Temporal Changes in SGLT2 Inhibitor and GLP-1 Receptor Agonist Use in Patients With Chronic Kidney Disease and Type 2 Diabetes, 2012-2023: A US Cohort Study

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SUPPLEMENTAL MATERIALS

Table S1. Description of Optum's de-identified Clinformatics® Data Mart Database (Optum® CDM)

Feature	US, Optum® CDM
Country population	336 million[a]
Database population	68 million (15-20 million annual covered lives)
Database type	Administrative health claims from commercial health plan and Medicare Advantage members
Drug dictionary codes/ therapeutic classification	NDCs
Capture of medication information	Outpatient pharmacy dispensing records
Disease and procedure coding system(s)	ICD-9-CM/ICD-10-CM CPT, HCPCS
Data privacy standards	Optum® CDM was designed to fully comply with HIPAA Privacy Rules. Techniques used to de-identify data include: Removing all direct identifiers for an individual, including name, street address, social security number, phone numbers, and date of birth Reducing the number of data elements that might be matched with an external data source or censoring their content Restrictions from data-use agreements with clients
Definition of type 1 diabetes	Recorded diagnoses from medical claims for encounter data from all available healthcare sites (e.g., inpatient hospital, outpatient hospital, ED, physician's office, surgery center) for all types of provided services. At least two diagnosis codes for type 1 diabetes during the baseline period [− all available, 0 days) were required.

Feature	US, Optum® CDM
Definition of type 2 diabetes	Recorded diagnoses from medical claims for encounter data from all available healthcare sites (e.g., inpatient hospital, outpatient hospital, ED, physician's office, surgery center) for all types of provided services. One diagnosis code for type 2 diabetes during the baseline period (all available, 0 days) was required.
Medical conditions	Recorded diagnoses from medical claims for encounter data from all available healthcare sites (e.g., inpatient hospital, outpatient hospital, ED, physician's office, surgery center) for all types of provided services.
Estimation of days' supply of index medication	Estimated day count the drug supply should last is reported in the data set.
Obesity	BMI not available; obesity defined by diagnosis codes.

BMI = body mass index; Optum® CDM = Optum's de-identified Clinformatics® Data Mart Database; CPT = Current Procedural Terminology; ED = emergency department; GP = general practitioner; HCPCS = Healthcare Common Procedure Coding System; HIPAA = Health Insurance Portability and Accountability Act; ICD-10-CM = *International Classification of Diseases, Tenth Revision, Clinical Modification*; ICD-9-CM = *International Classification of Diseases, Ninth Revision, Clinical Modification*; ICPC = International Classification of Primary Care; NDC = National Drug Code; US = United States.

[a] Population data from the 2023 US census (https://www.census.gov/popclock/).

Table S2. Medication Codes

Drug substance	ATC
SGLT2i drugs	
dapagliflozin	A10BK01, A10BX09 (historical code)
canagliflozin	A10BK02
empagliflozin	A10BK03
ertugliflozin	A10BK04
ipragliflozin	A10BK05
sotagliflozin	A10BK06
luseogliflozin	A10BK07
dapagliflozin and metformin	A10BD15
dapagliflozin, metformin, and saxagliptin	A10BD25
dapagliflozin and saxagliptin	A10BD21
empagliflozin and linagliptin	A10BD19
empagliflozin and metformin	A10BD20
canagliflozin and metformin	A10BD16
ertugliflozin and metformin	A10BD23
ertugliflozin and sitagliptin	A10BD24
GLP-1 RA drugs	
Exenatide	A10BJ01
Liraglutide	A10BJ02
Lixisenatide	A10BJ03
Albiglutide	A10BJ04
Dulaglutide	A10BJ05
Semaglutide	A10BJ06
Lixisenatide and insulin glargine	A10AE54
Liraglutide and insulin degludec	A10AE56
sMRA drugs	
Spironolactone	C03DA01
Potassium canrenoate	C03DA02
Canrenone	C03DA03

Drug substance	ATC
Eplerenone	C03DA04
Finerenone (ns-MRA)	
Finerenone	C03DA05

ATC = Anatomical Therapeutic Chemical; GLP-1 RA = glucagon-like peptide-1 receptor agonist; ns-MRA = nonsteroidal mineralocorticoid receptor antagonists; sMRA = steroidal mineralocorticoid receptor antagonists; SGLT2i = sodium-glucose cotransporter 2 inhibitors.

Table S3. Medication Other Than GLD Recorded 180 Days Before or on the Index Date for the SGLT2i and GLP-1 RA Cohorts

	SGLT2i			GLP-1 RA		
	Earlier period (N = 56,219) [1]	Later period (N = 94,080)	SMD (later vs. earlier)	Earlier period (N = 70,158) [2]	Later period (N = 72,816)	SMD (later vs. earlier)
Cardiovascular medications, n (%)						
Thiazide-like diuretics	17,919 (31.9)	26,012 (27.6)	−0.093	23,031 (32.8)	22,236 (30.5)	−0.049
Loop diuretics	12,595 (22.4)	30,757 (32.7)	0.232	17,894 (25.5)	18,163 (24.9)	−0.013
Potassium-sparing diuretics	1,255 (2.2)	1,534 (1.6)	−0.044	1,703 (2.4)	1,514 (2.1)	−0.023
ACE inhibitors	22,793 (40.5)	31,159 (33.1)	−0.154	28,644 (40.8)	24,253 (33.3)	−0.156
ARB	29,637 (52.7)	55,551 (59.0)	0.128	36,000 (51.3)	40,225 (55.2)	0.079
Beta-blockers	28,416 (50.5)	54,843 (58.3)	0.156	35,476 (50.6)	36,771 (50.5)	−0.001
Direct renin inhibitors	40 (0.1)	23 (< 0.1)	−0.021	59 (0.1)	15 (< 0.1)	−0.028
Angiotensin receptor-neprilysin inhibitors	1,354 (2.4)	5,039 (5.4)	0.153	625 (0.9)	1,567 (2.2)	0.103
Calcium channel blockers	18,711 (33.3)	35,476 (37.7)	0.093	23,752 (33.9)	24,937 (34.2)	0.008
Other antihypertensives	3,519 (6.3)	6,574 (7.0)	0.029	4,939 (7.0)	4,500 (6.2)	−0.035
Statins	43,609 (77.6)	75,405 (80.1)	0.063	53,632 (76.4)	56,981 (78.3)	0.043
Anticoagulants	6,480 (11.5)	17,606 (18.7)	0.202	7,786 (11.1)	9,594 (13.2)	0.064
Digoxin	1,106 (2.0)	1,679 (1.8)	−0.013	1,164 (1.7)	644 (0.9)	−0.069
Nitrates and other vasodilators	4,645 (8.3)	11,103 (11.8)	0.118	5,920 (8.4)	6,312 (8.7)	0.008

	SGLT2i			GLP-1 RA		
	Earlier period (N = 56,219) [1]	**Later period (N = 94,080)**	**SMD (later vs. earlier)**	**Earlier period (N = 70,158) [2]**	**Later period (N = 72,816)**	**SMD (later vs. earlier)**
Aspirin and other antiplatelet agents	7,970 (14.2)	14,431 (15.3)	0.033	9,339 (13.3)	8,949 (12.3)	−0.031
Lipid-lowering drugs other than statins	9,573 (17.0)	14,374 (15.3)	−0.048	11,962 (17.1)	11,588 (15.9)	−0.031
Other medications of interest, n (%)						
Anti-inflammatory drugs (NSAIDs)	9,668 (17.2)	14,077 (15.0)	−0.061	12,271 (17.5)	13,834 (19.0)	0.039
Acetaminophen	9,675 (17.2)	13,385 (14.2)	−0.082	14,200 (20.2)	12,244 (16.8)	−0.088
Anticonvulsants	1,862 (3.3)	3,180 (3.4)	0.004	2,882 (4.1)	3,228 (4.4)	0.016
Anti-infectives, n (%)						
Antibacterial agents	14,964 (26.6)	23,244 (24.7)	−0.044	20,959 (29.9)	20,062 (27.6)	−0.051
Antifungal agents	3,254 (5.8)	4,659 (5.0)	−0.037	5,172 (7.4)	5,684 (7.8)	0.016
Antitubercular agents	45 (0.1)	61 (0.1)	−0.006	64 (0.1)	44 (0.1)	−0.011
Chemotherapeutic agents	1,653 (2.9)	2,689 (2.9)	−0.005	2,031 (2.9)	2,117 (2.9)	0.001
Bronchodilators	7,987 (14.2)	16,621 (17.7)	0.095	11,135 (15.9)	13,476 (18.5)	0.07

ACE = angiotensin-converting enzymes; ARB = angiotensin receptor blockers; GLD = glucose-lowering drug; GLP-1 RA = glucagon-like peptide-1 receptor agonists; NSAID = nonsteroidal anti-inflammatory drug; SGLT2i = sodium-glucose cotransporter 2 inhibitors.

Note: Earlier period (1 January 2012–30 June 2021) results were previously reported [1,2].

Table S4. Markers of Type 2 Diabetes Severity at the Index Date in the SGLT2i and GLP-1 RA Cohorts

	SGLT2i			GLP-1 RA		
	Earlier period (N = 56,219) [1]	**Later period (N = 94,080)**	**SMD (later vs. earlier)[a]**	**Earlier period (N = 70,158) [2]**	**Later period (N = 72,816)**	**SMD (later vs. earlier)[a]**
Time from first recorded type 2 diabetes code at index date (years)						
Mean (SD)	5.1 (3.4)	5.9 (4.1)	0.223	4.9 (3.4)	5.7 (4.1)	0.223
Median (1st, 99th percentile)	4.2 (0, 14)	5.1 (0, 16)	-	4 (0, 14)	4.8 (0, 16)	-
Medications for type 2 diabetes (hypoglycemic agents) ever prescribed from 180 days before and including the index date, n (%)						
GLP-1 RA and fixed-dose combinations	9,989 (17.8)	15,754 (16.7)	−0.027	N/A	N/A	-
SGLT2i and fixed-dose combinations	N/A	N/A	-	9,359 (13.3)	17,010 (23.4)	0.261
Metformin and fixed-dose combinations	33,851 (60.2)	43,614 (46.4)	−0.28	36,888 (52.6)	36,704 (50.4)	−0.043
Sulfonylureas and fixed-dose combinations	21,746 (38.7)	26,363 (28.0)	−0.228	26,089 (37.2)	21,080 (28.9)	−0.176
Alpha-glucosidase inhibitors	343 (0.6)	320 (0.3)	−0.039	369 (0.5)	260 (0.4)	−0.025
Thiazolidinediones	5,285 (9.4)	6,811 (7.2)	−0.078	6,334 (9.0)	5,895 (8.1)	−0.033
DPP-4i and fixed-dose combinations	13,457 (23.9)	12,276 (13.0)	−0.283	17,042 (24.3)	10,655 (14.6)	−0.246

	SGLT2i			GLP-1 RA		
	Earlier period (N = 56,219) [1]	**Later period (N = 94,080)**	**SMD (later vs. earlier)[a]**	**Earlier period (N = 70,158) [2]**	**Later period (N = 72,816)**	**SMD (later vs. earlier)[a]**
Meglitinides (including repaglinide, nateglinide, mitiglinide)	760 (1.4)	969 (1.0)	−0.03	1,000 (1.4)	718 (1.0)	−0.04
Number of type 2 diabetes drug classes ever used 180 days before and including the index date, n (%)						
No therapy	9,013 (16.0)	27,036 (28.7)	0.308	16,185 (23.1)	18,646 (25.6)	0.059
Monotherapy	19,470 (34.6)	36,605 (38.9)	0.089	23,640 (33.7)	26,831 (36.8)	0.066
Dual therapy	18,676 (33.2)	22,837 (24.3)	−0.199	19,721 (28.1)	18,395 (25.3)	−0.064
Triple therapy	7,740 (13.8)	6,641 (7.1)	−0.221	8,635 (12.3)	7,237 (9.9)	−0.075
Quadruple therapy or more	1,320 (2.3)	961 (1.0)	−0.103	1,977 (2.8)	1,707 (2.3)	−0.03
Insulin use recorded 180 days before and including the index date, n (%)	18,447 (32.8)	27,369 (29.1)	−0.081	31,424 (44.8)	25,213 (34.6)	−0.209
HbA_{1c}, n (%)						
HbA_{1c} ≤ 53 mmol/mol or ≤ 7%	7,006 (12.5)	18,486 (19.6)	0.197	7,235 (10.3)	12,512 (17.2)	0.201
HbA_{1c} > 53 mmol/mol and ≤ 63.9 mmol/mol or > 7% and ≤ 8%	8,662 (15.4)	11,972 (12.7)	−0.077	8,846 (12.6)	8,921 (12.3)	−0.011
HbA_{1c} > 63.9 mmol/mol and ≤ 74.9 mmol/mol or > 8% and ≤ 9%	6,930 (12.3)	7,582 (8.1)	−0.141	8,228 (11.7)	6,850 (9.4)	−0.076
HbA_{1c} > 74.9 mmol/mol or > 9%	9,261 (16.5)	8,079 (8.6)	−0.24	12,498 (17.8)	8,894 (12.2)	−0.157
HbA_{1c} missing	24,360 (43.3)	47,961 (51.0)	0.154	33,351 (47.5)	35,639 (48.9)	0.028

	SGLT2i			GLP-1 RA		
	Earlier period (N = 56,219) [1]	**Later period (N = 94,080)**	**SMD (later vs. earlier)[a]**	**Earlier period (N = 70,158) [2]**	**Later period (N = 72,816)**	**SMD (later vs. earlier)[a]**
Other key diagnoses, n (%)						
Hyperkalemia	3,639 (6.5)	9,896 (10.5)	0.145	5,368 (7.7)	5,554 (7.6)	−0.001
Amputation	991 (1.8)	2,185 (2.3)	0.04	1,676 (2.4)	1,679 (2.3)	−0.005
Diabetes Severity Complications Index						
Key diagnoses for scoring of index score, n (%)						
Retinopathy	12,937 (23.0)	24,691 (26.2)	0.075	17,400 (24.8)	18,301 (25.1)	0.008
Nephropathy	33,245 (59.1)	44,587 (47.4)	−0.237	45,553 (64.9)	30,148 (41.4)	−0.485
Neuropathy	22,737 (40.4)	38,614 (41.0)	0.012	31,388 (44.7)	31,302 (43.0)	−0.035
Cerebrovascular	6,854 (12.2)	14,880 (15.8)	0.105	8,670 (12.4)	9,210 (12.6)	0.009
Cardiovascular	28,862 (51.3)	59,596 (63.3)	0.245	35,373 (50.4)	38,497 (52.9)	0.049
Peripheral vascular disease	16,026 (28.5)	32,330 (34.4)	0.126	20,546 (29.3)	22,678 (31.1)	0.04
Metabolic complications	3,343 (5.9)	5,725 (6.1)	0.006	4,994 (7.1)	4,434 (6.1)	−0.041
Index score						
Mean (SD)	2.9 (2.1)	3.3 (2.2)	0.189	3.1 (2.2)	2.9 (2.2)	−0.096
Median (1st, 99th percentile)	3 (0, 8)	3 (0, 9)	-	3 (0, 9)	3 (0, 9)	-

DPP-4i = dipeptidyl peptidase-4 inhibitors; GLP-1 RA = glucagon-like peptide-1 receptor agonists; HbA_{1c} = hemoglobin A_{1c} (glycated hemoglobin); N/A = not applicable; NR = not reportable; SD = standard deviation; SGLT2i = sodium-glucose cotransporter 2 inhibitors; SMD = standardized mean difference; sMRA = steroidal mineralocorticoid receptor antagonists; uACR = urine albumin-creatinine ratio.

Note: Earlier period (1 January 2012–30 June 2021) results were previously reported [1,2]. [a]* "-" indicates SMD not evaluated or not applicable for given variable.

Table S5. Baseline Markers of Severity for Kidney Dysfunction at the Index in the SGLT2i and GLP-1 RA Cohorts

	SGLT2i			GLP-1 RA		
	Earlier period (N = 56,219) [1]	Later period (N = 94,080)	SMD (later vs. earlier)[a]	Earlier period (N = 70,158) [2]	Later period (N = 72,816)	SMD (later vs. earlier)[a]
Time from first recorded CKD code at index date (based on all available data)						
Mean (SD)	3.8 (2.9)	4.8 (3.6)	0.308	3.6 (2.8)	4.6 (3.6)	0.327
Median (1st, 99th percentile)	3.1 (0, 12)	4.0 (0, 15)	-	2.8 (0, 12)	3.7 (0, 15)	-
CKD stage based on eGFR or diagnosis code[†], n (%)						
Stage 1: ≥ 90, normal or high	6,063 (10.8)	4,146 (4.4)	−0.242	6,015 (8.6)	4,919 (6.8)	−0.068
Stage 2: 60-89, mildly decreased	17,470 (31.1)	19,236 (20.4)	−0.245	17,872 (25.5)	18,324 (25.2)	−0.007
Stage 3: mildly to severely decreased	14,800 (26.3)	48,996 (52.1)	0.547	19,345 (27.6)	32,005 (44.0)	0.347
Stage 3a: 45-59, mildly to moderately decreased	9,414 (16.7)	21,545 (22.9)	0.155	11,239 (16.0)	15,938 (21.9)	0.15
Stage 3b: 30-44, moderately to severely decreased	3,521 (6.3)	15,999 (17.0)	0.34	6,376 (9.1)	8,964 (12.3)	0.104
Stage 3 without specification of substage	1,865 (3.3)	11,452 (12.2)	0.336	1,730 (2.5)	7,103 (9.8)	0.308
Stage 4: 15-29, severely decreased	1,380 (2.5)	5,391 (5.7)	0.166	3,590 (5.1)	3,514 (4.8)	−0.013
Stage 5: < 15 OR treated by dialysis, kidney failure	345 (0.6)	346 (0.4)	−0.035	343 (0.5)	282 (0.4)	−0.015
Unspecified stage	4,818 (8.6)	7,487 (8.0)	−0.022	7,763 (11.1)	5,038 (6.9)	−0.145

	SGLT2i			GLP-1 RA		
	Earlier period (N = 56,219) [1]	Later period (N = 94,080)	SMD (later vs. earlier)[a]	Earlier period (N = 70,158) [2]	Later period (N = 72,816)	SMD (later vs. earlier)[a]
No assessment of eGFR or diagnosis code in the year before index date	11,343 (20.2)	8,478 (9.0)	−0.32	15,230 (21.7)	8,734 (12.0)	−0.262
CKD stage based on diagnosis only,[b] n (%)						
Stage 1: ≥ 90, normal or high	1,291 (2.3)	1,001 (1.1)	−0.096	1,398 (2.0)	887 (1.2)	-0.062
Stage 2: 60-89, mildly decreased	8,220 (14.6)	9,437 (10.0)	−0.14	8,997 (12.8)	8,371 (11.5)	−0.041
Stage 3: mildly to severely decreased	4,510 (8.0)	41,302 (43.9)	0.897	4,048 (5.8)	25,894 (35.6)	0.791
Stage 3a: 45-59, mildly to moderately decreased	1,202 (2.1)	13,744 (14.6)	0.462	1,000 (1.4)	9,456 (13.0)	0.459
Stage 3b: 30-44, moderately to severely decreased	806 (1.4)	11,207 (11.9)	0.429	787 (1.1)	6,126 (8.4)	0.347
Stage 3 without specification of substage	2,502 (4.5)	16,351 (17.4)	0.424	2,261 (3.2)	10,312 (14.2)	0.396
Stage 4: 15-29, severely decreased	1,316 (2.3)	4,810 (5.1)	0.147	3,491 (5.0)	3,123 (4.3)	−0.033
Stage 5: < 15 OR treated by dialysis, kidney failure	0 (0)	0 (0)	-	0 (0)	0 (0)	-
Unspecified stage	7,289 (13.0)	10,282 (10.9)	−0.063	11,543 (16.5)	7,192 (9.9)	−0.195
No diagnosis code in the year before index	33,593 (59.8)	27,248 (29.0)	−0.652	40,681 (58.0)	27,349 (37.6)	−0.418
CKD stage based on eGFR only,[b] n (%)						
Stage 1: ≥ 90, normal or high	6,119 (10.9)	4,259 (4.5)	−0.24	5,965 (8.5)	5,057 (6.9)	−0.058
Stage 2: 60-89, mildly decreased	14,536 (25.9)	16,985 (18.1)	−0.189	14,293 (20.4)	16,064 (22.1)	0.041
Stage 3: mildly to severely decreased	14,069 (25.0)	34,138 (36.3)	0.246	19,729 (28.1)	21,967 (30.2)	0.045
Stage 3a: 45-59, mildly to moderately decreased	10,093 (18.0)	19,324 (20.5)	0.066	12,229 (17.4)	13,801 (19.0)	0.039

	SGLT2i			GLP-1 RA		
	Earlier period (N = 56,219) [1]	**Later period (N = 94,080)**	**SMD (later vs. earlier)[a]**	**Earlier period (N = 70,158) [2]**	**Later period (N = 72,816)**	**SMD (later vs. earlier)[a]**
Stage 3b: 30-44, moderately to severely decreased	3,976 (7.1)	14,814 (15.7)	0.275	7,500 (10.7)	8,166 (11.2)	0.017
Stage 3 without specification of substage	NA	NA	-	NA	NA	-
Stage 4: 15-29, severely decreased	810 (1.4)	3,779 (4.0)	0.159	1,892 (2.7)	2,377 (3.3)	0.033
Stage 5: < 15 OR treated by dialysis, kidney failure	392 (0.7)	471 (0.5)	−0.025	416 (0.6)	370 (0.5)	−0.011
No assessment of eGFR in the year before index date	20,293 (36.1)	34,448 (36.6)	0.011	27,863 (39.7)	26,981 (37.1)	−0.055
CKD stage based on uACR[b], n (%)						
A1: < 30, normal to mildly increased	6,301 (11.2)	8,141 (8.7)	−0.085	7,159 (10.2)	7,790 (10.7)	0.016
A2: 30-300, moderately increased (formerly “microalbuminuria”)	6,857 (12.2)	9,473 (10.1)	−0.068	7,967 (11.4)	7,250 (10.0)	−0.045
A3: > 300, severely increased (includes nephrotic syndrome, > ~ 2,000)	2,736 (4.9)	5,773 (6.1)	0.056	3,691 (5.3)	3,003 (4.1)	−0.054
No assessment of uACR recorded in year before index date	40,325 (71.7)	70,693 (75.1)	0.077	51,341 (73.2)	54,773 (75.2)	0.047
“Any historical use” of drug classes						
Drug classes used, n (%)						
Finerenone	N/A	38 (< 0.1)	-	N/A	30 (< 0.1)	-

	SGLT2i			GLP-1 RA		
	Earlier period (N = 56,219) [1]	**Later period (N = 94,080)**	**SMD (later vs. earlier)[a]**	**Earlier period (N = 70,158) [2]**	**Later period (N = 72,816)**	**SMD (later vs. earlier)[a]**
SGLT2i and fixed-dose combinations	3,864 (6.9)	10,532 (11.2)	0.151	9,769 (13.9)	16,703 (22.9)	0.234
GLP-1 RA and fixed-dose combinations	10,968 (19.5)	19,360 (20.6)	0.027	9,249 (13.2)	14,186 (19.5)	0.171
sMRA	5,297 (9.4)	13,139 (14.0)	0.142	6,454 (9.2)	8,190 (11.2)	0.068
ACEi or ARB	49,332 (87.7)	83,940 (89.2)	0.046	61,102 (87.1)	63,418 (87.1)	0
Number of drug classes used, n (%)						
0	5,534 (9.8)	7,740 (8.2)	−0.056	7,307 (10.4)	6,866 (9.4)	−0.033
1	34,588 (61.5)	53,513 (56.9)	−0.095	42,704 (60.9)	37,334 (51.3)	−0.194
2	13,545 (24.1)	25,646 (27.3)	0.073	16,766 (23.9)	21,317 (29.3)	0.122
3	2,425 (4.3)	6,521 (6.9)	0.114	3,186 (4.5)	6,639 (9.1)	0.182
4	127 (0.2)	659 (0.7)	0.07	195 (0.3)	658 (0.9)	0.082
> 4	N/A	N/A	N/A	N/A	N/A	N/A
“Any previous use” of drug classes						
Drug classes used, n (%)						
Finerenone	N/A	209 (0.2)	-	N/A	166 (0.2)	-
SGLT2i and fixed-dose combinations	N/A	N/A	-	9,255 (13.2)	16,391 (22.5)	0.245
GLP-1 RA and fixed-dose combinations	9,885 (17.6)	16,204 (17.2)	−0.009	N/A	N/A	-
sMRA	4,273 (7.6)	10,233 (10.9)	0.113	5,163 (7.4)	6,133 (8.4)	0.039
ACEi or ARB	46,279 (82.3)	77,009 (81.9)	−0.012	57,027 (81.3)	58,037 (79.7)	−0.04

	SGLT2i			GLP-1 RA		
	Earlier period (N = 56,219) [1]	**Later period (N = 94,080)**	**SMD (later vs. earlier)[a]**	**Earlier period (N = 70,158) [2]**	**Later period (N = 72,816)**	**SMD (later vs. earlier)[a]**
Number of drug classes used, n (%)						
0	7,958 (14.2)	13,029 (13.8)	−0.009	10,842 (15.5)	11,359 (15.6)	0.004
1	36,758 (65.4)	59,893 (63.7)	−0.036	47,715 (68.0)	43,754 (60.1)	−0.166
2	10,830 (19.3)	19,715 (21.0)	0.042	11,073 (15.8)	16,146 (22.2)	0.164
3	673 (1.2)	1,440 (1.5)	0.029	528 (0.8)	1,547 (2.1)	0.115
≥4	N/A	N/A	N/A	N/A	N/A	N/A
“Any recent use” of drug classes						
Drug classes used, n (%)						
Finerenone		224 (0.2)	-		199 (0.3)	-
SGLT2i and fixed-dose combinations	N/A	N/A	-	7,895 (11.3)	14,492 (19.9)	**0.24**
GLP-1 RA and fixed-dose combinations	8,655 (15.4)	13,228 (14.1)	−0.038	N/A	N/A	-
sMRA	3,669 (6.5)	8,966 (9.5)	0.111	4,165 (5.9)	4,991 (6.9)	0.038
ACEi or ARB	41,452 (73.7)	68,229 (72.5)	−0.027	50,855 (72.5)	51,831 (71.2)	−0.029
Number of drug classes used, n (%)						
0	11,963 (21.3)	20,387 (21.7)	0.01	16,339 (23.3)	16,397 (22.5)	−0.018
1	35,173 (62.6)	57,618 (61.2)	−0.027	45,059 (64.2)	42,378 (58.2)	−0.124
2	8,646 (15.4)	15,198 (16.2)	0.021	8,424 (12.0)	12,990 (17.8)	0.164
3	437 (0.8)	875 (0.9)	0.017	336 (0.5)	1,049 (1.4)	0.099

	SGLT2i			GLP-1 RA		
	Earlier period (N = 56,219) [1]	**Later period (N = 94,080)**	**SMD (later vs. earlier)[a]**	**Earlier period (N = 70,158) [2]**	**Later period (N = 72,816)**	**SMD (later vs. earlier)[a]**
≥4	N/A	N/A	N/A	N/A	N/A	N/A
Clinical conditions associated with risk of CKD						
Hypertension, n (%)	52,558 (93.5)	89,006 (94.6)	0.047	65,828 (93.8)	67,617 (92.9)	−0.039
Glomerulonephritis (all causes), n (%)	965 (1.7)	878 (0.9)	−0.069	1,515 (2.2)	452 (0.6)	−0.132
Renovascular disease, n (%)	532 (0.9)	1,286 (1.4)	0.039	661 (0.9)	712 (1.0)	0.004
Autoimmune disease, n (%)	3,387 (6.0)	5,334 (5.7)	−0.015	4,525 (6.4)	4,687 (6.4)	−0.001
Polycystic kidney disease, n (%)	170 (0.3)	318 (0.3)	0.006	329 (0.5)	223 (0.3)	−0.026
Gout or hyperuricemia, n (%)	6,046 (10.8)	12,465 (13.2)	0.077	8,193 (11.7)	7,780 (10.7)	−0.032
Hospitalizations for acute kidney injury in the previous year						
n (%)	557 (1.0)	1,488 (1.6)	-	941 (1.3)	861 (1.2)	-
Mean (SD)	1.0 (0.3)	1.1 (0.3)	0.234	1.1 (0.3)	1.1 (0.3)	−0.153
Median (1st, 99th percentile)	1 (1, 2)	1 (1, 2)	-	1 (1,2)	1 (1,2)	-

ACEi = angiotensin-converting enzyme inhibitors; ARB = angiotensin receptor blockers; CKD = chronic kidney disease; eGFR = estimated glomerular filtration rate; GLP-1 RA = glucagon-like peptide-1 receptor agonists; NA = not available; N/A = not applicable; SD = standard deviation; SGLT2i = sodium-glucose cotransporter 2 inhibitors; SMD = standardized mean difference; sMRA = steroidal mineralocorticoid receptor antagonists; uACR = urine albumin-to-creatinine ratio.

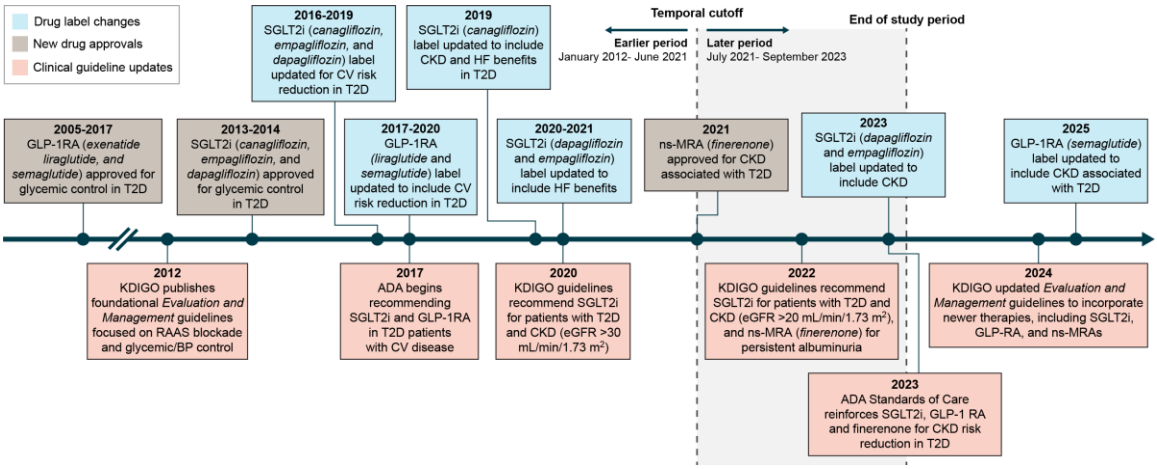
Note: Recent use: defined in the 90 days before the index date (study days [−90,−1]); Previous use: defined using the remaining time of the previous year (study days [−365,−91]); Any historical use: defined as before the year before the index date (study days [−∞,−366]). Earlier period (1 January 2012–30 June 2021) results were previously reported [1,2].

[a] "-" indicates SMD not evaluated or not applicable for given variable.

[b] Lookback period for these variables is the year before or on the index date (study days [−365,0]).

[c] For reporting compliance, data in some patient groups are suppressed ("N/A").

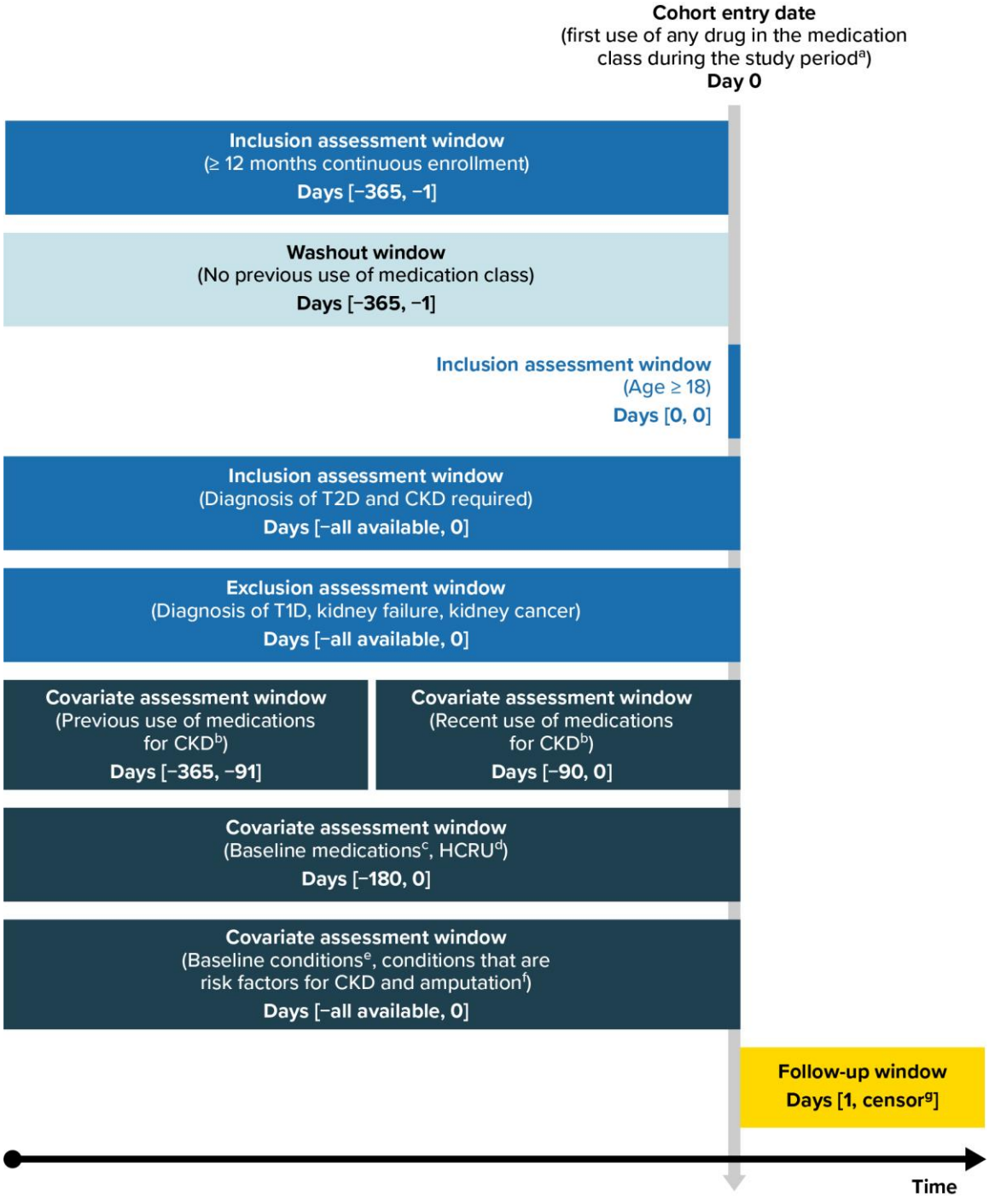
Figure S1. Study Timeline Relative to New Drug Approvals, Label Expansions, and Updated Clinical Guideline Recommendations for Adult CKD-type 2 Diabetes Indications in the US



ACE = angiotensin-converting enzyme; ADA = American Diabetes Association; ARB = angiotensin receptor blockers; BP = blood pressure; CKD = chronic kidney disease; CV = cardiovascular; eGFR = estimated glomerular filtration rate; GLP-1 RA = glucagon-like peptide-1 receptor agonists; KDIGO = Kidney Disease Improving Global Outcomes; ns-MRA = nonsteroidal mineralocorticoid receptor antagonists; RAAS = renin-angiotensin-aldosterone system; SGLT2i = sodium-glucose cotransporter 2 inhibitors; T2D = type 2 diabetes; US = United States.

Note: Approval references: GLP-1 RA [exenatide 2005 [3], liraglutide 2010 [4], semaglutide 2017 [5]], SGLT2i [canagliflozin 2013 [6], empagliflozin 2014 [7], dapagliflozin 2014 [8]], ns-MRA [finerenone 2021 [9]]; Label change references: GLP-1 RA [liraglutide 2017 [10], semaglutide 2020 [11], semaglutide 2025 [12]], SGLT2i [empagliflozin 2016 [13], canagliflozin 2018 [14], canagliflozin 2019 [15], dapagliflozin 2019 [16], dapagliflozin 2020 [17], empagliflozin 2021 [18], dapagliflozin 2021 [19], empagliflozin 2023 [20]]; Guideline references: KDIGO [2012 [21], 2020 [22], 2022 [23], 2024 [24]], ADA [2017 [25], 2023 [26]].

Figure S2. Variable Assessment Windows Relative to the Study Index Date for Medication-Specific Cohorts



ACEi = angiotensin-converting enzyme inhibitors; ARB = angiotensin receptor blocker; CKD = chronic kidney disease; COPD = chronic obstructive pulmonary disease; CVD = cardiovascular disease; GLP-1 RA = glucagon-like peptide-1 receptor agonist; GP = general practitioner; HCRU = healthcare resource use; HIV = human immunodeficiency virus; MRA = mineralocorticoid receptor antagonist; SGLT2i = sodium-glucose cotransporter 2 inhibitors; T1D = type 1 diabetes; T2D = type 2 diabetes.

[a] Study period: 9 July 2012 through 30 September 2023.

[b] SGLT2i, GLP-1 RA, other nonsteroidal MRA, ACEi, ARB.

[c] Cardiovascular medications (antihypertensives, beta-blockers, direct renin inhibitors, angiotensin receptor-neprilysin inhibitor, lipid-lowering medications, anticoagulants, aspirin and other antiplatelets [e.g., clopidogrel, ticlopidine, prasugrel], digoxin, nitrates), anti-inflammatory drugs, antibiotics, other (acetaminophen, anticonvulsants, antifungals, antituberculars, chemotherapeutic agents).

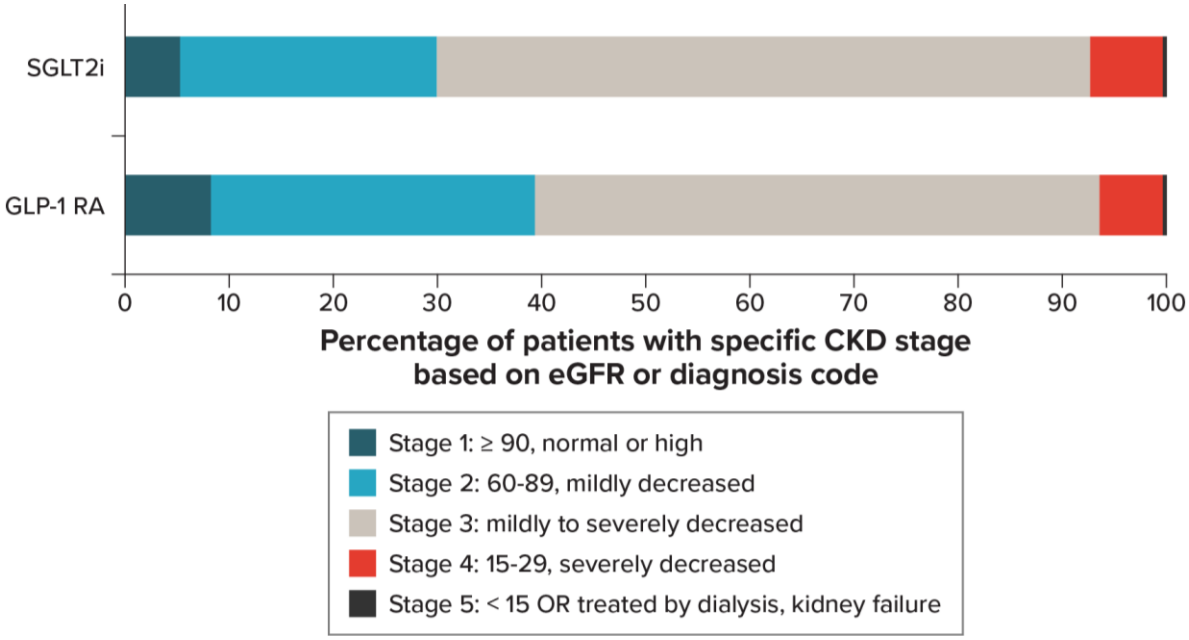
[d] HCRU measures: GP visits, hospital visits, hospitalizations, specialist visits, emergency department visits.

[e] Baseline conditions: chronic CVD, hypertension, diabetes severity and complications, hyperlipidemia, lifestyle CVD risk factors (obesity), stage of CKD, other kidney disorders, liver disease, HIV infection, dementia, COPD, and malignancies (other than kidney).

[f] Conditions predisposing individuals to CKD include hypertension, glomerulonephritis, renovascular disease, polycystic kidney disease, and autoimmune disease; amputations refer to amputations of the lower extremities.

[g] Censored at the earliest of date of death, disenrollment, developing kidney cancer, kidney failure, or end of the study period.

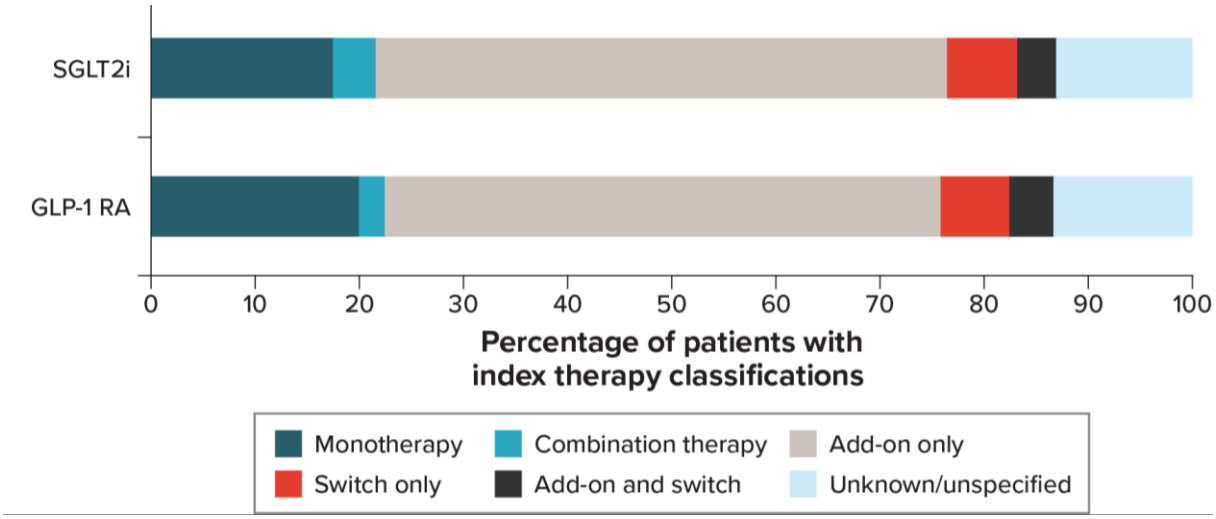
Figure S3. Definition of CKD Stage at the Index Date Based on eGFR Value or Diagnosis Code in the SGLT2i and GLP-1 RA Cohorts



CKD = chronic kidney disease; eGFR = estimated glomerular filtration rate; GLP-1 RA = glucagon-like peptide-1 receptor agonists; SGLT2i = sodium-glucose cotransporter 2 inhibitors; uACR = urine albumin-to-creatinine.

Note: All patients met the inclusion eligibility criteria for CKD, which was assessed through diagnosis codes, eGFR test results, or uACR test results. Percentages were calculated among patients who have staging information available.

Figure S4. Classification of Index Therapy in the SGLT2i and GLP-1 RA Cohorts



GLP-1 RA = glucagon-like peptide-1 receptor agonists; SGLT2i = sodium-glucose cotransporter 2 inhibitors.

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