliflozin and placebo groups, respectively; hazard ratio [HR] 0.74 [95% CI 0.63–0.88,  $P < 0.001$ ]. This trial included patients with type 2 diabetes, CKD, and risks for cardiovascular disease who received standard care in addition to treatment/placebo for an average of 16 months.

Meanwhile, the SOLOIST-WHF trial (Bhatt et al., *New England Journal of Medicine*, doi.org/fs2f) enrolled 1,222 patients with type 2 diabetes who were recently hospitalized with worsening HF. The authors reported that sotagliflozin reduced the same composite end point by a relative 33% compared to placebo (51.0 vs. 76.3 events per 100 patient-years, HR 0.67, 95% CI 0.52–0.85,  $P < 0.001$ ).

Despite both trials ending early because of a loss of funding and uncertainties related to the

coronavirus disease 2020 pandemic (bit.ly/3cvqrul), the SCORED trial still met its original primary end point of first occurrence of cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke with an HR of 0.84 (95% CI 0.72–0.99). The trial also met its co-primary end point of first occurrence of cardiovascular death or hospitalization for HF with an HR of 0.77 (95% CI 0.66–0.91). Meanwhile, the SOLOIST-WHF trial identified a significant reduction in hospitalizations/urgent visits for HF, but not a significant reduction in cardiovascular deaths.

There were more gastrointestinal adverse events associated with the treatment compared to placebo in both studies. A number of other adverse events associated with sotagliflozin were reported in the SCORED trial, but not in the SOLOIST-WHF trial.

“It is now clear that most patients with type 2 diabetes and either kidney disease or heart failure should be on an SGLT2 inhibitor,” said Deepak Bhatt, lead author of both studies. “SCORED provides further randomized clinical trial evidence that SGLT2 inhibitors should be part of the standard of care for patients with type 2 diabetes mellitus and kidney disease. And SOLOIST-WHF demonstrates that early, in-hospital initiation of SGLT2 inhibitors is safe, effective, and should become the standard of care in patients with type 2 diabetes mellitus and heart failure.”

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