

Health-System and Sex Differences in Cardioprotective Diabetes Therapy Among Adults With Type 2 Diabetes and Established ASCVD: A Two-Center EHR Study

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Abstract

Background

Despite compelling evidence that sodium–glucose cotransporter-2 inhibitors (SGLT2i) and glucagon-like peptide-1 receptor agonists (GLP-1RA) reduce cardiovascular risk, their implementation among patients most likely to benefit remains suboptimal. We evaluated prescribing patterns, institutional variation, sex disparities, and neighborhood-level socioeconomic disadvantage among adults with type 2 diabetes mellitus (T2DM) and established atherosclerotic cardiovascular disease (ASCVD).

Methods

We conducted a retrospective cohort study of 16,765 adults with T2DM and ASCVD receiving care at Weill Cornell Medicine (n = 8,669) or Houston Methodist (n = 8,096) between 2016 and 2023. ASCVD was characterized by subtype, including coronary artery disease (CAD), peripheral artery disease (PAD), and stroke/cerebrovascular disease. Prescription prevalence of SGLT2i and GLP-1RA therapy was compared across institutions, ASCVD subtypes, sex, and neighborhood socioeconomic disadvantage measured using the Area Deprivation Index (ADI). Pooled prevalence estimates and sex-specific odds ratios (ORs) were calculated using meta-analytic methods.

Results

Only 28.3% (95% CI 17.3–42.6) of eligible adults received an SGLT2i, with substantially higher use at Weill Cornell than at Houston Methodist (35.2% vs. 22.2%; $P < 0.001$). GLP-1RA therapy was prescribed to 27.8% (95% CI 23.1–33.0), also with significant institutional variation (30.4% vs. 25.3%; $P < 0.001$). Across both health systems, women had 29% lower odds of receiving an SGLT2i than men (OR 0.71, 95% CI 0.66–0.77; $P < 0.001$), whereas overall GLP-1RA prescribing did not differ by sex. Analyses across CAD, PAD, and stroke and by ADI further evaluated whether treatment gaps varied according to ASCVD phenotype and neighborhood disadvantage.

Conclusions

Fewer than one in three adults with T2DM and established ASCVD received either class of guideline-recommended cardioprotective therapy. By examining distinct ASCVD subtypes and neighborhood-level deprivation across two health systems, this study demonstrates that treatment gaps extend beyond overall medication use and must be understood within patients' clinical and socioeconomic contexts. Marked institutional variation and persistent sex disparities in SGLT2i prescribing identify an urgent need for health system–level strategies to standardize care, improve equitable access, and translate cardiovascular outcome evidence into routine practice.

Introduction

Type 2 diabetes mellitus (T2DM) is a prevalent and growing global health challenge, strongly associated with a heightened risk of cardiovascular disease (CVD), the leading cause of morbidity and mortality among affected individuals (1–3). Although both men and women develop T2DM, important sex- and gender-based differences exist in diagnosis, management, and outcomes. Men are more likely to develop T2DM at a lower body mass index and at a younger age, often due to greater visceral adiposity; meanwhile, women are frequently diagnosed later in life, often after menopause, and more commonly in the setting of obesity and additional metabolic risk factors (4–6). Importantly, T2DM confers a greater relative risk of coronary heart disease, stroke, and CVD-related mortality in women compared with men, effectively eliminating the cardioprotective advantage historically observed in women (7–9).

In recent years, the advent of glucose-lowering agents with proven cardiovascular benefit—namely, glucagon-like peptide-1 receptor agonists (GLP-1RA) and sodium-glucose cotransporter-2 inhibitors (SGLT2i)—has transformed the management of T2DM. Both drug classes have demonstrated robust reductions in major adverse cardiovascular events and heart failure outcomes in patients with T2DM and established atherosclerotic cardiovascular disease (ASCVD) (10–12). Despite strong guideline recommendations for their use, real-world uptake of these therapies remains suboptimal. Furthermore, variations in prescribing patterns by patient preference, sex, race, socioeconomic status, and clinical characteristics raise concerns about access to these therapies, particularly in populations already at elevated risk of adverse cardiovascular outcomes (13).

More specifically, prior studies suggest that women with T2DM—particularly those with comorbidities such as ischemic heart disease, heart failure, and chronic kidney disease—may be less likely to be prescribed SGLT2 inhibitors compared with men (14–16). However, data examining sex differences in GLP-1 receptor agonist prescribing remain limited, and existing studies of SGLT2i use are often derived from single healthcare systems, which may limit generalizability. In addition, many electronic health record (EHR)–based analyses lack cross-site phenotype validation and harmonization, raising the possibility that observed differences may reflect variation in data capture or clinical workflows rather than consistent patterns in care. Furthermore, the extent to which such differences are reproducible across institutions has not been well characterized. Because prescribing patterns may be influenced by local practice environments, a multi-system approach may help distinguish patient-level factors from system-level variation.

To address these gaps, the present study evaluates prescribing patterns of SGLT2i and GLP-1RA among patients with T2DM and ASCVD across two geographically distinct healthcare systems. Using a meta-analytic framework to combine institutional data, we provide pooled estimates of overall and subgroup-specific medication use. These findings aim to characterize real-world prescribing patterns across diverse clinical settings.

We hypothesized that use of SGLT2i and GLP-1RA would vary meaningfully by sex, health system, ASCVD subtype, and neighborhood socioeconomic disadvantage. We therefore examined prescribing across

two large health systems to identify clinical and structural differences that may contribute to the underuse of cardioprotective diabetes therapies in routine practice.

Materials and Methods

We conducted a retrospective cohort study of adults (≥ 18 years) with T2DM and established ASCVD treated within two large academic health systems (Weill Cornell Medicine and Houston Methodist). Eligible patients were identified from electronic health records between June 2016 and August 2023 using ICD-10 codes, laboratory values, and medication data. T2DM was defined using a validated algorithm requiring at least two outpatient ICD-10 codes separated by ≥ 6 months plus supporting evidence (HbA1c $> 6.5\%$, random glucose > 200 mg/dL, and prescriptions for glucose-lowering medications). Patients were required to have a documented sex. Individuals who were pregnant or receiving dialysis during the study period were excluded. ASCVD was defined by ICD-10 codes indicating coronary artery disease, peripheral arterial disease, or ischemic stroke. Supplementary Figure S1 provides the electronic medical record (EMR) algorithm used, and supplementary tables provide the ICD-10 codes for CVD.

Data Collection

Baseline demographic and clinical characteristics (Table 1) were extracted from structured EHR fields, including age, sex, race/ethnicity, insurance type, area deprivation index (ADI), comorbidities, laboratory results, and medication histories. BMI was calculated from recorded height and weight at baseline. Cardiovascular risk factors, including hypertension, dyslipidemia, smoking status, and chronic kidney disease, were defined by a combination of diagnostic codes and laboratory thresholds. Major adverse cardiovascular events (MACE) were adjudicated using diagnostic and procedure codes.

Table 1
Characteristics of Patients With Type 2 Diabetes and ASCVD Across Two Institutions

Variable	Total (N = 16,765)	Cornell (N = 8,669)	Houston Methodist (N = 8,096)	p-value
Sex	nan	nan	nan	< .001
Male	9847 (58.7)	4892(56.4)	4955 (61.2)	nan
Female	6918 (41.3)	3777 (43.6)	3141 (38.8)	nan
Age in years, mean(sd)	70.5 (10.5)	71.5 (11.3)	69.4 (9.7)	< .001
<45 yrs	231 (1.38)	132 (1.52)	99 (1.2)	0.196
45 to 54 yrs	989 (5.90)	501 (5.78)	488 (6.0)	nan
55 to 64 yrs	3432 (20.5)	1806 (20.8)	1,626 (20.1)	nan
≥65 yrs	12113 (72.3)	6230 (71.9)	5,883 (72.7)	nan
Race/ethnicity	nan	nan	nan	< .001
Non-Hispanic White	7787 (46.5)	3243 (37.4)	4,544 (56.1)	nan
Non-Hispanic Black	2769 (16.5)	1667 (19.2)	1,102 (13.6)	nan
Non-Hispanic Asian	1407 (8.39)	543 (6.26)	864 (10.7)	nan
Non-Hispanic Other	884 (5.27)	605 (6.98)	279 (3.4)	nan
Hispanic	2506 (15.0)	1414 (16.3)	1,092 (13.5)	nan
Unknown Ethnicity	1412 (8.42)	1197 (13.8)	215 (2.7)	nan
Insurance Type	nan	nan	nan	< .001
Medicaid	1068 (6.37)	1068 (12.3)	0 (0.00)	nan
Medicare	10403 (62.1)	6004 (69.3)	4,399 (53.5)	nan
Private	3346 (20.0)	1451 (16.7)	1,895 (23.4)	nan
Uninsured (Self-pay) or Other or NA	1948 (11.6)	146 (1.68)	1802 (22.3)	nan
ADI Category	nan	nan	nan	< .001
Quintile I (Least Deprived)	7408 (44.2)	6010 (69.3)	1,398 (17.3)	nan
Quintile II	3533 (21.1)	1146 (13.2)	2,387 (29.5)	nan
Quintile III	2291 (13.7)	300 (3.46)	1,991 (24.6)	nan
Values are presented as mean (SD) or n (%). P-values were calculated using chi-square tests for categorical variables and two-sample t tests for continuous variables. ASCVD = atherosclerotic cardiovascular disease.				

Variable	Total (N = 16,765)	Cornell (N = 8,669)	Houston Methodist (N = 8,096)	p-value
Quintile IV	1570 (9.36)	122 (1.41)	1,448 (17.9)	nan
Quintile V (Most Deprived)	930 (5.55)	119 (1.37)	811 (10.0)	nan
ADI N/A	1033 (6.16)	972 (11.2)	61 (0.8)	nan
BMI Classes	N = 16428	N = 8567	N = 7861	< .001
Underweight (BMI < 18.5)	202 (1.23)	148 (1.73)	54 (0.7)	nan
Healthyweight (BMI 18.5–24.9)	3081 (18.8)	1758 (20.5)	1,323 (16.8)	nan
Overweight (BMI 25-29.9)	5642 (34.3)	2988 (34.9)	2,654 (33.8)	nan
Obese Class I (BMI 30-34.9)	4299 (26.2)	2167 (25.3)	2,132 (27.1)	nan
Obese Class II (BMI 35-39.9)	1942 (11.8)	895 (10.5)	1,047 (13.3)	nan
Obese Class III (BMI ≥ 40)	1262 (7.68)	611 (7.13)	651 (8.3)	nan
FIB-4 Categories	N = 13408	N = 7657	N = 5751	P = 0.570
Low (Houston:<1.3; Cornell:<1.45)	6222 (46.4)	3533 (46.1)	2,689 (46.8)	nan
Moderate (Houston: 1.3–2.66; Cornell:1.45–3.25)	6301 (47.0)	3627 (47.4)	2,674 (46.5)	nan
High (Houston:≥2.67; Cornell:>3.25)	885 (6.60)	497 (6.49)	388 (6.7)	nan
HbA1C Categories	N = 13394	N = 7654	N = 5740	< .001
Low (≤ 7.0)	8126 (60.7)	4455 (58.2)	3,671 (64.0)	nan
Moderate (7.1–7.9)	2614 (19.5)	1508 (19.7)	1,106 (19.3)	nan
High (8.0-8.9)	1290 (9.63)	786 (10.3)	504 (8.8)	nan
Very High (≥ 9.0)	1364 (10.2)	905 (11.8)	459 (8.0)	nan
CV Risk factors	nan	nan	nan	nan
Hypertension	nan	nan	nan	< .001
No	1998 (11.9)	1567 (18.1)	431 (5.3)	nan
Yes	14767 (88.1)	7102 (81.9)	7,665 (94.7)	nan
Values are presented as mean (SD) or n (%). P-values were calculated using chi-square tests for categorical variables and two-sample t tests for continuous variables. ASCVD = atherosclerotic cardiovascular disease.				

Variable	Total (N = 16,765)	Cornell (N = 8,669)	Houston Methodist (N = 8,096)	p-value
Dyslipidemia	nan	nan	nan	< .001
No	3432 (20.5)	444 (5.12)	2,988 (36.9)	nan
Yes	13333 (79.5)	8225 (94.9)	5,108 (63.1)	nan
Smoking current	nan	nan	nan	< .001
No	15666 (93.4)	8248 (95.1)	7,418 (91.6)	nan
Yes	1099 (6.56)	421 (4.89)	678 (8.4)	nan
Charlson's comorbidity index	nan	nan	nan	P = 0.700
1–3 CCI	9123 (54.4)	4705 (54.3)	4,418 (54.6)	nan
>=4 CI	7642 (45.6)	3964 (45.7)	3,678 (45.4)	nan
Comorbidities	nan	nan	nan	nan
Renal disease	nan	nan	nan	< .001
No	12650 (75.5)	6295 (72.6)	6,355 (78.5)	nan
Yes	4115 (24.6)	2374 (27.4)	1,741 (21.5)	nan
Chronic pulmonary disease	nan	nan	nan	< .001
No	13187 (78.7)	6971 (80.4)	6,216 (76.8)	nan
Yes	3578 (21.3)	1698 (19.6)	1,880 (23.2)	nan
Heart failure	nan	nan	nan	< .001
No	13362 (79.7)	6628 (76.5)	6,734 (83.2)	nan
Yes	3403 (20.3)	2041 (23.5)	1,362 (16.8)	nan
Atrial fibrillation	nan	nan	nan	< .001
No	14232 (84.9)	7197 (83.0)	7,035 (86.9)	nan
Yes	2533 (15.1)	1472 (17.0)	1,061 (13.1)	nan
Pancreatitis	nan	nan	nan	0.581
No	16095 (99.2)	8607 (99.3)	8,028 (99.2)	nan
Yes	130 (0.80)	62 (0.76)	68 (0.84)	nan
Values are presented as mean (SD) or n (%). P-values were calculated using chi-square tests for categorical variables and two-sample t tests for continuous variables. ASCVD = atherosclerotic cardiovascular disease.				

Variable	Total (N = 16,765)	Cornell (N = 8,669)	Houston Methodist (N = 8,096)	p-value
Any Cancer	nan	nan	nan	< .001
No	13166 (78.5)	6711 (77.4)	6,455 (79.7)	nan
Yes	3599 (21.5)	1958 (22.6)	1,641 (20.3)	nan
Thyroid cancer	nan	nan	nan	0.013
No	16660 (99.4)	8602 (99.2)	8,058 (99.5)	nan
Yes	105 (0.63)	67 (0.77)	38 (0.47)	nan
MACE outcomes	nan	nan	nan	nan
4 component MACE	nan	nan	nan	< .001
No	8642 (51.6)	3591 (41.4)	5,051 (62.4)	nan
Yes	8123 (48.5)	5078 (58.6)	3,045 (37.6)	nan
Values are presented as mean (SD) or n (%). P-values were calculated using chi-square tests for categorical variables and two-sample t tests for continuous variables. ASCVD = atherosclerotic cardiovascular disease.				

Medication Exposure

Prescription data for SGLT2 inhibitors (SGLT2i) and glucagon-like peptide-1 receptor agonists (GLP-1RA) (Table 2) were obtained from the electronic health record (EHR) active medication lists at the time of cohort ascertainment. Medication use was identified through structured EHR medication fields using standardized drug-class queries that captured all agents within each therapeutic class. Prevalence estimates were calculated overall and stratified by sex and institution.

Table 2
Meta-analysis of Prevalence of GLP-1RA and SGLT2i Prescription Stratified by Sex

Outcome	Total (N = 16,765)	Cornell (N = 8,669)	Houston Methodist (N = 8,096)	P value (Cornell vs. Houston)
Overall SGLT2i use				
Yes, n (%)	4853 (29.0)	3054 (35.2)	1799 (22.2)	
Prevalence (95% CI)	28.3% (17.3–42.6); I ² = 99.7%, P < 0.001	35.2% (34.2–36.3)	22.2% (21.3–23.1)	< 0.001
SGLT2i use in men				
Yes, n (%)	3132 (31.8)	1896 (38.8)	1236 (24.9)	
Prevalence (95% CI)	31.5% (19.6–46.3); I ² = 99.5%, P < 0.001	38.8% (37.4–40.1)	24.9% (23.7–26.2)	< 0.001
SGLT2i use in women				
Yes, n (%)	1721 (24.9)	1158 (30.7)	563 (17.9)	
Prevalence (95% CI)	23.7% (13.5–38.3); I ² = 99.3%, P < 0.001	30.7% (29.2–32.2)	17.9% (16.6–19.3)	< 0.001
Overall GLP-1RA use				
Yes, n (%)	4683 (27.9)	2634 (30.4)	2049 (25.3)	
Prevalence (95% CI)	27.8% (23.1–33.0); I ² = 98.1%, P < 0.001	30.4% (29.4–31.4)	25.3% (24.4–26.3)	< 0.001
GLP-1RA use in men				
Yes, n (%)	2715 (27.6)	1526 (31.2)	1189 (24.0)	
Prevalence (95% CI)	27.5% (21.0–35.0); I ² = 98.4%, P < 0.001	31.2% (29.9–32.5)	24.0% (22.8–25.2)	< 0.001
Legend: Prevalence of sodium–glucose co-transporter-2 inhibitor (SGLT2i) and glucagon-like peptide-1 receptor agonist (GLP-1RA) use across two institutional cohorts. Values represent counts with percentages and 95% confidence intervals. P values compare prevalence between cohorts. Prevalence values in the source dataset denote pooled estimates derived from meta-analysis.				

Outcome	Total (N = 16,765)	Cornell (N = 8,669)	Houston Methodist (N = 8,096)	P value (Cornell vs. Houston)
GLP-1RA use in women	N = 6,918	N = 3,777	N = 3,141	
Yes, n (%)	1968 (28.5)	1108 (29.3)	860 (27.4)	
Prevalence (95% CI)	28.5% (27.4–29.5); I ² = 69.0%, P = 0.073	29.3% (27.9–30.8)	27.4% (25.8–29.0)	0.073
Legend: Prevalence of sodium–glucose co-transporter-2 inhibitor (SGLT2i) and glucagon-like peptide-1 receptor agonist (GLP-1RA) use across two institutional cohorts. Values represent counts with percentages and 95% confidence intervals. P values compare prevalence between cohorts. Prevalence values in the source dataset denote pooled estimates derived from meta-analysis.				

Statistical Analysis

Sex differences in medication use were assessed using chi-square tests for categorical variables and two-sample t-tests for continuous variables. Multivariable logistic regression was used to estimate adjusted odds ratios (ORs) for SGLT2i and GLP-1RA prescribing in women versus men, adjusting for age, race/ethnicity, comorbidities, HbA1c, insurance status, and ADI (Table 3). Subgroup analyses were conducted by cardiovascular disease type (coronary artery disease [CAD], peripheral artery disease [PAD], and stroke), age group, race/ethnicity, socioeconomic quintile, glycemic control category, and comorbidities (renal disease, chronic kidney disease [CKD], heart failure). Institution-specific ORs were generated and pooled using random-effects meta-analysis. All analyses were performed separately within each institution before deriving pooled estimates, and statistical significance was defined as two-sided $p < 0.05$.

Table 3

Adjusted Odds Ratios for SGLT2i and GLP1RA Prescription Among Women vs. Men in the Overall Cohort and in Subgroups

	SGLT2i			GLP1RA		
	Cornell OR (95% CI), p	Houston OR (95% CI), p	Overall OR (95% CI), p	Cornell OR (95% CI), p	Houston OR (95% CI), p	Overall OR (95% CI), p
Overall cohort (T2DM with ASCVD)	0.74 (0.67–0.82), p<.001, N = 8567	0.67 (0.59–0.75), p<.001, N = 7995	0.71 (0.66–0.77), p<.001	1.02 (0.92–1.13), P = 0.718, N = 8567	1.28 (1.15–1.43), P<.001, N = 7995	1.14 (0.91–1.43), P = 0.243
CAD	0.71 (0.63–0.80), p<.001, N = 5816	0.70 (0.61–0.80), p<.001, N = 5948	0.71 (0.65–0.77), p<.001	1.04 (0.91–1.18), P = 0.567, N = 5816	1.27 (1.13–1.45), P<.001, N = 5948	1.15 (0.95–1.40), P = 0.161
PAD	0.78 (0.65–0.92), p = 0.005, N = 2615	0.77 (0.61–0.98), p = 0.034, N = 1716	0.78 (0.68–0.89), p<.001	1.17 (0.98–1.41), P = 0.091, N = 2615	1.44 (1.14–1.84), P = 0.003, N = 1716	1.26 (1.09–1.46), P = 0.002
Stroke	0.80 (0.69–0.94), p = 0.005, N = 3390	0.59 (0.47–0.75), p<.001, N = 1867	0.70 (0.52–0.94), p = 0.017	1.01 (0.85–1.19), P = 0.924, N = 3390	1.25 (0.99–1.58), P = 0.060, N = 1867	1.09 (0.95–1.25), P = 0.235
Age < 45	1.16 (0.49–2.75), p = 0.738, N = 132	0.32 (0.07–1.40), p = 0.129, N = 91	0.84 (0.40–1.78), p = 0.652	1.21 (0.53–2.78), P = 0.647, N = 132	2.14 (0.96–2.66), P = 0.059, N = 97	1.83 (1.19–2.82), P = 0.006
Age 45–54	0.72 (0.48–1.08), p = 0.108, N = 494	0.66 (0.41–1.05), p = 0.083, N = 483	0.69 (0.51–0.94), p = 0.020	1.77 (1.17–2.68), P = 0.007, N = 494	1.35 (0.89–2.04), P = 0.157, N = 483	1.55 (1.15–2.07), P = 0.004
Age 55–64	0.75 (0.61–0.92), p = 0.007, N = 1773	0.68 (0.53–0.87), p = 0.002, N = 1607	0.72 (0.62–0.84), p<.001	1.29 (1.04–1.59), P = 0.021, N = 1773	1.51 (1.20–1.88), P<.001, N = 1607	1.39 (1.19–1.62), P<.001

Odds ratios (OR) represent the likelihood of SGLT2i and GLP1RA prescription among women compared with men, adjusted for age, race/ethnicity, comorbidities, HbA1c, insurance status, and ADI. Subgroup analyses were performed for cardiovascular disease type, age groups, race/ethnicity, socioeconomic strata, glycemic control, and comorbid conditions. ASCVD = atherosclerotic cardiovascular disease; CAD = coronary artery disease; PAD = peripheral arterial disease; HF = heart failure; ADI = area deprivation index.

	SGLT2i			GLP1RA		
	Cornell OR (95% CI), p	Houston OR (95% CI), p	Overall OR (95% CI), p	Cornell OR (95% CI), p	Houston OR (95% CI), p	Overall OR (95% CI), p
Age ≥ 65	0.70 (0.62–0.78), p<.001, N = 6168	0.66 (0.57–0.75), p<.001, N = 5808	0.68 (0.63–0.75), p<.001	0.84 (0.74–0.95), P = 0.006, N = 6168	1.21 (1.05–1.38), P = 0.006, N = 5808	1.01 (0.70–1.44), P = 0.969
Race White	0.68 (0.57–0.80), p<.001, N = 3219	0.56 (0.48–0.66), p<.001, N = 4497	0.61 (0.55–0.69), p<.001	1.00 (0.84–1.19), P = 0.971, N = 3219	1.26 (1.09–1.46), P = 0.002, N = 4497	1.13 (0.90–1.41), P = 0.296
Race Black	0.94 (0.75–1.18), p = 0.594, N = 1650	0.84 (0.62–1.14), p = 0.263, N = 1091	0.90 (0.75–1.08), p = 0.272	1.35 (1.05–1.72), P = 0.017, N = 1650	1.49 (1.11–2.01), P = 0.009, N = 1091	1.41 (1.16–1.70), P < 0.001
Race Asian	0.68 (0.47–1.01), p = 0.054, N = 539	0.66 (0.46–0.96), p = 0.029, N = 854	0.67 (0.51–0.87), p = 0.003	0.95 (0.60–1.50), P = 0.813, N = 539	1.14 (0.76–1.70), P = 0.539, N = 852	1.05 (0.78–1.42), P = 0.738
Race Hispanic	0.82 (0.65–1.03), p = 0.084, N = 1393	0.87 (0.64–1.17), p = 0.359, N = 1073	0.84 (0.70–1.01), p = 0.058	1.14 (0.90–1.45), P = 0.289, N = 1393	1.26 (0.95–1.67), P = 0.109, N = 1073	1.19 (0.99–1.43), P = 0.063
ADI Quintile 1	0.72 (0.64–0.81), p<.001, N = 5936	0.67 (0.49–0.91), p = 0.009, N = 1377	0.71 (0.64–0.80), p<.001	1.03 (0.91–1.16), P = 0.699, N = 5936	1.33 (1.01–1.74), P = 0.040, N = 1377	1.07 (0.96–1.20), P = 0.202
ADI Quintile 2	0.73 (0.56–0.94), p = 0.017, N = 1133	0.55 (0.45–0.69), p<.001, N = 2361	0.62 (0.52–0.73), p<.001	1.08 (0.82–1.44), P = 0.584, N = 1133	1.34 (1.08–1.62), P = 0.006, N = 2361	1.24 (1.06–1.47), P = 0.009

Odds ratios (OR) represent the likelihood of SGLT2i and GLP1RA prescription among women compared with men, adjusted for age, race/ethnicity, comorbidities, HbA1c, insurance status, and ADI. Subgroup analyses were performed for cardiovascular disease type, age groups, race/ethnicity, socioeconomic strata, glycemic control, and comorbid conditions. ASCVD = atherosclerotic cardiovascular disease; CAD = coronary artery disease; PAD = peripheral arterial disease; HF = heart failure; ADI = area deprivation index.

	SGLT2i			GLP1RA		
	Cornell OR (95% CI), p	Houston OR (95% CI), p	Overall OR (95% CI), p	Cornell OR (95% CI), p	Houston OR (95% CI), p	Overall OR (95% CI), p
ADI Quintile 3	0.89 (0.51–1.55), p = 0.672, N = 296	0.73 (0.58–0.92), p = 0.008, N = 1974	0.75 (0.61–0.93), p = 0.009	1.21 (0.67–2.19), P = 0.530, N = 296	1.32 (1.06–1.64), P = 0.014, N = 1974	1.31 (1.06–1.60), P = 0.011
ADI Quintile 4	1.68 (0.61–4.65), p = 0.318, N = 119	0.71 (0.55–0.92), p = 0.012, N = 1426	0.75 (0.58–0.96), p = 0.022	1.00 (0.33–3.02), P = 0.997, N = 119	1.37 (1.05–1.78), P = 0.020, N = 1426	1.35 (1.04–1.74), P = 0.023
ADI Quintile 5	1.30 (0.48–3.55), p = 0.604, N = 119	0.79 (0.55–1.15), p = 0.226, N = 798	0.84 (0.59–1.19), p = 0.319	1.49 (0.54–4.14), P = 0.444, N = 119	0.94 (0.66–1.34), P = 0.727, N = 798	0.99 (0.71–1.38), P = 0.943
HbA1c ≤ 7.0	0.66 (0.58–0.77), p < .001, N = 4433	0.61 (0.51–0.74), p < .001, N = 3648	0.64 (0.57–0.72), p < .001	1.01 (0.87–1.17), P = 0.909, N = 4433	1.32 (1.12–1.56), P = 0.001, N = 3648	1.15 (0.89–1.50), P = 0.292
HbA1c 7.1–7.9	0.84 (0.66–1.05), p = 0.124, N = 1497	0.66 (0.49–0.87), p = 0.004, N = 1094	0.76 (0.64–0.91), p = 0.003	1.13 (0.88–1.45), P = 0.350, N = 1497	1.49 (1.11–2.02), P = 0.008, N = 1094	1.27 (1.04–1.53), P = 0.016
HbA1c 8.0–8.9	0.99 (0.72–1.35), p = 0.947, N = 781	0.82 (0.53–1.28), p = 0.393, N = 499	0.93 (0.72–1.20), p = 0.573	0.91 (0.65–1.26), P = 0.552, N = 781	0.91 (0.58–1.42), P = 0.665, N = 499	0.91 (0.70–1.19), P = 0.487
HbA1c ≥ 9.0	0.81 (0.61–1.09), p = 0.159, N = 895	0.60 (0.38–0.93), p = 0.024, N = 451	0.74 (0.58–0.95), p = 0.016	1.06 (0.78–1.42), P = 0.717, N = 895	0.93 (0.60–1.42), P = 0.726, N = 458	1.02 (0.79–1.30), P = 0.901

Odds ratios (OR) represent the likelihood of SGLT2i and GLP1RA prescription among women compared with men, adjusted for age, race/ethnicity, comorbidities, HbA1c, insurance status, and ADI. Subgroup analyses were performed for cardiovascular disease type, age groups, race/ethnicity, socioeconomic strata, glycemic control, and comorbid conditions. ASCVD = atherosclerotic cardiovascular disease; CAD = coronary artery disease; PAD = peripheral arterial disease; HF = heart failure; ADI = area deprivation index.

	SGLT2i			GLP1RA		
	Cornell OR (95% CI), p	Houston OR (95% CI), p	Overall OR (95% CI), p	Cornell OR (95% CI), p	Houston OR (95% CI), p	Overall OR (95% CI), p
Renal No	0.76 (0.68–0.85), p<.001, N = 6212	—	—	1.12 (.99–1.27), P = 0.064, N = 6212		
Renal Yes	0.73 (0.61–0.88), p = 0.001, N = 2355	—	—	0.81 (0.67–0.99), P = 0.039, N = 2355		
HF No	0.77 (0.69–0.86), p<.001, N = 6543	0.64 (0.56–0.73), p<.001, N = 6652	0.70 (0.59–0.84), p<.001	1.03 (0.92–1.16), P = 0.588, N = 6543	1.29 (1.14–1.45), P<.001, N = 6652	1.15 (0.92–1.44), P = 0.209
HF Yes	0.73 (0.60–0.88), p = 0.001, N = 2024	0.81 (0.63–1.04), p<.105, N = 1343	0.76 (0.65–0.88), p<.001	0.89 (0.71–1.12), P = 0.324, N = 2024	1.23 (0.93–1.63), P = 0.174, N = 1332	1.01 (0.85–1.21), P = 0.894
Odds ratios (OR) represent the likelihood of SGLT2i and GLP1RA prescription among women compared with men, adjusted for age, race/ethnicity, comorbidities, HbA1c, insurance status, and ADI. Subgroup analyses were performed for cardiovascular disease type, age groups, race/ethnicity, socioeconomic strata, glycemic control, and comorbid conditions. ASCVD = atherosclerotic cardiovascular disease; CAD = coronary artery disease; PAD = peripheral arterial disease; HF = heart failure; ADI = area deprivation index.						

Meta-analyses of GLP-1RA and SGLT2i prevalence and sex-specific ORs were conducted using R (Version 4.4.2; meta package). Missing data were handled using complete case analysis, with < 1.2% missingness across key variables. Heterogeneity was assessed using the Cochrane Q test ($p < 0.05$) and the I^2 statistic, with values > 50% indicating moderate-to-high heterogeneity. Random-effects models were applied in the presence of heterogeneity. Pooled prevalence estimates and odds ratios were calculated using fixed- or random-effects models, as appropriate, with between-study variance estimated using inverse-variance methods. Confidence intervals for pooled estimates were wide, reflecting variability between sites.

Results

Table 1 summarizes the baseline characteristics of 16,765 patients across Cornell ($n = 8,669$) and Houston Methodist ($n = 8,096$). Among 16,765 patients, the mean age was 70.5 years, with most (72.3%) aged ≥ 65 . Men comprised 58.7% overall, with a higher proportion at Houston Methodist (61.2%) than

Cornell (56.4%). Racial distribution differed significantly, with more Non-Hispanic White patients at Houston Methodist (56.1% vs. 37.4%) and more Non-Hispanic Black and Other/unknown patients at Cornell. Across the cohort, ADI levels varied substantially between institutions, with Cornell patients far more likely to reside in the least deprived areas (Quintile I: 69.3% vs. 17.3%) and Houston Methodist patients more frequently represented in higher-deprivation quintiles (Quintiles II–V totaling 82.0% vs. 19.4%). Cardiovascular risk factors were highly prevalent, including hypertension in 88.1% and dyslipidemia in 79.5%, while smoking was more common at Houston Methodist (8.4% vs. 4.9%). Nearly half of the cohort experienced MACE, with markedly higher rates at Cornell (58.6%) compared to Houston Methodist (37.6%).

Table 2 presents the pooled prevalence of SGLT2i and GLPRA prescription by sex, as described by meta-analysis. Across 16,765 individuals, the pooled prevalence of SGLT2i use was 28.3% (95% CI, 17.3–42.6; $I^2 = 99.7\%$, $P < 0.001$), with significantly higher use in the Cornell cohort compared with Houston Methodist (35.2% vs. 22.2%, $P < 0.001$). This pattern persisted when stratified by sex: SGLT2i prescriptions were less common in women than men overall (23.7% vs. 31.5%), as well as within each cohort (Cornell: 30.7% vs. 38.8%; Houston Methodist: 17.9% vs. 24.9%; all $P < 0.001$). For GLP-1RA use, the pooled prevalence was 27.8% (95% CI, 23.1–33.0; $I^2 = 98.1\%$, $P < 0.001$), again higher at Cornell than Houston Methodist (30.4% vs. 25.3%, $P < 0.001$). Among men, GLP-1RA use was more frequent at Cornell than Houston Methodist (31.2% vs. 24.0%, $P < 0.001$), whereas among women the prevalence was similar between cohorts (29.3% vs. 27.4%, $P = 0.073$).

Across the overall cohort, women had significantly lower odds of SGLT2i use compared with men (Table 3: OR 0.71, 95% CI 0.66–0.77, $p < 0.001$). This disparity was consistent across major cardiovascular subgroups, including CAD (OR 0.71, 95% CI 0.65–0.77), PAD (OR 0.78, 95% CI 0.68–0.89), and stroke (OR 0.70, 95% CI 0.52–0.94). Age-stratified analyses revealed that the sex gap was pronounced among patients aged 45–54 (OR 0.69, 95% CI 0.51–0.94), 55–64 (OR 0.72, 95% CI 0.62–0.84) and ≥ 65 (OR 0.68, 95% CI 0.63–0.75), while differences were not statistically in patients < 45 . By race, sex disparities were strongest among White (OR 0.61, 95% CI 0.55–0.69) and Asian patients (OR 0.67, 95% CI 0.51–0.87), whereas no significant differences were observed among Black patients (OR 0.90, 95% CI 0.75–1.08). Socioeconomic gradients (ADI quintiles) showed variable patterns, with significant disparities in Quintiles 1–4 but not Quintile 5. Regarding glycemic control, women were less likely to receive SGLT2i at lower and moderately elevated HbA1c levels ($\leq 7.9\%$), with no differences at high HbA1c (8.0–8.9%). Disparities were also consistent in patients with and without heart failure.

In contrast to SGLT2i, in the overall cohort, women had similar GLP-1RA use compared with men (Table 3: OR 1.14, 95% CI 0.91–1.43, $p = 0.243$). Between sites, the adjusted odds of GLP-1RA prescription were similar for women and men at Cornell (OR 1.02, 95% CI 0.92–1.13; $P = 0.718$), whereas women at Houston Methodist had significantly higher odds of receiving a GLP-1RA (OR 1.28, 95% CI 1.15–1.43; $P < 0.001$). This pattern persisted across multiple clinical subgroups, with Cornell showing largely null associations—odds ratios generally near 1.0 and not statistically significant—while Houston consistently demonstrated increased odds of GLP-1RA prescribing for women, particularly among

patients with CAD, PAD, moderate hyperglycemia, and those aged 55–64 (ORs 1.27–1.51, all $P < 0.01$). Notably, sex-related differences diverged in the oldest age group (≥ 65 years), where Cornell showed lower odds for women (OR 0.84, $P = 0.006$) and Houston showed higher odds (OR 1.21, $P = 0.006$). The pooled meta-analytic estimates were generally intermediate and nonsignificant across subgroups, indicating heterogeneity between institutions but no consistent overall sex difference.

Discussion

This study provides several important insights into the characterization of patients with T2DM and secondary ASCVD across two major healthcare systems. We observed both shared and distinct clinical and sociodemographic features between the Cornell and Houston cohorts. Patients in Houston were younger (mean age 69.4 years) and predominantly male, and there were striking between-site differences in social deprivation (Area Deprivation Index [ADI]) and cardiovascular outcomes (MACE). This highlights the profound influence of social determinants of health on ASCVD burden, access to care, and survival (17,18)(15,16). Importantly, we also identified meaningful differences in prescribing patterns across sites and between sexes. While men and women were prescribed GLP-1RAs at similar rates, women were about 25% less likely to be prescribed SGLT2i. Both sites demonstrated underutilization of these evidence-based therapies (approximately 28% prevalence of use), echoing prior evidence that real-world adoption remains suboptimal despite strong randomized trial data supporting cardiovascular benefit (12,15)(17).

Feasibility of Multisite EMR-Based Cohort Development

Multisite cardiovascular and diabetes research is inherently challenging due to variability in EMR systems, coding architectures, and clinical workflows (19,20). Despite these barriers, the present study demonstrates the feasibility of a harmonized, flexible, and replicable approach to identifying comparable cohorts and stratifying T2D patients by ASCVD risk across two independent institutions. The stepwise methodology, developed at Houston Methodist and subsequently adapted at Cornell, preserved local context while maximizing analytical comparability. Such frameworks have the potential to enhance multisite population health surveillance and support quality improvement efforts across health systems with diverse clinical environments and infrastructures (20).

Inter-Institutional Variability and the Role of Social Determinants

Our findings reveal both conserved and variable cohort characteristics. Common features—such as older age and male predominance—reflect longstanding sex differences in ASCVD pathophysiology and plaque biology (21). In contrast, marked inter-site differences in ADI, race/ethnicity, and MACE outcomes highlight the importance of contextual, environmental, and structural determinants of cardiovascular health.

Cornell patients were substantially more socioeconomically advantaged, with 69.3% living in ADI Quintile I compared with only 17.3% at Houston. Consistent with extensive literature (15, 22, 23) demonstrating

that socioeconomic deprivation is associated with higher cardiovascular risk, worse ASCVD outcomes, reduced access to preventive care, and lower treatment adherence, this socioeconomic gradient would be expected to favor *lower* cardiovascular risk among the Cornell cohort. Therefore, the higher prevalence of MACE observed at Cornell likely reflects differences in referral patterns, case mix, or ascertainment rather than socioeconomic context alone.

Furthermore, our T2DM ASVCD cohorts included a lower proportion of non-Hispanic White patients than national ASCVD datasets (46.5% pooled vs. 80.7% reported) (18). This possibly reflects the intersection of diabetes and ASCVD, as diabetes prevalence remains higher among many non-White racial and ethnic groups (17). Such demographic variations underscore the importance of contextualized approaches when interpreting variations and designing targeted interventions.

Sex-Based Prescribing Differences

We observed lower odds of SGLT2i prescribing among women compared with men (combined OR 0.71). This finding is consistent with national analyses demonstrating lower SGLT2i use among women, racial and ethnic minorities (15), but should be interpreted as a descriptive difference in prescribing patterns, as the underlying causes cannot be determined from this observational analysis. Although models adjusted for comorbidities and subgroup analyses demonstrated similar patterns across clinical strata, residual confounding by indication is likely.

Several factors may contribute to these differences, including variation in comorbidity profiles, safety considerations, patient preferences, and clinician prescribing behavior (24, 25). For example, adverse effects such as genital infections—which occur more frequently in women—may influence treatment selection and patient preference for SGLT2 inhibitors (26). The absence of a consistent difference in GLP-1RA prescribing suggests that class-specific considerations may play a role.

In contrast, GLP-1RA prescribing did not significantly differ by sex, differing from earlier reports of gender inequities in GLP-1RA use (15). This divergence may indicate institution-specific policies, localized clinician awareness, or temporal improvements in GLP-1RA prescribing—supported by recent meta-analytic evidence of broad effectiveness and safety across diverse populations (23). Nonetheless, the overall underuse of both SGLT2i and GLP-1RA—even at Cornell, the higher-prescribing site—represents a major gap in the delivery of evidence-based cardioprotective therapy. Given the robust reductions in cardiovascular and renal events demonstrated in EMPA-REG OUTCOME and other major trials (12), closing these gaps remains a public health priority.

Clinical and Public Health Implications

Overall use of SGLT2i and GLP-1RA remained modest across both institutions, with approximately 28% of eligible patients receiving these therapies. This likely reflects multiple factors, including evolving evidence and guideline recommendations over the study period (2016–2023), cost and access considerations, and variability in clinical adoption. Earlier years in the study period may reflect lower

baseline uptake prior to widespread dissemination of cardiovascular outcome data and guideline recommendations. During the study period, agents such as empagliflozin and liraglutide—among the earliest to demonstrate cardiovascular benefit—were commonly used in clinical practice; however, drug-specific prescribing patterns were not evaluated in this analysis.

These findings highlight opportunities to better understand factors influencing treatment selection in routine clinical practice. Approaches such as clinical decision support tools, risk stratification strategies, and workflow optimization may help support appropriate use of evidence-based therapies. In addition, broader structural factors—including formulary design and insurance coverage—may influence prescribing patterns and warrant further investigation (27).

Limitations

Several limitations should be acknowledged. First, as an observational study using EMR data, residual confounding is likely, and we were unable to fully account for factors such as contraindications, intolerance, or patient preferences that may influence prescribing decisions. Second, medication exposure was defined based on active prescriptions and does not distinguish between new initiation and long-term use, nor does it capture adherence. Third, the study period includes years prior to widespread adoption of cardiovascular indications for SGLT2i and GLP-1RA, which may contribute to lower observed use. Fourth, EMR-derived data may introduce misclassification or incomplete coding. Fifth, substantial heterogeneity ($I^2=69\%$) suggests variability across sites, and pooled estimates should be interpreted with caution. Wide confidence intervals for some pooled estimates reflect between-site variability and differences in baseline characteristics, which may limit precision of effect estimates. Finally, results from two academic health systems may not be generalizable to other practice settings. Moreover, cost and insurance coverage are likely to influence prescribing patterns, particularly for newer therapies. The recent introduction of generic SGLT2 inhibitors may improve access and uptake moving forward.

Conclusion

Our EMR-based framework identified patients with T2DM and ASCVD across two healthcare systems and demonstrated variation in prescribing patterns of SGLT2i and GLP-1RA therapies. These findings provide insight into real-world use of cardioprotective diabetes therapies across diverse clinical settings. Further work is needed to better understand the clinical, patient-level, and system-level factors that influence treatment selection and to evaluate how uptake evolves over time.

Declarations

1. Ethics approval and consent to participate

This retrospective observational study was approved by the Institutional Review Boards of Weill Cornell Medicine protocol number: 12-8985 and Houston Methodist Research Institute 57-10934. The requirement for individual informed consent was waived by both Institutional Review Boards because the

study involved retrospective analysis of existing electronic health record data and posed minimal risk to participants. All methods were performed in accordance with applicable institutional guidelines and regulations and the Declaration of Helsinki.

2. Consent for publication

Not applicable. The manuscript does not contain identifiable individual participant information.

3. Availability of data and materials

The datasets analyzed in this study are not publicly available because they contain protected health information derived from institutional electronic health records and are subject to institutional privacy, data-use, and regulatory restrictions. Deidentified data may be available from the corresponding author upon reasonable request and subject to approval by the participating institutions and their respective Institutional Review Boards.

4. Competing interests

C.P., A.R., E.S., X.M., and R.G. declare that they have no competing interests. K.N. has served in advisory roles for Novo Nordisk, Novartis, and Esperion; served on the Amgen speakers' bureau; received research support from the National Institutes of Health, Novartis, Esperion, and the Jerold B. Katz Academy of Translational Research; and had advisory or consulting relationships with Quest Diagnostics and Regeneron. A.S. and E.A. declare that they have no relevant competing interests. S.R.K. serves as a consultant for Medpace, is co-editor of *Healio Endocrine Today*, and has received research funding awarded to Weill Cornell Medicine from Fractyl Laboratories. All authors affirm that any potential competing interests relevant to this work have been disclosed.

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6. Authors' contributions

K.N., A.S., E.A., and S.R.K. conceived and designed the study. C.P., A.R., E.S., S.R.K., and R.G. contributed to data acquisition, cohort development, and data validation. R.G., X.M., and SRK performed the data analyses. C.P., A.R., K.N., A.S., and E.A. contributed to the interpretation of the findings. C.P. and S.R.K. drafted the manuscript. All authors critically reviewed the manuscript for important intellectual content, contributed to its revision, approved the final version, and agreed to be accountable for all aspects of the work.

Guarantor: Sangeeta R. Kashyap, MD, is the guarantor of this work and, as such, had full access to the study data and takes responsibility for the integrity of the data, the accuracy of the analyses, and the decision to submit the manuscript for publication.

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Artificial intelligence use

The authors used generative artificial intelligence tools to assist with language editing, grammar, and readability. Artificial intelligence was not used for data collection, data analysis, statistical modeling, interpretation of results, generation of scientific conclusions, or reference retrieval. All content, analyses, and conclusions were developed and verified by the authors, who take full responsibility for the accuracy and integrity of the manuscript.

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Figures

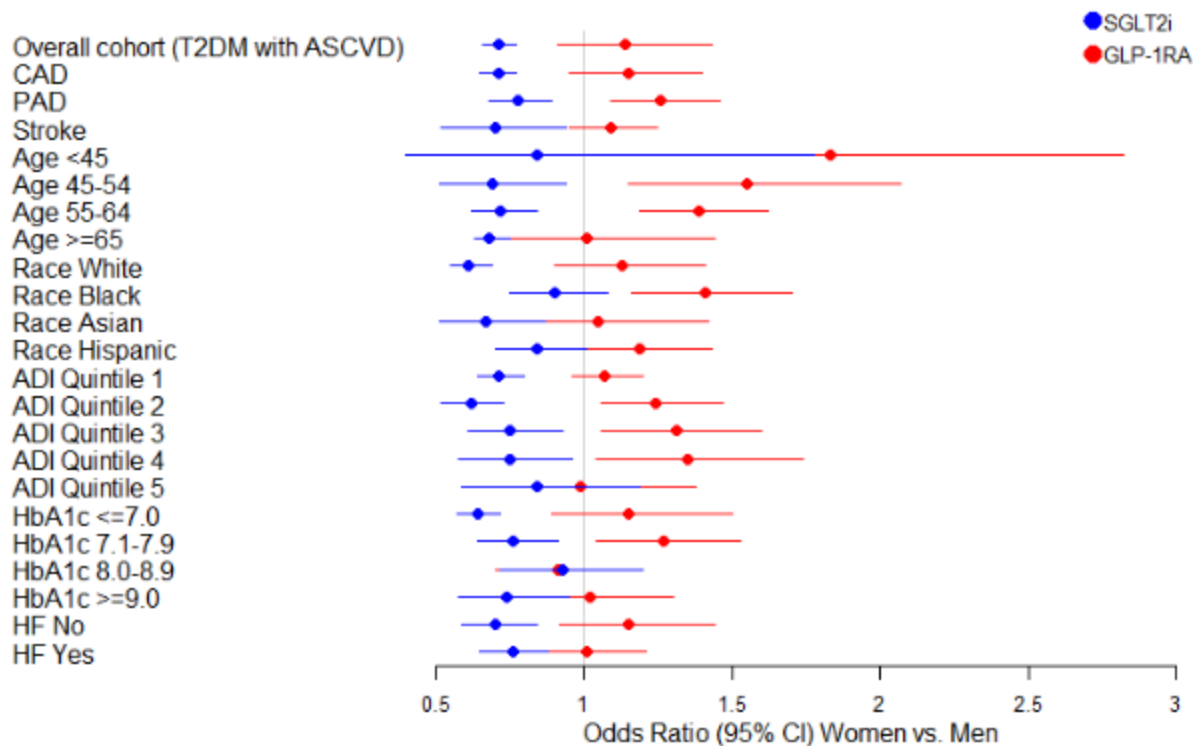


Figure 1

Forest Plot of SGLT2 and GLPRA Across Clinical Subgroups

Figure 1 Legend: Forest plot showing odds ratios (ORs) and 95% confidence intervals (CIs) for SGLT2 inhibitor (blue) and GLP-1 receptor agonist (red) prescribing among women compared with men in the overall cohort and across ASCVD, demographic, Area Deprivation Index (ADI), glycemic, and heart failure subgroups. ORs below 1.0 indicate lower odds of prescribing among women; ORs above 1.0 indicate higher odds among women. The vertical line denotes no sex difference (OR=1.0). ADI quintile 1 represents the least neighborhood deprivation and quintile 5 the greatest deprivation. ASCVD, atherosclerotic cardiovascular disease; CAD, coronary artery disease; CI, confidence interval; GLP-1RA, glucagon-like peptide-1 receptor agonist; HbA1c, glycated hemoglobin; HF, heart failure; PAD, peripheral artery disease; SGLT2i, sodium–glucose cotransporter-2 inhibitor; T2DM, type 2 diabetes mellitus

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