Supplementary Appendix to "The Outcomes of SGLT-2 Inhibitor Utilization in Diabetic Kidney Transplant Recipients"

TriNetX is the global federated health research network providing access to electronic medical records (diagnoses, procedures, medications, laboratory values, genomic information) across large healthcare organizations (HCOs). It provides a diverse range of data, including patient demographics, medical diagnoses (coded using ICD-10-CM), various medical procedures (recorded with ICD-10 Procedure Coding System, Current Procedural Terminology codes, or Systematized Nomenclature of Medicine - Clinical Terms), prescribed drugs (categorized by the Anatomical Therapeutic Chemical Classification system or RxNorm), laboratory tests (classified by Logical Observation Identifiers Names and Codes), genetic data (notated according to the Human Genome Variation Society standards), and detailed records of healthcare service use. This report was run on the set of HCOs grouped into a network called Research. This network included 83 HCO(s). The analysis process includes two main steps:
1) Defining the cohorts through query criteria;
2) Setting up and running the analysis.

According to the detailed description of the database provided and can be found at the website: https://trinetx.com/trust-security/, TriNetX is recognized as an ISO/IEC 27001:2013 certified entity, demonstrating its commitment to maintaining a robust Information Security Management System (ISMS). This international standard outlines the criteria for the creation, implementation, operation, surveillance, assessment, preservation, and enhancement of a documented ISMS, tailoring it to the specific risks faced by the organization. Emphasizing a risk-based methodology, ISO/IEC 27001:2013 advocates for suitable and balanced security measures that safeguard information assets, thereby instilling confidence in TriNetX's stakeholders, including its members and clients. The ISMS of TriNetX underpins the architecture and functionalities required to handle the data assets, personnel, operations, and technology that form the backbone of the TriNetX platform. Further information regarding TriNetX's ISO/IEC 27001:2013 Certification can be found in the Schellman ISO Certificate Directory (https://www.schellman.com/certificate-directory).

TriNetX has established systems and protocols that align with the European Union's (EU) criteria for the extraterritorial transfer of data from the EU to its platform, emphasizing the safeguarding and enhancement of the confidentiality, integrity, availability, and resilience of systems and services that process Personal Data. To guarantee that information is adequately de-identified in accordance with the Health Information Portability and Accountability Act (HIPAA) Privacy Rule, TriNetX employs the Expert Determination method. For this purpose, the services of Bradley Malin, Ph.D., are utilized. Furthermore, TriNetX adheres to the standards set by the Brazilian General Data Protection Law (LGPD), demonstrating its commitment to transparency by entering into Data Protection

Addendums with Brazilian healthcare organizations. According to the agreements between HCOs and TriNetX, all data provided to TriNetX will undergo pseudonymization and/or de-identification by the HCOs. TriNetX also offers assistance to HCOs in establishing pseudonymization processes if they are not already in place. Additionally, expert determination is used by TriNetX to ensure that data made available to end-users is sufficiently de-identified. To manage data consistently, TriNetX has formed a Data Trust team, which includes employees from its legal, privacy, compliance, and security departments. This team is tasked with evaluating data throughout its lifecycle, ensuring responsible and accountable data management. This information is based on the source document from TriNetX's official website (https://trinetx.com/trust-privacy/).

Cohorts definition

Query Criteria for Cohort 1 (query name: SGLT-2i users):
This query was run on the network Research with 83 HCO(s) queried and 83 HCO(s) responded. A total of 57 provider(s) responded with patients.

Query Criteria for Cohort 2 (query name: SGLT-2i non-users):
This query was run on the network Research with 83 HCO(s) queried and 83 HCO(s) responded. A total of 76 provider(s) responded with patients.

The specific codes used to identify diabetic kidney transplant recipients are outlined in **Supplemental Table S7**, while the codes utilized for querying SGLT-2i use, and the criteria for exclusions are detailed in **Supplemental Table S8**.

Analysis Setup

This analysis included outcomes that occurred in the time window that started 90 days after the first occurrence of the index event and ended 1825 days after the first occurrence of the index event. The index event only includes events that occurred up to 20 years ago. Patients whose index event occurred 20 years or more ago are excluded. In this analysis, 0 patients in Cohort 1 and 0 patients in Cohort 2 were excluded because they met the index event more than 20 years ago. Index events for the Compare Outcomes analysis were derived from the cohort definitions. Index events were defined separately for each cohort and were based on the criteria used in the original cohort definition.

The Survival analyses support the “exclude patients with outcomes prior to the window” setting. This option can exclude patients from the analysis if they are not at risk for an outcome (e.g., if the outcome is a chronic disease). When "exclude patients with the outcome prior to the time window" is not checked, all patients in the cohort are included in the analysis, regardless of whether they had the outcome prior to the time window. When "exclude patients with the outcome prior to the time window" is checked, patients are excluded from the analysis if their record includes the outcome

prior to the beginning of the time window. This selection will exclude all patients with the outcome prior to the index event. If the start of the time window for the analysis falls some days after the index event, patients will also be excluded if they have the outcome between the index event and the start of the time window.

The Kaplan-Meier Analysis estimates probability of the outcome at a respective time interval (daily time interval is used in this analysis). In order to account for the patients who exited the cohort during the analysis period, and therefore should not be included in the analysis, censoring is applied. In this analysis, patients are removed from the analysis (censored) after the last fact in their record. The output summary includes: Patients in each Cohort (count of patients meeting query criteria); Patients with Outcome (of the patients in the cohort, count of patients that had the outcome in the time window); Median Survival (the number of days when the survival drops below 50%; the "-" indicates that survival does not drop below 50% during the time window); and Survival Probability at End of Time Window (the % survival at the end of the time window). In addition, Log-Rank test, Hazard Ratio and test for Proportionality.

Supplemental Table S9 details the criteria for each outcome, specifying that for definitions encompassing multiple terms, the presence of at least one term is required for a match.

For a balanced comparison between the study groups, we incorporated a variety of demographic factors such as age, sex, and ethnic and racial backgrounds. Moreover, we scrutinized various comorbidities and concurrent medication use. We conducted propensity score matching based on 45 characteristics, including demographic factors such as age at Index, race (White), ethnicity (not Hispanic or Latino), and sex (male). Our analysis also encompassed a range of comorbidities, identified through ICD-10-CM codes. These included primary hypertension (I10), dyslipidemia (E78), heart failure (I50), liver diseases (K70-K77), chronic lower respiratory diseases (J40-J4A), systemic connective tissue disorders (M30-M36), neoplasms (C00-D49), overweight and obesity (E66), T2DM-related complications like nephropathy, ophthalmopathy, and neuropathy (E11.2-E11.4), nephrotic syndrome (N04), cystic kidney disease (Q61), and smoking (Z72.0). Medication use was classified according to the Anatomical Therapeutic Chemical Classification System, covering Corticosteroids (ATC:H02), Insulin (ATC:A10A), Biguanides (ATC:A10BA), GLP-1 agonists (ATC:A10BJ), DPP-4 inhibitors (ATC:A10BH), Sulfonylureas (ATC:A10BB), Thiazolidinediones (ATC:A10BG), HMG-CoA reductase inhibitors (ATC:C10AA), ACE inhibitors/ARBs (ATC:C09), Beta-blockers (ATC:C07), Calcium channel blockers (ATC:C08), and Diuretics (ATC:C03). Additionally, we accounted for potential confounding factors by analyzing physical examination findings and laboratory tests, which included systolic and diastolic blood pressure, body mass index (BMI), serum sodium and potassium levels, estimated glomerular filtration rate (eGFR), triglyceride and cholesterol levels, hemoglobin A1c (HbA1c), alanine aminotransferase (ALT), aspartate aminotransferase (AST), total bilirubin, and brain-type natriuretic peptide (BNP). These conditions were verified through diagnoses in the electronic health records of patients, spanning from a year to a day before the index date. The specific diagnosis and medication

codes utilized in our study are summarized in **Supplemental Table S10**.

Methods for New-User Analysis

In this analysis, we utilized the TriNetX system to classify kidney transplant recipients into two distinct groups based on their SGLT-2i medication usage prior to the transplant event:

- New SGLT-2i users were defined as patients who had no recorded SGLT-2i medication codes prior to the kidney transplant.
- Long-term SGLT-2i users were defined as patients who had documented SGLT-2i medication codes before the transplant event.

This classification was conducted to allow a new-user design subgroup analysis, enhancing the clarity and precision of the study results by distinguishing between the effects of initiating SGLT-2i after transplant versus continued use from pre-transplant periods. The outcomes of interest, including all-cause mortality, major adverse cardiovascular events (MACE), and major adverse kidney events (MAKE), were assessed with hazard ratios adjusted for age, sex, and race due to their potential interactions with kidney disease outcomes. The adjusted hazard ratios and 95% confidence intervals were calculated using Cox proportional hazards models.

Supplemental Table S1. Primary and Secondary Outcomes in the Study Population with Diabetic KTR among SGLT-2i Users (n = 1,970) Versus Non-Users (n = 1,970)

Outcome	Patients with outcome				aHR	*p*-value*	*E*-value	
	6 months	1 year	3 years	5 years	(95% CI)		For aHR	For Upper Bound of 95% CI
All-cause mortality								
SGLT-2i users	10	16	32	41	0.32	<0.001	5.70	3.87
SGLT-2i non-users	18	45	136	188	[0.22 - 0.45]			
MACE†								
SGLT-2i users	10	21	52	72	0.48	<0.001	3.59	2.61
SGLT-2i non-users	22	62	168	229	[0.37 - 0.62]			
MAKE								
SGLT-2i users	67	99	156	176	0.52	<0.001	3.26	2.61
SGLT-2i non-users	111	199	353	444	[0.43 - 0.62]			

***** The log-rank test was used to assess differences in outcome probabilities between cohorts, with significance determined at a two-sided p-value < 0.05.

† Patients who had experienced a MACE prior to the specified time window were excluded. After exclusion, there were 1,623 SGLT-2i users and 1,651 SGLT-2i non-users.

Abbreviation:

aHR, adjusted hazard ratio; CI, confidence interval; KTR, kidney transplant recipient; MACE, major adverse cardiovascular event; MAKE, major adverse kidney event; SGLT-2i, sodium-glucose cotransporter 2 inhibitor.

Supplemental Table S2. Incidence Rate Ratios for Outcomes of Interest among SGLT-2i Users Versus Non-Users

Outcome	Participants, n	Patients with Outcome, n	Mean follow-up years	Crude Incidence Rate/1,000 Person-Years	Incidence Rate Ratio (95% CI)
All-cause mortality	3940	229	3.0	19.18	0.20 [0.14 - 0.28]
SGLT-2i users	1970	41	3.2	6.56	
SGLT-2i non-users	1970	188	2.9	33.05	
MACE*	3274	301	3.1	30.05	0.30 [0.23 - 0.40]
SGLT-2i users	1623	72	3.1	14.11	
SGLT-2i non-users	1651	229	3.0	46.63	
MAKE	3940	620	3.0	51.93	0.36 [0.30 - 0.43]
SGLT-2i users	1970	176	3.2	28.15	
SGLT-2i non-users	1970	444	2.9	78.06	

* Patients who had experienced a MACE prior to the specified time window were excluded.

Abbreviation:

CI, confidence interval; MACE, major adverse cardiovascular event; MAKE, major adverse kidney event; SGLT-2i, sodium-glucose cotransporter 2 inhibitor.

Supplemental Table S3. Absolute Risks, Risk Differences, Risk Ratio, and Odds Ratio for All-Cause Mortality among SGLT-2i Users Versus Non-Users

	Patients with Outcome, n	Absolute Risks	Risk Difference (95% CI)	*p*-value* for Risk Difference	Risk Ratio (95% CI)	Odds Ratio (95% CI)
1 year post-transplant						
SGLT-2i users	16/1970	0.81%	-1.47%	<0.001	0.36	0.35
SGLT-2i non-users	45/1970	2.28%	[-2.24% to -0.70%]		[0.20 - 0.63]	[0.20 - 0.62]
3 years post-transplant						
SGLT-2i users	32/1970	1.62%	-5.28%	<0.001	0.24	0.22
SGLT-2i non-users	136/1970	6.90%	[-6.53% to -4.03%]		[0.16 - 0.34]	[0.15 - 0.33]
5 years post-transplant						
SGLT-2i users	41/1970	2.08%	-7.46%	<0.001	0.22	0.20
SGLT-2i non-users	188/1970	9.54%	[-8.90% to -6.02%]		[0.16 - 0.30]	[0.14 - 0.28]

* The log-rank test was used to assess differences in outcome probabilities between cohorts, with significance determined at a two-sided p-value < 0.05.

Abbreviation:

CI, confidence interval; SGLT-2i, sodium-glucose cotransporter 2 inhibitor.

Supplemental Table S4. Outcomes Excluding Patients with Different Dialysis-Related Codes within the First 1-3 Months Post-Transplant*

Outcome	aHR after matching (95% CI)	*p*-value†
Only excluded patients with mortality or dialysis-related diagnosis codes: 2,063 SGLT-2i users vs. 28,057 non-users		
All-cause mortality	0.35 [0.25 - 0.49]	<0.001
MACE	0.50 [0.39 - 0.63]	<0.001
MAKE	0.52 [0.45 - 0.61]	<0.001
Only excluded patients with mortality or dialysis-related procedure codes: 2,723 SGLT-2i users vs. 35,362 non-users		
All-cause mortality	0.31 [0.23 - 0.42]	<0.001
MACE	0.53 [0.43 - 0.65]	<0.001
MAKE	0.76 [0.69 - 0.84]	<0.001

* In the SGLT-2i user group, 972 patients were excluded due to having dialysis-related diagnosis codes within 1-3 months post-transplantation, and 312 patients were excluded due to having dialysis-related procedure codes in the same timeframe. Among these, 244 patients were excluded for having both types of codes. In the SGLT-2i non-user group, 12,232 patients were excluded due to dialysis-related diagnosis codes, and 4,927 due to dialysis-related procedure codes within the first 1-3 months post-transplant. Of these, 3,704 patients were excluded for having both diagnostic and procedure codes. The specific codes used for these exclusions are detailed in **Supplemental Table S8**.

† The log-rank test was used to assess differences in outcome probabilities between cohorts, with significance determined at a two-sided p-value < 0.05.

Abbreviation:

aHR, adjusted hazard ratio; CI, confidence interval; MACE, major adverse cardiovascular event; MAKE, major adverse kidney event; SGLT-2i, sodium-glucose cotransporter 2 inhibitor.

Supplemental Table S5. Comparative Analysis of Outcomes Based on SGLT-2i Usage in the First 3 Months and Continued Usage from 3 to 6 Months Post-Transplant*

Outcome	aHR after matching (95% CI)	*p*-value†
All-cause mortality	0.47 [0.30 - 0.73]	<0.001
MACE	0.66 [0.49 - 0.90]	0.008
MAKE	0.56 [0.45 - 0.70]	<0.001

* Comparison of SGLT-2i users in the first 3 months with continued usage from 3 to 6 months post-transplant and non-users in the first 3 months with continued non-usage from 3 to 6 months post-transplant. Patients were categorized based on the presence of medication codes during these time periods to determine continued usage or non-usage of SGLT-2i.

† The log-rank test was used to assess differences in outcome probabilities between cohorts, with significance determined at a two-sided p-value < 0.05.

Abbreviation:

aHR, adjusted hazard ratio; CI, confidence interval; MACE, major adverse cardiovascular event; MAKE, major adverse kidney event; SGLT-2i, sodium-glucose cotransporter 2 inhibitor.

Supplemental Table S6. Comparison of HbA1c Levels Between SGLT-2i Users and Non-Users at 3-6, 6-9, and 9-12 Months Post-Transplant

	Before matching			After matching		
	SGLT-2i users	**SGLT-2i non-users**	***p*-value***	**SGLT-2i users**	**SGLT-2i non-users**	***p*-value***
Post-transplant HbA1c (%)†						
3 to 6 months	7.5 ± 1.6	7.1 ± 1.7	<0.001	7.5 ± 1.6	7.4 ± 1.6	0.049
6 to 9 months	7.5 ± 1.5	7.1 ± 1.7	<0.001	7.5 ± 1.5	7.4 ± 1.7	0.262
9 to 12 months	7.5 ± 1.5	7.2 ± 1.7	<0.001	7.5 ± 1.5	7.4 ± 1.7	0.393

***** The log-rank test was used to assess differences in outcome probabilities between cohorts, with significance determined at a two-sided p-value < 0.05.

† Plus–minus values are means ±SD.

Abbreviation:

HbA1c, hemoglobin A1c; SGLT-2i, sodium-glucose cotransporter 2 inhibitor.

Supplemental Table S7. Code Use for Query Criteria of Diabetic Kidney Transplant Recipients (KTR)

Code use for Kidney Transplant			
The cohort	**Code type**	**Code**	**Code name**
Patients must have any of	diagnosis	UMLS:ICD10CM:Z94.0	Kidney transplant status
	procedure	UMLS:ICD10PCS:0TY00Z0	Transplantation of Right Kidney, Allogeneic, Open Approach
	procedure	UMLS:ICD10PCS:0TY10Z0	Transplantation of Left Kidney, Allogeneic, Open Approach
	procedure	UMLS:ICD10PCS:0TY10Z1	Transplantation of Left Kidney, Syngeneic, Open Approach
	procedure	UMLS:ICD10PCS:0TY00Z1	Transplantation of Right Kidney, Syngeneic, Open Approach
	procedure	UMLS:ICD10PCS:0TY10Z2	Transplantation of Left Kidney, Zooplastic, Open Approach
	procedure	UMLS:ICD10PCS:0TY00Z2	Transplantation of Right Kidney, Zooplastic, Open Approach
	procedure	UMLS:SNOMED:70536003	Transplant of kidney
	procedure	UMLS:SNOMED:175902000	Cadaveric renal transplant
	procedure	UMLS:CPT:1008098	Renal Transplantation Procedures
Date constraint	The terms in this group occurred between Jun 1, 2015 and Jun 1, 2023		
Code use for Type 2 Diabetes			
The cohort	**Code type**	**Code**	**Code name**
Patients must have	diagnosis	UMLS:ICD10CM:E11	Type 2 diabetes mellitus

Supplemental Table S8. Code Use for Query Criteria of Sodium-Glucose Co-Transporter 2 Inhibitor (SGLT-2i) and Exclusion

Code use for SGLT-2i				
	The cohort	**Code type**	**Code**	**Code name**
	Patients must have (SGLT-2i users) Patients cannot have (SGLT-2i non-users)	medication	NLM:ATC:A10BK	Sodium-glucose co-transporter 2 (SGLT2) inhibitors
Code use for Exclusion				
	The cohort	**Code type**	**Code**	**Code name**
	Patients cannot have	demographics	Deceased	Deceased
	or	diagnosis	UMLS:ICD10CM:R99	Ill-defined and unknown cause of mortality
	or	procedure	UMLS:CPT:90937	Hemodialysis procedure requiring repeated evaluation(s) with or without substantial revision of dialysis prescription
	or	procedure	UMLS:CPT:90947	Dialysis procedure other than hemodialysis (eg, peritoneal dialysis, hemofiltration, or other continuous renal replacement therapies) requiring repeated evaluations by a physician or other qualified health care professional, with or without substantial revision of dialysis prescription
	or	procedure	UMLS:CPT:90945	Dialysis procedure other than hemodialysis (eg, peritoneal dialysis, hemofiltration, or other continuous renal replacement therapies), with single evaluation by a physician or other qualified health care professional
	or	procedure	UMLS:CPT:1012752	Hemodialysis Procedures
	or	procedure	UMLS:CPT:90935	Hemodialysis procedure with single evaluation by a physician or other qualified health care professional
	or	procedure	UMLS:SNOMED:302497006	Hemodialysis

or	procedure	UMLS:CPT:1012740	Dialysis Services and Procedures
or	diagnosis	UMLS:ICD10CM:Z99.2	Dependence on renal dialysis

Supplemental Table S9. Compare Outcome Definitions

Mortality		
Code type	**Code**	**Code name**
Demographics	Deceased	Deceased
Diagnosis	UMLS:ICD10CM:R99	Ill-defined and unknown cause of mortality
Settings for the performed analyses		
Kaplan - Meier survival analysis		excluding patients with outcome prior to the time window
Major adverse cardiovascular event (MACE)		
Code type	**Code**	**Code name**
Demographics	Deceased	Deceased
Diagnosis	UMLS:ICD10CM:R99	Ill-defined and unknown cause of mortality
Diagnosis	UMLS:ICD10CM:I21	Acute myocardial infarction
Diagnosis	UMLS:ICD10CM:I46	Cardiac arrest
Diagnosis	UMLS:ICD10CM:I61	Nontraumatic intracerebral hemorrhage
Diagnosis	UMLS:ICD10CM:I63	Cerebral infarction
Settings for the performed analyses		
Kaplan - Meier survival analysis		excluding patients with outcome prior to the time window
Major adverse kidney event (MAKE)		
Code type	**Code**	**Code name**
Demographics	NA	Deceased
Diagnosis	UMLS:ICD10CM:R99	Ill-defined and unknown cause of mortality
Procedure	UMLS:CPT:90937	Hemodialysis procedure requiring repeated evaluation(s) with or without substantial revision of dialysis prescription
Procedure	UMLS:CPT:90947	Dialysis procedure other than hemodialysis (eg, peritoneal dialysis, hemofiltration, or other continuous renal replacement therapies) requiring repeated evaluations by a physician or other qualified health care professional, with or without substantial revision of dialysis prescription
Procedure	UMLS:CPT:90945	Dialysis procedure other than hemodialysis (eg, peritoneal dialysis, hemofiltration, or other continuous renal replacement therapies), with single evaluation by a physician or other qualified health care professional
Procedure	UMLS:CPT:1012752	Hemodialysis Procedures
Procedure	UMLS:CPT:90935	Hemodialysis procedure with single evaluation by a physician or other qualified health care professional
Procedure	UMLS:SNOMED:302497006	Hemodialysis
Procedure	UMLS:CPT:1012740	Dialysis Services and Procedures

Diagnosis	UMLS:ICD10CM:Z99.2	Dependence on renal dialysis
Laboratory	TNX:8001	Glomerular filtration rate/1.73 sq M.predicted [Volume Rate/Area] in Serum, Plasma or Blood by Creatinine-based formula (MDRD) (at most 14.00 mL/min/{1.73_m2} (most recent occurrence))
Settings for the performed analyses		
Kaplan - Meier survival analysis		including patients with outcome prior to the time window

Diabetic ketoacidosis (DKA)		
Code type	**Code**	**Code name**
Diagnosis	UMLS:ICD10CM:E11.1	Type 2 diabetes mellitus with ketoacidosis
Settings for the performed analyses		
Kaplan - Meier survival analysis		excluding patients with outcome prior to the time window

Osteoporotic fracture		
Code type	**Code**	**Code name**
Diagnosis	UMLS:ICD10CM:M80	Osteoporosis with current pathological fracture
Settings for the performed analyses		
Kaplan - Meier survival analysis		excluding patients with outcome prior to the time window

Appendicitis		
Code type	**Code**	**Code name**
Diagnosis	UMLS:ICD10CM:K35	Acute appendicitis
Diagnosis	UMLS:ICD10CM:K36	Other appendicitis
Diagnosis	UMLS:ICD10CM:K37	Unspecified appendicitis
Settings for the performed analyses		
Kaplan - Meier survival analysis		excluding patients with outcome prior to the time window

Hematologic malignancy		
Code type	**Code**	**Code name**
Diagnosis	UMLS:ICD10CM:C81-C96	Malignant neoplasms of lymphoid, hematopoietic and related tissue
Settings for the performed analyses		
Kaplan - Meier survival analysis		excluding patients with outcome prior to the time window

Common cold		
Code type	**Code**	**Code name**
Diagnosis	UMLS:ICD10CM:J00	Acute nasopharyngitis [common cold]
Settings for the performed analyses		
Kaplan - Meier survival analysis		excluding patients with outcome prior to the time window

Irritable bowel syndrome		
Code type	**Code**	**Code name**
Diagnosis	UMLS:ICD10CM:K58	Irritable bowel syndrome
Settings for the performed analyses		

Kaplan - Meier survival analysis		excluding patients with outcome prior to the time window
Burn		
Code type	**Code**	**Code name**
Diagnosis	UMLS:ICD10CM:T20-T25	Burns and corrosions of external body surface, specified by site
Settings for the performed analyses		
Kaplan - Meier survival analysis		excluding patients with outcome prior to the time window
Suicide attempt & ideation		
Code type	**Code**	**Code name**
Diagnosis	UMLS:ICD10CM:T14.91	Suicide attempt
Diagnosis	UMLS:ICD10CM:R45.851	Suicidal ideations
Settings for the performed analyses		
Kaplan - Meier survival analysis		excluding patients with outcome prior to the time window
Acute myocardial infarction (AMI)		
Code type	**Code**	**Code name**
Diagnosis	UMLS:ICD10CM:I21	Acute myocardial infarction
Settings for the performed analyses		
Kaplan - Meier survival analysis		excluding patients with outcome prior to the time window
Stroke		
Code type	**Code**	**Code name**
Diagnosis	UMLS:ICD10CM:I61	Nontraumatic intracerebral hemorrhage
Diagnosis	UMLS:ICD10CM:I63	Cerebral infarction
Settings for the performed analyses		
Kaplan - Meier survival analysis		excluding patients with outcome prior to the time window
Incident dialysis		
Code type	**Code**	**Code name**
Procedure	UMLS:CPT:90937	Hemodialysis procedure requiring repeated evaluation(s) with or without substantial revision of dialysis prescription
Procedure	UMLS:CPT:90947	Dialysis procedure other than hemodialysis (eg, peritoneal dialysis, hemofiltration, or other continuous renal replacement therapies) requiring repeated evaluations by a physician or other qualified health care professional, with or without substantial revision of dialysis prescription
Procedure	UMLS:CPT:90945	Dialysis procedure other than hemodialysis (eg, peritoneal dialysis, hemofiltration, or other continuous renal replacement therapies), with single evaluation by a physician or other qualified health care professional

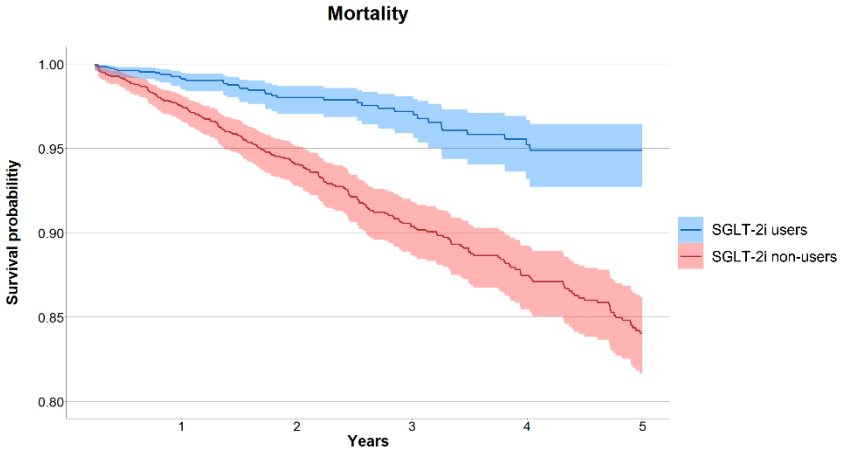
Procedure	UMLS:CPT:90935	Hemodialysis procedure with single evaluation by a physician or other qualified health care professional
Procedure	UMLS:CPT:1012752	Hemodialysis Procedures
Procedure	UMLS:SNOMED:302497006	Hemodialysis
Procedure	UMLS:CPT:1012740	Dialysis Services and Procedures
Diagnosis	UMLS:ICD10CM:Z99.2	Dependence on renal dialysis
Settings for the performed analyses		
Kaplan - Meier survival analysis		including patients with outcome prior to the time window
Acute kidney injury (AKI)		
Code type	**Code**	**Code name**
Diagnosis	UMLS:ICD10CM:N17	Acute kidney failure
Settings for the performed analyses		
Kaplan - Meier survival analysis		including patients with outcome prior to the time window
Urinary tract infection (UTI)		
Code type	**Code**	**Code name**
Diagnosis	UMLS:ICD10CM:N39.0	Urinary tract infection, site not specified
Diagnosis	UMLS:ICD10CM:N30	Cystitis
Diagnosis	UMLS:ICD10CM:N10	Acute pyelonephritis
Settings for the performed analyses		
Kaplan - Meier survival analysis		excluding patients with outcome prior to the time window
Urogenital candidiasis		
Code type	**Code**	**Code name**
Diagnosis	UMLS:ICD10CM:B37.3	Candidiasis of vulva and vagina
Diagnosis	UMLS:ICD10CM:B37.4	Candidiasis of other urogenital sites
Settings for the performed analyses		
Kaplan - Meier survival analysis		excluding patients with outcome prior to the time window

Supplemental Table S10. Diagnosis and Medication Codes Used in the Study

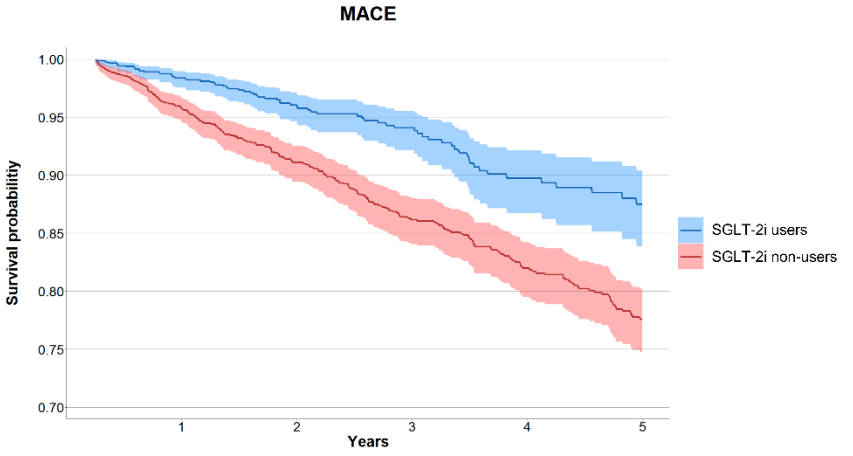
Diagnosis Code		
Disease	**Code (ICD-10-CM)**	**Code name**
Hypertension	I10	Essential (primary) hypertension
Heart failure	I50	Heart failure
DM nephropathy	E11.2	Type 2 diabetes mellitus with kidney complications
DM ophthalmology	E11.3	Type 2 diabetes mellitus with ophthalmic complications
DM neuropathy	E11.4	Type 2 diabetes mellitus with neurological complications
Liver diseases	K70-K77	Diseases of liver
Chronic lower respiratory diseases	J40-J4A	Chronic lower respiratory diseases
Systemic connective tissue disorders	M30-M36	Systemic connective tissue disorders
Neoplasms	C00-D49	Neoplasms
Dyslipidemia	E78	Disorders of lipoprotein metabolism and other lipidemias
Obesity	E66	Overweight and obesity
Nephrotic syndrome	N04	Nephrotic syndrome
Cystic kidney disease	Q61	Cystic kidney disease
Gout	M10	Gout
Proteinuria	R80	Proteinuria
Smoking	Z72.0	Tobacco use
Medication Code		
Drug	**Code**	**Code name**
Corticosteroids	ATC:H02	CORTICOSTEROIDS FOR SYSTEMIC USE
Insulin	ATC:A10A	INSULINS AND ANALOGUES
Biguanides	ATC:A10BA	Biguanides
Glucagon-like peptide-1 (GLP-1) agonists	ATC:A10BJ	Glucagon-like peptide-1 (GLP-1) analogues
Dipeptidyl peptidase 4 (DPP-4) inhibitors	ATC:A10BH	Dipeptidyl peptidase 4 (DPP-4) inhibitors
Sulfonylureas	ATC:A10BB	Sulfonylureas
Thiazolidinediones	ATC:A10BG	Thiazolidinediones
HMG-CoA reductase inhibitors	ATC:C10AA	HMG CoA reductase inhibitors
Angiotensin-converting enzyme	ATC:C09	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM

inhibitor/Angiotensin II receptor blocker		
Beta-blockers	ATC:C07	BETA BLOCKING AGENTS
Calcium channel blocker	ATC:C08	CALCIUM CHANNEL BLOCKERS
Diuretics	ATC:C03	DIURETICS
Vitamin C	ATC:A11G	ASCORBIC ACID (VITAMIN C), INCL. COMBINATIONS
Tacrolimus	RXNORM:42316	tacrolimus
Mycophenolate mofetil (MMF)	RXNORM:68149	mycophenolate mofetil

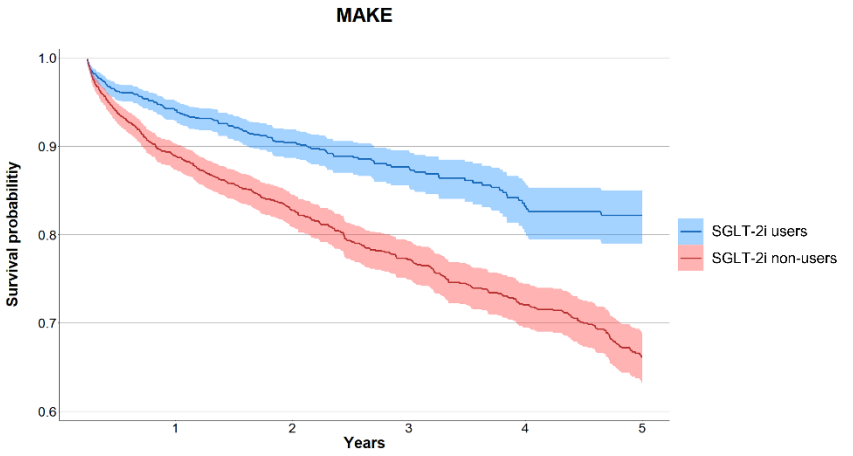
Supplemental Figure S1. Kaplan-Meier Survival Curves for Outcomes of Interest. (A) All-cause mortality; (B) Major adverse cardiovascular events (MACE); (C) Major adverse kidney events (MAKE). Source data are provided as a Source Data file.



A All-cause mortality



B Major adverse cardiovascular events (MACE)

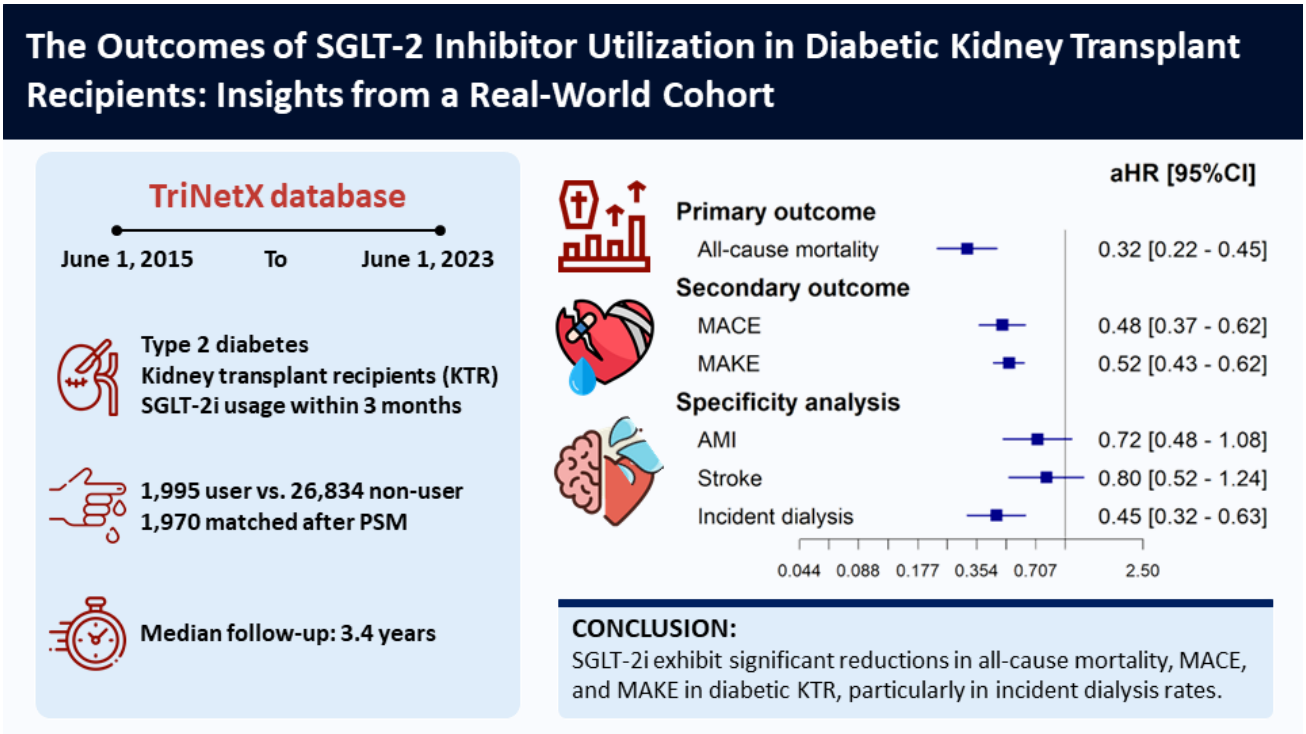


C Major adverse kidney events (MAKE)

Abbreviation:

MACE, major adverse cardiovascular event; MAKE, major adverse kidney event; SGLT-2i, sodium-glucose cotransporter 2 inhibitor.

Supplemental Figure S2. Graphical Abstract



Abbreviation:

aHR, adjusted hazard ratio; AMI, acute myocardial infarction; CI, confidence interval; KTR, kidney transplant recipient; MACE, major adverse cardiovascular event; MAKE, major adverse kidney event; PSM, propensity score matching; SGLT-2i, sodium-glucose cotransporter 2 inhibitor.