

# VALUE-BASED *Cardiology*<sup>™</sup>

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## Surgeon General Issues Call to Action on Hypertension

by Mary Caffrey

**US SURGEON GENERAL JEROME M. ADAMS, MD, MPH,** issued a nationwide call to action for providers and health systems to do more to control hypertension, which affects nearly half the adult population and contributes to some of the most common and expensive conditions in Medicare, such as chronic kidney disease, heart failure, and cognitive decline.

Adams announced the initiative in a viewpoint appearing in *JAMA*, and published the full, 52-page call to action document on HHS' website.

The call to action outlines the enormous cost of having 108 million adults with hypertension, along with the multiple factors that contribute to it, especially among minority populations. Inequalities in social, economic, and environmental conditions—the social determinants of health—play a role. So do “psychosocial and socioeconomic stressors,” such as depression, joblessness, neighborhood poverty, and financial stress—all of which may be on the rise due to coronavirus disease 2019 (COVID-2019).

## Risk Predictor Model Aims to Reduce HF Hospitalization in Patients With T2D

by Gianna Melillo

**BY COLLECTING DATA FROM** electronic medical records (EMRs) of patients with type 2 diabetes mellitus (T2DM), researchers were able to construct a risk prediction model of hospitalizations due to heart failure (HHF) for patients with the disease, according to a study published in *Clinical Cardiology*.

In this EMR-based retrospective cohort study, data from 54,452 patients receiving care from a single integrated healthcare system in the northeast United States were compiled in order to determine the strongest predictors of HHF.

Patients with T2DM were divided into 2 independent data sets, and the variables leading to HHF in each group were evaluated. The data were then combined to determine the 9 main variables contributing to HHF ( $P = .0001$ ). Between 2001 and 2016, subjects were followed for an average of 6.6 years.

The strongest predictors of HHF in patients with T2DM are:

- Age
- Coronary artery disease
- Blood urea nitrogen
- Atrial fibrillation
- Hemoglobin A1c
- Blood albumin
- Systolic blood pressure
- Chronic kidney disease
- Smoking history

“High-risk” patients were classified as such if they met a quantitative threshold of >5% probability of HHF within 5 years.

The study included patients with preexisting T2DM, defined as “patients meeting the diagnostic criteria within two years of the first EMR-documented encounter;” and newly diagnosed patients with T2DM, or “those first meeting diagnostic criteria more than 2 years after the first EMR-documented encounter.” Any patients with T2DM with previously documented HHF were excluded.

According to researchers, “T2DM affects nearly 10% of the United States adult population, and the morbidity and mortality associated with T2DM are often attributable to cardiovascular (CV) disorders.” In addition, 44% of hospital admissions relating to heart failure list diabetes as a comorbidity.

The most common CV risk factors listed in patients’ EMRs were hypertension (72%), hyperlipidemia (71%), coronary artery disease (21%) and prior myocardial infarction (5%).

These findings prompted researchers to create a prediction model aimed at reducing costly hospital visits and guiding therapeutic decisions.

The authors state, “The practical intent of risk prediction models is to identify high-risk patients such that cost-efficient provision of advanced management strategies (eg, a novel, efficacious, yet expensive pharmaceutical) can be directed toward those patients most likely to experience untoward events, thus minimizing the number needed to treat for benefit.”

Researchers hope future studies will evaluate the calibration of their model in new settings, to better gauge when providers should take action to prevent such hospitalizations.

#### Reference:

Williams BA, Geba D, Cordova JM, Shetty SS. A risk prediction model for heart failure hospitalization in type 2 diabetes mellitus [published online December 14, 2019]. *Clin Cardiol*. doi:10.1002/clc.23298.

The HHS document describes a 3-step process:

- **Awareness:** increasing the percentage of people who know they have high blood pressure
- **Treatment:** increasing the percentage receiving guideline-recommended care
- **Control:** increasing the percentage of the population who have hypertension lowered below specific thresholds.

In JAMA, Adams and co-author Janet S. Wright, MD, write that a larger share of the US adult population had uncontrolled hypertension in 2017-2018 (53.8%) compared with 2013-2014; in late 2017, the American Heart Association and American College of Cardiology lowered the level of what is considered hypertension or high blood pressure from 140/90 to 130/80, based on clinical trial data that supported controlling blood pressures at lower levels.

Adams’ message comes when the focus on disparities in health care and outcomes is brighter than ever, in part because minorities are dying at higher rates from COVID-2019. Part of the call to action is to address disparities in neighborhood-level conditions that contribute to hypertension.

“Setting blood pressure control as a population health priority also draws attention to the profound disparities associated with hypertension,” Adams and Wright wrote in JAMA.

The call to action has 3 major goals:

1. Making hypertension a national priority and “galvanizing action” by both payers and employers to promote blood pressure control by eliminating co-pays for key medications or blood pressure monitors.
  2. Creating community supports for hypertension control. Community-level investments in places to exercise, ride bicycles, and find affordable, healthy food, “should be a priority,” they wrote. Systems should be in place so that people with high blood pressure no where to go for help.
- “The reason to establish this goal is not merely to describe these health inequities, but to do so as a catalyzing step toward their elimination,” they said.**
3. Providing the best care for patients with hypertension. Adams writes that the best health systems can achieve hypertension control rates of 70% or better, but this a team approach, standardization, metrics and accountability, and strategies for self-monitoring.

In his message in the HHS document, Adams writes that while hypertension is a condition associated with the elderly, it does not begin in old age, nor is it limited to this group. “All ages are impacted, and early identification and long-term control can preserve cardiovascular health now and into the future,” he writes. “We know that lifestyle changes, such as being physically active and adopting a healthy diet, can promote hypertension control, yet many communities have significant barriers that prevent people from making these changes.”

The final section of the HHS document outlines the “sectors” that can contribute to the solution. Government has a role in funding research, but the document calls on “public health professionals, health care professionals, and their professional associations and societies” to take the initiative to “make the case” for investing in hypertension control.

#### Reference

Adams JM, Wright JS. A national commitment to improve the care of patients with hypertension in the US. *JAMA*. Published online October 7, 2020. doi:10.1001/jama.2020.20356

# ESC Research Report: Managed Care, Social Determinants in Cardiology

by Mary Caffrey

**BELOW ARE SELECTED ABSTRACTS** presented at the European Society of Cardiology 2020 Congress, which was held in a virtual format due to the coronavirus disease 2019 pandemic.

Prescribing patterns in diabetes and heart failure. Data presented by researchers from Novartis, makers of sacubitril/valsartan (Entresto), show that US physicians are more likely to prescribe the heart failure (HF) drug alongside a sodium glucose co-transporter 2 (SGLT2) inhibitor to younger, male patients with a better renal profile.

Patients with type 2 diabetes (T2D) are 2 to 4 times more likely to develop HF than persons without diabetes, and HF is also a risk factor for diabetes. SGLT2 inhibitors have been shown to lower blood glucose in patients with T2D and prevent hospitalization for HF (HFH) in this same group, and since 2015, cardiovascular outcomes trials have shown some evidence of protection against renal decline.

Emil Loefroth, PhD, of Novartis Sweden presented findings analyzing Optum claims data on US prescribing patterns for sacubitril/valsartan. This is an angiotensin receptor neprilysin inhibitor that reduces the risk for cardiovascular death or HFH in patients with HF with reduced ejection fraction; it is being evaluated by the FDA for patients with HF with preserved ejection fraction. Of the 2.3 million patients with HF identified, 41.6% had a T2D diagnosis.

Among them, 560 patients were simultaneously prescribed sacubitril/valsartan and an SGLT2 inhibitor (cohort 1), while 1566 were prescribed sacubitril/valsartan alongside a glucagon-like peptide-1 (GLP-1) receptor agonist or a dipeptidyl peptidase-4 inhibitor (DPP-4) inhibitor (cohort 2). Loefroth and his fellow researchers found:

Cohort 1 had a smaller share of women (27.9%) than cohort 2 (35.0%).

The patients in cohort 1 were younger (mean age, 61.4 years) compared with cohort 2 (mean age, 66.4 years).

The share of patients with stage 3 chronic kidney disease (estimated glomerular filtration rate <60 to >30 mL/min/1.73 m<sup>2</sup>) was 11.8% in cohort 1 and 24.4% in cohort 2.

Where data were available, the median NT-proBNP differed between the cohorts, at 914 (2154) pg/mL for cohort 1 and 2290 (5301) pg/ml for cohort 2, indicating a much healthier profile for the first group. However, complete values were available for only 17.7% of cohort 1 and 19.0% of cohort 2.

Data used were derived from the Optum database between July 1, 2014, and December 31, 2019. The index date for each patient was the date for the second prescription of “overlapping interest,” so it is not possible to tell which drug was prescribed

first. Sacubitril/valsartan was approved by the FDA in July 2015, while the first SGLT2 inhibitor was approved in March 2013 (canagliflozin) and the second in January 2014 (dapagliflozin). The first DPP-4 inhibitor was approved in 2006, and the first GLP-1 receptor agonist was approved in 2012.

Since the end of data collection, the FDA has approved canagliflozin for a renal indication based on the April 2019 CREDENCE trial for patients with T2D. This past weekend, data from DAPA-CKD showed that dapagliflozin could prevent renal decline in patients with HF regardless of diabetes status.

## Reference

Loefroth E, Hughes M, Shi Y, et al. Patient and clinical characteristics of heart failure patients concomitantly prescribed SGLT2 inhibitors and sacubitril/valsartan, a database cohort study using the Optum electronic health record data. Presented at: the European Society of Cardiology 2020 Congress; August 28, 2020.

Socioeconomic status in acute coronary syndrome. The connection between social determinants of health and outcomes is gaining attention in the United States, and much has been made of the lack of access to health care among the poor.

But a study presented from Australia at ESC 2020 found that socioeconomic status can affect outcomes after a hospitalization for acute coronary syndrome (ACS), even in countries with universal health coverage. In short, the poorer patients were more likely to die early compared with the wealthiest patients, even though they took medications. Far fewer from the poor groups took part in cardiac rehabilitation.

Researchers linked SNAPSHOT ACS data and its 18-month follow-up to admissions data from across Australia, as well as the national death index and pharmacy benefits data for a period of 3 years following discharge for ACS. Data were divided into 5 groupings, with group 1 having the lowest socioeconomic status and group 5 having the highest, based on the country's national economic statistics bureau, using residential postal codes as a marker. Outcomes were cardiac rehabilitation participation and smoking rates 18 months after discharge, the use of at least 3 of 4 indicated therapies, all-cause death, and cardiovascular disease (CVD) rates 36 months after discharge.

Results. Among 1655 patients with ACS (median [SD] age, 68 [13.5] years), 65% of whom were male, 21% were in group 1, 22% in group 2, 23% in group 3, 18% in group 4, and 15% in group 5. After 18 months, follow-up was done with 61% of the patients, with comparable loss to follow-in across each group. Patients in groups 1 and 2 had the lowest participation rates in

cardiac rehab compared with those in the group 5 (odds ratio [OR], 0.60; 95% CI, 0.36-0.99 for group 1; OR, 0.56; 95% CI, 0.35-0.91 for group 2). Odds of smoking were higher among those in group 3 than in group 5 (OR, 2.60; 95% CI, 1.15-5.89), but other patterns were seen.

By 36 months after discharge, there was no difference in the odds of using at least 3 of 4 medications among the groups. Even so, patients from group 1 (OR, 1.96; 95% CI, 1.19-3.21) and group 2 (OR, 1.91; 95% CI, 1.19-3.07) were more likely to die than those in group 5. The odds of CVD readmission did not differ across groups.

## Reference

Hyun K, Brieger D, Briffa T, et al. The impact of socioeconomic status on secondary prevention of the acute coronary syndrome. Presented at: the European Society of Cardiology 2020 Congress; August 28, 2020.

Predicting readmission in CAD. Risk calculators have been developed to assess the likelihood of a second event in coronary artery disease (CAD), but their value has been limited without information on which patients would benefit from intensive management. Investigators at the Baker Heart and Diabetes Institute in Melbourne, Australia, applied an existing risk score to predict readmission of patients with CAD and determine if higher-risk patients get more benefit from intensive medical and interventional strategies.

The study covered 19,940 patients admitted to a hospital in 2010 with CAD; they were followed through 2015. A risk score validated through PEGASUS-TIMI54 was used to stratify patients based on risk of future events, with a score of 6 as the

cutoff. Patients who scored below 6 were low risk, while those who scored  $\geq 6$  were high risk and recommended for intervention. The primary outcome was all-cause readmission; other outcomes were all-cause mortality and days alive and out of the hospital within 5 years of discharge.

Results. The 6573 high-risk patients included more males and Indigenous people, with more comorbidities who were more likely to be readmitted or dead at 5 years than the low-risk group, who numbered 13,367. Patients who were taking beta-blockers, ACE inhibitors or ARBs, or who had percutaneous coronary intervention (PCI, a stent) were less likely to be readmitted and showed a negative interaction with predicted risks—indicating that the benefits increased for the higher-risk patients. Conversely, those who had coronary artery bypass graft (CABG), were more likely to be readmitted (HR, 1.44; 95% CI, 1.15-1.80) and showed a negative interaction with patients predicted risks.

The authors wrote that patients who receive CABG are more likely to be readmitted than those who do not receive this procedure, with “this trend reduced for patients with higher risks.” The analysis of secondary outcomes suggest that interventions reduce mortality risks, with CABG having the strongest effect (HR, 0.34; 95% CI, 0.29-0.48). Results suggest high-risk patients who receive statins, PCI, and CABG have improved survival odds.

## Reference

Huynh Q, Ngheim S, Byrnes J, et al. Secondary prevention in coronary artery disease: a risk-guidance may be beneficial. Presented at: the European Society of Cardiology 2020 Congress; August 28, 2020.

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# PBMI Analysis Finds Jardiance Use Could Save Employers Thousands of Dollars

by Gianna Melillo

**RESULTS FROM AN ANALYSIS CONDUCTED** by the Pharmacy Benefit Management Institute (PBMI) show that the use of Jardiance (empagliflozin) among employees with type 2 diabetes (T2D) and cardiovascular disease (CVD) can save employers around \$737,000 per 10,000 covered lives each year. In the United States, 56% of Americans receive health insurance coverage through employer-sponsored plans.

Sharon Frazee, PhD, MPH, senior vice president of research and data innovation at PBMI, presented the results in a recent webinar.

“Employers are the main source of health insurance in the United States today, and because of this, employers end up sharing a significant portion of the cost of treating diabetes and CVD,” she said.

The webinar, “Improving Total Cost of Care for Patients With Type 2 Diabetes and Cardiovascular Disease,” focused on the

wide-ranging financial and clinical impacts diabetes care has on employers and patients alike. This is, in part, due to the costly and complex comorbidities often faced by patients with diabetes. “The risk of death from CVD among adults with diabetes is twice that of adults without diabetes,” Frazee said.

Beyond the reduction of cardiovascular events, clinical research found that medications containing empagliflozin lower glycated hemoglobin and reduce bodyweight in patients up to 2.9%, when used alongside adjustments in diet and exercise.

“Diabetes impacts 1 in 10 Americans, and among this 1 in 10, 1 in 5 had CVD. Given the prevalence costs and clinical progression associated with diabetes, plan design that encourages better management of diabetes may be in the best interests of both payers and patients,” Frazee concluded.

Researchers gathered data on commercially ensured, employer-sponsored populations to determine savings resulting from Jardiance use. They then compared the data to patients using other antidiabetic agents.

On average, patients incur direct pharmacy and medical costs totaling \$53,027 per person per year (in 2018 dollars). In an average commercially ensured, employer-sponsored population, 0.67% of members would meet the criteria for receiving Jardiance. By covering that small fraction of the population's costs, employers' inclusion savings could reach approximately \$737,000 per 10,000 lives covered annually.

Along with direct costs, "employers also have indirect costs due to workdays absent and reduced performance at work," Frazee said. In 2017, the American Diabetes Association found the "total cost of diagnosed diabetes is \$90 billion in reduced productivity alone," according to the webinar.

The use of Jardiance resulted in an annual cost savings of \$13,704 per patient, per year, researchers found. Most of these savings come from reduced medical costs as opposed to prescription drug costs.

"The aim of the analysis conducted by PBMI was to provide a better understanding of the cost outcomes for patients with T2D and CVD, treated with Jardiance, compared to similar patients treated with other antidiabetic medications," Frazee said.

The results of the study are not generalizable due to the fact that data were only collected from employer-sponsored, commercially ensured patients. For Medicare populations, Frazee notes, diabetes costs can be more than 3 times higher.

Data was sourced from an Armetrx database of patients' deidentified medical and prescription drug claims. Beginning on the index date, data was collected for 12 months on a per patient per month basis.

For the Jardiance cohort, the average patient total cost of care was \$3580.72 per patient per month compared with \$4503.90 in the non-Jardiance cohort.

"By shifting patients who meet criteria to this drug, financial savings are possible," Frazee said.

## Patients Take Different Statins, but Vascepa Benefits Are the Same

by Mary Caffrey, Gianna Melillo

**THE BENEFITS OF TAKING ICOSAPENT ETHYL**, the purified omega-3 fatty acid sold as Vascepa, were consistent across statins of different strengths and types, according to the latest data from the REDUCE-IT study presented during the 2020 Congress of the European Society of Cardiology (ESC), being presented in a virtual format.

Icosapent ethyl, first approved to treat high triglycerides, has since received a cardiovascular (CV) indication after REDUCE-IT showed that a 4g per day dose reduced the risk of first-time CV events by 25% and first and future events by 30%. Subsequent studies have sought to better understand the mechanisms of how icosapent ethyl produces these results.

In this latest round of data from the study, lead study author Deepak Bhatt, MD, MPH, of Brigham and Women's Hospital Heart & Vascular Center and Harvard Medical School, sought to examine the relationship between low density lipoprotein (LDL) cholesterol pathways and the CV benefits of icosapent ethyl, by examining whether there were major differences in benefit by statin type or by statin group (lipophilic vs lipophobic); according to the abstract presented at ESC, 96.1% of the patients in the study fell into one of these statin groups.

In an interview, Bhatt told *The American Journal of Managed Care*® that the analysis further supports the main findings of REDUCE-IT. "We looked at patients who are on really intense statins, things like atorvastatin and rosuvastatin, or more modest types of statins, such as simvastatin or pravastatin," he said. "We also bunched it by hydrophobic and hydro-

philic statins."

"The bottom line was, any way you sliced it there was a benefit, a consistent benefit favoring icosapent ethyl versus placebo, irrespective of the actual statin type or category of statin."

Results. CV outcomes were similar across different statin types (interaction,  $P = .61$ ) and across lipophilic/lipophobic categories (interaction,  $P = .51$ ). Hazard ratio (HR) results by individual statin type were as follows, all favoring icosapent ethyl (all 95% CI):

- Atorvastatin: HR, 0.80 (0.68-0.94),  $P = .0054$
- Simvastatin: HR, 0.76 (0.64-0.90),  $P = .0017$
- Rosuvastatin: HR, 0.68 (0.54-0.85),  $P = .0009$
- Pravastatin: HR, 0.88 (0.62-1.25),  $P = .47$

Among the 2 main statin groups, the HR on lipophilic statins was 0.78 (0.69-0.87),  $P < .0001$ ; for lipophobic statins, HR, 0.73 (0.66-0.88),  $P = .0012$ .

In the abstract, Bhatt and co-authors wrote that the LDL cholesterol changes and CV risk reduction in the study "appear independent of the type of concomitant statin therapy."

They concluded, "These data provide clinicians with additional insight regarding concomitant statin therapy considerations when prescribing icosapent ethyl and suggest there are important mechanisms of action for the substantial CV risk reduction observed with icosapent ethyl that are distinct from the LDL receptor pathway."

Reference

Bhatt DL, Miller M, Steg P, for the REDUCE-IT Investigators. REDUCE-IT outcomes by baseline statin type. Presented at ESC Congress 2020: Abstract 218514.

# Quality of Care, Mortality Consistent Among MA, FFS Medicare Enrollees With Heart Failure

by Maggie L. Shaw

**REPORTS OF MEDICARE ADVANTAGE (MA)** patients receiving higher-quality care for their cardiovascular disease prompted an observational, retrospective, cohort study of MA patients with heart failure and their fee-for-service (FFS) enrollee counterparts. The results, published in *JAMA Cardiology*, show that mortality and the quality of care in both patients groups were consistent for those hospitalized for heart failure.

One-third of Medicare beneficiaries are enrolled in MA plans, the private insurance option for plan participants.

The primary outcomes of the study were in-hospital mortality, discharge disposition, length of stay (LOS) 4 days or less, and 4 heart failure achievement measures for 262,626 patients enrolled in the Get With the Guidelines-Heart Failure (GWTG-HF) registry:

- Receipt of evidence-based  $\beta$ -blockers when indicated
- Angiotensin-converting enzyme inhibitor, angiotensin II receptor blockers, or angiotensin receptor-neprilysin inhibitors at discharge
- Left ventricular function
- Postdischarge appointments by Medicare insurance type

For the 2 groups (MA = 35.6% [93,549]; FFS = 64.4%

[169,077]), overall results show that standardized mean differences were less than 10% for age, sex, comorbidities, or objective measures (eg, vital signs, lab values) and for all heart failure achievement measures. Median (interquartile range [IQR]) age was also similar in the groups, at 78 (IQR, 70-85) years for MA enrollees and 78 (IQR, 69-86) years for FFS members.

All patients included in the study had to be 18 years or older; have heart failure; and have Medicare insurance coverage between January 1, 2014, and December 31, 2018; and list FFS Medicare or MA as their only source of payment.

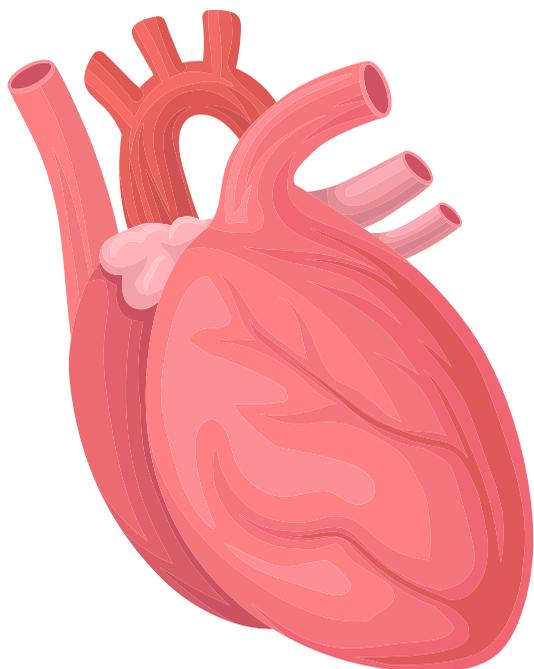
However, discharge to home was more likely to happen for patients in MA vs FFS plans (adjusted odds ratio [aOR], 1.16; 95% CI, 1.13-1.19;  $P < .001$ ), and they had a lower odds of hospital discharge within 4 days (AOR, 0.97; 95% CI, 0.93-1.00;  $P = .04$ ). Mortality remained consistent (aOR, 0.98; 95% CI, 0.92-1.03;  $P = .42$ ) between the groups.

Further analysis produced these results for patients in MA vs FFS plans:

- More likely to have diabetes (47.4% vs 45.4%), hyperlipidemia (59.8% vs 58.3%), peripheral vascular disease (13.0% vs 12.5%), and coronary artery disease (52.0% vs 51.5%)

**“Among patients hospitalized with heart failure, no observable benefit was noted in quality of care or in-hospital mortality between those enrolled in MA vs FFS Medicare, except lower use of post-acute care facilities”**

- Less likely to receive long-term dialysis (3.4% vs 5.0%)
- More often admitted to Midwest hospitals (26.4% vs 21.2%;  $P < .001$ )
- Less likely to be discharged to skilled nursing facilities (16.1% vs 17.5%;  $P < .001$ ) or inpatient rehab (1.9% vs 3.2%;  $P < .001$ )
- More likely to receive anticoagulation therapy for atrial fibrillation or atrial flutter (aOR, 1.13; 95% CI, 1.06-1.21;  $P < .001$ )
- More likely to receive discharge instructions (aOR, 1.11; 95% CI, 1.03-1.20;  $P = .008$ )



Overall mortality was just 2.9% for MA enrollees and 3.0% (P = .05) for FFS enrollees.

“Among patients hospitalized with heart failure, no observable benefit was noted in quality of care or in-hospital mortality between those enrolled in MA vs FFS Medicare, except lower use of post-acute care facilities,” the authors concluded. “As MA continues to grow, it will be important to ensure that participating private plans provide an added value to the patients they cover to justify the higher administrative costs compared with traditional FFS Medicare.”

Study limitations that may restrict generalization of their

findings are that hospital participation in the GWTG-HF registry is voluntary, which means those not participating could differ as could their patient demographics; the GWTG-HF registry does not contain data on patient social determinants of health; and not all patients enrolled in MA or FFS Medicare were included in the analysis.

#### Reference

Figuroa JF, Wadhera WK, Frakt, AB, et al. Quality of care and outcomes among Medicare Advantage vs fee-for-service Medicare patients hospitalized with heart failure. *JAMA Cardiol*. Published online September 2, 2020. doi:10.1001/jamacardio.2020.3638

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# New Renal, HF Results Seen in 2020 ACC Pathway on CV Risk Reduction

by Mary Caffrey

**CARDIOLOGISTS SHOULD CONSIDER** screening patients who have heart failure (HF), diabetic kidney disease (DKD), or atherosclerotic cardiovascular disease (ASCVD) for type 2 diabetes (T2D) once a year if they meet the criteria for prediabetes, according to an updated American College of Cardiology (ACC) document on new drug classes developed for T2D that have shown a range of benefits in cardiovascular care.

Regular screening is just one recommendation in the 2020 Expert Consensus Decision Pathway (ECDP) on Novel Therapies for Cardiovascular Risk Reduction With Type 2 Diabetes, published today in the *Journal of the American College of Cardiology*. It comes nearly 2 years after the inaugural document discussed 2 groups of therapies—sodium glucose co-transporter 2 (SGLT2) inhibitors, and glucagon-like peptide-1 (GLP-1) receptor agonists—that have transformed T2D treatment and are now changing the way physicians prevent heart and renal failure.

“An important paradigm shift in the care of patients with diabetes and cardiovascular disease is underway,” Sandeep R. Das, MD, MPH, FACC, co-chair of writing committee for the ECDP, said in a statement. “Patients and physicians can now choose from a number of medications that have important proven benefits on cardiovascular and renal outcomes, in addition to their effects on blood glucose.”

Among key updates in the 2020 ACC pathway:

- The authors say the need for patients to get started on SGLT2 inhibitors or GLP-1 RAs upon discharge after a heart attack “must be weighed” when hospitals decide what drugs to put on formulary.
- Unlike the 2018 pathway document, which singled out one

therapy from each class as “preferred,” the 2020 version makes no such distinctions, but some approved drugs in each class are not discussed in language on therapy initiation.

**“It’s important that we disconnect the benefits of both the SGLT2 inhibitors and the GLP-1 receptor agonists. The cardiovascular benefits that have been demonstrated are completely independent of glucose control,” McGuire said, and guidelines in both the United States and Europe reflect this.**

Both the SGLT2 inhibitor and GLP-1 RA classes were first approved to lower blood glucose, but they were found to have other benefits, including the ability to prevent heart attacks, strokes, renal decline, or cardiovascular death; or to reduce heart failure for hospitalization. The benefits were revealed in the first wave of cardiovascular outcomes trials, which were required by FDA and led to publication of the initial pathway in November 2018.

Since then, leaders of ACC have sought to educate members about the value of prescribing these drug classes in patients with heart failure or who have demonstrated ASCVD. However, cardiologists sometimes have resisted using drugs

that were first approved for diabetes, in part because they don't want to "own" responsibility for a patient's glycated hemoglobin level (A1C), a quality measure that can get reported to Medicare.

In a forthcoming interview to be published with *The American Journal of Managed Care*®, Darren K. McGuire, MD, MHSc, of UT Southwestern Medical Center, said there's been a rapid embrace of new evidence among the fellows he trains at the cardiology clinic at Parkland Hospital in Dallas, Texas. But among cardiologists generally, he said uptake has been "dismal."

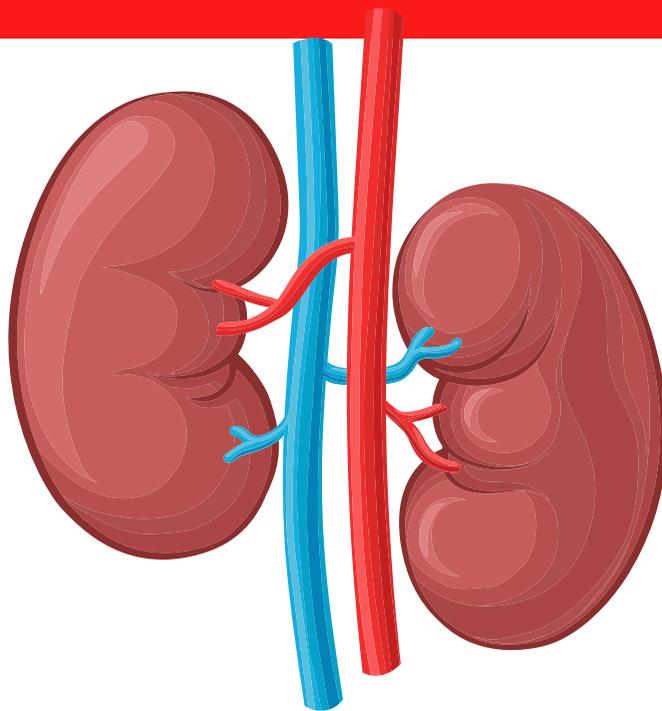
"It's important that we disconnect the benefits of both the SGLT2 inhibitors and the GLP-1 receptor agonists. The cardiovascular benefits that have been demonstrated are completely independent of glucose control," McGuire said, and guidelines in both the United States and Europe reflect this.

"It doesn't require the need for more glucose control," he said. "You simply use the risk of the patient to prescribe the medication. It's not that you're forgetting the glucose control. That's still going to be left up to the providers who've been managing it all along, but we'll be adding these."

September will mark 5 years since the scientific community was stunned with results from the EMPA-REG OUTCOME trial, which was the first to show a drug to lower blood glucose, empagliflozin, could also provide cardiovascular (CV) benefits.

**"It doesn't require the need for more glucose control," he said. "You simply use the risk of the patient to prescribe the medication. It's not that you're forgetting the glucose control. That's still going to be left up to the providers who've been managing it all along, but we'll be adding these."**

The race was on among competitors in the 2 emerging drug classes to show which individual therapy was more likely to reduce heart attacks, CV death, or heart or renal failure. In the 2018 pathway, the ACC authors singled out empagliflozin (Jardiance, Eli Lilly/Boehringer Ingelheim) among the SGLT2 inhibitors and liraglutide (Victoza, Novo Nordisk) among the GLP-1 RAs as "preferred," on the strength of CV outcomes trial results reported at that time.



New evidence. Since then, more clinical trial findings have been reported, and this has increased available data across the 2 classes for the ECDP Writing Committee and the Solution Set Oversight Committee to evaluate. Among the newer studies, the DAPA-HF trial found that the SGLT2 inhibitor dapagliflozin (Farxiga, AstraZeneca) reduced the risk of worsening HF or CV death for patients with HF with reduced ejection fraction (HFrEF), regardless of diabetes status. CREDENCE found that the SGLT2 inhibitor canagliflozin (Invokana, Janssen) could reduce the risk of renal decline or renal death in patients with T2D and chronic kidney disease (CKD).

More recently, the DAPA-CKD trial was stopped early, and sponsors of the EMPEROR-Reduced trial for empagliflozin in HFrEF say it has achieved all primary and secondary endpoints.

Among the treatment recommendations, the authors write:

- An SGLT2 inhibitor with demonstrated CV benefit is recommended for patients with T2D and HF, especially reduced ejection fraction (HFrEF).
- Diagnosis of T2D, when ASCVD, DKD, or HFrEF is present, or a diagnosis of ASCVD when any of the other conditions are present, "offers the opportunity to begin the patient-clinician discussion" about taking an SGLT2 inhibitor.
- GLP-1 RAs are recommended for those patients with established or very high risk ASCVD.
- Decisions on prescribing these medications for CV or kidney risk reduction "should not be contingent" on a patient's A1C level; however, the document stops short of saying metformin is not needed, and in fact, says most patients will likely take it.