Disclaimer
The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

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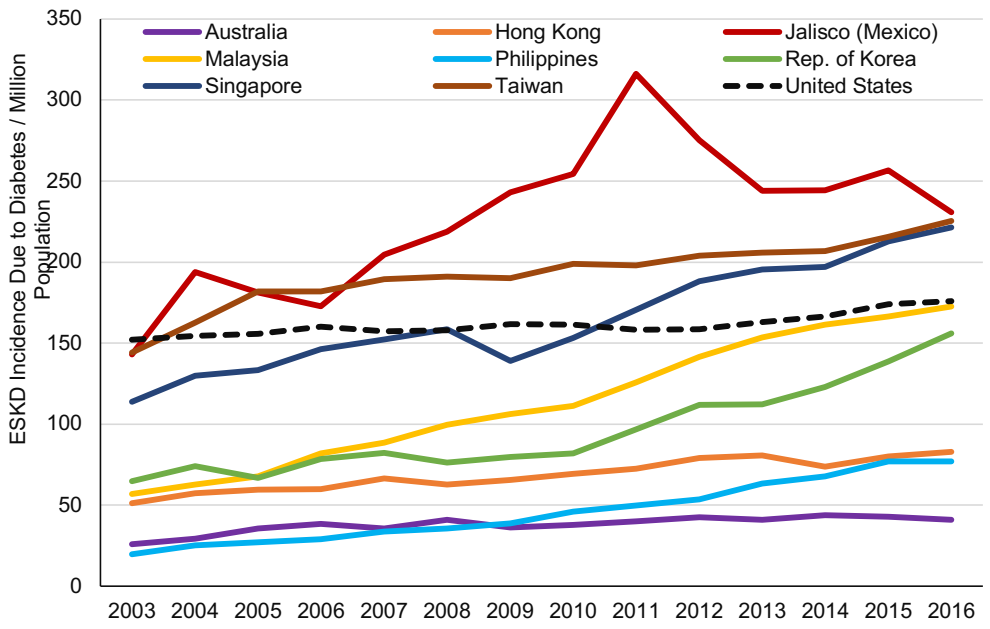
Figure 4. Trends in the unadjusted incidence of diabetes-related ESKD, 2003–2016 [4]. The countries with the largest average yearly change in ESKD incidence from 2003 to 2016 are represented, plus the United States.



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SGLT2s Show Promise for Kidney Protection

Benefits Seen in Patients with and without Diabetes

By Bridget M. Kuehn

Results from 2 large clinical trials of sodium-glucose cotransporter 2 (SGLT2) inhibitors presented at the European Society of Cardiology (ESC) Congress 2020 show that the drugs may offer substantial kidney-protecting benefits.

The hotly awaited results of the Phase III Dapagliflozin And Prevention of Adverse Outcomes in Chronic Kidney Disease (DAPA-CKD) trial showed a 39% reduction in a composite outcome of sustained reduction in estimated glomerular filtration rate of at least 50%, end stage kidney disease, or renal or cardiac death in patients taking the drug compared with patients taking a placebo (1). The trial, which was stopped early because of the strong benefit (2), enrolled 4304 patients with chronic kidney disease from 386 centers in 21 countries and included patients with diabetes and without. All participants were already taking an angiotensin-converting enzyme (ACE) inhibitor or angiotensin receptor blocker (ARB). Comparable benefits were seen in patients with and without diabetes.

"The DAPA-CKD trial has shown dapagliflozin's potential as a long-awaited new treatment option for patients with chronic kidney disease," said lead author Hiddo Heerspink, PhD, professor in the department of clinical pharmacy and pharmacology at the University Medical Center Groningen in the Netherlands in a press briefing at ESC Congress 2020.

Heart *and* kidney benefits

Results of the Empagliflozin Outcome Trial in Patients with Chronic Heart Failure and a Reduced Ejection Fraction (EMPEROR-Reduced) trial were also presented and published during the meeting (3). The trial enrolled 3730 patients with heart failure with reduced ejection fraction who were simultaneously treated with the drug and standard heart failure therapy.

It showed that empagliflozin reduced the risk of hospitalization for heart failure by about 30% compared with placebo in both patients with and without diabetes. Previously, results of the Dapagliflozin and Prevention of Adverse Outcomes in Heart Failure (DAPA-HF) trial demonstrated that dapagliflozin reduced the risk of worsening heart failure or cardiovascular death in patients with or without diabetes (4).

"We believe the important results of DAPA-HF and EMPEROR-Reduced trials should be sufficient to establish SGLT2 inhibitors as a new standard of care for patients with heart failure and reduced ejection," said lead author Milton Packer, MD, distinguished scholar in cardiovascular science at Baylor University Medical Center in Dallas, Texas.

In addition to demonstrating heart benefits, empagliflozin slowed the progressive kidney function decline seen in patients with heart failure and reduced by 50% the risk of a composite end point of needing chronic dialysis, kidney transplant, or sustained declines in estimated glomerular filtration rate.

Class benefits

The results of the DAPA-CKD trial showed a comparable magnitude of kidney benefit to the Canagliflozin and Renal Events in Diabetes with Established Nephropathy Clinical Evaluation (CREDENCE) trial of the SGLT2 inhibitor canagliflozin, which was also stopped early in July 2018 (5).

"DAPA-CKD really reinforced a major point from CREDENCE, how the SGLT2s are great drugs to reduce the need for dialysis and improve mortality in patients who have diabetic kidney disease," said Christos Argyropoulos, MD, PhD, chief of the division of nephrology at the University of New Mexico School of Medicine, who noted diabetes contributes to about 40% of cases of chronic kidney disease. "It also added the twist that the drugs may work to the same degree and improve the same outcomes in patients who don't have diabetes but do have chronic kidney disease."

There are currently multiple theories about how

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SGLT2s

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SGLT2 inhibitors protect the kidneys, but Argyropoulos said they likely help by stopping hyperfiltration and the resulting damage that occurs when the kidneys overwork.

"A big part of kidney disease development and progression is the kidneys sensing that something has happened to them and trying to compensate by working extra," he said. "This process, called hyperfiltration, causes secondary kidney damage, which makes more kidney tissue stop working." The SGLT2s seem to be able to slow the kidneys down and make them last longer, he said.

There are still some questions that need to be answered about this class of drugs. For example, it would be helpful to know who is likely to have rare but serious side effects like diabetic ketoacidosis.

"The next thing that we would have to do is find ways to use these drugs more safely, or at least detect these complications," Argyropoulos said.

It will also be important to manage or prevent common side effects, such as genital yeast infections in both men and women taking the drugs. Although these infections are easy to treat, repeated infections may make patients want to stop taking the drugs, Argyropoulos said.

The growing number of trials supporting substantial kidney benefits of SGLT2 inhibitors is a major development for the field of nephrology, Argyropoulos said. In fact, he said it's likely the biggest development since the emergence of ARBs and ACE-inhibitors.

"We are really talking about a once every 20 years type of event for nephrology."

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Take Action to Increase Access to Immunosuppressive Medication

ASN needs your help to ensure kidney transplant patients are able to access life-saving immunosuppressive medications.

Congress has introduced the Comprehensive Immunosuppressive Drug Coverage for Kidney Transplant Patients Act (H.R. 5534/S. 3353), bipartisan legislation that would remove Medicare's three-year limit for coverage of immunosuppressive drugs.

According to a pre-pandemic Department of Health & Human Services report, hundreds of kidney transplant patients lose their transplant due to an inability to afford immunosuppressive medication. This is not only costly to the health of the patient, but also to Medicare as the patient returns to dialysis. A recent analysis by the non-partisan Congressional Budget Office found that extending coverage of immunosuppressive drugs would save Medicare $70 million over a period of 10 years.

ASN and stakeholder organizations have urged Congress to pass this legislation before time runs out. However, your legislators need to hear from you as a constituent. Urge them to pass the Comprehensive Immunosuppressive Drug Coverage for Kidney Transplant Patients Act, which will save lives and taxpayer dollars.

Visit the following link and send a pre-composed email to your members of Congress: www.asn-online.org/policy/lac.aspx.