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Prescription Patterns of Cardiovascular- and Kidney-Protective Therapies Among Patients With Type 2 Diabetes and Chronic Kidney Disease

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OBJECTIVE

To assess the prevalence and correlates of prescription of sodium–glucose cotransporter 2 inhibitors (SGLT2i) and/or glucagon-like peptide 1 receptor agonists (GLP1-RA) in individuals with type 2 diabetes mellitus (T2DM) with and without chronic kidney disease (CKD).

RESEARCH DESIGN AND METHODS

This was a cross-sectional analyses of SGLT2i and GLP1-RA prescriptions from 1 January 2019 to 31 December 2020 in the Veterans Health Administration System. The likelihood of prescriptions was examined by the presence or absence of CKD and by predicted risks of atherosclerotic cardiovascular disease (ASCVD) and end-stage kidney disease (ESKD).

RESULTS

Of 1,197,880 adults with T2DM, SGLT2i and GLP1-RA were prescribed to 11% and 8% of patients overall, and to 12% and 10% of those with concomitant CKD, respectively. In adjusted models, patients with severe albuminuria were less likely to be prescribed SGLT2i or GLP1-RA versus nonalbuminuric patients with CKD, with odds ratios (ORs) of 0.91 (95% CI 0.89, 0.93) and 0.97 (0.94, 1.00), respectively. Patients with a 10-year ASCVD risk >20% (vs. <5%), had lower odds of SGLT2i use (OR 0.66 [0.61, 0.71]) and GLP1-RA prescription (OR 0.55 [0.52, 0.59]). A 5-year ESKD risk >5%, compared with <1%, was associated with lower likelihood of SGLT2i prescription (OR 0.63 [0.59, 0.67]) but higher likelihood of GLP1-RA prescription (OR 1.53 [1.46, 1.61]).

CONCLUSIONS

Among a large cohort of patients with T2DM, prescription of SGLT2i and GLP1-RA was low in those with CKD. We observed a "risk-treatment paradox," whereby patients with higher risk of adverse outcomes were less likely to receive these therapies.

The sodium–glucose cotransporter 2 inhibitors (SGLT2i) and the glucagon-like peptide 1 receptor agonists (GLP1-RA) afford substantial cardiovascular and kidney-protective effects (1–3). This has triggered a paradigm shift from a glucose-centric approach to

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type 2 diabetes mellitus (T2DM) management toward a recommended strategy that incorporates therapies based on their ability to lower risk for cardiovascular disease (CVD) and chronic kidney disease (CKD) progression. However, the adoption of this new paradigm may be slow given the traditional practice of using medications for diabetes based on glycemic targets.

As a class, the SGLT2i substantially reduce the risk of major adverse CVD events encompassing atherosclerotic CVD (ASCVD), incident and progressive heart failure, and CVD mortality (1,4). In addition, clinical trials of SGLT2i conducted exclusively in patients with CKD have demonstrated marked reductions in the risk of progression to end-stage kidney disease (ESKD) (5,6). Similarly, the GLP1-RA, including liraglutide, semaglutide, albiglutide, and dulaglutide, have demonstrated marked cardiovascular-protective effects in individuals with T2DM (2). Although dedicated trials of GLP1-RA evaluating primary kidney outcomes have not been conducted, these agents significantly reduce the risk of worsening albuminuria and kidney function decline, both powerful indicators of subsequent adverse kidney and cardiovascular events (3,7).

The protective cardiovascular and kidney effects derived from SGLT2i and GLP1-RA prompted major scientific guidelines, including the American Diabetes Association (ADA) and the Kidney Disease Improving Global Outcomes (KDIGO) in 2020, to recommend their prescription in individuals with T2DM regardless of glycemic control if they have established CVD, are at high risk of ASCVD, or have CKD (8,9). For patients with T2DM and CKD, an SGLT2i is recommended (8,9). For those with an estimated glomerular filtration rate (eGFR) less than adequate for SGLT2i prescription, or in those with high ASCVD risk or established ASCVD, a GLP1-RA may be preferred (9). While the use of these medications in this subset of patients is expected to increase with time, studying baseline prescription patterns is necessary to guide subsequent implementation efforts.

Recent studies have shown that use of SGLT2i and GLP1-RA is low among patients with T2DM and established CVD (10). Yet, less is known about contemporary prescription of these medications among patients with T2DM and concomitant CKD—an exceptionally high-risk population in whom rapid adoption of these therapies could lead to substantial reductions in the burden of CVD and CKD. Accordingly, in this study, we investigated current prescription patterns of SGLT2i and GLP1-RA in >1 million patients with T2DM who received primary care in the Veterans Health Administration (VHA) System during 2019 and 2020. The main objectives were to *1*) characterize prescription according to diabetes management and control, including hemoglobin A_{1c} concentrations, and use of other medications for diabetes; *2*) evaluate prescription prevalence and correlates among patients with CKD; and *3*) assess prescription use according to predicted risks for ASCVD and ESKD.

RESEARCH DESIGN AND METHODS

Study Setting

The Kidney Health Research Collaborative (KHRC) data registry is a unified data repository to enhance research initiatives aimed at improving the care of patients with CKD. It has curated data from the VHA Corporate Data Warehouse, which is a comprehensive national repository of data from the VHA electronic health record (EHR). The Corporate Data Warehouse contains individual patient sociodemographic characteristics, outpatient and inpatient clinical encounters, medication prescriptions and fills, medical conditions, procedures, and laboratory results. Data are sourced from >130 hospitals and 1,000 outpatient and skilled nursing facilities, and VA external fee-for-service claims.

Study Population

All VHA patients with T2DM and at least two primary care encounters between 1 January 2019 and 31 December 2020 were included (Supplementary Fig. 1). Ascertainment of T2DM combined ICD-10 codes, hemoglobin A_{1c} values, and prescription of antidiabetes medications following the validated electronic Medical Records and Genomics (e-MERGE) algorithm for ascertainment of T2DM in the EHR (Supplementary Fig. 2 and Supplementary Table 1) (11).

Patients were excluded if they were receiving hospice care, had an invalid date of birth, or did not have a sex classification (n = 20,865). Because SGLT2i and GLP1-RA are not indicated in patients with ESKD and have not been studied in patients who have received a kidney transplant, we excluded patients with an eGFR <15 mL/min/1.73 m^2 (stage 5 CKD), those undergoing chronic dialysis treatment, and kidney transplant recipients (n = 32,243). After these exclusions, the final study sample comprised 1,197,880 Veterans Affairs Health Care System patients with T2DM.

Key Covariates

Ascertainment of CKD used the validated e-Phenotype algorithm for the EHR that combines eGFR and urinary albumin-to-creatinine ratio (ACR) values obtained during outpatient clinic visits (12). CKD was defined as at least two measures of eGFR <60 mL/min/1.73 m^2 and/or an ACR >30 mg/g obtained >90 days apart. The prevalence of prescription by each CKD stage was assessed using the KDIGO staging system—eGFR stages G1 to G5 and ACR stages A1 to A3 (13). Because the urinary protein-to-creatinine ratio (PCR) is often ordered by providers in lieu of the ACR, we used the recommended KDIGO equivalent values to assign measured PCR values to A1 to A3 categories (Supplementary Table 2). Among patients with CKD, the Kidney Failure Risk Equation was calculated to estimate the 5-year risk of ESKD (14). The Kidney Failure Risk Equation is based on four variables to predict ESKD risk: age, sex, ACR, and eGFR.

We defined atherosclerotic CVD based on the ICD-10 codes for ischemic heart disease or ischemic stroke being present on at least two inpatient and/or outpatient encounters following published methods (Supplementary Table 1) (15). For individuals without prevalent ASCVD, the 10-year ASCVD risk was calculated using the American Heart Association/American College of Cardiology pooled cohort equation excluding patients ≥80 years (16).

SGLT2i and GLP1-RA Prescription

Prevalent SGLT2i or GLP1-RA prescription was defined as any active prescription from 1 January 2019 through 31 December 2020. The SGLT2i empagliflozin and the GLP1-RA semaglutide are included in the VHA national formulary. In addition to these medications, we assessed for the prescription of the SGLT2i ertugliflozin, canagliflozin,

and dapagliflozin and for the GLP1-RA liraglutide, albiglutide, and dulaglutide as nonformulary prescriptions. We included only GLP1-RA for which cardiovascular-protective effects have been demonstrated. For each medication class, prevalent medication prescription estimates were calculated overall and stratified by characteristics of diabetes control and management: the most recent hemoglobin A_{1c} value, the prescription of other medications for diabetes, and specialty treatment by endocrinology. In addition, prevalent prescription estimates were stratified by presence or absence of established CKD, by ASCVD and ESKD risk thresholds, and by clinic visits to endocrinology, nephrology, and cardiology.

Other Covariates

VHA does not systematically collect individual-level information on socioeconomic status in structured data fields. Therefore, we used the median per capita income of residential ZIP Code and the ZIP Code-level social deprivation index as proxies for socioeconomic status using data derived from the American Community Survey (17,18). Patients with >50% health coverage for service-connected conditions and those in whom diabetes is a service-connected condition do not have copayments for their medications for diabetes. Thus, we were able to assess prescriptions in the subset of patients who did not have any cost-sharing for these medications. Rurality was assessed using Rural-Urban Commuting Area codes, which consider population density as well as how closely a community is linked socioeconomically to large urban centers (19). Disparities in diabetes care have been described for patients with substance use disorder, including unhealthy alcohol use, and for patients with underlying mental illness (20,21). Therefore, we assessed alcohol with the Alcohol Use Disorder Identification Test Consumption (AUDIT-C), with unhealthy alcohol use defined as an AUDIT-C score ≥3 for women and ≥4 for men (22). Smoking status in the VA Health Care System is recorded as part of routine care under "health factors" (23). A mental health diagnosis comprised the presence of an ICD-10 code encompassing posttraumatic health disorder or other severe mental illness following published methods (24). Frailty was assessed with the validated VA frailty index, which encompasses variables related to mobility, functional status, cognition and mood, sensory impairment (e.g., hearing, or visual impairment), and other geriatric syndromes (e.g., incontinence) (25).

Statistical Analysis

Frequency and percentage are reported for categorical variables, and mean and SD are reported for continuous variables. We constructed crude and multivariable logistic regression models to investigate the associations of the following variables with prescription of SGLT2i and GLP1-RA: diabetes control and management (hemoglobin A_{1c} concentration and concomitant prescription of other antidiabetes medications), presence and stage of CKD, and predicted ASCVD and ESKD risk. Multivariable models adjusted for age, sex, race/ethnicity, ZIP Code median income, ZIP Code social deprivation index, service-connected disability and diabetes, rurality, smoking status, unhealthy alcohol use, hypertension, BMI, mental health diagnosis, frailty, and coronavirus disease 2019 (COVID-19) diagnosis. Because of overlap, separate models were constructed to evaluate the association of a visit to an endocrinology provider (yes/no) and the number of endocrinology visits with prescription for SGLT2i and GLP1-RA. Similarly, separate models were constructed to assess the association of CKD and KDIGO CKD stages with each prescription. Multivariable models simultaneously assessed the associations between eGFR and ACR category with each medication class. To account for the correlation among individuals within VA facilities, robust SEs were estimated with the empirical ("sandwich") estimator.

All statistical analyses were conducted using SAS version 8.1 software (SAS Institute, Cary, NC) for Unix.

RESULTS

Between 1 January 2019 and 31 December 2020, we identified 1,197,880 patients with T2DM who met the inclusion and exclusion criteria. Of these, 11% and 8% were prescribed an SGLT2i or a GLP1-RA, respectively (Supplementary Fig. 1). Nearly all of these prescriptions (>99%) were filled. Close to 99% of SGLT2i prescriptions were for empagliflozin specifically. For GLP1-RA, 41% of prescriptions were for liraglutide, 28% for dulaglutide, 26% for semaglutide, and 5% for albiglutide. Most patients (57%) without a prescription for an SGLT2i or a GLP1-RA had a hemoglobin A_{1c} <7% compared with <30% who were prescribed an SGLT2i, a GLP1-RA, or both medications. Compared with patients without a prescription, patients with prescriptions for either or both medications were more likely to have hypertension, obesity (BMI ≥30 kg/m^2), ASCVD, heart failure, and CKD (Table 1).

Prescription of SGLT2i and GLP1-RA According to Diabetes Management and Control

All variables related to diabetes management and control were strongly associated with SGLT2i or GLP1-RA prescription. Compared with patients who were not prescribed additional medications for diabetes, those with three or more prescriptions (other than prescriptions for SGLT2i or GLP1-RA) were more than four times as likely to be prescribed an SGLT2i or a GLP1-RA in multivariable analyses (Supplementary Table 3). Patients with higher hemoglobin A_{1c} were more likely to be prescribed both medication classes compared with patients with hemoglobin A_{1c} <7%. Patients who were seen by an endocrinologist (13%) and those with a greater number of visits were substantially more likely to be prescribed an SGLT2i or a GLP1-RA compared with patients without endocrinology visits during the study period. Of specific medications, prescription of insulin was associated with nearly two- and threefold higher odds of being prescribed an SGLT2i or a GLP1-RA, respectively (Supplementary Table 4).

Prescription of SGLT2i and GLP1-RA Among Patients With CKD

Overall, 35% of patients had CKD, the great majority of whom were not prescribed an SGLT2i or a GLP1-RA (Table 2). Of all patients with T2DM, 658,632 (55%) had ACR or PCR ordered during the study period. The strongest correlates of albuminuria testing were BMI, hypertension diagnosis, and a nephrology visit (Supplementary Table 5).

Among patients with CKD, lower eGFR (for SGLT2i) and higher ACR (for both SGLT2i and GLP1-RA) were associated with lower prescription of these medications

Table 1—Demographic and clinical characteristics of patients with type 2 diabetes mellitus in the VHA health care system from 2019 to 2020 by prescription of SGLT2i and GLP1-RA agents

Characteristics	None *n* = 1,011,176	SGLT2i *n* = 128,523	GLP1-RA *n* = 92,496	GLP1-RA and SGLT2i *n* = 34,315
Sociodemographic				
Age, mean (SD), years	68 (11)	65 (10)	68 (11)	64 (9)
Female sex	40,037 (4)	4,750 (4)	5,312 (6)	1,685 (5)
Race				
White	710,980 (70)	95,959 (75)	69,733 (75)	26,050 (76)
Black	204,954 (20)	20,618 (16)	14,371 (16)	5,017 (15)
Asian or Asian Pacific Islander	20,615 (2)	2,921 (2)	1,975 (2)	849 (2)
American Indian or Alaska Native	8,462 (1)	1,117 (1)	852 (1)	304 (1)
Ethnicity				
Hispanic/Latino	71,956 (7)	9,317 (7)	6,043 (7)	2,287 (7)
Service-connected disability >50%	422,886 (42)	61,186 (48)	45,876 (50)	17,405 (51)
Diabetes service connection	241,043 (24)	38,252 (30)	28,775 (31)	10,769 (31)
Lowest ZIP Code median income quartile (<$44,818)	255,797 (25)	28,098 (22)	19,595 (21)	7,033 (20)
Highest social deprivation index quartile (score >73)	24,6047 (24)	28,459 (22)	20,539 (22)	7,304 (21)
Rural or highly rural ZIP Code	377,858 (37)	47,649 (37)	34,746 (38)	12,724 (37)
Lifestyle				
Unhealthy alcohol use	79,504 (8)	7,648 (6)	4,207 (5)	1,618 (5)
Current smoking	155,768 (15)	17,635 (14)	11,080 (12)	3,936 (11)
Diabetes management and control				
Hemoglobin A_{1c} ≤7% (53 mmol/mol)	572,691 (57)	32,602 (25)	25,900 (28)	7,842 (23)
Diabetes medications other than SGLT2i or GLP1-RA				
None	235,455 (23)	3,602 (3)	2,154 (2)	424 (1)
One	409,144 (40)	23,582 (18)	18,454 (20)	5,106 (15)
Two	248,427 (25)	55,501 (43)	41,486 (45)	15,671 (46)
Three or more	118,150 (12)	45,838 (36)	30,402 (33)	13,114 (38)
Endocrinology visit	105,801 (10)	34,961 (27)	32,544 (35)	13,409 (39)
Clinical characteristics				
Hypertension	985,389 (97)	126,414 (98)	91,256 (99)	33,881 (99)
BMI ≥30 kg/m^2	549,224 (54)	82,354 (64)	66,313 (72)	24,531 (71)
ASCVD	317,094 (31)	55,128 (43)	36,581 (40)	14,761 (43)
Heart failure	97,496 (10)	18,514 (14)	14,191 (15)	5,264 (15)
CKD	345,322 (34)	50,337 (39)	43,648 (47)	14,627 (43)
Mental health diagnosis	218,381 (22)	29,984 (23)	23,413 (25)	8,707 (25)
COVID-19 diagnosis	26,629 (3)	4,636 (4)	3,506 (4)	1,374 (4)

Data are presented as *n* (%) unless otherwise specified.

(Table 2). The inverse associations between ACR and prescription of SGLT2i and GLP1-RA were observed across all eGFR categories for SGLT2i but not for GLP1-RA (Fig. 1).

Prescription of SGLT2i and GLP1-RA According to ASCVD and ESKD Risk

Among patients without established ASCVD, higher ASCVD risk was associated with lower prescription of SGLT2i and GLP1-RA (Table 3). Indeed, for patients with a 10-year ASCVD risk >20%, the prevalence odds of prescription for an SGLT2i or a GLP1-RA were lower compared with a 10-year ASCVD risk <5%. Among patients with CKD, those with higher ESKD risk were less likely to be prescribed an SGLT2i but more likely to be prescribed a GLP1-RA (Table 3). Sensitivity analyses that assessed these associations across age strata yielded results consistent with the main analyses (Supplementary Table 6*A* and *B*).

Sensitivity analyses that excluded 299 patients and 945 patients with prescriptions for SGLT2i and GLP1-RA, respectively, prior to 1 January 2019, but no prescriptions during the study period, yielded results consistent with the main findings (Supplementary Table 7).

CONCLUSIONS

In this study, we present a detailed analysis of contemporary prescription patterns of SGLT2i and GLP1-RA among a large cohort of patients with T2DM receiving primary care in the VHA, a large integrated health care system in the U.S. For patients with CKD, we found lower prevalent odds of prescription of SGLT2i with lower eGFR, and of SGLT2i and GLP1-RA with worsening albuminuria. Higher risks for ASCVD (for SGLT2i and GLP1-RA) and ESKD (for SGLT2i) were inversely associated with these prescriptions; these results remained robust across age-groups.

The results from this study should be contextualized with respect to clinical trial results demonstrating the cardiorenal-protective effects of these medications, which have informed current guidelines. For SGLT2i, the first trial in patients with T2DM demonstrating the protective cardiorenal effects of SGLT2i was the Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes (EMPA-REG) trial, which was published in 2015 (26). Among patients with albuminuric CKD,

Table 2—Association between the presence of CKD and prescription of SGLT2i and GLP1-RA among VA patients with T2DM during the years 2019 and 2020

	SGLT2i prescription			GLP1-RA prescription	
			Multivariable model*		Multivariable model*
	n	% Prescribed	OR (95% CI)	% Prescribed	OR (95% CI)
CKD†					
Absent	610,528	11	Reference	7	Reference
Present	424,680	12	0.98 (0.97, 1.00)	10	1.13 (1.12, 1.15)
Unknown	162,672	8	0.85 (0.81, 0.90)	5	0.81 (0.75, 0.86)
KDIGO CKD stage‡					
eGFR, mL/min/1.73 m^2					
G1: ≥90	88,959	16	Reference	11	Reference
G2: 60–89	192,723	15	1.02 (0.99, 1.05)	11	0.99 (0.94, 1.04)
G3a: 45–59	94,564	12	0.93 (0.89, 0.96)	9	1.02 (0.98, 1.07)
G3b: 30–44	24,056	9	0.72 (0.69, 0.76)	12	1.17 (1.11, 1.22)
G4:15–29	23,588	4	0.42 (0.39, 0.45)	12	1.09 (1.03, 1.15)
ACR, mg/g					
A1: <30	125,732	11	Reference	9	Reference
A2: 30–300	185,413	13	0.96 (0.95, 0.98)	11	1.01 (0.98, 1.03)
A3: >300	71,935	12	0.91 (0.89, 0.93)	13	0.97 (0.94, 1.00)
Unknown ACR/PCR	41,600	7	0.76 (0.72, 0.79)	7	0.80 (0.73, 0.87)
Nephrology visit					
No	1,133,361	11	Reference	7	Reference
Yes	64,519	13	1.05 (1.01, 1.09)	15	1.18 (1.14, 1.23)

*Multivariable model adjusted for age, sex, self-identified race/ethnicity, ZIP Code median income, ZIP Code area social deprivation index, VA diabetes and service connection, rurality, smoking status, unhealthy alcohol use, hypertension, BMI, mental health diagnosis, hemoglobin A_{1c}, antidiabetes medications, endocrinology visit, cardiology visit, nephrology visit, frailty, and COVID-19 diagnosis. †Separate models were fitted for CKD and CKD stage. ‡For eGFR category, models simultaneously adjust for ACR. For ACR category, models simultaneously adjust for eGFR.

the Canagliflozin and Renal Events in Diabetes with Established Nephropathy Clinical Evaluation (CREDENCE) and the Dapagliflozin in Patients with Chronic Kidney Disease (DAPA-CKD) were published in 2019 and 2020, respectively (5,6).

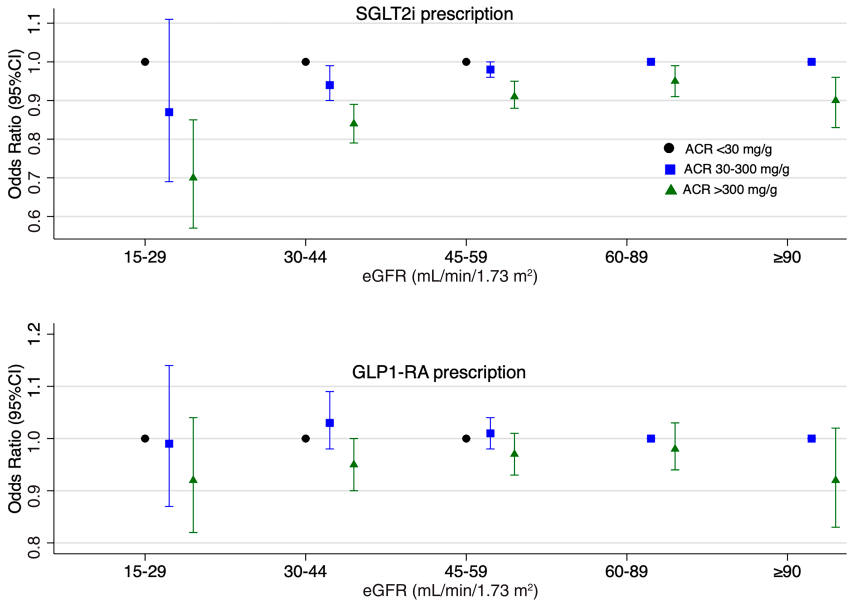

Figure 1—Association of albuminuria with SGLT2i and GLP1-RA prescription across eGFR categories among patients with CKD. Multivariable model adjusted for age, sex, self-identified race/ethnicity, ZIP Code median income, ZIP Code area social deprivation index, VA diabetes and service connection, rurality, smoking status, unhealthy alcohol use, hypertension, BMI, mental health diagnosis, hemoglobin A_{1c}, antidiabetes medications, endocrinology visit, cardiology visit, nephrology visit, frailty, and COVID-19 diagnosis.

Evidence of the kidney-protective effects of GLP1-RA stems from meta-analyses of landmark trials among patients with diabetes, including Liraglutide and Cardiovascular Outcomes in Type 2 Diabetes (LEADER) and Semaglutide and Cardiovascular Outcomes in Patients with Type 2 Diabetes (SUSTAIN-6), both published in 2016 (27,28). Responsive ADA and KDIGO guidelines recommending prescription of these medications to lower cardiac and kidney risk were only published in 2020. As such, the observed low prescription rates among patients with CKD may be expected. Indeed, recent studies suggest that while low, the prescription of these medications has increased incrementally over the past decade (29). Nonetheless, the impetus for this study was to establish a baseline and to motivate ongoing and future efforts to improve prescription among patients who would derive the largest benefit.

We observed that higher rates of prescription occur among patients with higher hemoglobin A_{1c} concentrations and that these medications are mainly prescribed as third- or fourth-line diabetes

Table 3—Association of ASCVD and ESKD risk and prescription of SGLT2i and GLP1-RA among VHA patients with T2DM during the years 2019 and 2020

		SGLT2i prescription		GLP1-RA prescription	
			Multivariable model*		Multivariable model*
	n	% Prescribed	OR (95% CI)	% Prescribed	OR (95% CI)
10-year ASCVD risk†					
<5%	35,500	13	Reference	11	Reference
5 to 7.4%	23,390	13	1.02 (0.96, 1.07)	11	0.99 (0.93, 1.06)
7.5 to 19.9%	146,616	12	0.91 (0.86, 0.96)	9	0.84 (0.79, 0.89)
>20%	538,036	8	0.66 (0.61, 0.71)	6	0.55 (0.52, 0.59)
Unknown	60,296	9	0.70 (0.65, 0.75)	6	0.54 (0.5, 0.59)
5-year ESKD risk‡					
<1%	165,955	14	Reference	10	Reference
1 to 2.9%	71,129	13	0.92 (0.89, 0.96)	11	1.20 (1.16, 1.24)
3 to 4.9%	23,186	12	0.86 (0.81, 0.92)	13	1.36 (1.3, 1.42)
>5%	54,719	9	0.63 (0.59, 0.67)	14	1.53 (1.46, 1.61)
Unknown	62,255	8	0.51 (0.45, 0.59)	9	0.81 (0.73, 0.89)

*Multivariable model adjusted for age, sex, self-identified race/ethnicity, ZIP Code median income, ZIP Code area social deprivation index, VA diabetes and service connection, rurality, smoking status, unhealthy alcohol use, hypertension, BMI, mental health diagnosis, hemoglobin A_{1c}, antidiabetes medications, endocrinology visit, cardiology visit, nephrology visit, frailty, and COVID-19 diagnosis. †ASCVD risk calculation excluded patients ≥80 years. ‡ESKD only calculated among patients with CKD and available ACR measurements.

medications. In addition, we found that while only 13% of patients visited an endocrinologist during the study period, these patients were substantially more likely to be prescribed an SGLT2i or a GLP1-RA. For SGLT2i, these results align with prescription trends in other health care systems that have shown that use rates are low for this medication class and that prescriptions are concentrated among subspecialty providers (30,31). From an equity perspective, the observed reliance on subspecialists to prescribe these medications may adversely disadvantage patients who rely on medical practices that lack readily available access to subspecialty care. To improve equitable medication access and to maximize population-level impacts of CVD and CKD risk reduction, implementation efforts should focus on improving prescriptions from primary care providers who care for the bulk of patients with T2DM.

The observed lower prevalence of SGLT2i prescription among patients with the highest severity of CKD is consistent with recently published studies in non-VHA health systems (32). Although the low prescription rates of SGLT2i are expected among patients with an eGFR <30 mL/min/1.73 m^2 in whom prior guidelines advised against their initiation, we found low prescription rates at CKD stages G3a and G3b, wherein prescription of SGLT2i could substantially prevent further CKD progression. Conversely, ACR is a major risk predictor of CVD and CKD progression independent of the GFR and is an essential component of CKD staging (33,34). The main SGLT2i trials among patients with diabetic kidney disease have used albuminuria as the main criterion for inclusion. Yet, although yearly testing for albuminuria is indicated among all patients with T2DM, and testing for albuminuria is integral in guiding SGLT2i or GLP1-RA selection, only 55% of patients had an ACR or PCR test over the 2-year study period. Furthermore, higher ACR was inversely associated with prescription of SGLT2i across all eGFR categories. The low rates of testing for albuminuria are consistent with those in other health systems (35). Because treatment of CKD at early stages is paramount both for the primary prevention of CVD and prevention of CKD progression to ESKD, overcoming the albuminuria detection and treatment gaps among patients with T2DM and CKD may lead to substantial population-level benefits in cardiovascular and kidney health.

Limitations of this study include that the VHA is an integrated health system with uniform pharmacy benefits offering discounted or free medications to its patients. Therefore, our results may not be generalizable to other health care systems where the substantial copayments or costs for these medications may be a major barrier to prescription (36); however, we anticipate that such a barrier may lead to even lower SGLT2i and GLP1-RA prescriptions in other settings. In addition, the observational and cross-sectional nature of this study precludes drawing causal inferences from the observed associations. Furthermore, we did not study prescription of other novel therapies that are now recommended for cardiorenal prevention. The 2022 ADA guidelines recommend that for patients with T2DM and CKD who are at increased risk for CVD events or CKD progression or who are unable to use an SGLT2i, the nonsteroidal mineralocorticoid receptor agonist finerenone should be used to reduce the risk of CKD progression and cardiovascular events (37).

In conclusion, we found low rates of prescription of SGLT2i and GLP1-RA among patients with CKD and in those at high ASCVD and ESKD risk. Considering the overwhelming evidence of cardiovascular and kidney protection, these results call for accelerated efforts to improve delivery of these medications to the highest-risk patients.

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