SUPPLEMENTAL MATERIAL

SUPPLEMENTAL TABLES

Supplemental Table 1. Inclusion and Exclusion Criteria Diagnosis Codes

Concept code	Concept name	Vocabulary
Inclusion Criteria		
Type 2 diabetes		
250.x0	Diabetes, type II or unspecified type, not stated as uncontrolled	ICD-9
250.x2	Diabetes, type II or unspecified type, uncontrolled	ICD-9
E11.x	Type 2 diabetes mellitus	ICD-10
Cerebrovascular disease		
430	Subarachnoid hemorrhage	ICD-9
431	Intracerebral hemorrhage	ICD-9
432.x	Other and unspecified intracranial hemorrhage	ICD-9
433.x	Occlusion and stenosis of precerebral arteries	ICD-9
434.x	Occlusion of cerebral arteries	ICD-9
435.x	Transient cerebral ischemia	ICD-9
436	Acute, but ill-defined, cerebrovascular disease	ICD-9
437.x	Other and ill-defined cerebrovascular disease	ICD-9
438.x	Late effects of cerebrovascular disease	ICD-9
I60.x-I69.x	Cerebrovascular diseases	ICD-10
G45.x	Transient cerebral ischemic attacks and related syndromes	ICD-10
Coronary artery disease		
410.x-414.x	Ischemic heart disease	ICD-9
I20.x	Angia pectoris	ICD-10
I21.x	ST elevation (STEMI) and non-ST elevation (NSTEMI) myocardial infarction	ICD-10
I22.x	Subsequent ST elevation (STEMI) and non-ST elevation (NSTEMI) myocardial infarction	ICD-10
I23.x	Certain current complications following ST elevation (STEMI) and non-ST elevation (NSTEMI) myocardial infarction (within the 28 day period)	ICD-10
I24.0	Acute coronary thrombosis not resulting in myocardial infarction	ICD-10
I25.x	Chronic ischemic heart disease	ICD-10

Heart failure

428.x	Heart failure	ICD-9
I50.x	Heart failure	ICD-10

Peripheral artery disease

440.2x	Atherosclerosis of native arteries of the extremities	ICD-9
443.81	Peripheral angiopathy in diseases classified elsewhere	ICD-9
443.89	Other specified peripheral vascular diseases	ICD-9
443.9	Peripheral vascular disease, unspecified	ICD-9
447.1	Stricture of artery	ICD-9
447.2	Rupture of artery	ICD-9
447.6	Arteritis, unspecified	ICD-9
447.8	Other specified disorders of arteries and arterioles	ICD-9
447.9	Unspecified disorders of arteries and arterioles	ICD-9
459.2	Compression of vein	ICD-9
459.3x	Chronic venous hypertension (idiopathic)	ICD-9
459.8x	Other specified diseases of the circulatory system	ICD-9
459.9	Unspecified circulatory system disorder	ICD-9
I70.2x	Atherosclerosis of native arteries of the extremities	ICD-10
I73.89	Other specified peripheral vascular diseases	ICD-10
I73.9	Peripheral vascular disease, unspecified	ICD-10
I77.1	Stricture of artery	ICD-10
I77.2	Rupture of artery	ICD-10
I77.6	Arteritis, unspecified	ICD-10
I77.8	Other specified disorders of arteries and arterioles	ICD-10
I77.9	Disorders of arteries and arterioles, unspecified	ICD-10
I79.8	Other disorders of arteries, arterioles and capillaries in diseases classified elsewhere	ICD-10
I87.1	Compression of vein	ICD-10
I87.3x	Chronic venous hypertension (idiopathic)	ICD-10
I99.8	Other disorder of the circulatory system	ICD-10
I99.9	Unspecified disorder of the circulatory system	ICD-10

Concept code	Concept name	Vocabulary
Exclusion Criteria		
Type 1 diabetes		
250.x1	Diabetes, type I [juvenile type], not stated as uncontrolled	ICD-9
250.x3	Diabetes, type I [juvenile type], uncontrolled	ICD-9
E10.x	Type 1 diabetes mellitus	ICD-10
Secondary diabetes		
249.x	Secondary diabetes mellitus	ICD-9
E08.x	Diabetes mellitus due to underlying condition	ICD-10
E09.x	Drug or chemical induced diabetes mellitus	ICD-10
E13.x	Other specified diabetes mellitus	ICD-10

Abbreviations: ICD-9, *International Classification of Disease, Ninth Revision*; ICD-10, *International Classification of Disease, Tenth Revision*.

Supplemental Table 2. Procedure and Diagnosis Codes for HHF, Stroke, MI, and BKA

Concept code	Concept name	Vocabulary
HHF		
428.x	Heart failure	ICD-9
I50.x	Heart failure	ICD-10
Stroke		
433.x1	Occlusion and stenosis of precerebral arteries- carotid artery	ICD-9
434.x1	Occlusion of cerebral arteries- cerebral embolism	ICD-9
436	Acute but ill-defined cerebrovascular disease	ICD-9
I63.x	Cerebral infarction	ICD-10
I67.8x	Other specified cerebrovascular disease	ICD-10
430	Subarachnoid hemorrhage	ICD-9
431	Intracerebral hemorrhage	ICD-9
I60.x	Nontraumatic subarachnoid hemorrhage	ICD-10
I61.x	Nontraumatic intracerebral hemorrhage	ICD-10
MI		
410.x	Acute myocardial infarction	ICD-9
I21.x	ST elevation (STEMI) and non-ST elevation (NSTEMI) myocardial infarction	ICD-10
BKA		
27880	Amputation, leg, through tibia and fibula	CPT-4
27881	Amputation, leg, through tibia and fibula; with immediate fitting technique including application of first cast	CPT-4
27882	Amputation, leg, through tibia and fibula; open, circular (guillotine)	CPT-4
27886	Amputation, leg, through tibia and fibula; re-amputation	CPT-4
27888	Amputation, ankle, through malleoli of tibia and fibula (eg, Syme, Pirogoff type procedures), with plastic closure and resection of nerves	CPT-4
28800	Amputation, foot; midtarsal (eg, Chopart type procedure)	CPT-4
28805	Amputation, foot; transmetatarsal	CPT-4
28810	Amputation, metatarsal, with toe, single	CPT-4
28820	Amputation, toe; metatarsophalangeal joint	CPT-4
28825	Amputation, toe; interphalangeal joint	CPT-4
84.11	Amputation of toe	ICD-9
84.12	Amputation through foot	ICD-9
84.13	Disarticulation of ankle	ICD-9
84.14	Amputation of ankle through malleoli of tibia and fibula	ICD-9
84.15	Other amputation below knee	ICD-9
84.16	Disarticulation of knee	ICD-9

Abbreviations: HHF, hospitalization for heart failure; MI, myocardial infarction; BKA, below-knee lower extremity amputation; CPT-4, *Current Procedural Terminology, 4th Edition*; ICD-9, *International Classification of Disease, Ninth Revision*; ICD-10, *International Classification of Disease, Tenth Revision*.

Supplemental Table 3. Number and Rate of Cardiovascular Outcomes and Mortality by Treatment in the Propensity-Matched ITT Cohort*

Outcome	Canagliflozin (n = 7,333)	Dapagliflozin (n = 1,955)	Empagliflozin (n = 3,341)	DPP-4 inhibitor (n = 3,806)	GLP-1 receptor agonist (n = 2,083)	TZD (n = 766)	SU (n = 2,747)	Insulin (n = 3,057)	Other (n = 310)
Composite of ACM and HHF, n	275	49	39	149	74	42	121	231	16
Follow-up, y	14,997.6	3,465.7	2,563..3	5,717.4	3,650.1	1,271.4	4,086.2	5,689.3	581.3
Incidence rate per 100 person-years	1.83	1.41	1.52	2.61	2.03	3.30	2.96	4.06	2.75
ACM, n	214	30	28	107	51	32	91	184	13
Follow-up, y	15,073.0	3,483.6	2,571.7	5,768.5	3,683.7	1,283.0	4,125.3	5,764.8	587.6
Incidence rate per 100 person-years	1.42	0.86	1.09	1.85	1.38	2.49	2.21	3.19	2.21
HHF, n	77	20	11	52	30	11	33	62	4
Follow-up, y	14,997.6	3,465.7	2,563.3	5,717.4	3,650.1	1,271.4	4,086.2	5,689.3	581.3
Incidence rate per 100 person-years	0.51	0.58	0.43	0.91	0.82	0.87	0.81	1.09	0.69
MACE, n	363	71	49	165	89	53	137	260	16
Follow-up, y	14,886.3	3,440.0	2,559.3	5,699.8	3,639.2	1,256.4	4,077.5	5,649.3	584.6
Incidence rate per 100 person-years	2.44	2.06	1.91	2.89	2.45	4.22	3.36	4.60	2.74
Nonfatal stroke, n	79	18	11	31	22	10	25	36	2
Follow-up, y	14,985.2	3,466.8	2,566.8	5,739.8	3,663.2	1,273.6	4,106.3	5,714.1	585.9
Incidence rate per 100 person-years	0.53	0.52	0.43	0.54	0.60	0.79	0.61	0.63	0.34
Nonfatal MI, n	85	24	12	36	20	15	30	48	1
Follow-up, y	14,974.1	3,456.7	2,564.3	5,728.6	3,659.7	1,264.6	4,096.0	5,698.3	586.3
Incidence rate per 100 person-years	0.57	0.69	0.47	0.63	0.55	1.19	0.73	0.84	0.17
Composite of MACE and HHF, n	419	88	60	198	111	61	161	303	19

Follow-up, y	14,832.3	3,423.3	2,552.2	5,662.5	3,608.3	1,249.3	4,049.3	5,604.0	579.3
Incidence rate per 100 person-years	2.82	2.57	2.35	3.50	3.08	4.88	3.98	5.41	3.28

Propensity matched using an exposure propensity score. Abbreviations: BKA, below-knee lower extremity amputation; ITT, intent-to-treat; DPP-4, dipeptidyl peptidase 4; GLP-1, glucagon-like peptide-1; TZD, thiazolidinedione; SU, sulfonylurea; ACM, all-cause mortality; HHF, hospitalization for heart failure; MACE, major adverse cardiovascular event; MI, myocardial infarction. *Patients within the non-SGLT2i cohort were able to simultaneously initiate medications across multiple non-SGLT2i medication classes; therefore, a single patient could contribute to >1 non-SGLT2i medication class cohort.

Supplemental Table 4. Number and Rate of Cardiovascular Outcomes and Mortality by Treatment in the Propensity-Matched On-Treatment Cohort*

Outcome	Canagliflozin (n = 7,333)	Dapagliflozin (n = 1,955)	Empagliflozin (n = 3,341)	DPP-4 inhibitor (n = 3,806)	GLP-1 receptor agonist (n = 2,083)	TZD (n = 766)	SU (n = 2,747)	Insulin (n = 3,057)	Other (n = 310)
Composite of ACM and HHF, n	89	22	21	95	31	16	61	121	7
Follow-up, y	8,218.4	2,016.7	1,896.8	3,664.5	2,042.4	735.4	2,318.7	3,359.2	223.0
Incidence rate per 100 person-years	1.08	1.09	1.11	2.59	1.52	2.18	2.63	3.60	3.14
ACM, n	72	13	14	64	16	12	45	92	4
Follow-up, y	8,228.1	2,022.2	1,899.9	3,688.2	2,048.4	735.6	2,333.6	3,380.7	223.4
Incidence rate per 100 person-years	0.88	0.64	0.74	1.74	0.78	1.63	1.93	2.72	1.79
HHF, n	20	9	7	36	16	4	17	34	3
Follow-up, y	8,218.4	2,016.7	1,896.8	3,664.5	2,042.4	735.4	2,318.7	3,359.2	223.0
Incidence rate per 100 person-years	0.24	0.45	0.37	0.98	0.78	0.54	0.73	1.01	1.35
MACE, n	144	35	29	98	39	26	72	139	6
Follow-up, y	8,168.3	2,003.2	1,892.9	3,651.2	2,033.3	729.2	2,310.3	3,326.7	222.8
Incidence rate per 100 person-years	1.76	1.75	1.53	2.68	1.92	3.57	3.12	4.18	2.69
Nonfatal stroke, n	39	6	7	19	14	6	10	24	2
Follow-up, y	8,198.2	2,016.3	1,896.9	3,673.1	2,040.4	732.9	2,325.9	3,355.8	222.8
Incidence rate per 100 person-years	0.48	0.30	0.37	0.52	0.69	0.82	0.43	0.72	0.90
Nonfatal MI, n	35	16	9	22	10	9	22	25	0
Follow-up, y	8,198.1	2,009.1	1,895.9	3,666.3	2,041.3	731.9	2,318.1	3,351.7	223.4
Incidence rate per 100 person-years	0.43	0.80	0.47	0.60	0.49	1.23	0.95	0.75	–
Composite of MACE and HHF, n	161	44	36	125	54	30	85	165	9
Follow-up, y	8,158.6	1,997.6	1,889.8	3,630.1	2,027.4	729.0	2,298.1	3,306.6	222.3
Incidence rate per 100 person-years	1.97	2.20	1.90	3.44	2.66	4.12	3.70	4.99	4.05

Propensity matched using an exposure propensity score. Abbreviations: BKA, below-knee lower extremity amputation; DPP-4, dipeptidyl peptidase 4; GLP-1, glucagon-like peptide-1; TZD, thiazolidinedione; SU, sulfonylurea; ACM, all-cause mortality; HHF, hospitalization for heart failure; MACE, major adverse cardiovascular event; MI, myocardial infarction. *Patients within the non-SGLT2i cohort were able to simultaneously initiate medications across multiple non-SGLT2i medication classes; therefore, a single patient could contribute to >1 non-SGLT2i medication class cohort.

Supplemental Table 5. Number and Rate of BKA Outcomes by SGLT2i Medication and Non-SGLT2i Matches in the Propensity-Matched Cohort*

Analytic Approach	Canagliflozin matched cohort		Dapagliflozin matched cohort		Empagliflozin matched cohort	
	Canagliflozin (n=7,333)	Non-SGLT2i (n=7,333)	Dapagliflozin (n=1,955)	Non-SGLT2i (n=1,955)	Empagliflozin (n=3,341)	Non-SGLT2i (n=3,341)
Intent-to-treat[†], n	29	9	3	4	3	5
Follow-up, y	15,045.7	12,247.0	3,478.2	3,290.8	2,567.9	5,445.0
Incidence rate per 100 person-years	0.19	0.07	0.09	0.12	0.12	0.09
On- treatment[†], n	12	4	2	2	3	3
Follow-up, y	8,217.9	7,122.9	2,020.3	1,931.0	1,898.4	3,193.5
Incidence rate per 100 person-years	0.15	0.06	0.10	0.10	0.16	0.09

Propensity matched using an exposure propensity score. Abbreviations: BKA, below-knee lower extremity amputation; SGLT2i, sodium glucose co-transporter 2 inhibitor. *The propensity model was developed based on available clinical characteristics of the entire study cohort. While each patient may have his/her own matched pair (based on propensity score), the specific sub-cohorts (e.g., canagliflozin vs. matched set; dapagliflozin vs. matched set, and empagliflozin vs. matched set) may not be equally balanced on all major confounding factors, particularly in relation to BKA. [†]Patients with prior BKA (n = 9) and their respective match were removed from analyses.

SUPPLEMENTAL FIGURES AND FIGURE LEGENDS

Supplemental Figure 1. Covariate balance of (A) selected and (B) total baseline characteristics.

A.
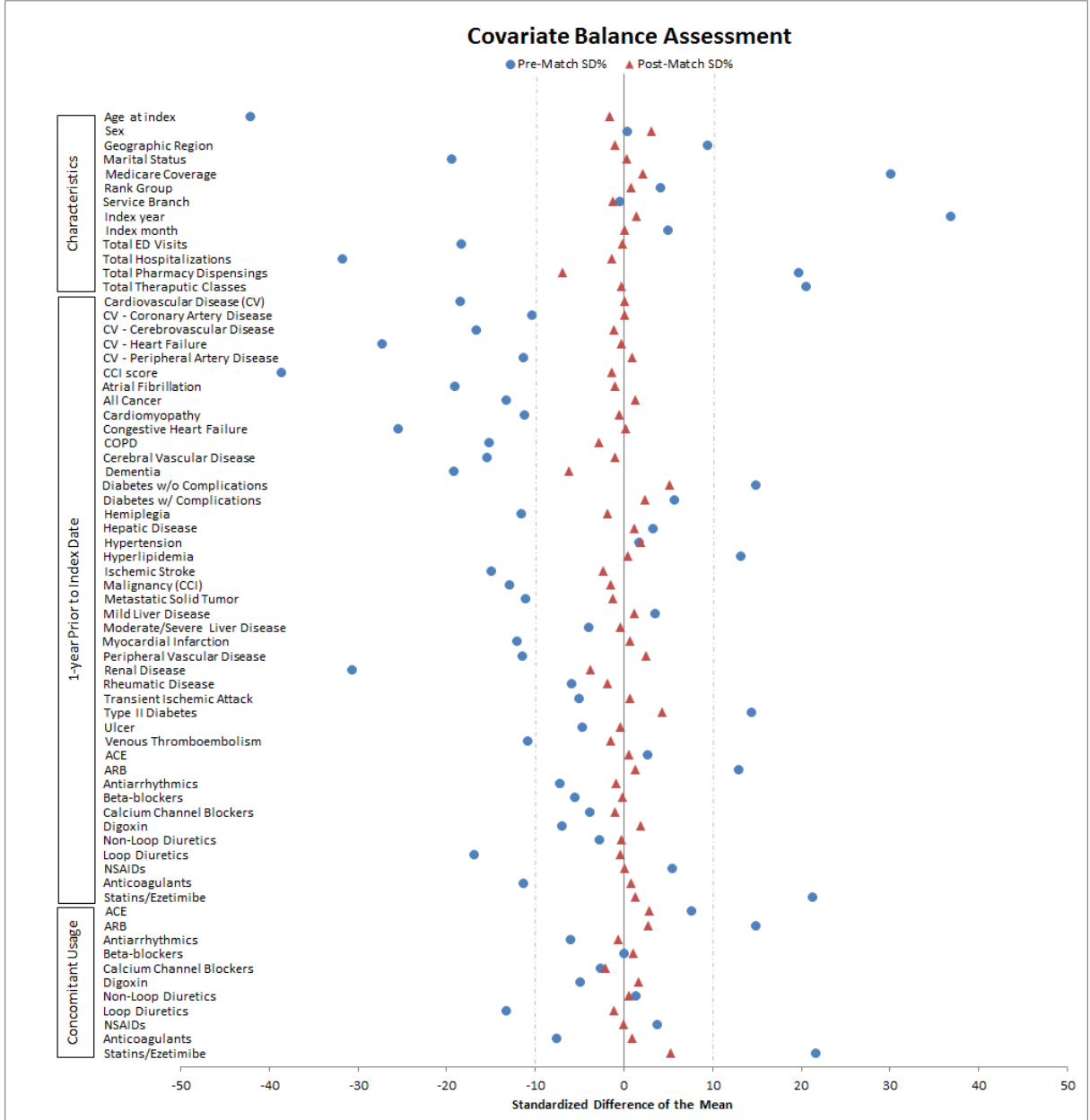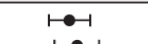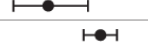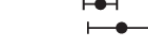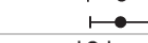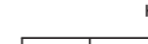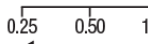
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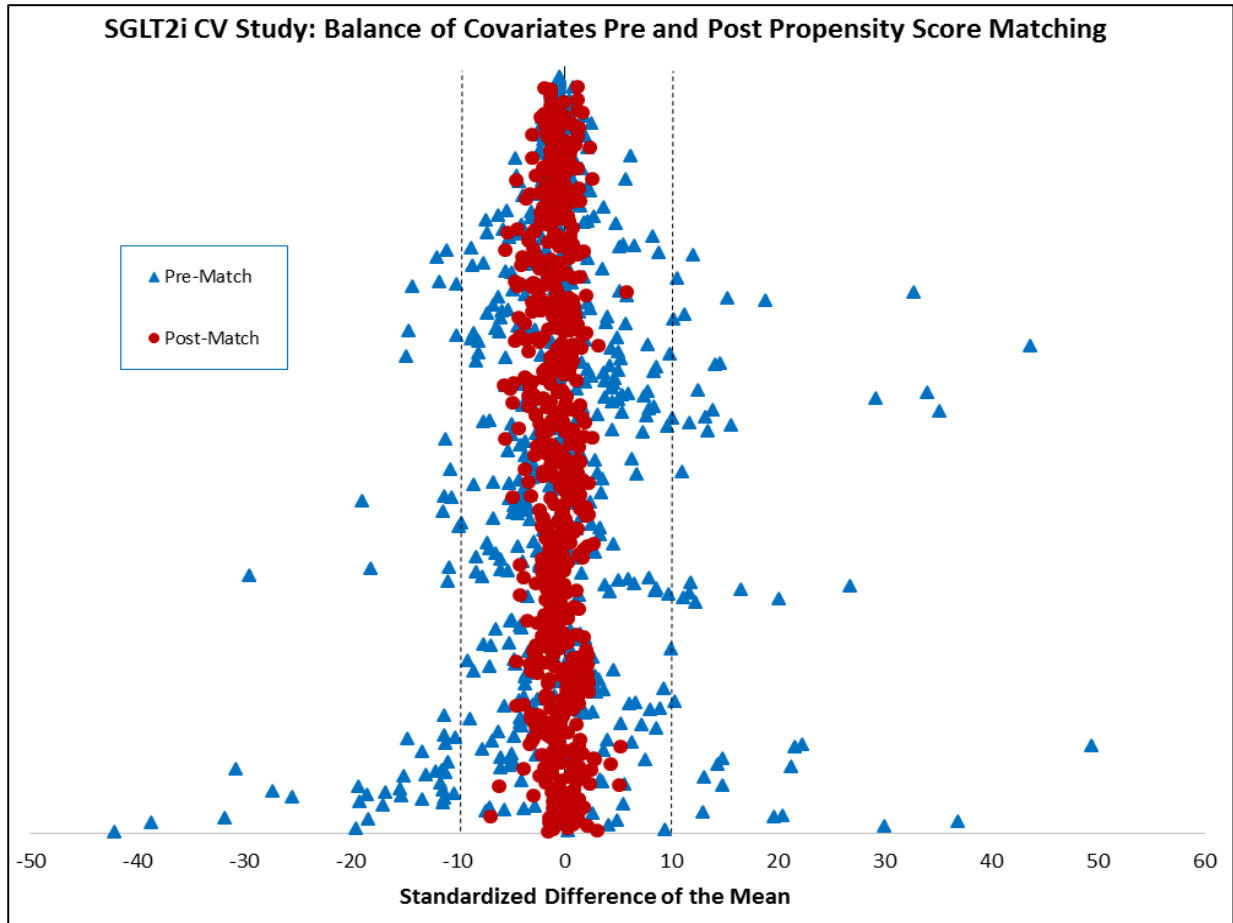
Abbreviations: ED, emergency department; SD, standardized difference; CV, cardiovascular; CVD, cardiovascular disease; CCI, Charlson comorbidity index; COPD, chronic obstructive pulmonary disease; ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; NSAID, nonsteroidal anti-inflammatory drug.

Supplemental Figure 2. Risk of cardiovascular and mortality outcomes for patients in the propensity-matched on-treatment cohort by treatment status.

	Non-SGLT2i (N = 12,629)		SGLT2i (N = 12,629)		Hazard ratio (95% CI)		P value
	Events (n)	Incidence rate per 100 patient-years	Events (n)	Incidence rate per 100 patient-years			
Composite of ACM and HHF	328	2.69	132	1.09	●—●	0.41 (0.33–0.50)	<0.0001
ACM	231	1.88	99	0.81	●—●	0.44 (0.35–0.55)	<0.0001
HHF	109	0.89	36	0.30	●—●	0.33 (0.23–0.49)	<0.0001
MACE	375	3.09	208	1.72	●—●	0.56 (0.47–0.66)	<0.0001
Nonfatal stroke	74	0.61	52	0.43	●—●	0.70 (0.49–0.99)	0.0438
Nonfatal myocardial infarction	86	0.71	60	0.50	●—●	0.69 (0.50–0.96)	0.0292
Composite of MACE and HHF	462	3.83	241	2.00	●—●	0.52 (0.45–0.61)	<0.0001
BKA*	9	0.07	17	0.14	●—●	2.01 (0.89–4.53)	0.0949

0.25   0.50   1.00   2.00   4.00

Favors SGLT2i   Favors Non-SGLT2i

Propensity matched using an exposure propensity score. Abbreviations: SGLT2i, sodium glucose co-transporter 2 inhibitor; CI, confidence interval; HHF, hospitalization for heart failure; MACE, major adverse cardiovascular event; BKA, below-knee lower extremity amputation. *Patients with prior BKA (n = 9) and their respective match were removed from analyses.

Supplemental Figure 3. Risk of the primary outcome in the propensity-matched ITT cohort stratified by treatment status and baseline subgroups.

Subgroup	Non-SGLT2i n/N	SGLT2i n/N	Hazard ratio (95% CI)		P value
Sex					0.3368
Female	231/5670	139/5474		0.62 (0.50–0.76)	
Male	395/6959	224/7155		0.54 (0.46–0.64)	
Age					0.9097
<65 y	130/5272	71/5292		0.58 (0.43–0.77)	
≥65 y	496/7357	292/7337		0.56 (0.49–0.65)	
Insulin usage, prior 12 months					0.5036
Yes	131/2093	106/2887		0.61 (0.47–0.79)	
No	495/10,536	257/9742		0.55 (0.47–0.64)	
GLP-1 usage, prior 12 months					0.2439
Yes	53/1026	52/2467		0.49 (0.33–0.72)	
No	573/11,603	311/10,162		0.61 (0.53–0.70)	
HF, any criterion					0.0201
Yes	265/2548	181/2495		0.68 (0.56–0.82)	
No	361/10,081	182/10,134		0.50 (0.42–0.59)	
HHF, prior 12 months					0.1558
Yes	68/320	50/278		0.75 (0.52–1.08)	
No	558/12,309	313/12,351		0.55 (0.48–0.64)	
PAD					0.5408
Yes	158/1946	88/1991		0.52 (0.40–0.68)	
No	468/10,683	275/10,638		0.59 (0.51–0.68)	
CV risk factors					0.3714
1	266/7386	143/7422		0.54 (0.44–0.66)	
2-3	360/5243	220/5207		0.60 (0.51–0.71)	
Renal disease, CCI component					0.1752
Yes	152/1552	95/1401		0.68 (0.53–0.88)	
No	474/11,077	268/11,228		0.55 (0.47–0.64)	
Chronic renal disease					0.1748
Yes	155/1565	97/1418		0.68 (0.52–0.87)	
No	471/11,064	266/11,211		0.55 (0.47–0.64)	

0.125   0.25   0.50   1.00   2.00

← Favors SGLT2i   Favors Non-SGLT2i →

Propensity matched using an exposure propensity score. Abbreviations: ITT, intent-to-treat; SGLT2i, sodium glucose co-transporter 2 inhibitor; CI, confidence interval; GLP-1, glucagon-like peptide-1; HF, heart failure; HHF, hospitalization for HF; PAD, peripheral artery disease; CV, cardiovascular; CCI, Charlson co-morbidity index.

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Supplemental Figure 4. Sensitivity analyses of the propensity-matched ITT cohort.*

Outcomes per model	Non-SGLT2i Events (n)	SGLT2i Events (n)	Hazard ratio (95% CI)	Hazard ratio (95% CI)	P value
ACM or HHF					
Primary	626	363		0.57 (0.50–0.65)	<0.0001
No insulin	395	289		0.69 (0.59–0.80)	<0.0001
No TZD	584	339		0.57 (0.50–0.65)	<0.0001
No SU	505	250		0.51 (0.44–0.59)	<0.0001
No insulin/TZD/SU	234	153		0.63 (0.52–0.77)	<0.0001
ACM					
Primary	475	272		0.57 (0.49–0.66)	<0.0001
No insulin	291	223		0.72 (0.61–0.86)	0.0003
No TZD	443	253		0.57 (0.49–0.66)	<0.0001
No SU	384	185		0.50 (0.42–0.59)	<0.0001
No insulin/TZD/SU	169	118		0.68 (0.54–0.86)	0.0011
HHF					
Primary	188	108		0.57 (0.45–0.73)	<0.0001
No insulin	126	78		0.58 (0.44–0.77)	0.0002
No TZD	177	101		0.57 (0.45–0.73)	<0.0001
No SU	155	78		0.53 (0.40–0.69)	<0.0001
No insulin/TZD/SU	83	41		0.48 (0.33–0.70)	0.0001
MACE					
Primary	714	483		0.67 (0.60–0.75)	<0.0001
No insulin	454	392		0.82 (0.71–0.94)	0.0035
No TZD	661	453		0.68 (0.60–0.76)	<0.0001
No SU	577	336		0.59 (0.52–0.68)	<0.0001
No insulin/TZD/SU	266	216		0.79 (0.66–0.95)	0.0100
Nonfatal stroke					
Primary	125	108		0.85 (0.66–1.10)	0.2190
No insulin	89	90		0.95 (0.71–1.28)	0.7559
No TZD	115	103		0.88 (0.67–1.15)	0.3476
No SU	100	79		0.80 (0.60–1.08)	0.1433
No insulin/TZD/SU	54	56		1.01 (0.69–1.46)	0.9763
Nonfatal MI					
Primary	148	121		0.81 (0.64–1.03)	0.0888
No insulin	100	94		0.89 (0.67–1.18)	0.4279
No TZD	133	112		0.84 (0.65–1.08)	0.1672
No SU	118	84		0.72 (0.55–0.96)	0.0250
No insulin/TZD/SU	56	48		0.83 (0.57–1.23)	0.3596
MACE or HHF					
Primary	845	567		0.66 (0.60–0.74)	<0.0001
No insulin	542	451		0.78 (0.69–0.89)	0.0001
No TZD	784	534		0.67 (0.60–0.75)	<0.0001
No SU	684	397		0.59 (0.52–0.67)	<0.0001
No insulin/TZD/SU	322	249		0.75 (0.63–0.88)	0.0006
BKA†					
Primary	18	35		1.99 (1.12–3.51)	0.0183
No insulin	9	27		2.87 (1.34–6.14)	0.0065
No TZD	17	34		2.05 (1.14–3.67)	0.0161
No SU	15	29		2.01 (1.08–3.75)	0.0283
No insulin/TZD/SU	2	20		3.83 (1.43–10.28)	0.0076

0.125 0.25 0.50 1.00 2.00 4.00 8.00 16.00
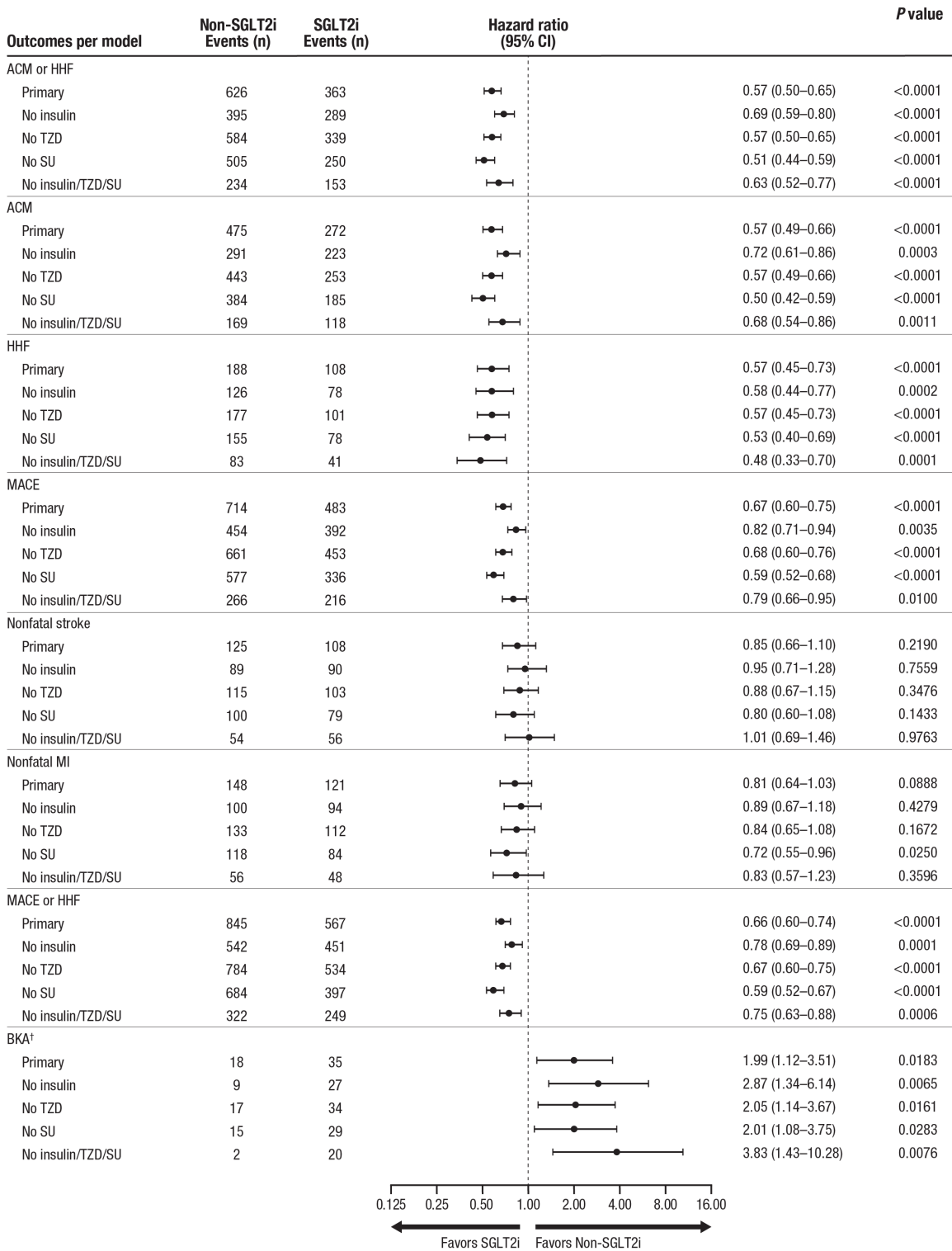
← Favors SGLT2i   Favors Non-SGLT2i →

Propensity matched using an exposure propensity score. Abbreviations: SGLT2i, sodium glucose co-transporter 2 inhibitor; CI, confidence interval; ACM, all-cause mortality; HHF, hospitalization for heart failure; TZD, thiazolidinedione; SU, sulfonylurea; MACE, major adverse cardiovascular event; MI, myocardial infarction; BKA, below-knee lower extremity amputation. *Cohort size: primary = 25,258; no

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insulin = 19,144; no TZD = 23,726; no SU = 19,764; no insulin/TZD/SU = 12,182. The cohort sizes for the BKA analysis were slightly smaller because patients with prior amputations were excluded from analysis. [†]Patients with prior BKA (n = 9) and their respective match were excluded from analysis.

Supplemental Figure 5. Risk of BKA in the propensity-matched ITT cohort stratified by treatment status and baseline subgroups.

Subgroup	Non-SGLT2i n/N	SGLT2i n/N	Hazard ratio (95% CI)		P value
Sex					0.3817
Female	7/5666	9/5469		1.33 (0.50–3.57)	
Male	11/6954	26/7151		2.38 (1.17–4.82)	
Age					0.5485
<65 y	4/5269	10/5289		2.44 (0.77–7.78)	
≥65 y	14/7351	25/7331		1.81 (0.94–3.48)	
Insulin usage, prior 12 months					0.2217
Yes	3/2089	14/2882		3.77 (1.10–12.93)	
No	15/10,531	21/9738		1.52 (0.78–2.96)	
GLP-1 usage, prior 12 months					0.0707
Yes	4/1024	5/2465		0.76 (0.20–2.89)	
No	14/11,596	30/10,155		2.41 (1.27–4.56)	
HF, any criterion					0.4866
Yes	6/2547	15/2493		2.51 (0.96–6.60)	
No	12/10,073	20/10,127		1.73 (0.85–3.51)	
HHF, prior 12 months					0.3473
Yes	1/320	5/277		5.11 (0.59–44.53)	
No	17/12,300	30/12,343		1.81 (0.99–3.28)	
PAD					0.5271
Yes	7/1944	17/1986		2.44 (1.01–5.91)	
No	11/10,682	18/10,637		1.68 (0.79–3.55)	
CV risk factors					0.7544
1	7/7379	12/7418		1.75 (0.69–4.45)	
2-3	11/5241	23/5202		2.13 (1.04–4.38)	
Renal disease, CCI component					0.6239
Yes	5/1549	7/1400		1.52 (0.49–4.65)	
No	13/11,071	28/11,220		2.20 (1.13–4.27)	
Chronic renal disease					0.3587
Yes	6/1562	7/1417		1.25 (0.43–3.64)	
No	12/11,058	28/11,203		2.39 (1.21–4.72)	

Axis: 0.125 0.25 0.50 1.00 2.00 4.00 8.00 16.00 32.00 64.00

← Favors SGLT2i   Favors Non-SGLT2i →

Propensity matched using an exposure propensity score. Abbreviations: BKA, below-knee lower extremity amputation; ITT, intent-to-treat; SGLT2i, sodium glucose co-transporter 2 inhibitor; CI, confidence interval; GLP-1, glucagon-like peptide-1; HF, heart failure; HHF, hospitalization for HF; PAD, peripheral artery disease; CV, cardiovascular; CCI, CCI, Charlson co-morbidity index.
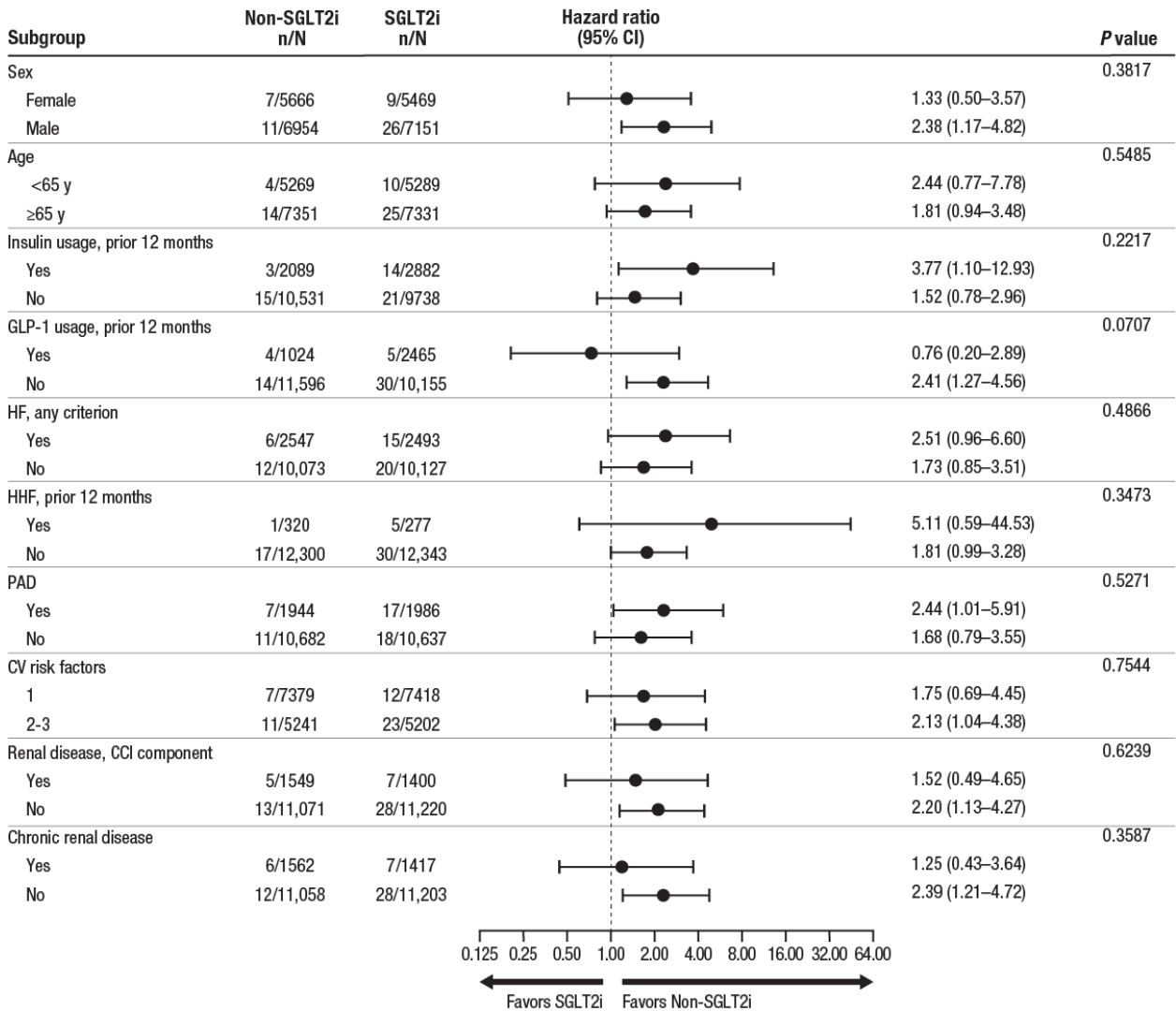
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