Kidney Medicine

Disparities in SGLT2 Inhibitor or Glucagon-Like Peptide 1 Receptor Agonist Initiation Among Medicare-Insured Adults With CKD in the United States

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Rationale & Objective: Information regarding disparities in initiating sodium/glucose cotransporter 2 inhibitors (SGLT2i) and glucagon-like peptide 1 receptor agonists (GLP-1RA) in patients with chronic kidney disease (CKD) is limited. We examined sociodemographic and clinical factors associated with the initiation of SGLT2i, GLP-1RA, or second-generation sulfonylureas in a Medicare Fee-For-Service patient population with CKD and type 2 diabetes.

Study Design: Retrospective cohort study.

Setting & Participants: The 20% random sample of Medicare Fee-For-Service claims, 2012-2018.

Exposures: Patients' sociodemographic and clinical factors.

Outcomes: Use of SGLT2i, GLP-1RA, or sulfonylureas.

Analytical Approach: Patients with a newly initiated prescription of SGLT2i, GLP-1RA, or second-generation sulfonylureas from January 1, 2013, to December 31, 2018, were identified. Multinomial logistic regression model was used to evaluate demographic and clinical factors associated with the initiation of SGLT2i, GLP-1RA, or second-generation sulfonylureas.

Results: The study cohort comprised 53,029 adults (aged greater than or equal to 18 years) with CKD and type 2 diabetes, of whom 10.0%, 17.4%, and 72.6% had a first prescription for SGLT2i, GLP-1RA, and sulfonylurea, respectively. Patients aged greater than or equal to 75 years versus those aged 65-74 years had lower odds to start SGLT2i or GLP-1RA compared with sulfonylureas. Black patients were associated with lower odds of initiation of SGLT2i (OR, 0.67; 95% CI, 0.61-0.74) and GLP-1RA (OR, 0.73; 95% CI, 0.68-0.79), compared with White patients. Hispanic and Asian patients had lower odds of initiation of GLP-1RA. Patients with cardiovascular disease or hyperlipidemia had higher odds to start SGLT2i or GLP-1RA.

Limitations: CKD and type 2 diabetes diagnosis; CKD stage; and patient clinical status were identified with diagnosis or procedure codes. There is potential for residual confounding with the use of retrospective data.

Conclusions: The results of this study identified disparities in the use of SGLT2i and GLP-1RA in patients with CKD. Black and older patients were significantly less likely to be initiated on SGLT2i or GLP-1RA than on second-generation sulfonylureas.

Visual Abstract included

Complete author and article information provided before references.

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An estimated 15% of US adults (aged greater than or equal to 18 years) (37 million people) have chronic kidney disease (CKD).[1] Diabetes is the leading cause.[2]

Editorial, •••

Diabetes has long been known to be associated with the development of cardiovascular and kidney disease.[3,4] Large clinical trials have shown benefits of newer glucose-lowering medications on cardiovascular and kidney outcomes in patients with CKD with type 2 diabetes.[5-14] Sodium/glucose cotransporter 2 inhibitors (SGLT2i) and glucagon-like peptide 1 receptor agonists (GLP-1RA) are recommended in patients with CKD with type 2 diabetes by the American Diabetes Association and KDIGO (Kidney Disease: Improving Global Outcomes) clinical guidelines.[15,16]

Although evidence of cardiovascular and kidney benefits from clinical trials evaluating SGLT2i and GLP-1RA is overwhelming, prescription of these newer glucose-lowering medications is low in both type 2 diabetes and patients with CKD.[17,18] A recent retrospective analysis using 2015-2019 data from the Optum Clinformatics Data Mart suggested that the prescription of SGLT2i was low in commercially insured patients with type 2 diabetes and showed racial/ethnic, sex, and socioeconomic disparities in the receipt of SGLT2i therapy versus other glucose-lowering medications.[18] Although the benefits of SGLT2i and GLP-1RA among patients with type 2 diabetes and CKD have been demonstrated, there is no evidence showing cardiovascular and kidney benefits of older glucose-lowering medications like sulfonylureas in this population; however, second-generation sulfonylureas (glyburide, glipizide, and glimepiride) are widely used.[17]

There is limited information examining the use of SGLT2i or GLP-1RA among patients with CKD with type 2 diabetes in the Medicare population perspective across different age, sex, race/ethnicity, or socioeconomic groups. Our study aimed to examine whether patients with CKD and type 2 diabetes were more likely to start SGLT2i and GLP-1RA, compared with the second-generation sulfonylureas in a more recent Medicare Fee-For-Service population. We also examined patients' sociodemographic and clinical factors associated with the initiation of SGLT2i, GLP-1RA, or second-generation sulfonylureas.

PLAIN-LANGUAGE SUMMARY

There is limited information on disparities of sodium/glucose cotransporter 2 inhibitors (SGLT2i) and glucagon-like peptide 1 receptor agonists (GLP-1RA) initiation among patients with chronic kidney disease (CKD) and type 2 diabetes in the Medicare population. We used a Medicare 20% random sample to examine whether patients with CKD and type 2 diabetes were more likely to start SGLT2i or GLP-1RA, compared with second-generation sulfonylureas across age, sex, race, and socioeconomic status. We found that Black and older patients and those with CKD stage 4-5 and a higher Elixhauser Comorbidity Index score were associated with lower odds of initiating SGLT2i or GLP-1RA than sulfonylureas. Our findings are important because this represents a health disparity issue that needs to be addressed to slow kidney disease progression in populations that are at higher risk of progressing to kidney failure.

METHODS

Data Source

We used data from a 20% random sample of Medicare Fee-For-Service claims. To conduct this study, we used claims data files that included patient demographic characteristics, health insurance enrollment, type of institutional care (inpatient, outpatient, home health, skilled nursing facility), physician visits, and Part D characteristic files (including prescription events) from January 1, 2012, to December 31, 2018.

Study Design and Cohort Selection

We conducted a retrospective cohort study design in patients with CKD with type 2 diabetes. We identified patients with CKD and type 2 diabetes from 2013 to 2018 and used the *International Classification of Diseases, Ninth Revision, Clinical Modification* or *International Classification of Diseases, Tenth Revision, Clinical Modification* diagnosis codes provided by the US Renal Data System.[19] We excluded diagnoses related to type 1 diabetes (*International Classification of Diseases, Ninth Revision, Clinical Modification*: 250.X1/250.X3, X=0-9; *International Classification of Diseases, Tenth Revision, Clinical Modification*: E10) to select patients more likely to have type 2 diabetes. Patients were considered to have type 2 diabetes if they had ≥1 diagnosis code from inpatient services, home health, or skilled nursing facilities or ≥2 diagnosis codes from physician claims or outpatient services on different dates within 365 days. The same method was used to identify patients with CKD. This method has been shown to increase sensitivity and specificity relative to when only 1 claim is used.[20] The first claim date was chosen for index diagnosis.

To establish CKD and type 2 diabetes diagnoses, the index date was defined by choosing the claims date for the latter of the 2 diagnoses. For example, if the date of diabetes diagnosis was June 15, 2013, and that of CKD diagnosis was July 12, 2014, then the diagnosis index date was July 12, 2014. Patients aged less than 18 years at the diagnosis index date were excluded. Next, we identified patients who filled a first prescription of SGLT2i, GLP-1RA, or second-generation sulfonylurea from January 1, 2013, to December 31, 2018. The first prescription date of SGLT2i, GLP-1RA, or sulfonylureas after the CKD and diabetes diagnosis index date was the prescription index date. We then created 3 mutually exclusive new user groups: SGLT2i, GLP-1RA, and sulfonylureas. For each treatment group, we excluded patients who had a prescription for any drug of interest (SGLT2i, GLP-1RA, or sulfonylureas) in the 12-month period before the prescription index fill date. We then applied the following inclusion criteria: continuous enrollment in Medicare Part A, Part B, and Part D in 1 year before or on the prescription index date.

Study Outcome

The outcome of the study was the initiation of glucose-lowering medications prescriptions (Table S1).

Study Covariates

To define the study covariates, we used a 1-year baseline period before the prescription index date. The covariates included age, sex, race/ethnicity (White, Black, Asian, Hispanic, and other/unknown), region (Northeast, Midwest, South, and West), income level, health insurance status, baseline glucose-lowering medication prescriptions (Table S2), CKD stage status, and comorbid conditions. Zip code–level household median income from the US Census Bureau (a community-level characteristic) was used to approximate personal income level. Low-income subsidy (LIS) status was included as a proxy measure of personal lower income status. The Medicare Part D program offers LIS benefits to enrollees with limited assets and income. Comorbid conditions were based on Elixhauser measures,[21] and confirmed if at least 1 inpatient or 2 physician/outpatient service claims on different days were identified during the baseline period. The Elixhauser Comorbidity Index includes a comprehensive set of 30 comorbid condition measures (covering acute and chronic conditions) and has been used to assess prevalent comorbid conditions in health research for examining medication use.[18,22] The Van Walraven method was used to calculate a comorbid condition index score.[23] Because laboratory-based information was not available in our data files, kidney function was defined by CKD stage-specific *International Classification of Diseases, Ninth Revision, Clinical Modification/International Classification of Diseases, Tenth Revision, Clinical Modification* diagnosis codes (Table S3) from outpatient or physician visit claims during the baseline period. The last claim code for the CKD stage (1-5) in the baseline period was selected.

Statistical Analysis

We described the baseline characteristics across individuals who initiated SGLT2i, GLP-1RA, or sulfonylureas (counts and percentages for categorical variables and means/medians for continuous variables). We used multinomial logistic regression models to evaluate factors associated with the initiation of SGLT2i and GLP-1RA compared with sulfonylureas. Estimated adjusted odds ratios (ORs) are reported with 95% confidence intervals (CIs). All statistical testing was 2-tailed, with P values of <0.05 designated as statistically significant. All statistical analyses were performed using SAS version 9.4 (SAS Institute Inc).

Two subgroup analyses were conducted using the same modeling approach as above: one was among patients with LIS and the other was by the median income level (<$60,000 and ≥$60,000). We also conducted a sensitivity analysis to exclude patients with CKD stages 4 and 5 and kidney failure because the initiation of SGLT2i was not recommended in patients with advanced CKD stages and kidney failure during the study timeframe.

This study was approved by the Hennepin Healthcare Human Subjects Research Committee (IRB-FY2021-35). A waiver of consent was issued because of data anonymity and the use of a large secondary data study.

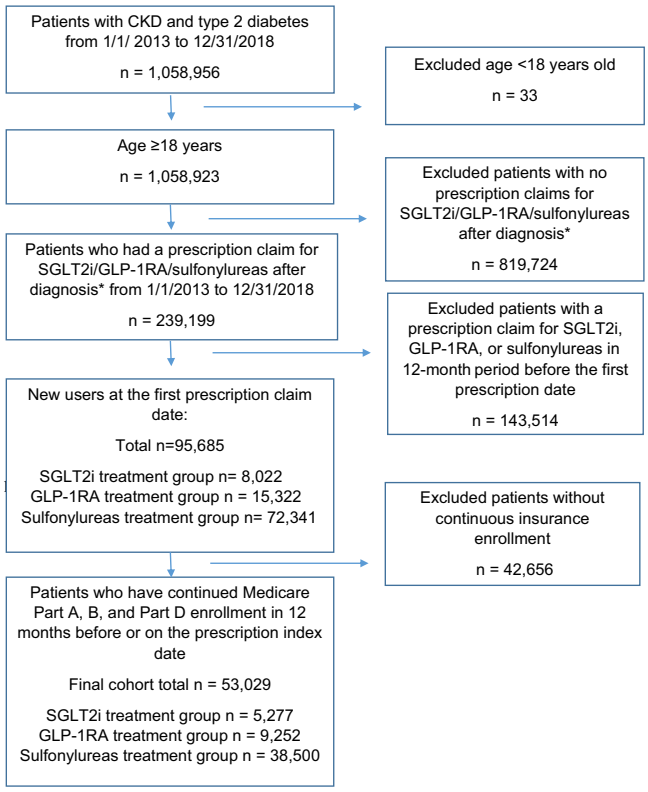

Figure 1. CONSORT (Consolidated Standards of Reporting Trials) diagram for patient selection. *Diagnosis is defined as patients with CKD and type 2 diabetes. CKD, chronic kidney disease; GLP-1RA, glucagon-like peptides-1 receptor agonists; SGLT2i, sodium-glucose cotransporter 2 inhibitors.

RESULTS

After applying study inclusion and exclusion criteria, the study cohort comprised 53,029 adults (aged greater than or equal to 18 years) with CKD and type 2 diabetes, of whom 10.0% (n = 5,277) had an initiating prescription for SGLT2i, 17.4% (n = 9,252) for GLP-1RA, and 72.6% (n = 38,500) for sulfonylureas. A CONSORT (Consolidated Standards of Reporting Trials) diagram for patient selection is provided in Figure 1. The overall mean ± SD age was 71.4 ± 10.9 years; SGLT2i and GLP-1RA users were younger than sulfonylurea users. Baseline insulin use was 47.5%, 69.7%, and 21.0% among users of SGLT2i, GLP-1RA, and sulfonylureas, respectively. The baseline characteristics of each treatment group are summarized in Table 1.

Demographic Differences in Initiating SGLT2i and GLP-1RA Versus Sulfonylureas

After adjusting for demographic and clinical factors (Table 2), patients aged greater than or equal to 75 years had lower odds to start SGLT2i or GLP-1RA than those aged 65-74 years, compared with sulfonylureas. Females had higher odds to initiate GLP-1RA (OR, 1.2; 95% CI, 1.13-1.26) than did males, but lower odds to initiate SGLT2i (OR, 0.88; 95% CI, 0.83-0.94). Black patients were associated with lower odds of initiation of SGLT2i (OR, 0.67; 95% CI, 0.61-0.74) or GLP-1RA (OR, 0.73; 95% CI, 0.68-0.79) than White patients. Hispanic and Asian patients had lower odds of initiation of GLP-1RA. A median household zip code income of ≥$100,000 was associated with higher odds of initiation of GLP-1RA than income of $60,000-$99,999 (OR, 1.21; 95% CI, 1.10-1.35). LIS status was not associated with the initiation of either SGLT-2i or GLP-1RA. Compared with patients living in the Midwest region, people living in the Northeast, South, or West had higher odds to start SGLT2i. There was no significant difference between regions in the initiation of GLP-1RA.

Clinical Difference in Initiating SGLT2i and GLP-1RA Versus Sulfonylureas

Patients with baseline insulin use had higher odds to initiate SGLT2i (OR, 3.78; 95% CI, 3.54- 4.04) or GLP-1RA (OR, 8.58; 95% CI, 8.11-9.07), compared with sulfonylureas. Baseline metformin use was associated with higher odds of initiating SGLT2i (OR, 1.15; 95% CI, 1.07-1.23) but lower odds of initiating GLP-1RA (OR, 0.85; 95% CI, 0.80- 0.90).

We also examined the odds of starting SGLT2i or GLP-1RA based on clinical characteristics. Compared with patients with CKD stage 3, patients with stages 4-5 had lower odds of starting SGLT2i (OR, 0.46; 95% CI, 0.37-0.57) or GLP-1RA (OR, 0.75; 95% CI, 0.67-0.85) than sulfonylureas; however, patients with CKD stage 1-2 were associated with higher odds of starting SGLT2i (OR, 1.80; 95% CI, 1.62-2.01). Patients with a history of cardiovascular

Table 1. Baseline Characteristics of Patients With CKD, Aged Greater Than or Equal To18 Years, With Type 2 Diabetes, Medicare 20% CKD Claims, 2013-2018

Baseline Characteristics	Overall Cohort	SGLT2i	GLP-1RA	Sulfonylureas
Total (N)	53,029	5,277	9,252	38,500
Age, y				
mean ± SD	71.4 ± 10.9	68.8 ± 10.6	66.8 ± 10.6	72.9 ± 10.6
median (IQR)	72.0 (66.0-78.0)	70.0 (65.0-75.0)	68.0 (61.0-73.0)	73.0 (67.0-80.0)
Age category, y				
18-64	10,262 (19.4%)	1,284 (24.3%)	2,903 (31.4%)	6,075 (15.8%)
65-74	22,090 (41.7%)	2,531 (48.0%)	4,387 (47.4%)	15,172 (39.4%)
75-84	15,137 (28.5%)	1,201 (22.8%)	1,703 (18.4%)	12,233 (31.8%)
≥85	5,540 (10.4%)	261 (4.9%)	259 (2.8%)	5,020 (13.0%)
Sex				
Male	25,951 (48.9%)	2,779 (52.7%)	4,156 (44.9%)	19,016 (49.4%)
Female	27,078 (51.1%)	2,498 (47.3%)	5,096 (55.1%)	19,484 (50.6%)
Race/ethnicity				
White	40,368 (76.1%)	4,034 (76.4%)	6,999 (75.6%)	29,335 (76.2%)
Black	7,491 (14.1%)	580 (11.0%)	1,364 (14.7%)	5,547 (14.4%)
Asian	1,489 (2.8%)	208 (3.9%)	191 (2.1%)	1,090 (2.8%)
Hispanic	1,815 (3.4%)	226 (4.3%)	350 (3.8%)	1,239 (3.2%)
Other/unknown	1,866 (3.5%)	229 (4.3%)	348 (3.8%)	1,289 (3.3%)
Region				
Midwest	12,043 (22.7%)	993 (18.8%)	2,079 (22.5%)	8,971 (23.3%)
Northeast	9,306 (17.5%)	930 (17.6%)	1,647 (17.8%)	6,729 (17.5%)
South	22,548 (42.5%)	2,243 (42.5%)	3,941 (42.6%)	16,364 (42.5%)
West	9,031 (17.0%)	1,107 (21.0%)	1,580 (17.1%)	6,344 (16.5%)
Other/unknown	101 (0.2%)	[a]	[a]	92 (0.2%)
LIS status				
Non-LIS	30,075 (56.7%)	2,821 (53.5%)	4,477 (48.4%)	22,777 (59.2%)
LIS	22,954 (43.3%)	2,456 (46.5%)	4,775 (51.6%)	15,723 (40.8%)
Zip code–level household median income				
≤$34,999	3,644 (6.9%)	357 (6.8%)	643 (6.9%)	2,644 (6.9%)
$35,000-$59,999	25,870 (48.8%)	2,519 (47.7%)	4,579 (49.5%)	18,772 (48.8%)
$60,000-$99,999	18,008 (34.0%)	1,856 (35.2%)	3,050 (33.0%)	13,102 (34.0%)
≥$100,000	4,293 (8.1%)	435 (8.2%)	765 (8.3%)	3,093 (8.0%)
Missing	1,214 (2.3%)	110 (2.1%)	215 (2.3%)	889 (2.3%)
CKD stage				
1/2	4,923 (9.3%)	640 (12.1%)	922 (10.0%)	3,361 (8.7%)
3	18,320 (34.5%)	1,323 (25.1%)	3,319 (35.9%)	13,678 (35.5%)
4/5	3,720 (7.0%)	98 (1.9%)	632 (6.8%)	2,990 (7.8%)
Unknown/unspecified	26,066 (49.2%)	3,216 (60.9%)	4,379 (47.3%)	18,471 (48.0%)
ESKD	1,465 (2.8%)	14 (0.3%)	300 (3.2%)	1,151 (3.0%)
Metformin use	30,674 (57.8%)	3,529 (66.9%)	4,941 (53.4%)	22,204 (57.7%)
Meglitinides use	1,096 (2.1%)	159 (3.0%)	252 (2.7%)	685 (1.8%)
Thiazolidinediones use	2,948 (5.6%)	491 (9.3%)	587 (6.3%)	1,870 (4.9%)
α-glucosidase inhibitors use	220 (0.4%)	26 (0.5%)	56 (0.6%)	138 (0.4%)
Bile acid sequestrants use	412 (0.8%)	69 (1.3%)	102 (1.1%)	241 (0.6%)
Dopamine-2 agonists use	31 (0.1%)	[a]	[a]	22 (0.1%)
DPP-4is use	11,607 (21.9%)	1,827 (34.6%)	2,279 (24.6%)	7,501 (19.5%)
Amylin mimetics use	43 (0.1%)	[a]	29 (0.3%)	[a]
Insulins use	17,059 (32.2%)	2,504 (47.5%)	6,451 (69.7%)	8,104 (21.0%)
Cardiovascular disease	35,213 (66.4%)	3,261 (61.8%)	6,006 (64.9%)	25,946 (67.4%)
Hypertension	49,392 (93.1%)	4,896 (92.8%)	8,708 (94.1%)	35,788 (93.0%)
Hyperlipidemia	42,224 (79.6%)	4,434 (84.0%)	7,658 (82.8%)	30,132 (78.3%)
Hypoglycemia events	3,738 (7.0%)	369 (7.0%)	925 (10.0%)	2,444 (6.3%)

(Continued)

Table 1 (Cont'd). Baseline Characteristics of Patients With CKD, Aged Greater Than or Equal To18 Years, With Type 2 Diabetes, Medicare 20% CKD Claims, 2013-2018

Baseline Characteristics	Overall Cohort	SGLT2i	GLP-1RA	Sulfonylureas
No. of Elixhauser comorbid conditions				
mean ± SD	6.6 ± 3.3	6.0 ± 3.0	6.7 ± 3.1	6.7 ± 3.4
median (IQR)	6.0 (4.0-9.0)	5.0 (4.0-8.0)	6.0 (4.0-9.0)	6.0 (4.0-9.0)
Elixhauser Comorbidity Index score				
mean ± SD	10.2 ± 10.0	7.3 ± 8.8	8.2 ± 9.1	11.1 ± 10.2
median (IQR)	8.0 (3.0-16.0)	5.0 (0.0-12.0)	6.0 (1.0-14.0)	9.0 (4.0-17.0)

Abbreviations: CKD, chronic kidney disease; DPP-4i, dipeptidyl peptidase 4 inhibitor; ESKD, end-stage kidney disease; GLP-1RA, glucagon-like peptides-1 receptor agonists; IQR, interquartile range; LIS, low-income subsidy; SGLT2i, sodium/glucose cotransporter 2 inhibitors.
[a]Counts of 10 or fewer patients.

disease or hyperlipidemia had higher odds to start SGLT2i or GLP-1RA. For the Elixhauser Comorbidity Index score, a higher value (greater comorbid condition burden) was associated with lower odds of starting SGLT2i (OR, 0.96; $P < 0.001$) or GLP-1RA (OR, 0.96; $P < 0.001$).

Subgroup and Sensitivity Analyses

Results were similar in the subgroup analyses among patients with LIS (Table S4). Patients who were aged greater than or equal to 75 years, were Black, had CKD stage 4-5, and had a higher Elixhauser Comorbidity Index score were associated with lower odds of initiation of SGLT2i or GLP-1RA. The subgroup analysis performed according to the median income level showed that Black patients were associated with a significantly lower rate of initiating SGLT2i and GLP-1RA than White patients at both income levels: <$60,000 (OR, 0.66 for SLGT2i; OR, 0.71 for GLP-1RA) and ≥$60,000 (OR, 0.65 for SLGT2i; OR, 0.74 for GLP-1RA) (Tables S5 and S6). The findings from the sensitivity analysis were similar to those from the main analysis (Table S7).

DISCUSSION

Our study compared the initiation of SGLT2i and GLP-1RA with second-generation sulfonylureas across race, age, sex, and socioeconomic factors in adult patients with CKD and type 2 diabetes using Medicare claims data. There were significant differences in age, sex, race/ethnicity racial/ethnical, socioeconomic groups, and clinical status of patients initiating SGLT2i and GLP-1RA, compared with second-generation sulfonylureas.

We observed racial/ethnic differences in the initiation of SGLT2i and GLP-1RA, with Black patients significantly less likely to start SGLT2i or GLP-1RA, compared with White patients, even after adjustment for community socioeconomic status and clinical factors. Hispanic and Asian patients were also associated with lower odds of initiation of GLP-1RA but not SGLT2i. Significantly lower rate of initiating SGLT2i and GLP-1RA in Black patients was also shown in the subgroup analysis among patients with LIS and in the subgroup analysis by the median income level (<$60,000 and ≥$60,000); Black patients were less likely to initiate the new agents regardless of income groups. Several prior studies in patients without CKD have demonstrated lower use of these agents among Black patients.[18,24,25] Similar to our finding, studies have shown that racial disparity persists at all levels of social economic status.[26,27]

Health disparities in Black patients with diabetes and CKD have been well documented. The Coronary Artery Risk Development in Young Adults study found that Black patients had significantly faster annualized estimated glomerular filtration rates of decline.[28] The US Renal Data System annual data reported that Black patients had the highest prevalence of end-stage kidney disease in racial and ethnic groups from 2000 to 2019.[29] Our research team showed that Medicare-enrolled Black patients with CKD had a higher risk of developing hypoglycemia than White patients.[30] Clinical studies have demonstrated the cardiovascular and kidney benefits of SGLT2i and GLP-1RA, especially the Canagliflozin and Renal Events in Diabetes with Established Nephropathy Clinical Evaluation (CREDENCE) and the Dapagliflozin and Prevention of Adverse Outcomes in Chronic Kidney Disease (DAPA-CKD) trials, which were specially designed to focus on patients with CKD.[6,8] The significant benefit of dapagliflozin on primary kidney outcomes was also shown in the Black subgroup. Given the benefits of the newer agents in cardiovascular and kidney outcomes, it is important to investigate barriers and to promote access and adherence to the newer glucose-lowering medications especially among higher risk patients with type 2 diabetes.

In addition to racial differences in the use of SGLT2i or GLP-1RA, we discovered differences in use based on sex and socioeconomic status. Interestingly, female patients were less likely to start SGLT2i but were more likely to start GLP-1RA, compared with male patients. A published study in the non-CKD population reported a similar finding that women were more likely to start a GLP-1RA than men but were less likely to start SGLT2i.[25] It may be that physicians are reluctant to start SGLT2i in women because of concern of increased risk of urinary tract infections (UTIs), but this has been refuted in a recent meta-analysis.[31] The 2 clinical trials, CREDENCE and DAPA-CKD, which specifically focused on patients with CKD, showed that risk of UTIs with SGLT2i was similar to that with placebo.[6,8] Compared

Table 2. Factors Associated With Initiating SGLT2i or GLP-1RA, Compared With Sulfonylureas (Multinomial Logistic Regression Analysis)

	SGLT2i vs Sulfonylureas				GLP-1RA vs Sulfonylureas			
Characteristic	Adjusted Odds Ratio	95% CI		*P* value	Adjusted Odds Ratio	95% CI		*P* value
Age category, y								
18-64	1.31	1.20	1.43	<0.001	1.55	1.44	1.67	<0.001
65-74	1.00				1.00			
75-84	0.63	0.59	0.68	<0.001	0.53	0.49	0.56	<0.001
≥85	0.39	0.34	0.45	<0.001	0.21	0.18	0.24	<0.001
Sex								
Male	1.00				1.00			
Female	0.88	0.83	0.94	<0.001	1.20	1.13	1.26	<0.001
Race/ethnicity								
White	1.00				1.00			
Black	0.67	0.61	0.74	<0.001	0.73	0.68	0.79	<0.001
Asian	1.23	1.04	1.46	0.02	0.74	0.62	0.88	<0.001
Hispanic	0.98	0.84	1.16	0.84	0.81	0.70	0.93	0.004
Other/unknown	1.03	0.88	1.20	0.70	0.94	0.82	1.08	0.36
Region								
Midwest	1.00				1.00			
Northeast	1.18	1.07	1.31	0.001	1.09	1.00	1.18	0.05
South	1.22	1.12	1.32	<0.001	1.03	0.96	1.10	0.38
West	1.46	1.32	1.61	<0.001	1.08	0.99	1.18	0.07
Other/unknown	0.32	0.11	0.92	0.03	0.18	0.07	0.48	<0.001
Low-income subsidy	1.01	0.94	1.09	0.78	0.98	0.92	1.05	0.59
Zip code–level household median income								
≤$34,999	0.95	0.84	1.09	0.49	0.87	0.78	0.98	0.02
$35,000-$59,999	0.94	0.88	1.01	0.07	0.94	0.88	1.00	0.04
$60,000-$99,999	1.00				1.00			
≥$100,000	0.97	0.86	1.10	0.65	1.21	1.10	1.35	<0.001
Missing	0.78	0.63	0.97	0.03	0.89	0.75	1.07	0.22
CKD stage								
1/2	1.80	1.62	2.01	<0.001	1.08	0.99	1.19	0.09
3	1.00				1.00			
4/5	0.46	0.37	0.57	<0.001	0.75	0.67	0.85	<0.001
Unknown/unspecified	1.61	1.50	1.73	<0.001	0.87	0.82	0.93	<0.001
ESKD	0.15	0.09	0.26	<0.001	0.74	0.63	0.89	<0.001
Metformin use	1.15	1.07	1.23	<0.001	0.85	0.80	0.90	<0.001
Meglitinides use	1.62	1.34	1.96	<0.001	1.76	1.48	2.09	<0.001
Thiazolidinediones use	1.85	1.65	2.07	<0.001	1.47	1.32	1.64	<0.001
α-glucosidase inhibitors use	0.94	0.61	1.47	0.80	1.22	0.85	1.74	0.29
Bile acid sequestrants use	2.11	1.58	2.82	<0.001	1.96	1.50	2.56	<0.001
DPP-4is use	2.15	2.01	2.30	<0.001	1.47	1.38	1.57	<0.001
Insulins use	3.78	3.54	4.04	<0.001	8.58	8.11	9.07	<0.001
Cardiovascular disease	1.08	1.00	1.16	0.04	1.13	1.06	1.20	<0.001
Hypertension	1.11	0.98	1.25	0.11	1.16	1.03	1.29	0.01
Hyperlipidemia	1.39	1.28	1.51	<0.001	1.22	1.14	1.31	<0.001
Hypoglycemia events	1.00	0.88	1.13	0.97	1.05	0.96	1.15	0.32
Elixhauser Comorbidity Index score	0.96	0.96	0.97	<0.001	0.96	0.96	0.97	<0.001
Year of prescription[a]	1.34	1.31	1.37	<0.001	1.40	1.38	1.43	<0.001

Abbreviations: CKD, chronic kidney disease; DPP-4i, dipeptidyl peptidase 4 inhibitor; GLP-1R, glucagon-like peptides-1 receptor agonists; SGLT2i, sodium/glucose cotransporter 2 inhibitors.
[a]For a 1-year change from previous to subsequent year (eg, from 2017 to 2018), initiating SGLT2i was 1.34 times as likely compared with starting sulfonylureas and initiating GLP-1RA was 1.4 times as likely.

with those with a median household income ranging from $60,000 to $99,999, those with a median income of ≥$100,000 were more likely and those with a median income <$60,000 were less likely to receive GLP-1RA.

SGLT2i and GLP-1RA are high-cost brand medications compared with generic sulfonylureas. The median retail prices for a 30-day supply ranged from $300 (interquartile range, $285-$303) for ertugliflozin to $942 (interquartile range, $931-$969) for liraglutide for Medicare beneficiaries in 2019 Part D plans. The median estimated annual out-of-pocket costs ranged from $1,097 (interquartile range, $932-$1,271) for empagliflozin to $2,447 (interquartile range, $2,441-$2,464) for liraglutide.[32] Further, the low rate of formulary inclusion in Medicare Part D program may also limit patients' access to certain high-cost glucose-lowering medications. Canagliflozin was included on <75% of Part D plan formularies in 2019 and 2020,[32,33] but coverage without prior authorization and without step therapy requirements was only 53.2% (95% CI, 49.1%-57.4%) in 2019 Part D plans.[32] However, we did not observe a significant difference in starting SGLT2i or GLP-1RA based on LIS status. Although LIS enrollees have limited assets and income, they also have lower premium and copayment because of cost-sharing requirements.

Two recent studies analyzed the use of SGLT2i based on sociodemographic and clinical factors. Both studies, however, focused on commercially insured and Medicare Advantage patients without CKD. Eberly et al[18] compared adult patients with type 2 diabetes who did and did not receive SGLT2i treatment using the Optum Clinformatics Data Mart from October 1, 2015, to June 30, 2019 in the primary focus. The subgroup analysis reported factors associated with SGLT2i use among patients with CKD and found, similar to our study, that Black patients and female patients were associated with lower rates of adoption of SGLT2i; patients with metformin and insulin use were associated with high rates. The study reported that higher median household income (≥$100,000 vs <$50, 000) was associated with a higher rate of adoption of SGLT2i. This is different from our finding; we did not observe a significant difference in starting SGLT2i based on the zip code–level median household income. The Optum study focused on the adoption of SGLT2i and did not examine GLP-1RA use in adult patients with type 2 diabetes with a younger median age using SGLT2i (58 vs 70 years) than our study. Further, Optum investigators evaluated comorbid conditions from the earliest date of available data to the date of cohort entry. Some patients may have had a relatively short baseline evaluation period, which could introduce bias in terms of number or type of comorbid conditions. Using a similar cohort design and the same Optum dataset, McCoy et al[24] examined adult patients (aged greater than or equal to 18 years) with type 1 or 2 diabetes for the use of SGLT2i treatment between 2013 and 2016. They also showed that SGLT2i users were younger, and SGLT2i were prescribed less frequently to women than men and Black versus White patients.

We observed that patients with CKD with cardiovascular disease had significantly higher initiation of SGLT2i or GLP-1RA than sulfonylureas. Five large randomized clinical trials (the EMPA-REG OUTCOME, the Canagliflozin Cardiovascular Assessment Study [CANVAS], the Dapagliflozin Effect on Cardiovascular Events–Thrombolysis in Myocardial Infarction 58 [DECLARE–TIMI 58], CREDENCE, and DAPA-CKD) demonstrated cardiovascular benefits, and kidney protective benefits of SGLT2i.[5-8,11,12,34] The clinical trials that may have impacted our results were the CANVAS (canagliflozin, published 2017), EMPA-REG OUTCOME (empagliflozin, 2015), the Trial to Evaluate Cardiovascular and Other Long-term Outcomes with Semaglutide in Subjects with Type 2 Diabetes (SUSTAIN-6) trial (semaglutide, 2016), and the Liraglutide Effect and Action in Diabetes: Evaluation of Cardiovascular Outcome Results (LEADER) trial (liraglutide, 2016), all of which demonstrated significant cardiovascular and kidney benefits of SGLT-2i and GLP-1RA.[5,11-14] Although enrolled participants in these 4 clinical trials had type 2 diabetes, they all included some patients with estimated glomerular filtration rate of < 60, and their primary outcome was major adverse cardiovascular events (ie, a composite outcome of death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke).

Consistent with other studies, we noted that older patients were significantly less likely to start SGLT2i or GLP-1RA than sulfonylureas, compared with younger patients. Older patients may be more likely to have multiple comorbid conditions, lower estimated glomerular filtration rates, polypharmacy, and financial barriers for new expensive medications, which may lead inertia in initiating novel medications. However, significant benefits of SGLT2i were shown among the subgroup patients (aged greater than or equal to 65 years) in the study of EMPAREG, CANVAS, DECLARE, and DAPA-CKD.[6-8,11,12,34]

Our study has several strengths. We provide a comparison between initiations of novel, tradename SGLT2i and GLP-1RA versus generic sulfonylureas with a nationally representative sample of Medicare beneficiaries with CKD and type 2 diabetes enrolled in Medicare Part D plans. Also, we used a new user design, which reduces the risk of selection bias that can occur when patients have been exposed to a drug class in the past. The Medicare claims database is large enough to create a population for >53,000 patients meeting study criteria. It provides comprehensive information on patient demographic characteristics, inpatient and outpatient diagnoses and procedures, and prescriptions. Finally, we used actual medication claims dispensing records rather than other data sources that might measure only prescribing patterns.

Our analysis also has limitations. The study only assessed the first prescription filled by new users after the diagnosis index date. Clinical characteristics were measured based on administrative claims. In our study, CKD stage and evidence of patients with CKD and type 2 diabetes were identified using diagnosis codes and could not be verified through medical record review or laboratory values. We used ≥1 inpatient claim or ≥2 physician/outpatient claims to increase sensitivity and specificity.[20] Approximately 49% of the CKD stage codes were CKD stage unknown or

unspecified in our study cohort; thus, our findings applied to patients with specific CKD stages known or determined. Our analysis cohort consisted of patients with CKD enrolled in Medicare Part D coverage; thus, usage patterns may differ for patients enrolled in the non-Part D prescription plans, Medicare Advantage plans, or other types of health insurance. However, approximately 75% of Medicare beneficiaries with CKD were enrolled in Medicare Part D in 2019.[29] In addition, Medicare Part D beneficiaries may have chosen to use drug discount cards or coupons in lieu of their Medicare Part D prescription benefits, and we could not capture that information. The Medicare data set does not include patients aged younger than 65 years, except for people with disabilities. The generalizability of our findings may not apply to younger patients with CKD and diabetes. Further, although Medicare claims that data sources of race/ethnicity information are commonly used in reports and studies of health disparities,[35,36] Jarrín et al[37] suggested high validity for Black patients and low sensitivity for Hispanic and Asian patients in Medicare beneficiary data files. Thus, there is a potential for misclassification in these race/ethnicity groups. Finally, zip code–level household median income was used to approximate personal income level, which is not included in Medicare claims data. Zip code–level household data are commonly used in Medicare studies.[18,22]

In conclusion, we identified several race-, sex-, and age-related disparities in use of SGLT2i and GLP-1RA among Medicare-insured adults diagnosed with type 2 diabetes and CKD. Of particular concern, Black patients were significantly less likely to be initiated on SGLT2i or GLP-1RA and were more likely to receive sulfonylureas, which have not showed cardiovascular or kidney benefits and are more likely to cause hypoglycemia. This represents a health disparity and a pharmacoequity issue that needs to be addressed to slow kidney disease progression in a population that is at higher risk of progressing to kidney failure. These findings should also be a call for public education and political action by kidney disease patient advocacy organizations such as the National Kidney Foundation, American Society of Nephrology, and American Association of Kidney Patients to eliminate health disparities in the prescription of newer diabetes agents that have been shown to slow the rate of CKD progression.

SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Table S1: Food and Drug Administration (FDA) approval dates for sulfonylureas, SGLT2i and GLP-1RA.

Table S2: Description of baseline glucose-lowering medications prescriptions in study patients.

Table S3: Chronic kidney disease stage-specific ICD-9/10-CM diagnosis codes.

Table S4: Factors associated with initiating SGLT2i, or GLP-1RA compared with sulfonylureas among CKD and type 2 diabetes patients with low-income subsidy (N=22,954), multinomial logistic regression analysis.

Table S5: Factors associated with initiating SGLT2i, or GLP-1RA compared with sulfonylureas among CKD and type 2 diabetes patients with the zip code linked median household income <$60,000 (N=29,514), multinomial logistic regression analysis.

Table S6: Factors associated with initiating SGLT2i, or GLP-1RA compared with sulfonylureas among CKD and type 2 diabetes patients with the zip code linked median household income ≥$60,000 (N=22,301), multinomial logistic regression analysis.

Table S7: Factors associated with initiating SGLT2i, or GLP-1RA compared with sulfonylureas excluding patients with stage 4 and 5 CKD and kidney failure (N=48,948), multinomial logistic regression analysis.

ARTICLE INFORMATION

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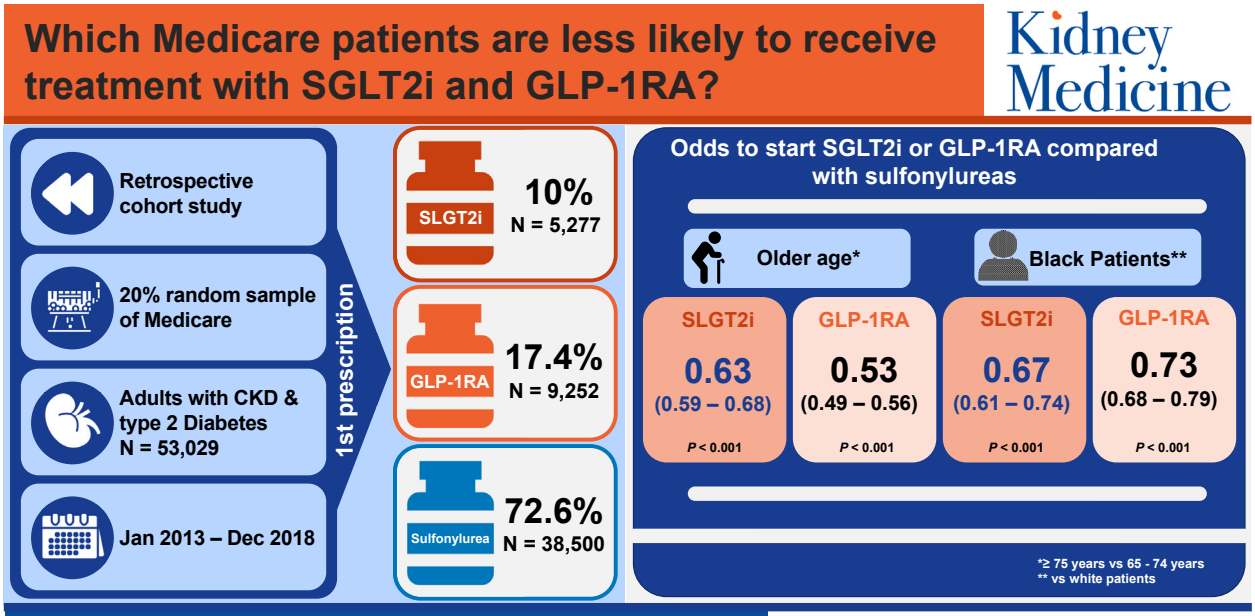
Which Medicare patients are less likely to receive treatment with SGLT2i and GLP-1RA?
Kidney Medicine
Retrospective cohort study
20% random sample of Medicare
Adults with CKD & type 2 Diabetes
N = 53,029
Jan 2013 – Dec 2018
1st prescription
SLGT2i
10%
N = 5,277
GLP-1RA
17.4%
N = 9,252
Sulfonylurea
72.6%
N = 38,500
Odds to start SGLT2i or GLP-1RA compared with sulfonylureas
Older age*
Black Patients**
SLGT2i
0.63
(0.59 – 0.68)
P < 0.001
GLP-1RA
0.53
(0.49 – 0.56)
P < 0.001
SLGT2i
0.67
(0.61 – 0.74)
P < 0.001
GLP-1RA
0.73
(0.68 – 0.79)
P < 0.001
*≥ 75 years vs 65 - 74 years
** vs white patients
Conclusion: Black and older patients with type 2 diabetes and CKD were significantly less likely to be initiated on SGLT2i or GLP-1RA than on 2nd generation sulfonylureas.
Reference: Zhao JZ, Weinhandl ED, Carlson AM, et al. Disparities in SGLT2 inhibitor or glucagon-like peptide 1 receptor agonist initiation among Medicare insured adults with CKD in the United States. Kidney Medicine, 2023.
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