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ORIGINAL ARTICLE

Adoption of New Glucose-Lowering Medications in the U.S. —The Case of SGLT2 Inhibitors: Nationwide Cohort Study

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Abstract

Background: High-quality diabetes care is evidence-based, timely, and equitable. Sodium-glucose

(AACE),[9] European Association for the Study of Diabetes (EASD),[7] and American Heart Association (AHA)[10] clinical guidelines.

CVD is the most common comorbidity among people with diabetes and contributes the most to their morbidity and mortality.[11] Nearly 74% of people with diabetes have hypertension,[1] 18% have coronary heart disease,[12] and 9%–22% have HF.[13] Similarly, severe hypoglycemia is a common, yet potentially preventable, adverse event in diabetes management, affecting as many as 17% of people with type 2 diabetes.[14] SGLT2i may be a preferred agent to be considered in these contexts; yet, little is known about how they were incorporated into real-world diabetes management and, specifically, whether their early use was aligned with the clinical contexts for which they are most beneficial.

Three SGLT2i were approved by the U.S. Food and Drug Administration (FDA) before publication of cardiovascular outcome trials demonstrating improved CVD, HF, and kidney outcomes with their use[3–6]: canagliflozin (March 2013), dapagliflozin (January 2014), and empagliflozin (August 2014). They act by inhibiting SGLT2 in the proximal convoluted tubule, thereby preventing active glucose reabsorption and facilitating glycosuria in a glucose-dependent, insulin-independent fashion. Early on, it was apparent that SGLT2i are not associated with weight gain or hypoglycemia, but can lower blood pressure and weight, thereby making them particularly attractive treatment options for overweight or obese patients, patients with comorbid HF or hypertension, patients at risk for hypoglycemia, and the elderly.[7] While approved as an add-on medication for the management of type 2 diabetes, SGLT2i have also been used off-label by patients with type 1 diabetes.[15–17]

The decision to initiate SGLT2i therapy is likely impacted by clinician familiarity,[18–23] patient interest, insurance coverage and cost considerations, and adverse effect concerns. Most notable safety concerns that emerged early on included genitourinary tract infections, dehydration, acute kidney