HHS Public Access

Author manuscript

Endocrine. Author manuscript; available in PMC 2022 August 01.

Published in final edited form as:

Endocrine. 2021 August ; 73(2): 480–484. doi:10.1007/s12020-021-02710-4.

Race And Sex Differences in the Initiation of Diabetes Drugs by Privately-Insured U.S. Adults

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Keywords

Type 2 diabetes; race; gender; disparities; pharmacotherapy; GLP-1 receptor agonist; SGLT2 inhibitor; health services research

INTRODUCTION

Differences in pharmacologic management of hyperglycemia may contribute to disparities in diabetes-related health outcomes among racial/ethnic minorities and women. Non-white patients with diabetes experience a disproportionate share of diabetes complications, including hypoglycemia[1] and cardiovascular and renal death,[2] compared to white patients. Similarly, women have an increased risk of all-cause, renal, and cardiovascular death compared to men.[3, 4]

Three classes of glucose-lowering medications have been introduced as treatment options over the past 15 years and are increasingly recommended as second-line agents in specific

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Author Contributions: R.G.M. is the guarantor of this manuscript; she had full access to the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. R.G.M. designed the study, interpreted the data, and wrote the manuscript. S.D.M., X.Y., T.D., P.N., L.R.S., and A.H.L contributed to the discussion and reviewed/edited the manuscript. H.K.V. analyzed the data and reviewed/edited the manuscript. N.D.S. supervised study design and data interpretation, contributed to the discussion, and reviewed/edited the manuscript.

Conflict of Interest: The authors have no conflicts of interest to declare.

Ethics approval: This study was exempt from review by the Mayo Clinic Institutional Review Board, as it involves research on de-identified data.

Availability of data and material: This study was conducted using de-identified data from OptumLabs Data Warehouse.

clinical contexts. Glucagon-like peptide-1 receptor agonists (GLP-1RA), sodium/glucose cotransporter-2 inhibitors (SGLT2i), and dipeptidyl peptidase-4 inhibitors (DPP4i) all have low hypoglycemia risk, while GLP-1RA and SGLT2i have additional cardiovascular and renal benefits.[5] We previously found low rates of early SGLT2i adoption by women and black patients in the U.S.,[6] while non-white patients in England were less likely to be prescribed both GLP-1RA and SGLT2i compared to white patients.[7] With greater experience using these medications and emerging evidence supporting their preferred use in the context of cardiovascular and kidney disease, prescribing practices may have changed. Yet, contemporary differences in the use of these medications as a function of both sex and race have not been examined.

METHODS

Study Design.

We retrospectively analyzed de-identified administrative claims data from OptumLabs® Data Warehouse (OLDW), which include medical and pharmacy claims and enrollment records for commercial and Medicare Advantage enrollees, representing a diverse mixture of ages, ethnicities and geographical regions across United States.[8] This study was exempt from review by the Mayo Clinic Institutional Review Board as it involves research on de-identified data and is reported in accordance with STROBE guidelines for observational cohort studies.[9]

Study Population.

Adults (≥18 years) with type 2 diabetes who filled ≥1 glucose-lowering medication between January 1, 2013 and December 31, 2018. Index date was set to the date of the first medication fill. Patients were required to have 12 months of medical and pharmacy claims prior to the index date. Diabetes was ascertained using Healthcare Effectiveness Data and Information Set criteria.[10]

Primary Outcomes.

Initiation of DPP-4i, GLP-1RA, and SGLT2i, defined as the first fill for a drug within each class and no fills for any other medications within the same class in the preceding 12 months. Patients were independently considered for each of the three drug class cohorts. Use was classified as first-line if there were no fills for any diabetes medications in the preceding 12 months.

Independent Variables.

Patients were categorized as White men, White women, non-White men, and non-White women. Patient age, sex, race/ethnicity, U.S. region of residency, and type of health plan (commercial vs. Medicare Advantage) were ascertained from enrollment files. Clinical variables included prescriber specialty and comorbidities. Comorbidities were ascertained using International Classification of Diseases 9^{th} and 10^{th} revisions (ICD) diagnosis codes from the 12 months preceding the index date, and included hypoglycemia- and hyperglycemia-related emergency department (ED)/hospital visits; Diabetes Complications Severity Index (DCSI) comorbidities of retinopathy, nephropathy, neuropathy, and peripheral

vascular disease;[11] and Charlson comorbidities of myocardial infarction (MI), HF, cerebrovascular disease, dementia, chronic obstructive pulmonary disease, cirrhosis, and cancer (except for non-melanoma skin cancer).[12] The total count of diabetes complications, per the DCSI,[11] was also included.

Statistical Analysis.

Baseline characteristics of White men, White women, non-White men, and non-White women are reported as frequencies with percentages for categorical data and means with standard deviations (SD) for continuous variables. Multivariable logistic regression was used to assess predictors for the use of GLP-1RA, SGLT2i, and DPP4i initiation for each race/sex group, adjusted for the aforementioned independent variables, with results presented as odds ratios and 95% confidence intervals. All analyses were conducted using SAS Enterprise Guide software version 7.1 (SAS Institute Inc., Cary, NC).

RESULTS

Our study population was comprised of 1,743,484 pharmacologically-treated adults with diabetes, including 596,481 (34.2%) White men, 534,892 (30.7%) White women, 285,344 (16.4%) non-White men, and 326,767 (18.7%) non-White women (Table). Women were older than men, and White patients were older than non-White patients. There were more White patients in the Midwest, and more non-White patients in the South. White patients more frequently had cardiovascular disease, COPD, and cancer. Non-White patients more frequently had retinopathy, nephropathy, and peripheral vascular disease. Prior hypoglycemia-related ED/hospital visits were more prevalent among non-White compared to White individuals, and women compared to men, while hyperglycemia-related ED/hospital visits were more prevalent among non-White patients and men.

Adjusted odds of GLP-1RA initiation were higher for White women (OR 1.43; 95% CI, 1.41–1.45) and non-White men (OR 1.12; 95% CI, 1.10–1.14), but lower for non-White women (OR 0.79; 95% CI, 0.78–0.81), compared to White men (Table). Odds of SGLT2i initiation were lower for all groups when compared to White men, ranging from OR 0.84 (95% CI, 0.82–0.85) for non-White men to OR 0.89 (95% CI 0.87–0.91) for non-White women. Finally, odds of DPP4i initiation were higher for non-White men (OR 1.11; 95% CI, 1.09–1.13) and non-White women (OR 1.16; 95% CI, 1.14–1.18), but same for White women, as compared to White men.

DISCUSSION

Cardiovascular and kidney diseases are leading causes of morbidity, disability, and mortality among patients with diabetes.[13–15] Racial/ethnic minorities[2] and women[3, 4] are disproportionately affected by these complications. GLP-1RA and SGLT2i medications can reduce the risks of both cardiovascular and renal complications, yet we observed some differences in the use of both of these medications as a function of race and sex.

After controlling for comorbidity burden and compared to White men, GLP-1RA were 43% more likely to be started by White women, 12% more likely to be started by non-White men,

and 21% less likely to be started by non-White women. GLP-1RA have the greatest weight loss potential of all glucose-lowering medications, such that their preferred use by White women may reflect prioritization of weight loss when choosing glucose-lowering therapy.[16] The increased odds of GLP-1RA initiation by non-White men compared to White men is reassuring, considering the disproportionately high burden of cardiovascular and kidney disease in this population.[2] In contrast, the low rates of GLP-1RA initiation by non-White women suggest an opportunity for cardiovascular risk reduction to narrow the cardiovascular mortality gap compared to White women.[17–19]

SGLT2i were at least 10% less likely to be started by all groups compared to White men. SGLT2i are the newest of the three therapeutic classes examined, and clinicians' prescribing decisions for new medications may be more susceptible to implicit bias. Non-White patients may also be more cautious about using newer therapeutics with a less established evidence base because of greater distrust of the medical and scientific communities.[20] And yet, DPP4i, which are less effective and without the additional cardiovascular and renal benefits of GLP-1RA and SGLT2i, were used more often by non-White than White patients of both sexes.

Our study design could not identify the underlying causes of preferential use of DPP-4i among non-White patients, or the avoidance of SGLT2i among women and non-White men and of GLP-1RA among non-White women. By relying on pharmacy fill data, we also could not differentiate between clinicians' failure to prescribe and patients' failure to fill these medications. These important questions would be best addressed by mixed research methods studies, directly asking patients and clinicians about factors affecting their choice of glucose-lowering medications. We also focused on the initiation of each medication class, not medication adherence or persistence, which may also vary among the race and sex groups. Finally, the study population was comprised of commercially insured and Medicare Advantage beneficiaries, and as such may not generalize to the broader U.S. population with diabetes.

While the race/sex differences in glucose-lowering medication use were not consistent, they were concerning as they reinforce the persistence of non-clinical factors influencing disease management. All patients had the same health coverage, and relevant clinical and non-clinical confounders were analytically accounted for. Further research is needed to delineate the root causes of these differences and pave the way toward ensuring greater equity in diabetes management and health outcomes.

Funding:

This effort was funded by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) of the National Institutes of Health (NIH) grant K23DK114497 (McCoy) and the Agency for Healthcare Research and Quality (AHRQ) Comparative Health System Performance Initiative grant 1U19HS024075 (Shah). Study contents are the sole responsibility of the authors and do not necessarily represent the official views of NIH.

In the past 36 months, Dr. McCoy also received support from an AARP® Quality Measure Innovation Grant and the NIDDK (P30DK111024). In the past 36 months, Dr. Shah has received research support through Mayo Clinic from the Food and Drug Administration (FDA) to establish Yale-Mayo Clinic Center for Excellence in Regulatory Science and Innovation (CERSI) program (U01FD005938); the Centers of Medicare and Medicaid Innovation under the Transforming Clinical Practice Initiative (TCPI); the AHRQ (R01HS025164; R01HS025402; R03HS025517); the National Heart, Lung and Blood Institute of the NIH (R56HL130496; R01HL131535); the

National Science Foundation; and the Patient Centered Outcomes Research Institute (PCORI) to develop a Clinical Data Research Network (LHSNet). Dr. Dunlay receives research support from the NIH (R01HL144529, R03HL135225, T32HL07111) and the FDA (U01FD005938). Dr. Noseworthy receives funding from NIH (R01AG062436–01A1, R21HL140205, R01HL131535, R01HS25402, R01HL143070) FDA (U01FD05938) and the American Heart Association (18SFRN34230146). Dr. Limper receives research support from the NIH (R01HL62150) and the Caerus Foundation and Three Lakes Partners Foundation. Dr. Yao receives funding from NIH (R01AG062436, R21HL140205, R01HS025402) and FDA (U01FD005938).

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Table.

Study Population.

Baseline characteristics of patients in the cohort. * Adjusted odds of starting GLP-1 receptor agonists (GLP-1RA), SGLT2 inhibitors (SGLT2i), and DPP-4 inhibitors (DPP-4i) were calculated using three indpependent logistic regression models that adjusted for patient age, U.S. region, insurance type (commercial vs. Medicare Advantage), year of prescription, baseline medications, treatment type (first-line vs. add-on), count of diabetes complications, comorbidities, and prescriber specialty.

	White Men	White Women	Non-White Men	Non-White Women
N	596,481	534,892	285,344	326,767
Age, years, mean (SD)	62.3 (12.2)	63.5 (13.3)	60.7 (13.3)	62.8 (13.8)
Age group, N (%)				
18–44 years	48919 (8.2%)	49809 (9.3%)	36969 (13.0%)	38065 (11.6%)
45–64 years	271174 (45.5%)	202564 (37.9%)	122717 (43.0%)	116011 (35.5%)
65–74 years	179555 (30.1%)	172937 (32.3%)	82003 (28.7%)	107278 (32.8%)
≥75 years	96833 (16.2%)	109582 (20.5%)	43655 (15.3%)	65413 (20.0%)
U.S. region, N (%)				
Midwest	180252 (30.2%)	159327 (29.8%)	37797 (13.2%)	44576 (13.6%)
Northeast	75535 (12.7%)	68362 (12.8%)	38761 (13.6%)	40084 (12.3%)
South	272616 (45.7%)	248222 (46.4%)	172525 (60.5%)	208509 (63.8%)
West	68078 (11.4%)	58981 (11.0%)	36261 (12.7%)	33598 (10.3%)
Insurance type, N (%)				
Commercial	300667 (50.4%)	221115 (41.3%)	141186 (49.5%)	124216 (38.0%)
Medicare Advantage	295814 (49.6%)	313777 (58.7%)	144158 (50.5%)	202551 (62.0%)
Diabetes complications count, N (%)				
0	267813 (44.9%)	254770 (47.6%)	137123 (48.1%)	150989 (46.2%)
1	163949 (27.5%)	140709 (26.3%)	70264 (24.6%)	82561 (25.3%)
2	89203 (15.0%)	75188 (14.1%)	39806 (14.0%)	48108 (14.7%)
3	46511 (7.8%)	39631 (7.4%)	22443 (7.9%)	26911 (8.2%)
≥4	29005 (4.9%)	24594 (4.6%)	15708 (5.5%)	18198 (5.6%)
Comorbidities, N (%)				
Retinopathy	66735 (11.2%)	66710 (12.5%)	38849 (13.6%)	50514 (15.5%)
Nephropathy	95467 (16.0%)	84277 (15.8%)	51781 (18.1%)	57943 (17.7%)
Neuropathy	120872 (20.3%)	118027 (22.1%)	55914 (19.6%)	77442 (23.7%)
Peripheral vascular disease	74971 (12.6%)	62329 (11.7%)	38724 (13.6%)	44294 (13.6%)
MI	28071 (4.7%)	15471 (2.9%)	10636 (3.7%)	8420 (2.6%)
CHF	52759 (8.8%)	48202 (9.0%)	24451 (8.6%)	30417 (9.3%)
Cerebrovascular disease	58181 (9.8%)	55049 (10.3%)	26707 (9.4%)	33606 (10.3%)
Dementia	12595 (2.1%)	19200 (3.6%)	6556 (2.3%)	11570 (3.5%)
COPD	73798 (12.4%)	79431 (14.8%)	27713 (9.7%)	39116 (12.0%)
Cancer	48727 (8.2%)	41538 (7.8%)	21068 (7.4%)	21940 (6.7%)
Cirrhosis	5533 (0.9%)	5014 (0.9%)	2680 (0.9%)	2584 (0.8%)
Severe hyperglycemia	3353 (0.6%)	2717 (0.5%)	2188 (0.8%)	1805 (0.6%)

	White Men	White Women	Non-White Men	Non-White Women
Severe hypoglycemia	3981 (0.7%)	4408 (0.8%)	2465 (0.9%)	3532 (1.1%)
Prescriber specialty				
Endocrinology	39060 (6.5%)	39936 (7.5%)	15431 (5.4%)	20157 (6.2%)
Family medicine	246146 (41.3%)	201986 (37.8%)	100642 (35.3%)	105277 (32.2%)
Internal medicine	179611 (30.1%)	156190 (29.2%)	96296 (33.7%)	107080 (32.8%)
Cardiology	5853 (1.0%)	3548 (0.7%)	4066 (1.4%)	3473 (1.1%)
Pediatrics	1548 (0.3%)	1386 (0.3%)	993 (0.3%)	1122 (0.3%)
Other	55585 (9.3%)	55910 (10.5%)	25657 (9.0%)	31113 (9.5%)
Unknown	68678 (11.5%)	75936 (14.2%)	42259 (14.8%)	58545 (17.9%)
Incidence of medication starts, N (%)				
GLP-1RA	35500 (6.0%)	37968 (7.1%)	14263 (5.0%)	19600 (6.0%)
SGLT2i	43997 (7.4%)	31186 (5.8%)	19265 (6.8%)	18444 (5.6%)
DPP4i	47548 (8.0%)	40082 (7.5%)	26144 (9.2%)	27159 (8.3%)
Adjusted odds of medication initiation, OR (95% CI), p-value*				
GLP-1RA	Ref	1.43 (1.41–1.45) *p<0.001*	1.12 (1.10–1.14) *p<0.001*	0.79 (0.78–0.81) *p<0.001*
SGLT2i	Ref	0.87 (0.86–0.89) *p<0.001*	0.84 (0.82–0.85) *p<0.001*	0.89 (0.87–0.91) *p<0.001*
DPP4i	Ref	0.99 (0.98–1.01) *p=0.47*	1.11 (1.09–1.13) *p<0.001*	1.16 (1.14–1.18) *p<0.001*