Race and ethnicity and pharmacy dispensing of SGLT2 inhibitors and GLP-1 receptor agonists in type 2 diabetes

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Summary

Background Sodium-Glucose Cotransporter 2 Inhibitors (SGLT2i) and Glucagon-Like Peptide-1 Receptor Agonists (GLP-1 RA) improve cardiorenal outcomes in patients with type 2 diabetes. Equitable use of SGLT2i and GLP-1 RA has the potential to reduce racial and ethnic health disparities. We evaluated trends in pharmacy dispensing of SGLT2i and GLP-1 RA by race and ethnicity.

Methods Retrospective cohort study of patients (≥18 years) with type 2 diabetes using 2014–2022 electronic health record data from six US care delivery systems. Entry was at earliest pharmacy dispensing of any type 2 diabetes medication. We used multivariable logistic regression to evaluate the association between pharmacy dispensing of SGLT2i and GLP1-RA and race and ethnicity.

Findings Our cohort included 687,165 patients (median 6 years of dispensing data; median 60 years; 0.3% American Indian/Alaska Native (AI/AN), 16.6% Asian, 10.5% Black, 1.4% Hawaiian or Pacific Islander (HPI), 31.1% Hispanic, 3.8% Other, and 36.3% White). SGLT2i was lower for AI/AN (OR 0.80, 95% confidence interval 0.68–0.94), Black (0.89, 0.86–0.92) and Hispanic (0.87, 0.85–0.89) compared to White patients. GLP-1 RA was lower for AI/AN (0.78, 0.63–0.97), Asian (0.50, 0.48–0.53), Black (0.86, 0.83–0.90), HPI (0.52, 0.46–0.57), Hispanic (0.69, 0.66–0.71), and Other (0.78, 0.73–0.83) compared to White patients.

Interpretation Dispensing of SGLT2is, and GLP-1 RAs was lower in minority group patients. There is a need to evaluate approaches to increase use of these cardiorenal protective drugs in patients from racial and ethnic minority groups with type 2 diabetes to reduce adverse cardiorenal outcomes and improve health equity.

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Keywords: SGLT2i; GLP-1 RA; Type 2 diabetes; Race and ethnicity; Cardiovascular disease; Renal disease

Introduction

Sodium-Glucose Cotransporter 2 Inhibitors (SGLT2i) and Glucagon-Like Peptide-1 Receptor Agonists (GLP-1 RA) reduce adverse cardiorenal outcomes in patients with type 2 diabetes and high cardiovascular disease, chronic kidney disease, heart failure, obesity, or elevated cardiovascular disease risk.[1] These findings prompted the American Diabetes Association,[2] the American

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Research in context

Evidence before this study

We searched for cross-sectional and longitudinal cohort studies investigating the use of SGLT2i and GLP-1 RA among patients with type 2 diabetes and reporting use by race and ethnicity, published in any language from 2005 (time of first GLP-1 RA introduction) until November 9, 2023, in PubMed, Embase and Google Scholar. Prior studies investigated racial and ethnic disparities in the use of SGLT2i and GLP-1 RA. These studies, however, had one or more of the following limitations: cohorts did not extend beyond 2019 or 2020, before the American Diabetes Association, the American College of Cardiology, and the European Society of Cardiology updated their SGLT2i and GLP-1 RA guidelines, used administrative or insurance claims-based databases, which lacked important clinical variables such as glycemic control and diabetes duration, included few racially and ethnically diverse groups, or few younger patients or women, and sample sizes were small.

Added value of this study

To our knowledge, this is the first U.S.-based study to evaluate the dispensing of SGLT2i and GLP-1 RA among racially and ethnically diverse patients over a span of time (2014–2022) that includes data after the American Diabetes Association, the American College of Cardiology, and the European Society of Cardiology updated their SGLT2i and GLP-1 RA guidelines in 2019/2020. In addition, this study uses data from real-world clinical settings that include patients with various insurance coverage, and the analyses account for important indications of initiating one of these drugs, including diabetes duration and control, which most prior studies did not account for, along with cardiovascular and chronic kidney disease risk factors. In our retrospective cohort study, we observed that compared to White patients, SGLT2i dispensing was lower for American Indian/Alaska Native, Black, and Hispanic patients, and GLP-1 RA dispensing was lower for American Indian/Alaska Native, Asian, Black, Hawaiian or Pacific Islander, Hispanic, and Other patients.

Implications of all the available evidence

Taken together, these findings highlight the need for targeted efforts towards more equitable use of these cardiorenal protective medications across racial and ethnic minority groups.

College of Cardiology,[3] and the European Society of Cardiology[4] to recommend that patients with type 2 diabetes with established or at risk of atherosclerotic cardiovascular disease, chronic kidney disease, or heart failure, be prescribed an SGLT2i or GLP-1 RA, irrespective of glycemic control or metformin use.

Recent studies have shown racial and ethnic disparities in the use of these medications.[5–10] These studies, however, had limitations: cohorts did not extend beyond 2019[5–7,10,11] or 2020,[8,9] used administrative or insurance claims-based databases,[5–7,10,11] included few racially and ethnically diverse groups,[5,8] or few younger patients or women,[6,8,9] sample sizes were small,[8] and important clinical variables such as glycemic control[5–7,11] and diabetes duration[5–9,11] were not available. Our study addresses these limitations, and to our knowledge, it is the first to evaluate the dispensing of SGLT2i and GLP-1 RA among racially and ethnically diverse patients using contemporary data (through 2022), which allows the evaluation of disparities over a span of time that includes data following the updated guidelines.[2–4] Additional unique contributions of this study are the use of data from real-world clinical settings that include patients with various insurance coverage, diabetes duration and control, and cardiovascular disease and chronic kidney disease risk factors.

In this study, we evaluated trends in pharmacy dispensing of SGLT2i and GLP-1 RA between 2014 and 2022 using data from six large not-for-profit care delivery systems with fully integrated administrative and electronic health records in the US. We estimated the proportion of patients with type 2 diabetes who received these medications by race and ethnicity, overall and by year, and by important demographic and clinical characteristics.

Methods

Study design, setting, and participants

This retrospective cohort study included patients with type 2 diabetes on glucose-lowering therapy from six large US healthcare delivery systems from 1/1/2014 to 12/13/2022. These sites (Geisinger in Pennsylvania, HealthPartners in Minnesota and Wisconsin, Henry Ford Health in Michigan, Kaiser Permanente Northern California [KPNC], Kaiser Permanente Southern California, and Kaiser Permanente Hawaii [KPHI]) are part of the Health Care Systems Research Network and serve approximately 10 million patients with over 600,000 living with type 2 diabetes. The index date (study entry or baseline date) was the latest of 1/1/2014 or the date of the first type 2 diabetes pharmacy dispensing after 1/1/2009. We included adult patients (aged ≥18 years) with evidence of type 2 diabetes (using a validated algorithm to discriminate from type 1 diabetes using a ratio of International Classification of Diseases (ICD)-9 and ICD-10 codes[12]; patients with evidence of type 1 diabetes [n = 21,686] or indeterminate [n = 148,709] were excluded), on glucose-lowering therapy,[2] 2 years of continuous health plan membership (allowing up to a 92-day administrative gap), and ≥ one hemoglobin A1C (HbA1c) in the two years prior to baseline. Patients with

evidence of SGLT2i or GLP-1 RA contraindications (multiple endocrine neoplasia, type 2, pancreatitis, pyelonephritis, necrotizing fasciitis, cystic fibrosis, or estimated glomerular filtration rate <30 mL/min/1.73 m^2) between 1/1/2009 and index date were excluded (n = 29,923). This study was approved by the KPNC institutional review board. This study followed the STROBE reporting guidelines.

Primary exposure

Race and ethnicity were collected from various registries and electronic health record data. Those with Latino or Hispanic ethnicity (hereafter Hispanic) were identified first. The remaining non-Hispanic participants were categorized into: American Indian/Alaskan Native (AI/AN), Asian, Black or African American (hereafter Black), Hawaiian and Pacific Islander (HPI), Multi-racial or Other/Unknown (hereafter Other), and White.

Primary outcome

Our outcomes of interest, annual pharmacy dispensing between 2014 and 2022 (yes/no) and dispensing at any point during the study period (yes/no) were generated separately for SGLT2i and GLP-1 RA. Patients contributed annual primary outcome data only in calendar years where the patient had at least one type 2 diabetes pharmacy dispensing. The data captures the use of SGLT2i or GLP-1 RA at least once or more in any given year, or during the entire study period (Table 1). If someone had a pharmacy dispensing of one of these drugs for a few months and stopped, they are counted in both the numerator and denominators for that drug in that given year (Figs. 1 and 2), or during the entire study period (Tables 2 and 3). Across each racial and ethnic group, we evaluated annual pharmacy dispensing rates of any SGLT2i or GLP-1 RA (Figs. 1 and 2) and pharmacy dispensing of SGLT2i, GLP-1 RA, or both, at any point between 2014 and 2022 (Tables 2 and 3, and Supplementary Table S1).

Covariates

Covariates were ascertained at baseline from the electronic health record, including patient demographics (age, sex, and insurance type), concurrent medication fills (metformin, or insulin filled in the same calendar year as the index date), diabetes control (most recent HbA1c within two years prior to index date), visits to specialists (endocrinology, cardiology, and nephrology within 1 year prior to the index date), and comorbidities (cerebrovascular disease, chronic kidney disease, congestive heart failure, myocardial infarction, peripheral vascular disease, dyslipidemia, and hypertension using ICD-9/10 data within two years prior to index date). Body mass index was calculated by dividing weight in kilograms by the square of height in meters. Those with a recorded body mass index in the two years prior to index date ≥30 kg/m^2 for non-Asian participants, or ≥27.5 for Asian participants, were identified as obese.[13] Those with missing or unknown sex (n = 18) or missing HbA1c (n = 20) were excluded. Household address at index date was used to ascertain median household income at the census tract level using data from the American Community Survey.[14] Baseline diabetes duration was calculated using data between 1/1/2009 and index date. The first instance of an inpatient diabetes diagnosis or the first of two other qualifying events within 2 years of each other was used to calculate diabetes duration at index date.[15] Other qualifying events included an outpatient diabetes diagnosis, any anti-hyperglycemic medication dispensing, a fasting plasma glucose ≥126 mg/dL, a random plasma glucose ≥200 mg/dL, or an HbA1c ≥ 6.5%. The two qualifying events could not both be a fill for metformin, thiazolidinediones, or liraglutide, and could not be during pregnancy.

Statistical analysis

Descriptive statistics were calculated for demographic and clinical characteristics and cardiovascular risk factors at baseline for the overall cohort and by dispensing medication (SGLT2i, GLP-1 RA, both, and neither) during the study period (Table 1). Age was presented as median [interquartile range] since it was not normally distributed (Kolmogorov–Smirnov Goodness-of-Fit test $p < 0.05$), and categorical measures were presented as No. (%). For each drug class, we evaluated annual trends of pharmacy dispensing by race and ethnicity between 2014 and 2022. We first used separate logistic regression models for each drug class with an interaction term between race and ethnicity and dispensing year, adjusting for age, sex, and site. We then output annual predicted dispensing rates for each drug class by race and ethnicity (Figs. 1 and 2). To evaluate the association between race and ethnicity and pharmacy dispensing of each drug class (SGLT2i, GLP-1 RA or both) ever dispensed between 2014 and 2022, we used three separate logistic regression models with race and ethnicity as the primary exposure. The three separate models were adjusted for demographics, concurrent type 2 diabetes medication fills, diabetes control, diabetes duration, visits to specialists, and comorbidities, including cardiovascular risk factors, at baseline and reported adjusted odds ratios (AORs) with 95% CIs (Tables 2 and 3, and Supplementary Table S1). We conducted sensitivity analyses including: 1) models adjusting only for age, sex, and site, to evaluate if racial and ethnic differences were stronger compared to the fully adjusted models; 2) stratified models within each insurance (Commercial, Medicare, and Medicaid), to evaluate if racial and ethnic differences persisted within each insurance, since our study lacked data on medication copayment; and 3) because there were site-specific pharmacy dispensing differences, we also conducted site-specific stratified models for KPNC and

Characteristic	Overall N = 687,165	SGLT2i N = 56,776	GLP-1 RA N = 20,329	Both N = 10,117	Neither N = 599,943
Age, median [IQR], y	60 [51, 69]	58 [50, 66]	54 [46, 62]	54 [47, 61]	61 [52, 70]
Sex					
Male	367,995 (53.6%)	33,346 (58.7%)	8834 (43.5%)	4977 (49.2%)	320,838 (53.5%)
Female	319,170 (46.4%)	23,430 (41.3%)	11,495 (56.5%)	5140 (50.8%)	279,105 (46.5%)
Race and ethnicity					
American Indian or Alaska Native	1978 (0.3%)	136 (0.2%)	63 (0.3%)	31 (0.3%)	1748 (0.3%)
Asian	114,148 (16.6%)	11,713 (20.6%)	1652 (8.1%)	1145 (11.3%)	99,638 (16.6%)
Black or African American	72,088 (10.5%)	5448 (9.6%)	2931 (14.4%)	1233 (12.2%)	62,476 (10.4%)
Hawaiian or Pacific Islander	9482 (1.4%)	1160 (2.0%)	235 (1.2%)	174 (1.7%)	7913 (1.3%)
Hispanic or Latino	213,777 (31.1%)	15,870 (28.0%)	5345 (26.3%)	2169 (21.4%)	190,393 (31.7%)
Multi-race or other or unknown	26,019 (3.8%)	2611 (4.6%)	956 (4.7%)	585 (5.8%)	21,867 (3.6%)
White	249,673 (36.3%)	19,838 (34.9%)	9147 (45.0%)	4780 (47.2%)	215,908 (36.0%)
Study entry					
2014	438,549 (63.8%)	41,096 (72.4%)	14,369 (70.7%)	8424 (83.3%)	374,660 (62.4%)
2015–2022	248,616 (36.2%)	15,680 (27.6%)	5960 (29.3%)	1693 (16.7%)	225,283 (37.6%)
Insurance type					
Commercial	409,249 (59.6%)	37,900 (66.8%)	14,949 (73.5%)	7710 (76.2%)	348,690 (58.1%)
Medicare	251,466 (36.6%)	16,648 (29.3%)	3953 (19.4%)	1786 (17.7%)	229,079 (38.2%)
Medicaid	25,050 (3.6%)	2069 (3.6%)	1249 (6.1%)	523 (5.2%)	21,209 (3.5%)
Other	1400 (0.2%)	159 (0.3%)	178 (0.9%)	98 (1%)	965 (0.2%)
Census tract household income					
First (lowest)	163,097 (23.7%)	12,796 (22.5%)	5235 (25.8%)	2488 (24.6%)	142,578 (23.8%)
Second	162,956 (23.7%)	13,356 (23.5%)	4803 (23.6%)	2372 (23.4%)	142,425 (23.7%)
Third	163,222 (23.8%)	14,137 (24.9%)	4523 (22.2%)	2225 (22.0%)	142,337 (23.7%)
Fourth (highest)	163,126 (23.7%)	13,921 (24.5%)	4114 (20.2%)	2081 (20.6%)	143,010 (23.8%)
Missing	34,764 (5.1%)	2566 (4.5%)	1654 (8.1%)	951 (9.4%)	29,593 (4.9%)
Concurrent diabetes meds- metformin	557,428 (81.1%)	46,288 (81.5%)	15,941 (78.4%)	8475 (83.8%)	486,724 (81.1%)
Concurrent diabetes meds- insulin	143,506 (20.9%)	12,570 (22.1%)	7533 (37.1%)	4150 (41.0%)	119,253 (19.9%)
Type 2 diabetes control					
HbA1c <7%	233,670 (34.0%)	15,858 (27.9%)	5290 (26.0%)	2040 (20.2%)	210,482 (35.1%)
HbA1c 7–<8	216,383 (31.5%)	19,402 (34.2%)	6188 (30.4%)	3216 (31.8%)	187,577 (31.3%)
HbA1c 8–<9	91,376 (13.3%)	8721 (15.4%)	3391 (16.7%)	2008 (19.8%)	77,256 (12.9%)
HbA1c 9–<11	82,490 (12.0%)	7693 (13.5%)	3368 (16.6%)	1851 (18.3%)	69,578 (11.6%)
HbA1c ≥ 11	63,246 (9.2%)	5102 (9.0%)	2092 (10.3%)	1002 (9.9%)	55,050 (9.2%)
Diabetes duration					
<1 year	138,474 (20.2%)	7992 (14.1%)	3555 (17.5%)	1142 (11.3%)	125,785 (21.0%)
1–2 years	57,246 (8.3%)	4446 (7.8%)	1774 (8.7%)	792 (7.8%)	50,234 (8.4%)
2–3 years	61,174 (8.9%)	5128 (9.0%)	1806 (8.9%)	859 (8.5%)	53,381 (8.9%)
3–4 years	60,350 (8.9%)	5348 (9.4%)	1820 (9.0%)	931 (9.2%)	52,251 (8.7%)
4 or more years	368,537 (53.6%)	33,830 (59.6%)	11,329 (55.7%)	6388 (63.1%)	316,990 (52.8%)
Missing	1384 (0.2%)	32 (0.1%)	45 (0.2%)	5 (0.0%)	1302 (0.2%)
Visits to an endocrinology specialist, No. per 12 months					
0	663,169 (96.5%)	54,643 (96.2%)	18,497 (91.0%)	9042 (89.4%)	580,987 (96.8%)
1	9189 (1.3%)	768 (1.4%)	623 (3.1%)	318 (3.1%)	7480 (1.2%)
2+	14,807 (2.2%)	1365 (2.4%)	1209 (5.9%)	757 (7.5%)	11,476 (1.9%)
Visits to a cardiology specialist, No. per 12 months					
0	603,479 (87.8%)	48,298 (85.1%)	17,530 (86.2%)	8608 (85.1%)	529,043 (88.2%)
1	44,485 (6.5%)	3978 (7.0%)	1512 (7.4%)	720 (7.1%)	38,275 (6.4%)
2+	39,201 (5.7%)	4500 (7.9%)	1287 (6.3%)	789 (7.8%)	32,625 (5.4%)
Visits to a nephrology specialist, No. per 12 months					
0	671,774 (97.8%)	55,399 (97.6%)	19,846 (97.6%)	9895 (97.8%)	586,634 (97.8%)
1	4532 (0.7%)	404 (0.7%)	164 (0.8%)	76 (0.8%)	3888 (0.6%)
2+	10,859 (1.6%)	973 (1.7%)	319 (1.6%)	146 (1.4%)	9421 (1.6%)

(Table 1 continues on next page)

Characteristic	Overall N = 687,165	SGLT2i N = 56,776	GLP-1 RA N = 20,329	Both N = 10,117	Neither N = 599,943
(Continued from previous page)					
Comorbidities					
Cerebrovascular disease	20,937 (3.0%)	1387 (2.4%)	426 (2.1%)	191 (1.9%)	18,933 (3.2%)
Chronic kidney disease	161,056 (23.4%)	14,705 (25.9%)	3810 (18.7%)	2121 (21.0%)	140,420 (23.4%)
Congestive heart failure	32,963 (4.8%)	3638 (6.4%)	558 (2.7%)	335 (3.3%)	28,432 (4.7%)
Myocardial infraction	9171 (1.3%)	1225 (2.2%)	202 (1.0%)	144 (1.4%)	7600 (1.3%)
Peripheral vascular disease	15,354 (2.2%)	1025 (1.8%)	306 (1.5%)	128 (1.3%)	13,895 (2.3%)
Dyslipidemia	406,129 (59.1%)	35,387 (62.3%)	11,533 (56.7%)	6455 (63.8%)	352,754 (58.8%)
Hypertension	414,180 (60.3%)	35,256 (62.1%)	12,004 (59.0%)	6415 (63.4%)	360,505 (60.1%)
Obesity	414,234 (60.3%)	36,084 (63.6%)	16,552 (81.4%)	7974 (78.8%)	353,624 (58.9%)

Abbreviations: GLP-1 RA, glucagon-like peptide-1 receptor agonist; IQR, interquartile range; SGLT2i, sodium-glucose cotransporter 2 inhibitor. Data presented as number (percentage), unless otherwise indicated.

Table 1: **Demographic and clinical characteristics of patients with type 2 diabetes in multiple integrated health care systems with and without pharmacy dispensing of SGLT2i and GLP-1 RA agents.**

KPHI, which had the highest racial and ethnic heterogeneity. These remaining sensitivity analyses are shown in the Supplementary Methods. We evaluated model assumptions and confirmed there was no multicollinearity and confirmed linearity in the logit function for continuous variables. All analyses were completed in R 3.4.1 (R Statistical Foundation for Computing).

Role of the funding source

The funders had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Results

Study participants

Our cohort included 687,165 patients with type 2 diabetes (median 60 years old, 46.5% female), who contributed a median [IQR] of 6 years [3–9] of pharmacy dispensing data (similar across all racial and ethnic groups) (Supplementary Figure S1). In our study, 12,976 (1.9%) patients were from Geisinger, 16,649 (2.4%) from Henry Ford Health, 14,339 (2.1%) from HealthPartners, 20,305 (3.0%) from KPHI, 279,632 (40.7%) from KPNC, and 343,264 (49.9%) from KPSC. During the study period, 56,776 (8.3%) received an SGLT2i, 20,329 (3.0%) received a GLP-1 RA, and 10,117 (1.5%) received both. Our sample included 1978 AI/AN (0.3%), 114,148 Asian (16.6%), 72,088 Black (10.5%), 9482 HPI (1.4%), 213,777 Hispanic (31.1%), 26,019 Other (3.8%), and 249,673 White patients (36.3%). Baseline characteristics of patients are summarized in Table 1.

Race and ethnicity differences in the pharmacy dispensing of SGLT2i and GLP-1 RA

In the overall cohort, predicted rates of dispensing of SGLT2i increased from 0.1% in 2014 to 12.2% in 2022 (Fig. 1) and increased from 0.3% to 3.4% for GLP-1 RA (Fig. 2). The predicted rate of SGLT2i increased from 0.2% in 2014 to 10.5% in 2022 among AI/AN, 0.02% to 14.0% among Asian, 0.06% to 12.0% among Black, 0.02% to 12.6% among HPI, 0.02% to 10.6% among Hispanic, 0.07% to 10.8% among Other, and 0.1% to 13.2% among White patients (Fig. 1). For GLP-1 RA, the predicted rates increased from 0.2% in 2014 to 4.4% in 2022 among AI/AN, 0.1% to 1.9% among Asian, 0.2% to 4.3% among Black, 0.1% to 1.6% among HPI, 0.1% to 3.1% among Hispanic, 0.2% to 2.4% among Other, and 0.5% to 4.5% among White patients (Fig. 2).

In the fully adjusted models, overall dispensing of an SGLT2i was lower for AI/AN (OR 0.80, 95% confidence interval 0.68–0.94), Black (OR 0.89, 0.86–0.92) and Hispanic (OR 0.87, 0.85–0.89) compared to White patients, higher for Asian (OR 1.11, 1.08–1.14), and not different for HPI (OR 1.01, 0.95–1.08), or Other patients (OR 1.04, 0.99–1.08) (Table 2).

Using equivalent multivariable analyses for GLP-1 RA, we found that dispensing was lower for AI/AN (OR 0.78, 0.63–0.97), Asian (OR 0.50, 0.48–0.53), Black (OR 0.86, 0.83–0.9), HPI (OR 0.52, 0.46–0.57), Hispanic (OR 0.69, 0.66–0.71), and Other (OR 0.78, 0.73–0.83) compared to White patients (Table 3). Dispensing of both drug classes was lower for Asian (OR 0.63, 0.59–0.68), Black (OR 0.78, 0.73–0.84), HPI (OR 0.62, 0.52–0.73), Hispanic (OR 0.65, 0.61–0.69), Other (OR 0.87, 0.78–0.95) and for AI/AN (OR 0.80, 0.54–1.13) adults, though for AI/AN patients, the association was not statistically significant (Supplementary Table S1). The primary race and ethnicity results of sensitivity analyses were consistent with the primary findings (Supplementary Tables S2–S17).

Risk factors differences in the pharmacy dispensing of SGLT2i and GLP-1 RA

In multivariable analyses, female sex was associated with lower odds of an SGLT2i dispensing (OR 0.86,

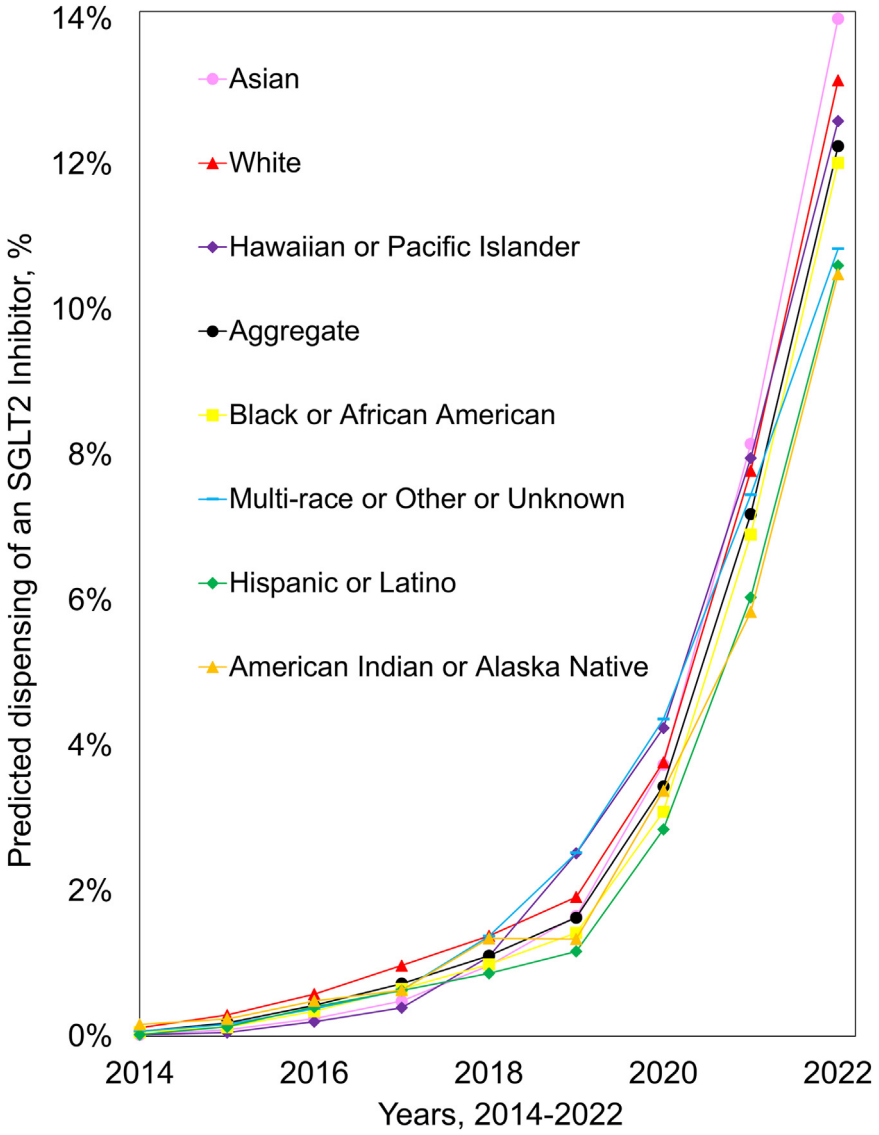

Fig. 1: Rates of pharmacy dispensing of an SGLT2i among patients with type 2 diabetes in multiple integrated health care systems (2014–2022), by race and ethnicity. Abbreviation: SGLT2i, sodium-glucose cotransporter 2 inhibitor.

0.84–0.87), but higher odds of a GLP-1 RA (OR 1.39, 1.35–1.42) (Tables 2 and 3). Compared to commercial, Medicaid and Medicare insurance were associated with lower odds of SGLT2i pharmacy dispensing (OR 0.88, 0.84–0.91, and 0.71, 0.69–0.73, respectively) and GLP-1 RA (OR 0.77, 0.73–0.81, and 0.64, 0.61–0.66, respectively). There was a positive linear association between median household income quartiles and odds of an SGLT2i or GLP-1 RA pharmacy dispensing. The OR for those in the highest income quartiles were 1.07 (1.05–1.10) and 1.22 (1.17–1.26), for SGLT2i and GLP-1 RA, respectively.

Concurrent use of metformin and insulin was associated with higher odds of an SGLT2i pharmacy dispensing (OR 1.14, 1.12–1.17 and 1.04, 1.02–1.06, respectively) and a GLP-1 RA (OR 1.10, 1.07–1.14 and 2.16, 2.10–2.23, respectively). There was an inverse J-shaped association between HbA1c categories and dispensing of these drugs with the strongest association in patients with a HbA1c between 8 and 9% (OR 1.42, 1.39–1.46 for SGLT2i; and 1.44, 1.39–1.50 for GLP-1 RA). There was a positive linear association with dispensing and diabetes duration category, with an OR of 2.23 (2.17, 2.29) for SGLT2i and 2.12 (2.04, 2.20) for GLP-1 RA, for those in the highest category (4+ years). Two or more visits to endocrinology and cardiology were associated with higher odds of an SGLT2i pharmacy dispensing (OR 1.35, 1.28–1.41; and OR 1.45, 1.40–1.50,

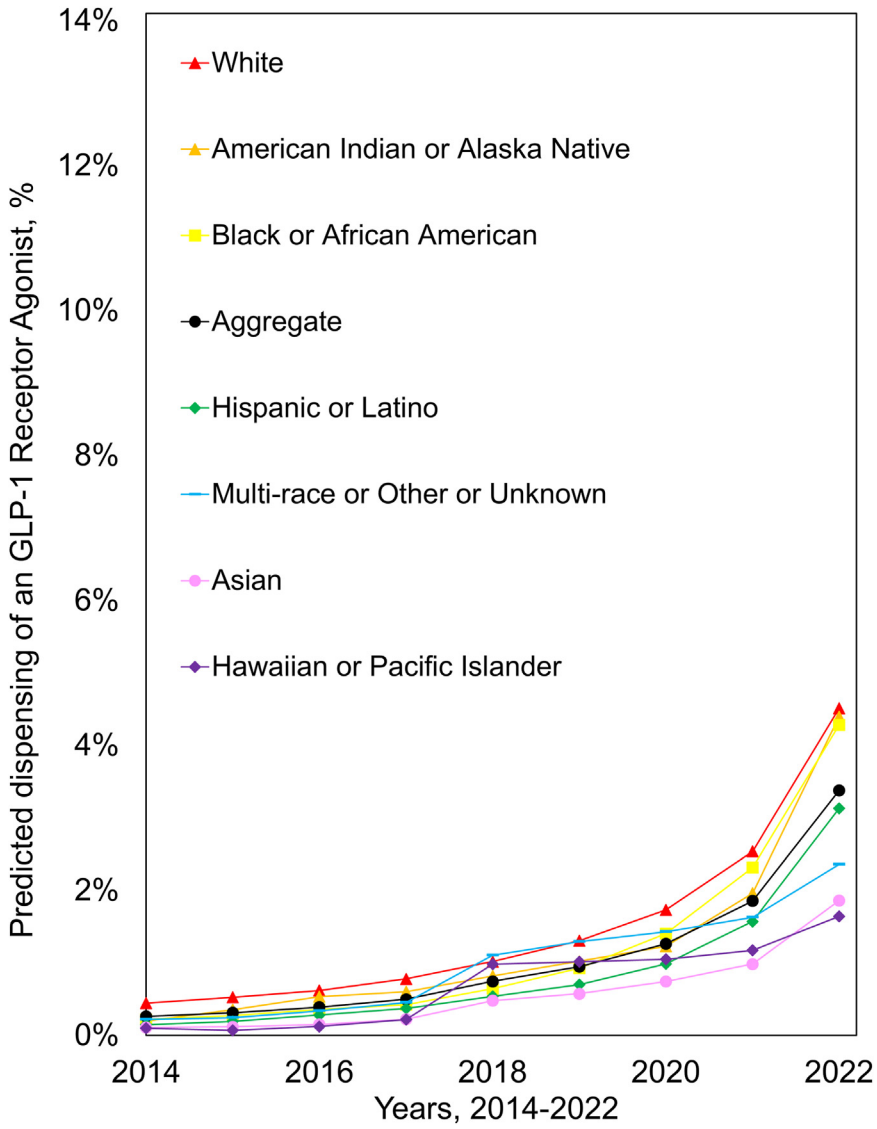

Fig. 2: Rates of pharmacy dispensing of a GLP-1 RA among patients with type 2 diabetes in multiple integrated health care systems (2014–2022), by race and ethnicity. Abbreviation: GLP-1 RA, glucagon-like peptide-1 receptor agonist.

respectively) and GLP-1 RA (OR 1.94, 1.83–2.05; and OR 1.23, 1.16–1.30, respectively), compared to patients without visits. However, visits to nephrology were associated with lower odds of an SGLT2i pharmacy dispensing (OR 0.94, 0.88–1.0) and GLP-1 RA (OR 0.84, 0.76–0.94) for patients with 2+ visits (Tables 2 and 3).

Chronic kidney disease was associated with higher odds of an SGLT2i pharmacy dispensing (OR 1.16, 1.13–1.18) but not with GLP-1 RA (OR 0.98, 0.95–1.01). Congestive heart failure was associated with higher odds of an SGLT2i pharmacy dispensing (OR 1.31, 1.26–1.36), but with lower odds of GLP-1 RA (OR 0.64, 0.60–0.69). Myocardial infarction history was associated with higher odds of an SGLT2i pharmacy dispensing (OR 1.37, 1.29–1.46) and was suggestive of being associated with lower odds of a GLP-1 RA (OR 0.90, 0.80–1.01), though the association did not reach the level of statistical significance. Peripheral vascular disease was associated with lower odds of an SGLT2i dispensing (OR 0.70, 0.66–0.75) and GLP-1 RA (OR 0.76, 0.69–0.85). Dyslipidemia, hypertension, and obesity were all associated with similar higher odds of an SGLT2i and GLP-1 RA pharmacy dispensing (OR point estimates between 1.13–1.18), except obesity was associated with much higher odds of GLP-1 RA (OR 2.09, 2.03–2.16) (Tables 2 and 3).

The demographic and clinical characteristics and cardiovascular risk factors among patients who had

Characteristic	AOR (95% CI)	P-value
Age, years	0.98 (0.98, 0.98)	<0.001
Sex		
Female	0.86 (0.84, 0.87)	<0.001
Male	Reference	
Race and ethnicity		
American Indian or Alaska Native	0.80 (0.68, 0.94)	0.007
Asian	1.11 (1.08, 1.14)	<0.001
Black or African American	0.89 (0.86, 0.92)	<0.001
Hawaiian or Pacific Islander	1.01 (0.95, 1.08)	0.731
Hispanic or Latino	0.87 (0.85, 0.89)	<0.001
Multi-race or other or unknown	1.04 (0.99, 1.08)	0.092
White	Reference	
Insurance type		
Commercial	Reference	
Medicare	0.71 (0.69, 0.73)	<0.001
Medicaid	0.88 (0.84, 0.91)	<0.001
Other	1.07 (0.93, 1.23)	0.351
Census tract household income		
First (lowest)	Reference	
Second	1.03 (1.01, 1.06)	0.006
Third	1.08 (1.05, 1.10)	<0.001
Fourth (highest)	1.07 (1.05, 1.10)	<0.001
Missing	0.85 (0.81, 0.89)	<0.001
Concurrent diabetes meds-		
Metformin	1.14 (1.12, 1.17)	<0.001
Insulin	1.04 (1.02, 1.06)	<0.001
Type 2 diabetes control		
HbA1c <7%	Reference	
HbA1c 7–<8	1.32 (1.3, 1.35)	<0.001
HbA1c 8–<9	1.42 (1.39, 1.46)	<0.001
HbA1c 9–<11	1.40 (1.37, 1.44)	<0.001
HbA1c ≥ 11	1.30 (1.26, 1.34)	<0.001
Diabetes duration, years		
Less than 1	Reference	
1–2	1.52 (1.46, 1.58)	<0.001
2–3	1.72 (1.66, 1.78)	<0.001
3–4	1.90 (1.83, 1.96)	<0.001
4 or more	2.23 (2.17, 2.29)	<0.001
Missing	0.37 (0.26, 0.51)	<0.001
Visits to an endocrinology specialist, No. per 12 months		
0	Reference	
1	1.09 (1.02, 1.17)	0.008
2+	1.35 (1.28, 1.41)	<0.001
Visits to a cardiology specialist, No. per 12 months		
0	Reference	
1	1.14 (1.10, 1.17)	<0.001
2+	1.45 (1.40, 1.50)	<0.001
Visits to a nephrology specialist, No. per 12 months		
0	Reference	
1	0.97 (0.88, 1.07)	0.593
2+	0.94 (0.88, 1.00)	0.055
Comorbidities		
Cerebrovascular disease	0.80 (0.75, 0.84)	<0.001
Chronic kidney disease	1.16 (1.13, 1.18)	<0.001

(Table 2 continues on next page)

Characteristic	AOR (95% CI)	P-value
(Continued from previous page)		
Congestive heart failure	1.31 (1.26, 1.36)	<0.001
Myocardial infraction	1.37 (1.29, 1.46)	<0.001
Peripheral vascular disease	0.70 (0.66, 0.75)	<0.001
Dyslipidemia	1.16 (1.13, 1.18)	<0.001
Hypertension	1.18 (1.16, 1.20)	<0.001
Obesity	1.18 (1.16, 1.20)	<0.001

Abbreviations: AOR, adjusted odds ratio; CI, confidence interval; HbA1c, hemoglobin A1C; SGLT2i, sodium-glucose cotransporter 2 inhibitor.

Table 2: **Factors associated with pharmacy dispensing of SGLT2i among patients with type 2 diabetes in multiple integrated health care systems.**

dispensing of both classes were similar to patients who received only a GLP-1 RA (Supplementary Table S1).

Discussion

In this retrospective cohort study using real-world clinical data from 687,165 patients with type 2 diabetes from six large care delivery systems in the US, we found racial and ethnic inequities in the pharmacy dispensing of SGLT2i and GLP-1 RA. AI/AN, Black and Hispanic patients were less likely to receive an SGLT2i pharmacy dispensing, while Asian patients were more likely to receive an SGLT2i compared to White patients. Patients from all racial and ethnic groups were less likely to receive a GLP-1 RA pharmacy dispensing compared to White patients. These racial and ethnic inequities persisted while accounting for other demographics, diabetes control, duration, and management, visits to specialists, and comorbidities, as well as in sensitivity analyses, including within insurance types and within two care delivery systems with the greatest racial and ethnic heterogeneity, confirming the robustness of our findings.

This study adds to the body of literature suggesting racial and ethnic disparities in the use of SGLT2i and GLP-1 RA. Only one prior study in the Veterans Health Administration system included AI/AN patients and also found underusage for both drug classes.[8] Among Asian patients, as in prior studies there was a disparity in GLP-1 RA use,[8,11] but in contrast to prior findings,[7,8] Asian patients were more likely to receive SGLT2is than White patients. This could be explained in part because our study was the first to disaggregate Asian and HPI patients. Due to variations in these heterogeneous groups, future studies should further investigate usage of these drugs within the diverse Asian and HPI population. Among Black and Hispanic patients, our study agreed with prior studies that found disparities for both drug classes,[5–9,11] except one study that found Hispanic patients were slightly more likely to receive an SGLT2i.[7] Lastly, for patients classified as Other, our study aligned with three prior studies that found less use of GLP-1 RA.[6,8,9]

In general, comorbidities were independently associated with pharmacy dispensing of these drugs, which aligns with national guidelines.[2–4] There were two notable exceptions; in our study, a concerning finding was that cerebrovascular disease and peripheral vascular disease were negatively associated with dispensing of these drugs.

This study uncovered marked racial and ethnic disparities in pharmacy dispensing of SGLT2i's and GLP-1 RA's. However, the extent to which these disparities are patient-, provider-, health system-related, or a combination of these remains unclear and should be the work of future studies. The existing literature suggests several reasons why patients from minority groups in the US may be less likely to receive SGLT2i and GLP-1 RA. These include high out-of-pocket costs,[16] insurance coverage, decreased access to health care, subspecialty care, or to providers familiar with the benefits of these drugs, limited health literacy,[17] structural racism,[5,18] or provider bias which may lead to the perception that specific patient groups are less inclined to adhere with treatment involving a newer and more expensive medication.[19,20]

This study has limitations. First, we did not examine providers' prescribing patterns over time; prior studies have found similar racial and ethnic disparities.[8,9] Second, our study lacked data on medication out-of-pocket costs. An analysis of Medicare Part D (which helps cover the cost of prescription drugs[21]) recipients showed annual out-of-pocket costs for SGLT2i were US$1298–1565 and US$2102–2230 for GLP-1 RA. Alternative annual therapies such as sulfonylureas (US$31–101) and thiazolidinediones (US$136) were less expensive.[22] A recent analysis from the Look AHEAD study found that when socioeconomic status was controlled for, racial and ethnic minority groups were still less likely to initiate newer diabetes medications,[23] suggesting barriers other than cost. Other studies have similarly observed cost-related lower medication adherence and glycemic control among racial and ethnic minority groups.[24] A recent study reported out-of-pocket cost to be an independent predictor of SGLT2i and GLP1RA initiation irrespective of race and ethnicity while another showed racial and ethnic

Characteristic	AOR (95% CI)	P-value
Age, years	0.96 (0.95, 0.96)	<0.001
Sex		
Female	1.39 (1.35, 1.42)	<0.001
Male	Reference	
Race and ethnicity		
American Indian or Alaska Native	0.78 (0.63, 0.97)	0.030
Asian	0.50 (0.48, 0.53)	<0.001
Black or African American	0.86 (0.83, 0.90)	<0.001
Hawaiian or Pacific Islander	0.52 (0.46, 0.57)	<0.001
Hispanic or Latino	0.69 (0.66, 0.71)	<0.001
Multi-race or other or unknown	0.78 (0.73, 0.83)	<0.001
White	Reference	
Insurance type		
Commercial	Reference	
Medicare	0.64 (0.61, 0.66)	<0.001
Medicaid	0.77 (0.73, 0.81)	<0.001
Other	1.20 (1.03, 1.39)	0.019
Census tract household income		
First (lowest)	Reference	
Second	1.05 (1.02, 1.09)	0.003
Third	1.10 (1.06, 1.14)	<0.001
Fourth (highest)	1.22 (1.17, 1.26)	<0.001
Missing	0.89 (0.84, 0.95)	<0.001
Concurrent diabetes meds		
Metformin	1.10 (1.07, 1.14)	<0.001
Insulin	2.16 (2.10, 2.23)	<0.001
Type 2 diabetes control		
HbA1c <7%	Reference	
HbA1c 7–<8	1.25 (1.21, 1.30)	<0.001
HbA1c 8–<9	1.44 (1.39, 1.50)	<0.001
HbA1c 9–<11	1.40 (1.35, 1.46)	<0.001
HbA1c ≥ 11	1.13 (1.07, 1.18)	<0.001
Diabetes duration, years		
Less than 1	Reference	
1–2	1.54 (1.46, 1.62)	<0.001
2–3	1.60 (1.52, 1.69)	<0.001
3–4	1.77 (1.68, 1.87)	<0.001
4 or more	2.12 (2.04, 2.20)	<0.001
Missing	0.37 (0.28, 0.50)	<0.001
Visits to an endocrinology specialist, No. per 12 months		
0	Reference	
1	1.48 (1.37, 1.60)	<0.001
2+	1.94 (1.83, 2.05)	<0.001
Visits to a cardiology specialist, No. per 12 months		
0	Reference	
1	1.14 (1.08, 1.19)	<0.001
2+	1.23 (1.16, 1.30)	<0.001
Visits to a nephrology specialist, No. per 12 months		
0	Reference	
1	1.04 (0.90, 1.20)	0.585
2+	0.84 (0.76, 0.94)	0.001
Comorbidities		
Cerebrovascular disease	0.80 (0.74, 0.88)	<0.001
Chronic kidney disease	0.98 (0.95, 1.01)	0.211

(Table 3 continues on next page)

Characteristic	AOR (95% CI)	P-value
(Continued from previous page)		
Congestive heart failure	0.64 (0.60, 0.69)	<0.001
Myocardial infraction	0.90 (0.80, 1.01)	0.086
Peripheral vascular disease	0.76 (0.69, 0.85)	<0.001
Dyslipidemia	1.13 (1.10, 1.16)	<0.001
Hypertension	1.17 (1.14, 1.20)	<0.001
Obesity	2.09 (2.03, 2.16)	<0.001

Abbreviations: AOR, adjusted odds ratio; CI, confidence interval; GLP-1 RA, glucagon-like peptide-1 receptor agonist; HbA1c, hemoglobin A1C.

Table 3: **Factors associated with pharmacy dispensing of an GLP-1 receptor agonist among patients with type 2 diabetes in multiple integrated health care systems.**

differences in anti-hyperglycemic medication initiation with narrower cost differences.[25] Another study showed a relationship between out-of-pocket costs and adherence and persistence of cardiometabolic medications that did not differ by race and ethnicity.[24] Further, in this study, within each insurance type in which copayments are similar, racial and ethnic differences persisted (see Supplementary Tables S3–S5, S9–S11, and S15–S17). Third, we did not evaluate patient preferences, particularly for the use of injectable drugs, which could explain some of the racial and ethnic differences. For instance, our study (not shown) agreed with prior studies that showed Asian and HPI patients with diabetes were less likely to use insulin.[26] Future studies should investigate patient preferences and the extent to which this may explain racial and ethnic differences. Fourth, outcome data was recorded on an annual basis (calendar year), and some patients contributed less than 12 months of data when either their index date started after January 1st of their study entry year, or if they left the cohort before study end, creating missing data. However, this missing data was similar across racial and ethnic groups, thus it is unlikely that this would have biased our results. Fifth, we did not evaluate pharmacy dispensing differences in administration frequency (daily vs weekly). Sixth, this data came from six integrated healthcare systems that are broadly representative of the regions they serve in terms of age, race and ethnicity, and sex distribution, nevertheless, the findings of this study may not generalize to the broader US population, particularly to the uninsured or underinsured population, or those living in the southern states.[27] Lastly, our study evaluated dispensing of these drugs but did not evaluate adherence to the drugs, and possible racial and ethnic differences in adherence over time and should be the work of a future study. The strengths of this study include the use of a large racially-, ethnically-, and geographically diverse sample of insured adult patients with type 2 diabetes from six sites across the US, follow-up through 2022, and the measurement of individual-level clinical data rather than self-reported information.

In conclusion, this study found pharmacy dispensing of SGLT2is was lower among AI/AN, Black, and Hispanic patients with type 2 diabetes, and pharmacy dispensing of GLP-1 RA medications was lower among all patients with type 2 diabetes from minority groups in six US large care delivery systems. Several racial and ethnic minority groups are disproportionally affected by cardiovascular disease[28] and chronic kidney disease[29] compared to their White counterparts. cardiovascular disease and chronic kidney disease are projected to rise and disproportionately impact racial and ethnic minority populations in the US.[30,31] Our work supports prior findings[5,6] and highlights the need to evaluate approaches to increase the use of these cardiorenal protective drugs in patients from racial and ethnic minority groups with type 2 diabetes to reduce adverse cardiorenal outcomes and improve health equity.

Contributors

All authors acquired and interpreted the data, critically revised the paper, and had final responsibility for the decision to submit for publication.

Concept and design: Rodriguez, Schmittdiel, Neugebauer.

Acquisition, analysis, or interpretation of data: Rodriguez, Finertie, Schmittdiel, Neugebauer.

Drafting of the manuscript: Rodriguez, Finertie, Gosiker.

Critical revision of the manuscript for important intellectual content: All authors.

Statistical analysis: Finertie.

Obtained funding: Neugebauer, O'Connor, Schmittdiel, Rodriguez.

Supervision: Rodriguez, Schmittdiel.

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Data sharing statement

Data from this study are not available.

Declaration of interests

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.lana.2024.100759.

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