SUPPLEMENTARY MATERIAL

Outcomes in Users of SGLT2 Inhibitors or GLP-1 RA With Type 2 Diabetes and Chronic Kidney Disease

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Appendix A: Description of Data Sources

Table A1. Summary of Characteristics of Participating Data Sources

Feature	Denmark, DNHR	Spain, VID	Japan, J-CKD-DB-Ex	US, Optum® EHR
General information				
Country population	5,974,086 [a]	Valencia region, 5,319,448 [b]	123,850,000 [c]	337 million [d]
Database population	5.8 million	5 million	--	
Database type	National health record databases capable of linkage with other databases through a unique personal identification number	Regional health record databases capable of linkage with other databases through a unique personal identification number	Hospital-based, longitudinal electronic medical record database	EHRs from multispecialty practices, small group practices, physician providers, and integrated delivery networks throughout the US
Drug dictionary codes/therapeutic classification	ATC	ATC	National drug codes in Japan, HOT codes	NDC [e]
Capture of medication information	Outpatient pharmacy dispensed prescriptions in Danish National Prescription Registry	Written prescription and dispensing information linked at the individual level. Prescription data were used to define the index date and dispensing data to estimate days covered with the medication.	Written prescriptions from hospital and outpatient encounters. Under Japanese regulation, any new medication should be renewed every 2 weeks during the first year that the medication is on the market, and for longer periods (e.g., 30 days) thereafter.	Written prescriptions records in the EHR. Prescription dispensing records are not captured.
Disease and procedure coding system(s)	ICD-10 Procedure codes: NCSP	ICD-9-CM, ICD-10-ES	ICD-10 Disease name code	ICD-9-CM/ICD-10-CM CPT, HCPCS

Feature	Denmark, DNHR	Spain, VID	Japan, J-CKD-DB-Ex	US, Optum® EHR
Data privacy standards	Cell frequencies (categorical variables) of less than 5 are not reported, and related cells have additional masking, if needed, to prevent back calculation; for continuous variables, 1st and 99th percentiles are reported instead of minimum and maximum values.	Categorical variables with low counts, or low frequencies for a specific level of a categorical variable, are not reported. Masking may occur to prevent back calculation of low counts. For continuous variables, the 1st and 99th percentiles are reported instead of minimum and maximum values.	Categorical variables with low counts are not reported. For continuous variables, the 1st and 99th percentiles are reported instead of minimum and maximum values. Masking may occur to prevent back calculation of low count events.	Fully compliant 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 number(s), 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
Study-specific information				
Definition of T1D	Aged < 30 years at first diabetes record (hospital diagnosis or medication prescription); if first diabetes record is on or after 1995, mandatory use of insulin around the first record is required.	ICD codes (recorded diagnosis on the index date in the electronic medical record in VID covering primary and secondary care)	ICD-10 codes	Two ICD-10-CM diagnosis codes during the baseline period (all available, 0 days) were required.

Feature	Denmark, DNHR	Spain, VID	Japan, J-CKD-DB-Ex	US, Optum® EHR
Definition of T2D	Redemption of prescription for a glucose-lowering medication from a community pharmacy or a hospital contact with a T2D diagnosis. Furthermore, aged ≥ 30 years at first diabetes record.	ICD codes (recorded diagnosis on the index date in the electronic medical record in VID covering primary and secondary care)	ICD-10 codes	One ICD-10-CM diagnosis code for T2D during the baseline period (all available, 0 days) was required.
Medical conditions	Diagnosis coded on or before the index date during an inpatient, outpatient, or emergency department visit using both primary and secondary diagnoses as recorded in the Danish National Patient Registry.	ICD codes (recorded diagnosis on the index date in the electronic medical record in VID covering primary and secondary care).	Recorded diagnoses in inpatient and outpatient settings in hospital care.	Medical conditions were obtained based on the presence of 1 ICD-10-CM diagnosis code for that condition during the baseline period. The absence of codes was deemed to indicate the absence of disease.
Obesity	BMI not available; obesity defined by diagnosis codes.	BMI available, but it may be affected by registration bias or selective reporting.	BMI not available; obesity defined by diagnosis codes.	BMI available

ATC = Anatomical Therapeutic Chemical classification system; BMI = body mass index; CPT = Current Procedural Terminology; DNHR = Danish National Health Registers; EHR = electronic health record; GP = general practitioner; HCPCS = Healthcare Common Procedure Coding System; HIPAA = Health Insurance Portability and Accountability Act; HOT = standard master codes for pharmaceutical products (http://www2.medis.or.jp/master/hcode/); ICD-10 = *International Classification of Diseases, Tenth Revision*; ICD-10-CM = *International Classification of Diseases, Tenth Revision, Clinical Modification*; ICD-10-ES = *International Classification of Diseases, Tenth Revision, Spanish Version*; ICD-9-CM = *International Classification of Diseases, Ninth Revision, Clinical Modification*; ICPC = International Classification of Primary Care; J-CKD-DB-Ex = Japan Chronic Kidney Disease Database Extension; NCSP = NOMESCO Classification of Surgical Procedures; NDC = National Drug Code; Optum® EHR = Optum® de-identified Electronic Health Record data set; PHARMO = PHARMO Data Network; T1D = type 1 diabetes; T2D = type 2 diabetes; US = United States; VID = Valencia Health System Integrated Database; WHO = World Health Organization.

[a] Population of Denmark from Statistics Denmark in August 2024. Available at: Population figures - Statistics Denmark (dst.dk).

[b] Population of Spain in 2024 by autonomous community. Available at: https://www.statista.com/statistics/445549/population-of-spain-by-autonomous-community/.

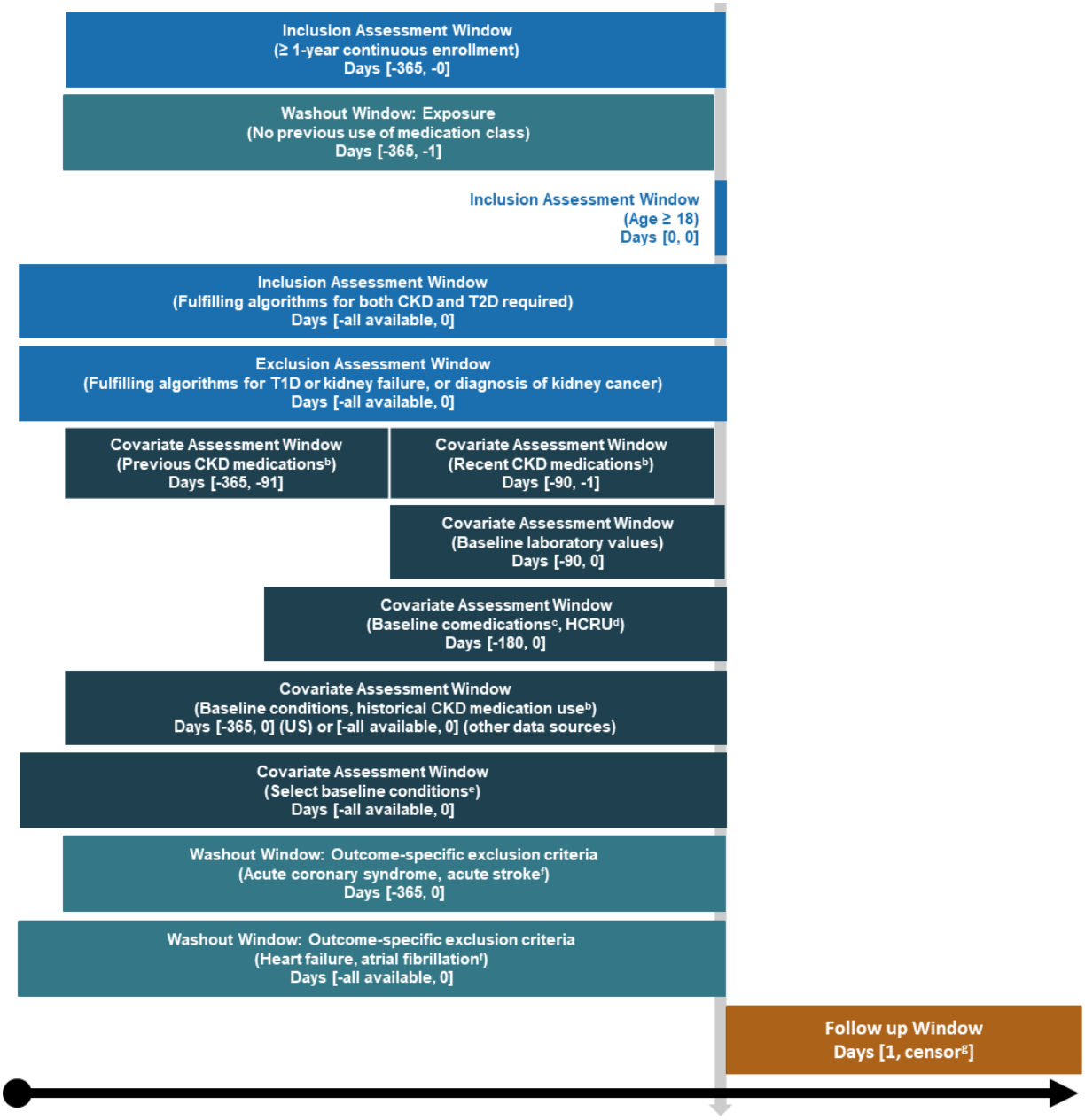
[c] Population data from Statistics Bureau of Japan 2024. Available at: https://www.stat.go.jp/english/index.html.

[d] Population data from the 2024 US census. Available at: https://www.census.gov/popclock/.

[e] NDCs corresponding to the relevant ATC codes were identifie

Appendix B: Variable Assessment and Classification of Index Medications

Figure B1. Variable Assessment Windows Relative to the Study Index Date for the SGLT2i and GLP-1 RA Cohorts



ACEi = angiotensin-converting enzyme inhibitors; ARB = angiotensin receptor blockers; CKD = chronic kidney disease; GLP-1 RA = glucagon-like peptide-1 receptor agonists; HCU = healthcare utilization; SGLT2i = sodium-glucose cotransporter 2 inhibitors; T2D = type 2 diabetes.

[a] Study period: 01 January 2012 through 31 December 2019.

[b] SGLT2i, GLP1 RA, ACEi, ARB.

[c] Cardiovascular medications (antihypertensives, cholesterol-lowering medications, anticoagulants, aspirin and other antiplatelets [e.g., clopidogrel, ticlopidine, prasugrel], digoxin, nitrates), anti-inflammatory medications, antibiotics, other (acetaminophen, anticonvulsants, antifungals, antituberculars, chemotherapeutic agents).

[d] Chronic cardiovascular disease, hypertension, diabetes severity and complications, hyperlipidemia, lifestyle cardiovascular disease risk factors (smoking, obesity), stage of CKD, other kidney disorders, liver disease, comorbidities, general practitioner visits, hospital visits, hospitalizations, specialist visits, emergency department visits.

[e] Conditions requiring ≥ 365 days for accurate assessment (e.g., amputation).

[f] Outcome-specific exclusion criteria were assessed in outcome-specific washout periods, but these washout periods were not applied before cohort selection; outcome-specific washout periods were applied separately before outcome-specific analyses.

[g] Censored at the earliest of the following: end of the study period (31 December 2019), disenrollment, death, discontinuation of medication class, or development of kidney failure or kidney cancer.

Note that unique individuals could be included in both cohorts if they separately met the eligibility criteria for both.

Source: Figure based on Schneeweiss et al. [1].

Table B1. List of Study Medications by Class and ATC Code

Medication class	Drug substance	ATC code
SGLT2i	Dapagliflozin	A10BK01
	Canagliflozin	A10BK02
	Empagliflozin	A10BK03
	Ertugliflozin	A10BK04
	Ipragliflozin	A10BK05
	Sotagliflozin	A10BK06
	Luseogliflozin	A10BK07
	Tofogliflozin	Not available
	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
	Canagliflozin and teneligliptin	Not available
	Ipragliflozin and sitagliptin	Not available
GLP-1 RA	Exenatide	A10BJ01
	Liraglutide	A10BJ02
	Lixisenatide	A10BJ03
	Albiglutide	A10BJ04
	Dulaglutide	A10BJ05
	Semaglutide	A10BJ06
	Lixisenatide and insulin glargine	A10AE54
	Liraglutide and insulin degludec	A10AE56

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

Table B2. Primary Outcome Definitions

Primary Outcome	Definition
Kidney failure	Identified through recorded diagnosis codes for CKD stage 5 or end-stage kidney disease, repeated eGFR measurements <15 mL/min/1.73m^2, dependence on dialysis, or kidney transplant
Acute coronary syndrome	Inpatient diagnosis of acute myocardial infarction or unstable angina
Stroke	Inpatient diagnosis of ischemic, hemorrhagic, or unspecific stroke
Congestive heart failure	Inpatient or emergency department diagnosis of heart failure
Atrial fibrillation	Inpatient, emergency department, or non-hospitalized diagnoses of atrial fibrillation

ATC = Anatomical Therapeutic Chemical; CKD = chronic kidney disease; eGFR = estimated glomerular filtration rate; GLP-1 RA = glucagon-like peptide-1 receptor agonists; SGLT2i = sodium-glucose cotransporter 2 inhibitors.

Appendix C: Additional Results

Table C1. Attrition of cohorts of SGLT2i users, by data source

	DNHR	VID	J-CKD-DB-Ex	Optum® EHR
All patients in the current database build	NE	NE	251,659	NE
All patients with recorded study medication use	92,508	107,814	4,833	510,549
Total number of potential index dates	1,090,250	2,372,569	7,709	3,062,715
Excluded due to potential index dates reported outside the study period	561,336 (51.5%)	0 (0%)	0 (0%)	1,450,997 (47.4%)
Total number of potential index dates during the study period	528,914	2,372,569	7,709	1,611,718
Excluded patients with < 12 months of lookback time at the potential index date	5,589 (1.1%)	5,794 (0.2%)	1,889 (24.5%)	28,998 (1.8%)
Excluded for a recorded prescription/dispensing of any SGLT2i during the 12 months before the potential index date	471,994 (89.2%)	2,259,458 (95.2%)	2,701 (35.0%)	1,244,991 (77.2%)
Excluded patients aged < 18 years at the potential index date	7 (< 0.1%)	84 (< 0.1%)	5 (0.1%)	158 (< 0.1%)
Excluded for no T2D diagnosis recorded on or before the potential index date	0 (0%)	3,721 (0.2%)	1,893 (24.6%)	87,498 (5.4%)
Excluded for no CKD diagnosis recorded on or before the potential index date	382,342 (72.3%)	1,811,782 (76.4%)	4,486 (58.2%)	1,287,922 (79.9%)
Patients with potential index dates meeting the inclusion criteria	13,272	23,632	1,335	64,740
Excluded for T1D identified on or before the potential index date	88 (0.7%)	0 (0%)	434 (32.5%)	1,435 (2.2%)
Excluded for kidney cancer recorded on or before the potential index date	91 (0.7%)	102 (0.4%)	46 (3.4%)	464 (0.7%)
Excluded for kidney failure recorded on or before the potential index date[a]	20 (0.2%)	240 (1.0%)	50 (3.7%)	1,089 (1.7%)
Number of patients with potential index dates eligible for study inclusion	13,076	23,293	835	61,828
Subsequent index dates removed due to inclusion of an earlier eligible index date	575 (4.4%)	889 (3.8%)	23 (2.8%)	6,593 (10.7%)
Final patient sample used for analyses	12,501	22,404	811	54,308

CKD = chronic kidney disease; DNHR = Danish National Health Registers; J-CKD-DB-Ex = Japan Chronic Kidney Disease Database Extension; NE = not estimable; Optum® EHR = Optum® de-identified Electronic Health Record data set; SGLT2i = sodium-glucose cotransporter 2 inhibitors; T1D = type 1 diabetes; T2D = type 2 diabetes; VID = Valencia Health System Integrated Database.

Note: The selection of each cohort involved evaluating multiple potential index dates per patient.

[a] Patients may have had more than 1 indicator of kidney failure.

Table C2. Attrition of cohorts of GLP-1 RA users, by data source

	DNHR	VID	J-CKD-DB-Ex	Optum® EHR
All patients in the current database build	NE	NE	251,659	NE
All patients with recorded study medication use	104,689	34,125	2,211	722,835
Total number of potential index dates	2,612,591	1,149,538	4,521	4,723,888
Excluded due to potential index dates reported outside the study period	1,148,801 (44.0%)	0 (0%)	0 (0%)	2,526,720 (53.5%)
Total number of potential index dates during the study period	1,463,790	1,149,538	4,521	2,197,168
Excluded patients with < 12 months of lookback time at the potential index date	49,679 (3.4%)	1,980 (0.2%)	1,609 (35.6%)	35,282 (1.6%)
Excluded for a recorded prescription/dispensing of any GLP-1 RA during the 12 months before the potential index date	1,410,936 (96.4%)	1,114,948 (97.0%)	2,181 (48.2%)	1,706,292 (77.7%)
Excluded patients aged < 18 years at the potential index date	286 (< 0.1%)	204 (< 0.1%)	4 (0.1%)	525 (< 0.1%)
Excluded for no T2D diagnosis recorded on or before the potential index date	0 (0%)	3,895 (0.3%)	1,183 (26.2%)	234,243 (10.7%)
Excluded for no CKD diagnosis recorded on or before the potential index date	1,043,130 (71.3%)	839,070 (73.0%)	2,371 (52.4%)	1,627,628 (74.1%)
Patients with potential index dates meeting the inclusion criteria	11,584	9,051	463	101,364
Excluded for T1D identified on or before the potential index date	158 (1.4%)	0 (0%)	160 (34.6%)	2,712 (2.7%)
Excluded for kidney cancer recorded on or before the potential index date	130 (1.1%)	68 (0.8%)	27 (5.8%)	1,192 (1.2%)
Excluded for kidney failure recorded on or before the potential index date[a]	86 (0.7%)	231 (2.6%)	86 (18.6%)	3,659 (3.6%)
Number of patients with potential index dates eligible for study inclusion	11,217	8,756	222	94,065
Subsequent index dates removed due to inclusion of an earlier eligible index date	521 (4.6%)	439 (5.0%)	2 (0.9%)	15,131 (16.1%)
Final patient sample used for analyses	10,696	8,317	219	78,934

CKD = chronic kidney disease; DNHR = Danish National Health Registers; GLP-1 RA = glucagon-like peptide-1 receptor agonists; J-CKD-DB-Ex = Japan Chronic Kidney Disease Database Extension; NE = not estimable; Optum® EHR = Optum® de-identified Electronic Health Record data set; T1D = type 1 diabetes; T2D = type 2 diabetes; VID = Valencia Health System Integrated Database.

Note: The selection of each cohort involved evaluating multiple potential index dates per patient.

[a] Patients may have had more than 1 indicator of kidney failure.

Table C3. Selected Baseline Characteristics of New Users of SGLT2i and GLP-1 RA Medications: DNHR

Characteristic	SGLT2i (n = 12,501)	GLP-1 RA (n = 10,696)
Age at the index date, years		
Mean (SD)	65.0 (11.3)	65.3 (11.5)
Median (1st, 99th percentiles)	66 (35, 87)	67 (34, 87)
Female sex, n (%)	4,485 (35.9%)	4,281 (40.0%)
Calendar year of index date, n (%)		
2012	0	435 (4.1%)
2013	123 (1.0%)	290 (2.7%)
2014	231 (1.8%)	270 (2.5%)
2015	666 (5.3%)	590 (5.5%)
2016	1,651 (13.2%)	1,024 (9.6%)
2017	2,663 (21.3%)	1,585 (14.8%)
2018	3,276 (26.2%)	2,526 (23.6%)
2019	3,891 (31.1%)	3,976 (37.2%)
Obesity, yes (by diagnosis), n (%)	3,558 (28.5%)	3,645 (34.1%)
Smoking, current smoker, n (%)	1,520 (12.2%)	1,408 (13.2%)
Alcohol abuse, n (%)	570 (4.6%)	462 (4.3%)
Duration of T2D at the index date, years, mean (SD)	11.4 (6.2)	11.8 (6.4)
Medications for T2D (hypoglycemic agents) ever prescribed from 180 days before and including the index date, n (%)		
GLP-1 RA and fixed-dose combinations	3,223 (25.8%)	NA
SGLT2i and fixed-dose combinations	NA	2,355 (22.0%)
Metformin and fixed-dose combinations	10,709 (85.7%)	8,212 (76.8%)
Sulfonylureas and fixed-dose combinations	2,198 (17.6%)	1,676 (15.7%)
Alpha-glucosidase inhibitors	NR	NR
Thiazolidinediones	10 (0.1%)	8 (0.1%)
Dipeptidyl peptidase-4 inhibitors and fixed-dose combinations	3,993 (31.9%)	3,958 (37.0%)
Meglitinides (e.g., repaglinide, nateglinide, mitiglinide)	46 (0.4%)	36 (0.3%)
Insulin use recorded in the 180 days before and including the index date, n (%)	4,134 (33.1%)	4,881 (45.6%)
HbA_{1c}, n (%)		

Characteristic	SGLT2i (n = 12,501)	GLP-1 RA (n = 10,696)
HbA_{1c} ≤ 53 mmol/mol or ≤ 7%	1,388 (11.1%)	1,290 (12.1%)
HbA_{1c} > 53 to ≤ 63.9 mmol/mol or > 7% to ≤ 8%	3,493 (27.9%)	2,562 (24.0%)
HbA_{1c} > 63.9 to ≤ 74.9 mmol/mol or > 8% to ≤ 9%	3,441 (27.5%)	2,956 (27.6%)
HbA_{1c} > 74.9 mmol/mol or > 9%	3,971 (31.8%)	3,613 (33.8%)
HbA_{1c} missing	208 (1.7%)	275 (2.6%)
Diabetes Severity Complications Index Score, mean (SD)	2.4 (1.6)	2.6 (1.7)
Hyperkalemia, n (%)	145 (1.2%)	140 (1.3%)
Duration of CKD at the index date, years, mean (SD)	3.5 (3.4)	3.7 (3.5)
CKD stage based on eGFR[a] or diagnosis code,[b] n (%)		
Stage 1: eGFR ≥ 90, normal or high	5,056 (40.4%)	3,507 (32.8%)
Stage 2: eGFR 60-89, mildly decreased	4,257 (34.1%)	2,958 (27.7%)
Stage 3: eGFR 30-59, mildly to severely decreased	2,887 (23.1%)	3,733 (34.9%)
Stage 3a: eGFR 45-59, mildly to moderately decreased	2,232 (17.9%)	2,354 (22.0%)
Stage 3b: eGFR 30-44, moderately to severely decreased	640 (5.1%)	1,359 (12.7%)
Stage 3 without specification of substage	15 (0.1%)	20 (0.2%)
Stage 4: eGFR 15-29, severely decreased	102 (0.8%)	353 (3.3%)
Stage 5: eGFR < 15 or treated by dialysis, kidney failure	NR	NR
Unspecified stage	NR	NR
Clinical conditions associated with risk of CKD,[b] n (%)		
Hypertension	9,973 (79.8%)	8,706 (81.4%)
Glomerulonephritis (all causes)	191 (1.5%)	193 (1.8%)
Renovascular disease	37 (0.3%)	36 (0.3%)
Autoimmune disease	614 (4.9%)	516 (4.8%)
Polycystic kidney disease	50 (0.4%)	46 (0.4%)
Gout or hyperuricemia	516 (4.1%)	567 (5.3%)
Cardiovascular medications,[c] n (%)		
Thiazide-like diuretics	1,800 (14.4%)	1,672 (15.6%)
Loop diuretics	2,636 (21.1%)	3,064 (28.6%)
Potassium-sparing diuretics	121 (1.0%)	115 (1.1%)
Beta-blockers	4,920 (39.4%)	4,366 (40.8%)
Calcium channel blockers	5,001 (40.0%)	4,263 (39.9%)
Statins	9,722 (77.8%)	8,239 (77.0%)
Aspirin and other antiplatelet agents	5,416 (43.3%)	4,644 (43.4%)

Characteristic	SGLT2i (n = 12,501)	GLP-1 RA (n = 10,696)
ACEi or ARB in the 90 days before the index date	7,660 (61.3%)	6,533 (61.1%)
Macrovascular complications of diabetes,[b] n (%)		
Coronary heart disease	3,645 (29.2%)	3,165 (29.6%)
Cerebrovascular disease	1,477 (11.8%)	1,314 (12.3%)
Peripheral vascular disease	1,865 (14.9%)	1,885 (17.6%)
Cardiovascular disease risk factors,[b] n (%)		
Hypercholesterolemia	4,237 (33.9%)	3,736 (34.9%)
Congestive heart failure	1,519 (12.2%)	1,427 (13.3%)
Healthcare utilization,[c] n (%), mean [SD]		
General practitioner (or primary care) visits	8,655 (69.2%) 6.7 [3.9]	7,457 (69.7%) 7.4 [4.3]
Hospital visits (as ambulatory patient)	8,710 (69.7%) 3.9 [3.9]	7,966 (74.5%) 4.1 [3.8]
Inpatient hospital admissions	1,988 (15.9%) 1.5 [1.0]	1,827 (17.1%) 1.5 [1.2]
Inpatient hospital admissions for congestive heart failure	251 (2.0%) 1.3 [0.7]	183 (1.7%) 1.4 [0.9]
Specialist visits	5,827 (46.6%) 1.7 [1.2]	5,069 (47.4%) 1.6 [1.2]
Emergency department visits	1,264 (10.1%) 1.3 [0.8]	1,175 (11.0%) 1.4 [1.6]

ACEi = angiotensin-converting enzyme inhibitors; ARB = angiotensin receptor blockers; CKD = chronic kidney disease; DNHR = Danish National Health Registers; eGFR = estimated glomerular filtration rate; GLP-1 RA = glucagon-like peptide-1 receptor agonists; HbA_{1c} = hemoglobin A_{1c}; NA = not available; NR = not reported; SD = standard deviation; SGLT2i = sodium-glucose cotransporter 2 inhibitors; T2D = type 2 diabetes.

[a] The lookback period is study days (−365, 0).

[b] The lookback period uses all available data: study days (−∞, 0).

[c] Evaluated in the 180 days before or on the index date; n = the number of patients with ≥ 1 healthcare visit of each type during this period.

Table C4. Selected Baseline Characteristics of New Users of SGLT2i and GLP-1 RA Medications: J-CKD-DB-Ex

Characteristic	SGLT2i (n = 811)	GLP-1 RA (n = 219)
Age at the index date, years		
Mean (SD)	66.5 (11.7)	66.8 (13.3)
Median (1st, 99th percentiles)	67.9 (36, 88)	68.6 (31, 91)
Female sex, n (%)	299 (36.9%)	97 (44.3%)
Calendar year of index date, n (%)		
2014	NA	NA
2015	83 (10.2%)	24 (11.0%)
2016	186 (22.9%)	41 (18.7%)
2017	172 (21.2%)	44 (20.1%)
2018	186 (22.9%)	45 (20.5%)
2019	184 (22.7%)	65 (29.7%)
Obesity, yes (by diagnosis), n (%)	79 (9.7%)	31 (14.2%)
Smoking, current smoker, n (%)	NA	NA
Alcohol abuse	23 (2.8%)	3 (1.4%)
Duration of T2D at the index date, years, mean (SD)	7.5 (4.7)	8.6 (5.4)
Medications for T2D (hypoglycemic agents) ever prescribed from 180 days before and including the index date, n (%)		
GLP-1 RA and fixed-dose combinations	145 (17.9%)	NA
SGLT2i and fixed-dose combinations	NA	105 (47.9%)
Metformin and fixed-dose combinations	458 (56.5%)	122 (55.7%)
Sulfonylureas and fixed-dose combinations	276 (34.0%)	79 (36.1%)
Alpha-glucosidase inhibitors	219 (27.0%)	85 (38.8%)
Thiazolidinediones	154 (19.0%)	38 (17.4%)
Dipeptidyl peptidase-4 inhibitors and fixed-dose combinations	629 (77.6%)	176 (80.4%)
Meglitinides (including repaglinide, nateglinide, mitiglinide)	145 (17.9%)	73 (33.3%)
Insulin use recorded in the 180 days before and including the index date, n (%)	385 (47.5%)	192 (87.7%)

Characteristic	SGLT2i (n = 811)	GLP-1 RA (n = 219)
HbA_{1c}, n (%)		
$HbA_{1c} \leq 53$ mmol/mol or $\leq 7\%$	258 (31.8%)	44 (20.1%)
$HbA_{1c} > 53$ to ≤ 63.9 mmol/mol or $> 7\%$ to $\leq 8\%$	275 (33.9%)	63 (28.8%)
$HbA_{1c} > 63.9$ to ≤ 74.9 mmol/mol or $> 8\%$ to $\leq 9\%$	161 (19.9%)	50 (22.8%)
$HbA_{1c} > 74.9$ mmol/mol or $> 9\%$	105 (12.9%)	58 (26.5%)
HbA_{1c} missing	12 (1.5%)	4 (1.8%)
Diabetes Severity Complications Index Score, mean (SD)	3.7 (2.1)	4.1 (2.2)
Hyperkalemia, n (%)	51 (6.3%)	29 (13.2%)
Duration of CKD at the index date, years, mean (SD)	2.5 (2.1)	2.6 (2.2)
CKD stage based on eGFR[a] or diagnosis code,[b] n (%)		
Stage 1: eGFR ≥ 90, normal or high	39 (4.8%)	13 (5.9%)
Stage 2: eGFR 60-89, mildly decreased	346 (42.7%)	76 (34.7%)
Stage 3: eGFR 30-59, mildly to severely decreased	377 (46.5%)	99 (45.2%)
Stage 3a: eGFR 45-59, mildly to moderately decreased	259 (31.9%)	48 (21.9%)
Stage 3b: eGFR 30-44, moderately to severely decreased	118 (14.5%)	51 (23.3%)
Stage 3 without specification of substage	0 (0%)	0 (0%)
Stage 4: eGFR 15-29, severely decreased	43 (5.3%)	29 (13.2%)
Stage 5: eGFR < 15 or treated by dialysis, kidney failure	3 (0.4%)	2 (0.9%)
Unspecified stage	0 (0%)	0 (0%)
Clinical conditions associated with risk of CKD,[b] n (%)		
Hypertension	683 (84.2%)	201 (91.8%)
Glomerulonephritis (all causes)	169 (20.8%)	39 (17.8%)
Renovascular disease	24 (3.0%)	7 (3.2%)
Polycystic kidney disease	0 (0%)	0 (0%)
Autoimmune disease	205 (25.3%)	68 (31.1%)
Gout or hyperuricemia	269 (33.2%)	75 (34.2%)
Cardiovascular medications,[c] n (%)		
Thiazide-like diuretics	55 (6.8%)	15 (6.8%)
Loop diuretics	102 (12.6%)	36 (16.4%)
Potassium-sparing diuretics	0 (0%)	0 (0%)
Beta-blockers	188 (23.2%)	44 (20.1%)
Calcium channel blockers	329 (40.6%)	122 (55.7%)
Statins	383 (47.2%)	123 (56.2%)

Characteristic	SGLT2i (n = 811)	GLP-1 RA (n = 219)
Aspirin and other antiplatelet agents	225 (27.7%)	77 (35.2%)
ACEi or ARB in the 90 days before the index date	441 (54.4%)	133 (60.7%)
Macrovascular complications of diabetes,[b] n (%)		
Coronary heart disease	479 (59.1%)	135 (61.6%)
Cerebrovascular disease	364 (44.9%)	120 (54.8%)
Peripheral vascular disease	142 (17.5%)	51 (23.3%)
Cardiovascular disease risk factors,[b] n (%)		
Hypercholesterolemia	644 (79.4%)	191 (87.2%)
Congestive heart failure	490 (60.4%)	124 (56.6%)
Healthcare utilization,[c] n (%), mean [SD]		
General practitioner (or primary care) visits	NA	NA
Hospital visits (as ambulatory patient)	NA	NA
Inpatient hospital admissions	198 (24.4%) 0.3 [0.6]	98 (44.7%) 0.6 [0.8]
Inpatient hospital admissions for congestive heart failure	158 (19.5%) 0.9 [3.5]	73 (33.3%) 1.6 [4.1]
Specialist visits	NA	NA
Emergency department visits	NA	NA

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; HbA_{1c} = hemoglobin A_{1c}; J-CKD-DB-Ex = Japan Chronic Kidney Disease Database Extension; NA = not available; SD = standard deviation; SGLT2i = sodium-glucose cotransporter 2 inhibitors; T2D = type 2 diabetes.

[a] The lookback period is study days (−365, 0).

[b] The lookback period uses all available data: study days (−∞, 0).

[c] Evaluated in the 180 days before or on the index date; n = the number of patients with ≥ 1 healthcare visit of each type during this period.

Table C5. Selected Baseline Characteristics of New Users of SGLT2i and GLP-1 RA Medications: VID

Characteristic	SGLT2i (n = 22,404)	GLP-1 RA (n = 8,317)
Age at the index date, years		
Mean (SD)	69.8 (11.1)	66.9 (10.6)
Median (1st, 99th percentiles)	70.8 (42, 91)	67.9 (40,88)
Female sex, n (%)	9,106 (40.6%)	3,768 (45.3%)
Calendar year of index date, n (%)		
2012	0 (0%)	195 (2.3%)
2013	5 (< 0.1%)	360 (4.3%)
2014	389 (1.7%)	605 (7.3%)
2015	2,403 (10.7%)	704 (8.5%)
2016	4,032 (18.0%)	936 (11.3%)
2017	4,264 (19.0%)	1,130 (13.6%)
2018	4,836 (21.6%)	1,820 (21.9%)
2019	6,475 (28.9%)	2,567 (30.9%)
Obesity, yes (by diagnosis), n (%)	15,221 (67.9%)	7,531 (90.6%)
Smoking, current smoker, n (%)	3,322 (14.8%)	1,184 (14.2%)
Alcohol abuse, n (%)	720 (3.2%)	243 (2.9%)
Duration of T2D at the index date, years, mean (SD)	9.0 (3.8)	9.1 (3.7)
Medications for T2D (hypoglycemic agents) ever prescribed from 180 days before and including the index date, n (%)		
GLP-1 RA and fixed-dose combinations	2,525 (11.3%)	NA
SGLT2i and fixed-dose combinations	NA	2,887 (34.7%)
Metformin and fixed-dose combinations	11,289 (50.4%)	5,396 (64.9%)
Sulfonylureas and fixed-dose combinations	2,947 (13.2%)	855 (10.3%)
Alpha-glucosidase inhibitors	80 (0.4%)	22 (0.3%)
Thiazolidinediones	676 (3.0%)	518 (6.2%)
Dipeptidyl peptidase-4 inhibitors and fixed-dose combinations	14,458 (64.5%)	5,389 (64.8%)
Meglitinides (including repaglinide, nateglinide, mitiglinide)	4,405 (19.7%)	1,865 (22.4%)
Insulin use recorded in the 180 days before and including the index date, n (%)	7,873 (35.1%)	4,850 (58.3%)

Characteristic	SGLT2i (n = 22,404)	GLP-1 RA (n = 8,317)
HbA_{1c}, n (%)		
$HbA_{1c} \leq 53$ mmol/mol or $\leq 7\%$	4,849 (21.6%)	1,228 (14.8%)
$HbA_{1c} > 53$ to ≤ 63.9 mmol/mol or $> 7\%$ to $\leq 8\%$	5,916 (26.4%)	1,940 (23.3%)
$HbA_{1c} > 63.9$ to ≤ 74.9 mmol/mol or $> 8\%$ to $\leq 9\%$	4,784 (21.4%)	1,941 (23.3%)
$HbA_{1c} > 74.9$ mmol/mol or $> 9\%$	4,216 (18.8%)	2,029 (24.4%)
HbA_{1c} missing	2,639 (11.8%)	1,179 (14.2%)
Diabetes Severity Complications Index Score, mean (SD)	4.1 (2.0)	4.4 (2.1)
Hyperkalemia, n (%)	1,936 (8.6%)	929 (11.2%)
Duration of CKD at the index date, years, mean (SD)	2.9 (2.2)	3.0 (2.4)
CKD stage based on eGFR[a] or diagnosis code,[b] n (%)		
Stage 1: eGFR ≥ 90, normal or high	5,103 (22.8%)	1,834 (22.1%)
Stage 2: eGFR 60-89, mildly decreased	7,722 (34.5%)	2,140 (25.7%)
Stage 3: eGFR 30-59, mildly to severely decreased	8,008 (35.7%)	3,384 (40.7%)
Stage 3a: eGFR 45-59, mildly to moderately decreased	5,444 (24.3%)	1,866 (22.4%)
Stage 3b: eGFR 30-44, moderately to severely decreased	2,269 (10.1%)	1,381 (16.6%)
Stage 3 without specification of substage	295 (1.3%)	137 (1.7%)
Stage 4: eGFR 15-29, severely decreased	434 (1.9%)	480 (5.8%)
Stage 5: eGFR < 15 or treated by dialysis, kidney failure	14 (0.1%)	17 (0.2%)
Unspecified stage	0	0
Clinical conditions associated with risk of CKD,[b] n (%)		
Hypertension	20,302 (90.6%)	7,762 (93.3%)
Glomerulonephritis (all causes)	671 (3.0%)	435 (5.2%)
Renovascular disease	241 (1.1%)	105 (1.3%)
Autoimmune disease	1,470 (6.6%)	591 (7.1%)
Polycystic kidney disease	76 (0.3%)	23 (0.3%)
Gout or hyperuricemia	6,156 (27.5%)	2,590 (31.1%)
Cardiovascular medications,[c] n (%)		
Thiazide-like diuretics	1,127 (5.0%)	478 (5.8%)
Loop diuretics	5,438 (24.3%)	2,665 (32.0%)
Potassium-sparing diuretics	330 (1.5%)	123 (1.5%)
Beta-blockers	7,626 (34.0%)	3,106 (37.4%)
Calcium channel blockers	5,586 (24.9%)	2,490 (29.9%)
Statins	16,691 (74.5%)	6,524 (78.4%)

Characteristic	SGLT2i (n = 22,404)	GLP-1 RA (n = 8,317)
Aspirin and other antiplatelet agents	9,247 (41.3%)	3,752 (45.1%)
ACEi or ARB in the 90 days before the index date	16,740 (74.7%)	6,462 (77.7%)
Macrovascular complications of diabetes,[b] n (%)		
Coronary heart disease	5,775 (25.8%)	2,169 (26.1%)
Cerebrovascular disease	2,828 (12.6%)	1,056 (12.7%)
Peripheral vascular disease	5,525 (24.7%)	2,493 (30.0%)
Cardiovascular disease risk factors,[b] n (%)		
Hypercholesterolemia	17,564 (78.4%)	6,664 (80.1%)
Congestive heart failure	910 (4.1%)	377 (4.5%)
Healthcare utilization,[c] n (%), mean [SD]		
General practitioner (or primary care) visits	22,111 (98.7%) 5.9 [4.3]	8,149 (98.0%) 6.3 [4.5]
Hospital visits (as ambulatory patient)	NA	NA
Inpatient hospital admissions	3,783 (16.9%) 0.2 [0.6]	1,460 (17.6%) 0.2 [0.6]
Inpatient hospital admissions for congestive heart failure	1,039 (4.6%) 0.1 [0.3]	368 (4.4%) 0.1 [0.3]
Specialist visits	16,799 (75.0%) 3.8 [4.7]	7,211 (86.7%) 5.2 [5.2]
Emergency department visits	6,300 (28.1%) 0.5 [1.0]	2,493 (30.0%) 0.5 [1.0]

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; HbA_{1c} = hemoglobin A_{1c}; NA = not available; SD = standard deviation; SGLT2i = sodium-glucose cotransporter 2 inhibitors; T2D = type 2 diabetes; VID = Valencia Health System Integrated Database.

[a] The lookback period is study days (−365, 0).

[b] The lookback period uses all available data: study days (−∞, 0).

[c] Evaluated in the 180 days before or on the index date; n = the number of patients with ≥ 1 healthcare visit of each type during this period.

Table C6. Selected Baseline Characteristics of New Users of SGLT2i and GLP-1 RA Medications: Optum® EHR

Characteristic	SGLT2i (n = 54,308)	GLP-1 RA (n = 78,934)
Age at the index date, years		
Mean (SD)	62.2 (11.0)	62.2 (10.9)
Median (1st, 99th percentiles)	63 (34, 84)	63, (34, 84)
Female sex, n (%)	24,121 (44.4%)	40,515 (51.3%)
Calendar year of index date, n (%)		
2012	0	2,938 (3.7%)
2013	824 (1.5%)	4,218 (5.3%)
2014	4,491 (8.3%)	5,272 (6.7%)
2015	7,607 (14.0%)	7,862 (10.0%)
2016	7,271 (13.4%)	10,037 (12.7%)
2017	9,038 (16.6%)	12,784 (16.2%)
2018	10,137 (18.7%)	16,131 (20.4%)
2019	14,940 (27.5%)	19,692 (24.9%)
Obesity, yes (by diagnosis), n (%)	24,113 (44.4%)	38,526 (48.8%)
Smoking, current smoker, n (%)	7,033 (13.0%)	9,849 (12.5%)
Alcohol abuse, n (%)	697 (1.3%)	987 (1.3%)
Duration of T2D at the index date, years, mean (SD)	4.9 (2.8)	4.8 (2.9)
Medications for T2D (hypoglycemic agents) ever prescribed from 180 days before and including the index date, n (%)		
GLP-1 RA and fixed-dose combinations	8,246 (15.2%)	NA
SGLT2i and fixed-dose combinations	NA	7,420 (9.4%)
Metformin and fixed-dose combinations	27,190 (50.1%)	33,585 (42.5%)
Sulfonylureas and fixed-dose combinations	16,330 (30.1%)	20,821 (26.4%)
Alpha-glucosidase inhibitors	192 (0.4%)	244 (0.3%)
Thiazolidinediones	2,990 (5.5%)	4,024 (5.1%)
Dipeptidyl peptidase-4 inhibitors and fixed-dose combinations	10,123 (18.6%)	12,749 (16.2%)
Meglitinides (including repaglinide, nateglinide, mitiglinide)	459 (0.8%)	619 (0.8%)
Insulin use recorded in the 180 days before and including the index date, n (%)	16,105 (29.7%)	30,742 (38.9%)
HbA_{1c}, n (%)		
$HbA_{1c} \leq 53$ mmol/mol or $\leq 7\%$	11,598 (21.4%)	17,365 (22.0%)

Characteristic	SGLT2i (n = 54,308)	GLP-1 RA (n = 78,934)
HbA_{1c} > 53 to ≤ 63.9 mmol/mol or > 7% to ≤ 8%	14,331 (26.4%)	18,938 (24.0%)
HbA_{1c} > 63.9 to ≤ 74.9 mmol/mol or > 8% to ≤ 9%	9,916 (18.3%)	13,931 (17.6%)
HbA_{1c} > 74.9 mmol/mol or > 9%	14,098 (26.0%)	20,937 (26.5%)
HbA_{1c} missing	4,365 (8.0%)	7,763 (9.8%)
Diabetes Severity Complications Index Score, mean (SD)	1.8 (1.8)	2.0 (1.9)
Hyperkalemia, n (%)	1,883 (3.5%)	3,681 (4.7%)
Duration of CKD at the index date, years, mean (SD)	4.7 (2.8)	4.7 (2.8)
CKD stage based on eGFR[a] or diagnosis code,[b] n (%)		
Stage 1: eGFR ≥ 90, normal or high	14,425 (26.6%)	16,653 (21.1%)
Stage 2: eGFR 60-89, mildly decreased	20,226 (37.2%)	24,339 (30.8%)
Stage 3: eGFR 30-59, mildly to severely decreased	14,022 (25.8%)	26,561 (33.6%)
Stage 3a: eGFR 45-59, mildly to moderately decreased	10,871 (20.0%)	17,135 (21.7%)
Stage 3b: eGFR 30-44, moderately to severely decreased	2,956 (5.4%)	8,948 (11.3%)
Stage 3 without specification of substage	195 (0.4%)	478 (0.6%)
Stage 4: eGFR 15-29, severely decreased	466 (0.9%)	2,334 (3.0%)
Stage 5: eGFR < 15 or treated by dialysis, kidney failure	9 (< 0.1%)	56 (0.1%)
Unspecified stage	1,189 (2.2%)	2,573 (3.3%)
Clinical conditions associated with risk of CKD,[b] n (%)		
Hypertension	46,750 (86.1%)	68,000 (86.1%)
Glomerulonephritis (all causes)	2,365 (4.4%)	3,765 (4.8%)
Renovascular disease	244 (0.4%)	453 (0.6%)
Autoimmune disease	4,027 (7.4%)	6,339 (8.0%)
Polycystic kidney disease	247 (0.5%)	431 (0.5%)
Gout or hyperuricemia	4,612 (8.5%)	7,701 (9.8%)
Cardiovascular medications,[c] n (%)		
Thiazide-like diuretics	12,477 (23.0%)	18,035 (22.8%)
Loop diuretics	6,570 (12.1%)	12,290 (15.6%)
Potassium-sparing diuretics	951 (1.8%)	1,480 (1.9%)
Beta-blockers	16,532 (30.4%)	24,054 (30.5%)
Calcium channel blockers	8,109 (14.9%)	12,015 (15.2%)
Statins	27,461 (50.6%)	38,788 (49.1%)
Aspirin and other antiplatelet agents	19,163 (35.3%)	29,237 (37.0%)
ACEi or ARB in the 90 days before the index date	22,157 (40.8%)	31,061 (39.4%)

Characteristic	SGLT2i (n = 54,308)	GLP-1 RA (n = 78,934)
Macrovascular complications of diabetes,[b] n (%)		
Coronary heart disease	13,005 (23.9%)	18,449 (23.4%)
Cerebrovascular disease	3,621 (6.7%)	5,587 (7.1%)
Peripheral vascular disease	7,829 (14.4%)	12,124 (15.4%)
Cardiovascular disease risk factors,[b] n (%)		
Hypercholesterolemia	45,314 (83.4%)	64,689 (82.0%)
Congestive heart failure	5,867 (10.8%)	10,378 (13.1%)

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; HbA_{1c} = hemoglobin A_{1c}; NA = not applicable; Optum® EHR = Optum® de-identified Electronic Health Record data set; SD = standard deviation; SGLT2i = sodium-glucose cotransporter 2 inhibitors; T2D = type 2 diabetes.

[a] The lookback period is study days (−365, 0).

[b] The lookback period uses all available data: study days (−∞, 0).

[c] Evaluated in the 180 days before or on the index date; n = the number of patients with ≥ 1 healthcare visit of each type during this period.

Table C7. Variables Used to Define Baseline CKD Stage for New Users of SGLT2i Medications by Data Source

	DNHR (N = 12,501)	VID (N = 22,404)	J-CKD-DB-Ex (N = 811)	Optum® EHR (N = 54,308)
CKD stage based on diagnosis only[a], n (%)	–	–	–	–
Stage 1: eGFR ≥ 90, normal or high	NR	122 (0.5%)	0 (0%)	796 (1.5%)
Stage 2: eGFR 60-89, mildly decreased	NR	579 (2.6%)	2 (0.2%)	3,251 (6.0%)
Stage 3: mildly to severely decreased	86 (0.7%)	819 (3.7%)	5 (0.6%)	784 (1.4%)
Stage 3a: eGFR 45-59, mildly to moderately decreased	0 (0%)	0 (0%)	0 (0%)	87 (0.2%)
Stage 3b: eGFR 30-44, moderately to severely decreased	0 (0%)	0 (0%)	0 (0%)	36 (0.1%)
Stage 3 without specification of substage	86 (0.7%)	819 (3.7%)	5 (0.6%)	661 (1.2%)
Stage 4: eGFR 15-29, severely decreased	24 (0.2%)	117 (0.5%)	0 (0%)	403 (0.7%)
Stage 5: eGFR < 15 OR treated by dialysis; kidney failure	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Unspecified stage	423 (3.4%)	0 (0%)	0 (0%)	4,252 (7.8%)
No diagnosis code at any time on or before the index date	11,955 (95.6%)	16,646 (74.3%)	804 (99.1%)	44,822 (82.5%)
CKD stage based on eGFR only[b], n (%)	–	–	–	–
Stage 1: eGFR ≥ 90, normal or high	5,059 (40.5%)	5,157 (23.0%)	39 (4.8%)	14,635 (26.9%)
Stage 2: eGFR 60-89, mildly decreased	4,268 (34.1%)	7,865 (35.1%)	346 (42.7%)	20,030 (36.9%)
Stage 3: mildly to severely decreased	2,887 (23.1%)	7,769 (34.7%)	377 (46.5%)	14,599 (26.9%)
Stage 3a: eGFR 45-59, mildly to moderately decreased	NR	5,466 (24.4%)	259 (31.9%)	11,392 (21.0%)
Stage 3b: eGFR 30-44, moderately to severely decreased	650 (5.2%)	2,303 (10.3%)	118 (14.5%)	3,207 (5.9%)
Stage 3 without specification of substage	0 (0%)	0 (0%)	0 (0%)	NA
Stage 4: eGFR 15-29, severely decreased	87 (0.7%)	344 (1.5%)	43 (5.3%)	406 (0.7%)
Stage 5: eGFR < 15 OR treated by dialysis, kidney failure	NR	14 (0.1%)	3 (0.4%)	12 (< 0.1%)
No assessment of eGFR in the year on or before the index date	NR	1,255 (5.6%)	3 (0.4%)	4,626 (8.5%)

	DNHR (N = 12,501)	VID (N = 22,404)	J-CKD-DB-Ex (N = 811)	Optum® EHR (N = 54,308)
CKD stage based on eGFR[b] or diagnosis code[a], n (%)	–	–	–	–
Stage 1: eGFR ≥ 90, normal or high	5,056 (40.4%)	5,103 (22.8%)	39 (4.8%)	14,425 (26.6%)
Stage 2: eGFR 60-89, mildly decreased	4,257 (34.1%)	7,722 (34.5%)	346 (42.7%)	20,226 (37.2%)
Stage 3: mildly to severely decreased	2,887 (23.1%)	8,008 (35.7%)	377 (46.5%)	14,022 (25.8%)
Stage 3a: eGFR 45-59, mildly to moderately decreased	2,232 (17.9%)	5,444 (24.3%)	259 (31.9%)	10,871 (20.0%)
Stage 3b: eGFR 30-44, moderately to severely decreased	640 (5.1%)	2,269 (10.1%)	118 (14.5%)	2,956 (5.4%)
Stage 3 without specification of substage	15 (0.1%)	295 (1.3%)	0 (0%)	195 (0.4%)
Stage 4: eGFR 15-29, severely decreased	102 (0.8%)	434 (1.9%)	43 (5.3%)	466 (0.9%)
Stage 5: eGFR < 15 OR treated by dialysis, kidney failure	NR	14 (0.1%)	3 (0.4%)	9 (< 0.1%)
Unspecified stage	NR	0 (0%)	0 (0%)	1,189 (2.2%)
No assessment of GFR in the year on or before the index date or diagnosis code any time on or before the index date	NR	818 (3.7%)	3 (0.4%)	3,971 (7.3%)
CKD stage based on UACR[b], n (%)	–	–	–	–
A1: UACR < 30, normal to mildly increased	2,997 (24.0%)	4,732 (21.1%)	148 (18.2%)	11,725 (21.6%)
A2: UACR 30-300, moderately increased (formerly 'microalbuminuria')	5,804 (46.4%)	8,396 (37.5%)	173 (21.3%)	16,269 (30.0%)
A3: UACR > 300, severely increased (includes nephrotic syndrome, > ~2,000)	1,564 (12.5%)	2,033 (9.1%)	96 (11.8%)	4,792 (8.8%)
No assessment of UACR recorded in the year on or before the index date	2,136 (17.1%)	7,243 (32.3%)	394 (48.6%)	21,522 (39.6%)

CKD = chronic kidney disease; DNHR = Danish National Health Registers; eGFR = estimated glomerular filtration rate; GFR = glomerular filtration rate; J-CKD-DB-Ex = Japan Chronic Kidney Disease Database Extension; NA = not applicable; NR = not reported; Optum® EHR = Optum® de-identified Electronic Health Record data set; SGLT2i = sodium-glucose cotransporter 2 inhibitors; UACR = urine albumin-to-creatinine ratio; VID = Valencia Health System Integrated Database.

[a] The lookback period for these variables is any time on or before the index date (study days (−∞, 0]).

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

Table C8. Variables Used to Define Baseline CKD Stage for New Users of GLP-1 RA Medications by Data Source

	DNHR (N = 10,696)	VID (N = 8,317)	J-CKD-DB-Ex (N = 219)	Optum® EHR (N = 78,934)
CKD stage based on diagnosis only[a], n (%)	–	–	–	–
Stage 1: eGFR ≥ 90, normal or high	NR	41 (0.5%)	0 (0%)	981 (1.2%)
Stage 2: eGFR 60-89, mildly decreased	NR	200 (2.4%)	0 (0%)	4,417 (5.6%)
Stage 3: mildly to severely decreased	228 (2.1%)	582 (7.0%)	8 (3.7%)	1,655 (2.1%)
Stage 3a: eGFR 45-59, mildly to moderately decreased	0 (0%)	0 (0%)	0 (0%)	143 (0.2%)
Stage 3b: eGFR 30-44, moderately to severely decreased	0 (0%)	0 (0%)	0 (0%)	87 (0.1%)
Stage 3 without specification of substage	228 (2.1%)	582 (7.0%)	8 (3.7%)	1,425 (1.8%)
Stage 4: eGFR 15-29, severely decreased	82 (0.8%)	132 (1.6%)	6 (2.7%)	1,858 (2.4%)
Stage 5: eGFR < 15 OR treated by dialysis; kidney failure	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Unspecified stage	626 (5.9%)	0 (0%)	0 (0%)	8,843 (11.2%)
No diagnosis code at any time before or on the index date	9,727 (90.9%)	5,411 (65.1%)	205 (93.6%)	61,180 (77.5%)
CKD stage based on eGFR only[b], n (%)	–	–	–	–
Stage 1: eGFR ≥ 90, normal or high	3,511 (32.8%)	1,858 (22.3%)	13 (5.9%)	16,865 (21.4%)
Stage 2: eGFR 60-89, mildly decreased	2,974 (27.8%)	2,183 (26.3%)	76 (34.7%)	24,016 (30.4%)
Stage 3: mildly to severely decreased	3,747 (35.0%)	3,296 (39.6%)	100 (45.7%)	28,255 (35.8%)
Stage 3a: eGFR 45-59, mildly to moderately decreased	NR	1,877 (22.6%)	48 (21.9%)	18,228 (23.1%)
Stage 3b: eGFR 30-44, moderately to severely decreased	1,391 (13.0%)	1,419 (17.1%)	52 (23.7%)	10,027 (12.7%)
Stage 3 without specification of substage	0 (0%)	0 (0%)	0 (0%)	NA
Stage 4: eGFR 15-29, severely decreased	319 (3.0%)	07 (4.9%)	28 (12.8%)	2,063 (2.6%)
Stage 5: eGFR < 15 OR treated by dialysis, kidney failure	NR	17 (0.2%)	2 (0.9%)	71 (0.1%)
No assessment of eGFR in the year before the index date	NR	556 (6.7%)	0 (0%)	7,664 (9.7%)

	DNHR (N = 10,696)	VID (N = 8,317)	J-CKD-DB-Ex (N = 219)	Optum® EHR (N = 78,934)
CKD stage based on eGFR[b] or diagnosis code[a], n (%)	–	–	–	–
Stage 1: eGFR ≥ 90, normal or high	3,507 (32.8%)	1,834 (22.1%)	13 (5.9%)	16,653 (21.1%)
Stage 2: eGFR 60-89, mildly decreased	2,958 (27.7%)	2,140 (25.7%)	76 (34.7%)	24,339 (30.8%)
Stage 3: mildly to severely decreased	3,733 (34.9%)	3,384 (40.7%)	99 (45.2%)	26,561 (33.6%)
Stage 3a: eGFR 45-59, mildly to moderately decreased	2,354 (22.0%)	1,866 (22.4%)	48 (21.9%)	17,135 (21.7%)
Stage 3b: eGFR 30-44, moderately to severely decreased	1,359 (12.7%)	1,381 (16.6%)	51 (23.3%)	8,948 (11.3%)
Stage 3 without specification of substage	20 (0.2%)	137 (1.7%)	0 (0%)	478 (0.6%)
Stage 4: eGFR 15-29, severely decreased	353 (3.3%)	480 (5.8%)	29 (13.2%)	2,334 (3.0%)
Stage 5: eGFR < 15 OR treated by dialysis, kidney failure	NR	17 (0.2%)	2 (0.9%)	56 (0.1%)
Unspecified stage	NR	0 (0%)	0 (0%)	2,573 (3.3%)
No assessment of GFR in the year before the index date or diagnosis code any time before or on the index date	NR	266 (3.2%)	0 (0%)	6,418 (8.1%)
CKD stage based on UACR[b], n (%)	–	–	–	–
A1: UACR < 30, normal to mildly increased	2,663 (24.9%)	1,691 (20.3%)	50 (22.8%)	16,526 (20.9%)
A2: UACR 30-300, moderately increased (formerly 'microalbuminuria')	4,556 (42.6%)	2,945 (35.4%)	44 (20.1%)	20,841 (26.4%)
A3: UACR > 300, severely increased (includes nephrotic syndrome, > ~2,000)	1,439 (13.5%)	981 (11.8%)	36 (16.4%)	7,496 (9.5%)
No assessment of UACR recorded in the year before the index date	2,038 (19.1%)	2,700 (32.5%)	89 (40.6%)	34,071 (43.2%)

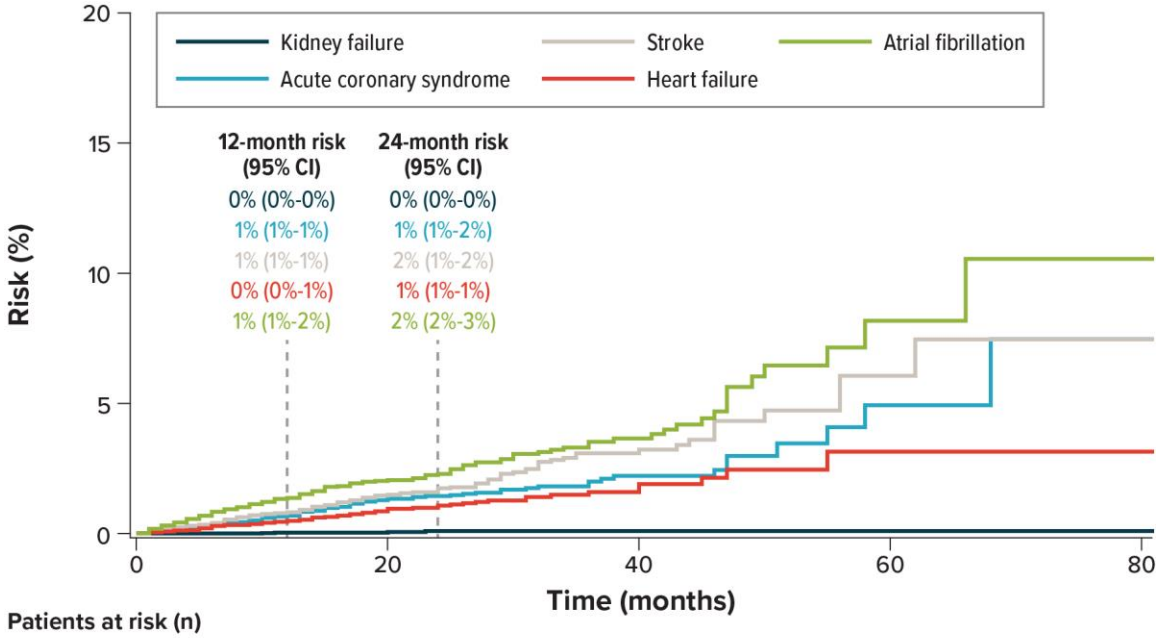
CKD = chronic kidney disease; DNHR = Danish National Health Registers; eGFR = estimated glomerular filtration rate; GFR = glomerular filtration rate; GLP-1 RA = glucagon-like peptide-1 receptor agonists; J-CKD-DB-Ex = Japan Chronic Kidney Disease Database Extension; NA = not applicable; NR = not reported; Optum® EHR = Optum® de-identified Electronic Health Record data set; UACR = albumin-to-creatinine ratio; VID = Valencia Health System Integrated Database.

[a] The lookback period for these variables is any time before or on the index date (study days (−∞, 0]).

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

Figure C1. Cumulative Incidence of Primary Outcomes: DNHR

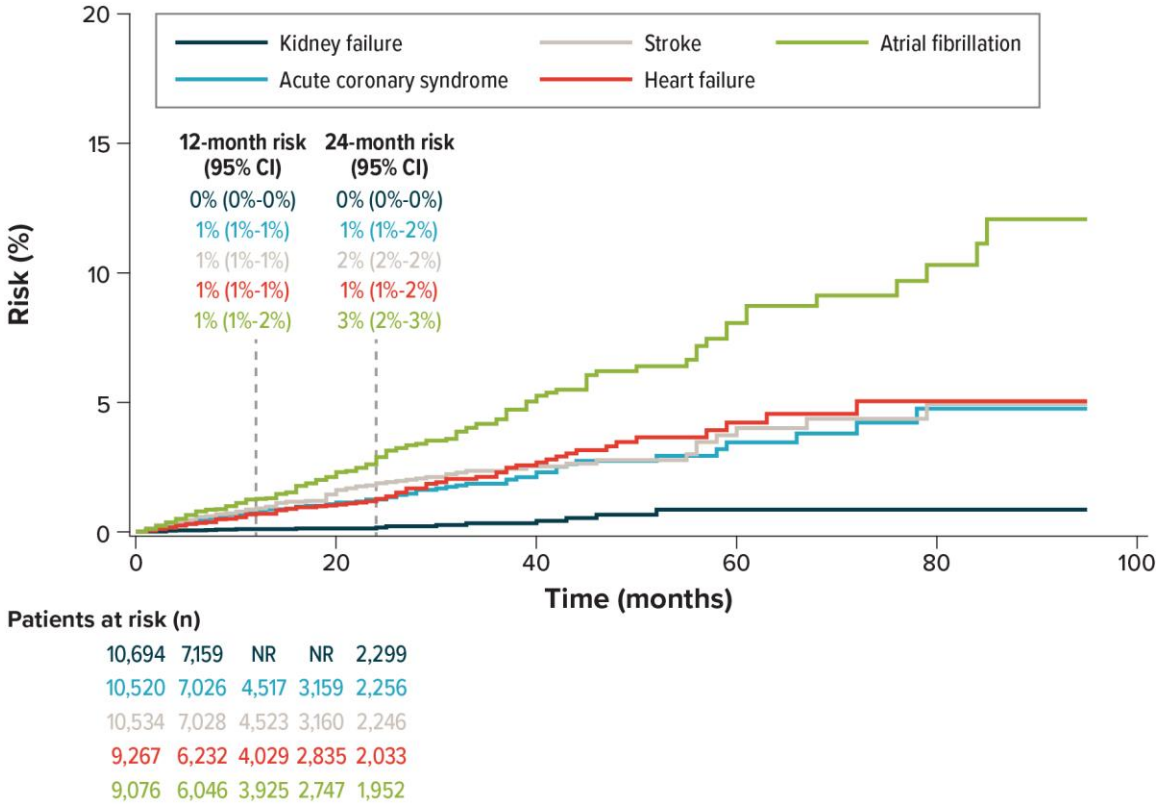
a. SGLT2i Cohort



Patients at risk (n)

12,501	8,256	NR	NR	NR
12,249	8,073	5,401	3,686	2,388
12,316	8,117	5,430	3,689	2,394
10,982	7,341	4,929	3,391	2,201
10,672	7,031	4,734	3,256	2,114

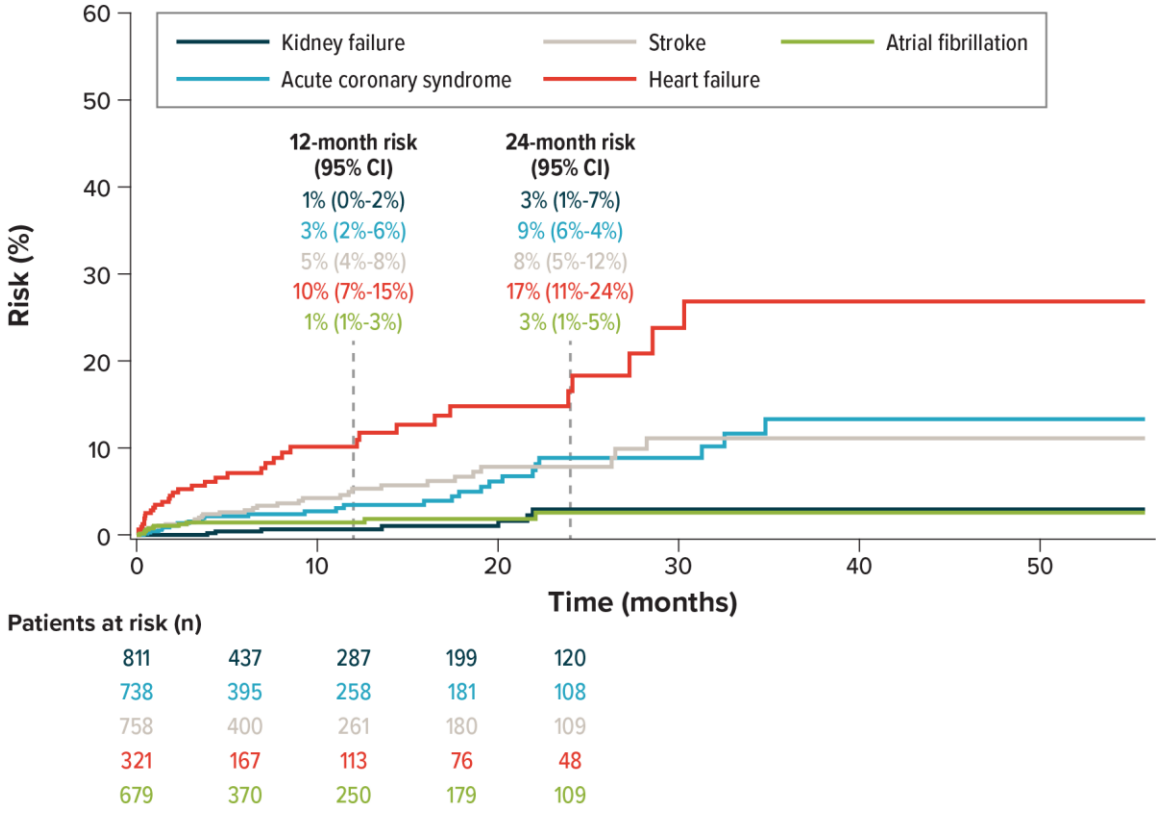
b. GLP-1 RA Cohort



DNHR = Danish National Health Registers; GLP-1 RA = glucagon-like peptide-1 receptor agonists; NR = not reported; SGLT2i = sodium-glucose cotransporter 2 inhibitors.

Figure C2. Cumulative Incidence of Primary Outcomes: J-CKD-DB-Ex

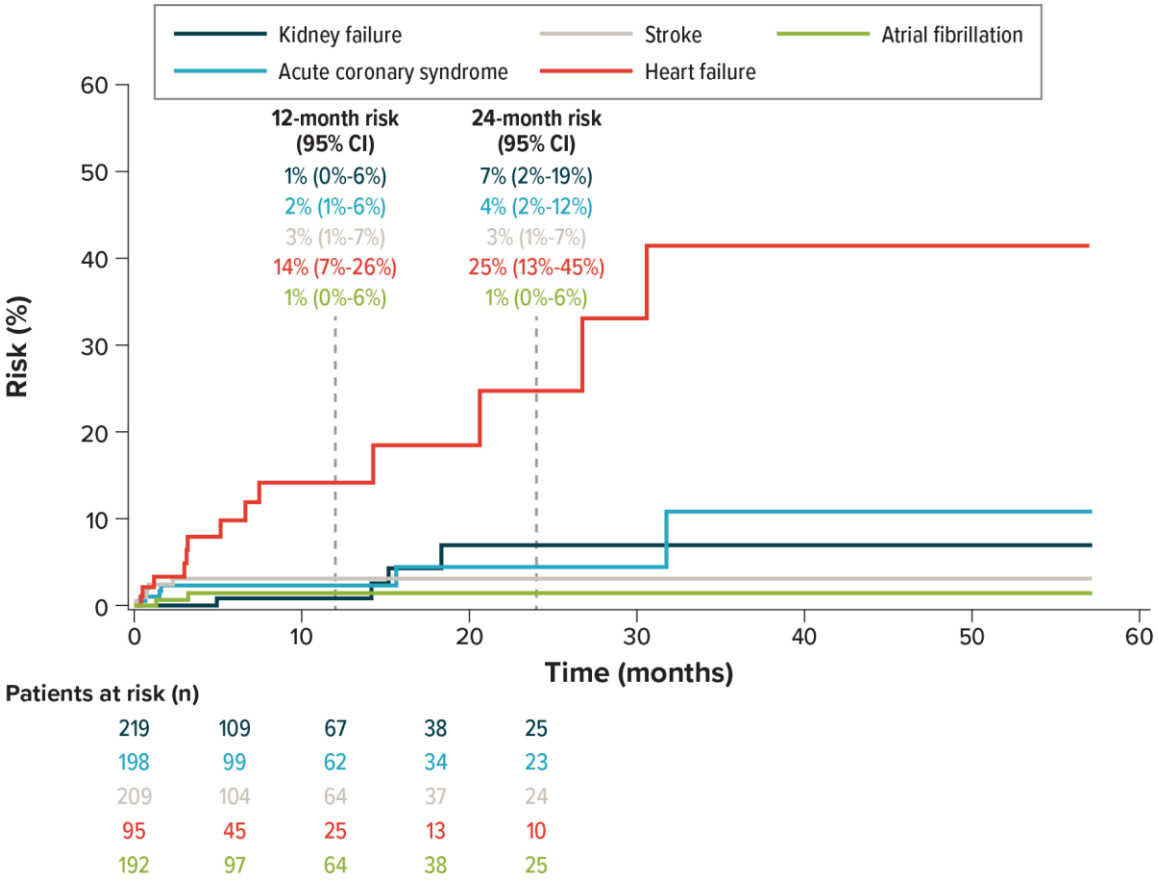
a. SGLT2i Cohort



Patients at risk (n)

811	437	287	199	120
738	395	258	181	108
758	400	261	180	109
321	167	113	76	48
679	370	250	179	109

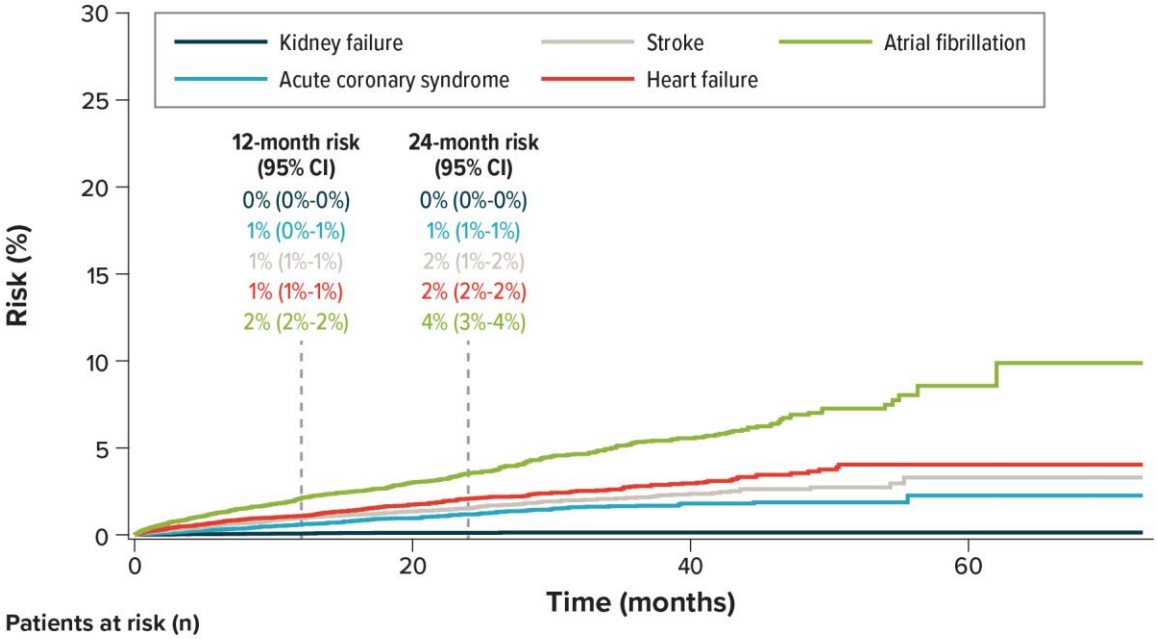
b. GLP-1 RA Cohort



GLP-1 RA = glucagon-like peptide-1 receptor agonists; J-CKD-DB-Ex = Japan Chronic Kidney Disease Database Extension; SGLT2i = sodium-glucose cotransporter 2 inhibitors.

Figure C3. Cumulative Incidence of Primary Outcomes: VID

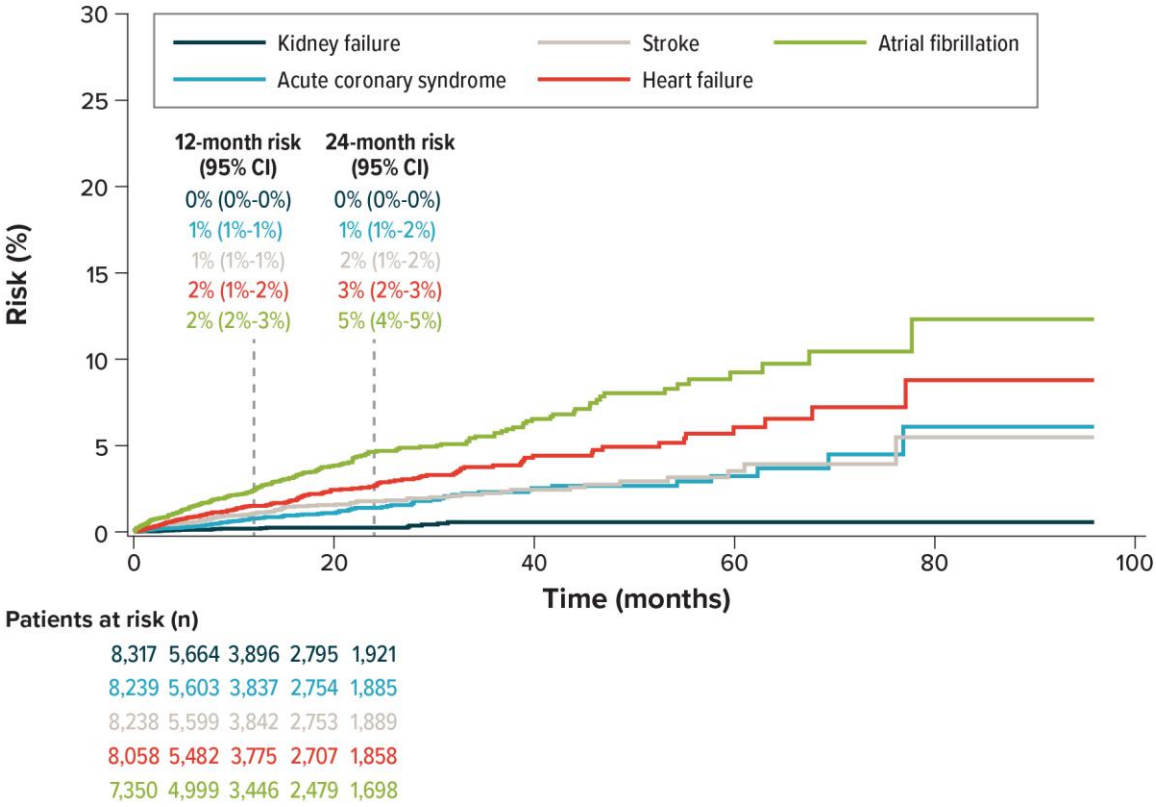
a. SGLT2i Cohort



Patients at risk (n)

22,404	14,754	10,215	7,775	5,611
22,066	14,520	10,039	7,622	5,491
22,206	14,575	10,084	7,669	5,514
21,573	14,234	9,882	7,528	5,450
19,755	13,003	9,046	6,883	4,963

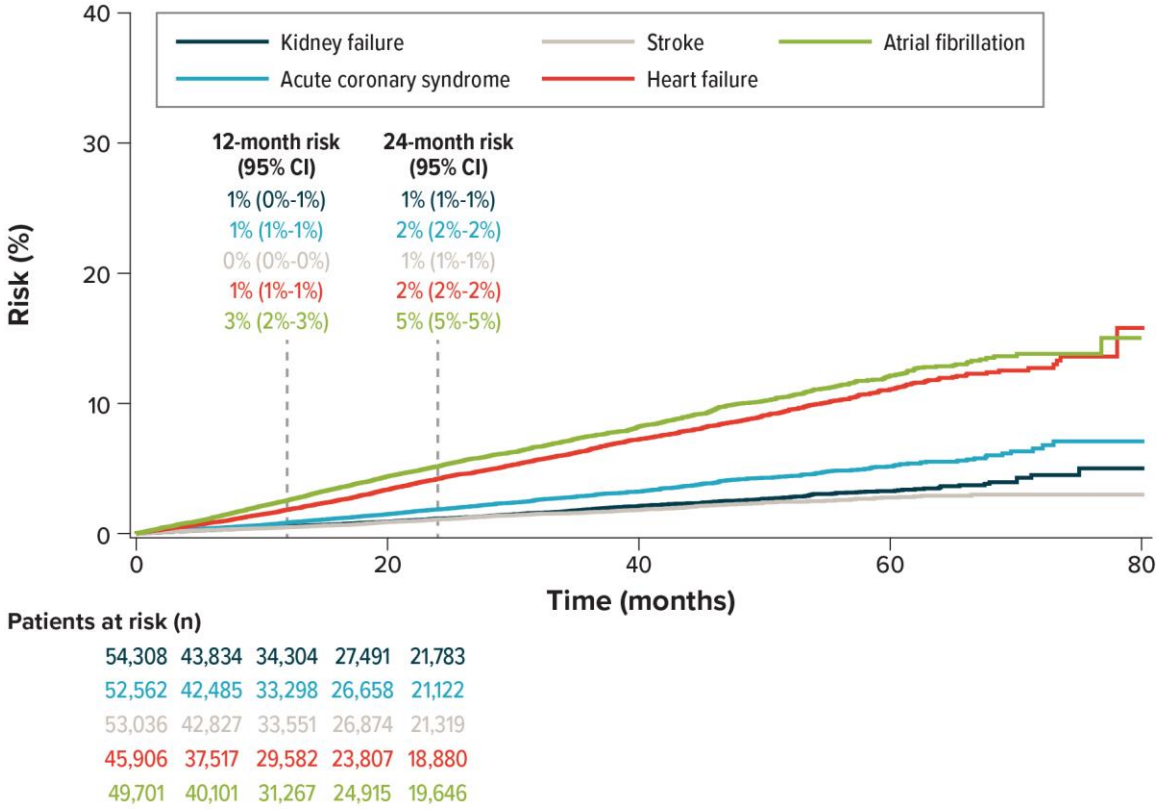
b. GLP-1 RA Cohort



GLP-1 RA = glucagon-like peptide-1 receptor agonists; SGLT2i = sodium-glucose cotransporter 2 inhibitors; VID = Valencia Health System Integrated Database.

Figure C4. Cumulative Incidence of Primary Outcomes: Optum® EHR

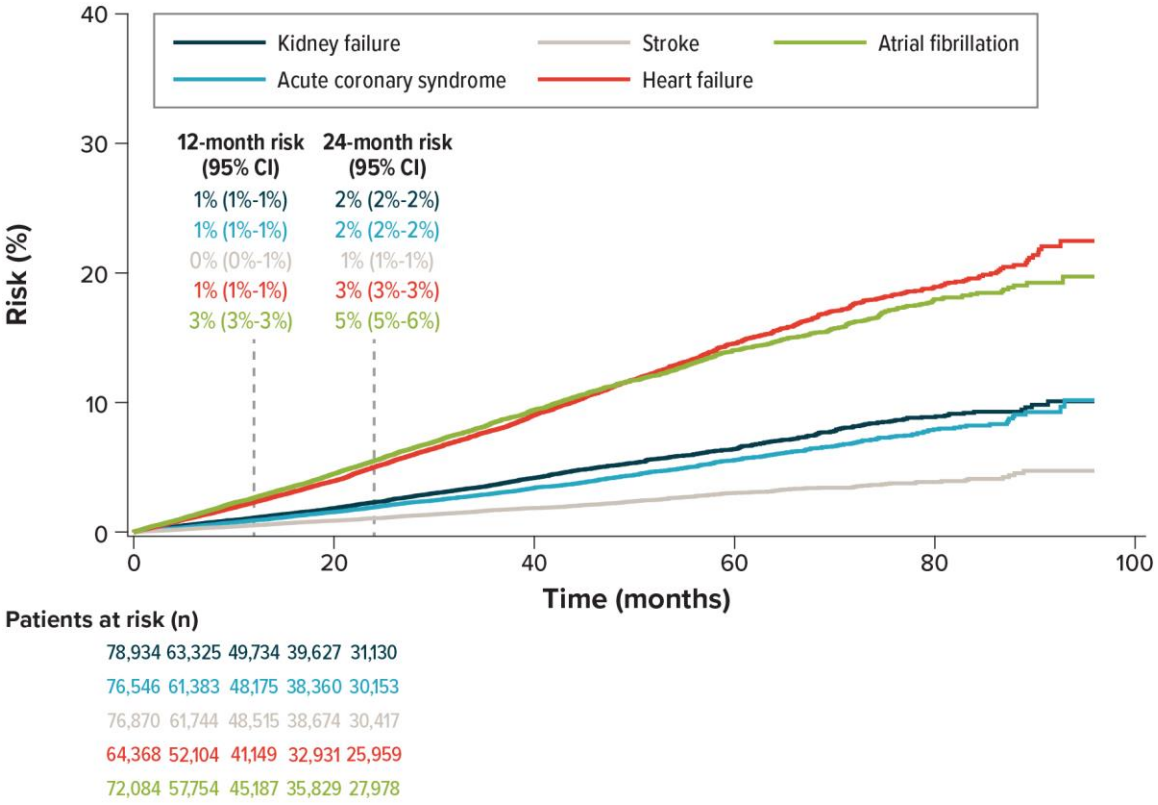
a. SGLT2i Cohort



Patients at risk (n)

Kidney failure	54,308	43,834	34,304	27,491	21,783
Acute coronary syndrome	52,562	42,485	33,298	26,658	21,122
Stroke	53,036	42,827	33,551	26,874	21,319
Heart failure	45,906	37,517	29,582	23,807	18,880
Atrial fibrillation	49,701	40,101	31,267	24,915	19,646

b. GLP-1 RA Cohort



GLP-1 RA = glucagon-like peptide-1 receptor agonists; Optum® EHR = Optum® de-identified Electronic Health Record data set; SGLT2i = sodium-glucose cotransporter 2 inhibitors.

SUPPLEMENTARY REFERENCES

1. Schneeweiss S, Rassen JA, Brown JS, et al. Graphical depiction of longitudinal study designs in health care databases. Ann Intern Med. 2019;170(6):398-406.