

Supplemental Online Content

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This supplemental material has been provided by the authors to give readers additional information about their work.

eMethods

Feasibility Analyses

Before conducting the main effectiveness and safety analyses, we performed a feasibility analysis comparing baseline characteristics of eligible patients with vs. without an HbA1c value recorded within 3 months before cohort entry. The aim was to investigate whether patients with HbA1c value in the de-identified Optum® Clinformatics® Data Mart Database were representative of the full insured population by sharing similar baseline characteristics of those without an HbA1c value. Balance of baseline characteristics between the two sub-populations was assessed with standardized differences, with meaningful imbalances set at values higher than 10% (see eTable 1).

Sensitivity Analyses

We inspected the robustness of the main findings through sensitivity analyses. We explored potential informative censoring by carrying forward the exposure to the first-used medication for one year from cohort entry, without considering drug discontinuation or switching, i.e., mimicking an “intention-to-treat” approach. To assess consistency of treatment effect across subgroups of patients with and without history of cardiovascular disease (defined as a diagnosis of MI, angina, coronary atherosclerosis or other forms of chronic ischemic heart disease, coronary procedure, congestive heart failure, ischemic stroke, peripheral artery disease or surgery, recorded within six months before cohort entry), we tested the significance of an interaction term between exposure and cardiovascular disease history in our primary effectiveness outcome models. Our primary cohort included users of insulin, which is generally prescribed in routine care as treatment intensification (or third-line therapy) in patients with T2D at an advanced stage. Comparisons involving both second-line therapies (SGLT2i and DPP-4i) and a third-line therapy (insulin) may introduce time-lag bias, as insulin users can have a more severe diabetes. This bias is compounded by the fact that the insulin users had already started insulin before cohort entry, unlike the new users of SGLT2i or DPP-4i. To address potential time-lag bias and thus test the internal validity of the primary effectiveness findings, we excluded from the original cohort patients on insulin and required patients to receive metformin at cohort entry. Additionally, as CVOTs showed an increased HHF rate in patients receiving saxagliptin or alogliptin compared to placebo, which resulted in an FDA warning, we conducted a sensitivity analysis for the HHF outcome redefining the comparator group as sitagliptin only, which had a neutral effect on HHF in CVOTs. Finally, to address the potential for unmeasured confounding associated with the high risk for recurrence for certain safety outcomes, we excluded from the original study population patients with a recent history of fracture of the pelvis, hip, humerus, radius and ulna, genital mycotic infection and DKA events at baseline. All secondary cohorts built for the sensitivity analyses were stratified by HbA1c levels and within each HbA1c stratum, PS was re-estimated and matching re-performed. The definitions of the secondary cohorts are reported in eTable 2.

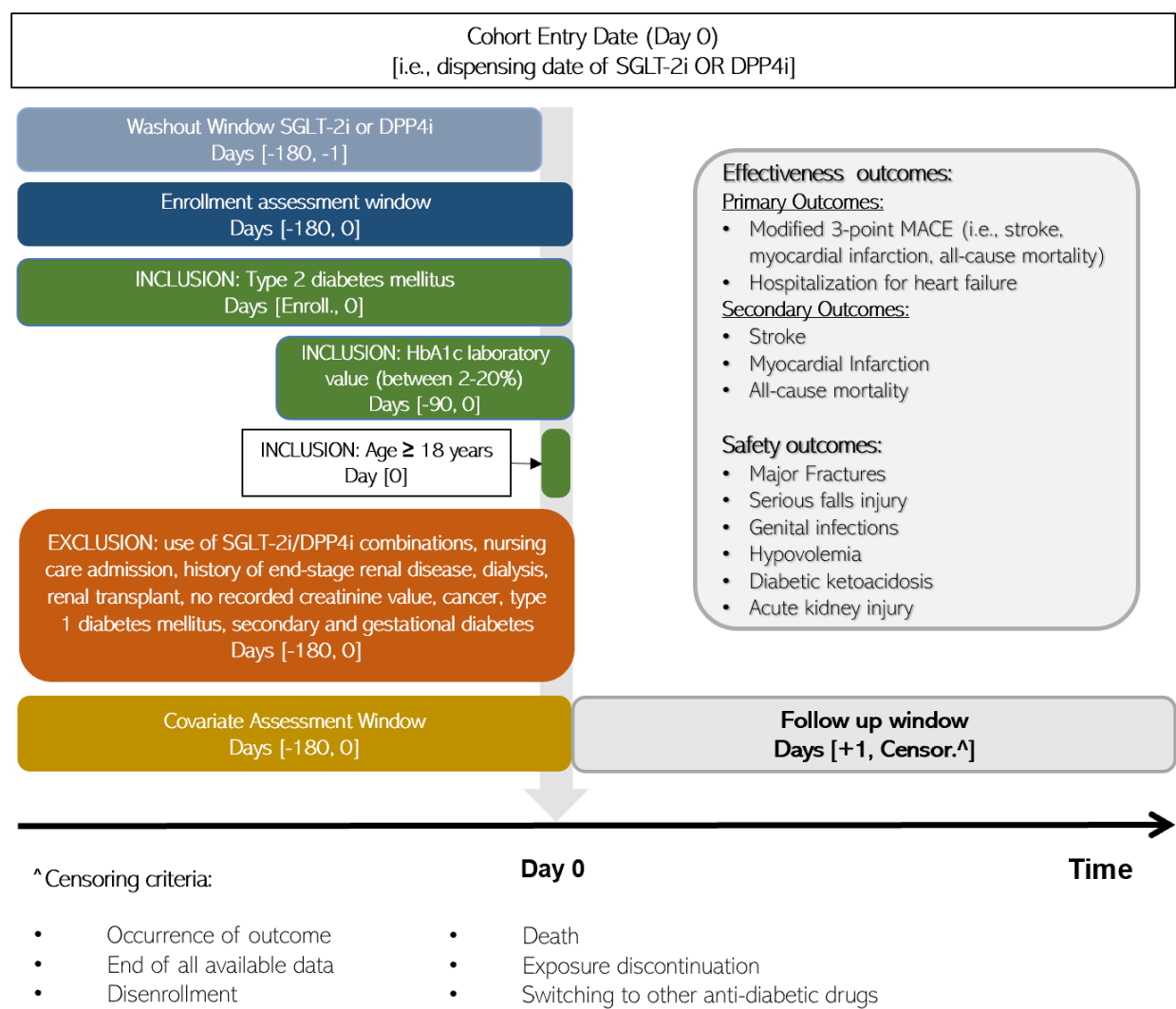
eTable 1. Baseline characteristics of eligible patients with vs. without a HbA_{1c} value within 3 months before cohort entry.

	Patients without HbA _{1c}	Patients with HbA _{1c}	St. Diff.
Number of patients	302,204	144,614	-
Demographics and lifestyle risk factors			
Age			
...mean (sd)	61.56 (12.52)	62.05 (12.37)	-0.04
...median [IQR]	63.00 [53, 70]	64.00 [53, 71]	--
Age Categories			
...18 - 39; n (%)	14,698 (4.9%)	6,496 (4.5%)	0.02
...40 - 44; n (%)	15,602 (5.2%)	6,938 (4.8%)	0.02
...45 - 49; n (%)	23,898 (7.9%)	11,167 (7.7%)	0.01
...50 - 54; n (%)	32,787 (10.8%)	14,947 (10.3%)	0.02
...55 - 59; n (%)	38,882 (12.9%)	17,784 (12.3%)	0.02
...60 - 64; n (%)	37,896 (12.5%)	17,402 (12.0%)	0.02
...65 - 69; n (%)	53,297 (17.6%)	27,360 (18.9%)	-0.03
...70 - 74; n (%)	40,592 (13.4%)	20,698 (14.3%)	-0.03
...75 - 79; n (%)	24,163 (8.0%)	12,171 (8.4%)	-0.01
...80 - 84; n (%)	13,915 (4.6%)	6,659 (4.6%)	0.00
...≥ 85; n (%)	6,474 (2.1%)	2,992 (2.1%)	0.00
Male; n (%)	160,326 (53.1%)	76,358 (52.8%)	0.01
Race			
...White; n (%)	161,982 (53.6%)	71,372 (49.4%)	0.08
Quarter/Year of Cohort Entry			
...Q2 2013; n (%)	7,232 (2.4%)	2,743 (1.9%)	0.03
...Q3 2013; n (%)	8,375 (2.8%)	3,084 (2.1%)	0.05
...Q4 2013; n (%)	8,256 (2.7%)	3,116 (2.2%)	0.03
...Q1 2014; n (%)	7,410 (2.5%)	3,010 (2.1%)	0.03
...Q2 2014; n (%)	7,567 (2.5%)	3,006 (2.1%)	0.03
...Q3 2014; n (%)	8,497 (2.8%)	3,647 (2.5%)	0.02
...Q4 2014; n (%)	8,565 (2.8%)	3,865 (2.7%)	0.01
...Q1 2015; n (%)	7,573 (2.5%)	3,680 (2.5%)	0.00
...Q2 2015; n (%)	7,272 (2.4%)	3,799 (2.6%)	-0.01
...Q3 2015; n (%)	7,701 (2.5%)	3,859 (2.7%)	-0.01
...Q4 2015; n (%)	7,448 (2.5%)	3,437 (2.4%)	0.01
...Q1 2016; n (%)	7,163 (2.4%)	3,997 (2.8%)	-0.03
...Q2 2016; n (%)	6,482 (2.1%)	3,953 (2.7%)	-0.04
...Q3 2016; n (%)	8,701 (2.9%)	4,684 (3.2%)	-0.02
...Q4 2016; n (%)	8,566 (2.8%)	4,319 (3.0%)	-0.01
...Q1 2017; n (%)	9,363 (3.1%)	4,659 (3.2%)	-0.01
...Q2 2017; n (%)	8,368 (2.8%)	4,664 (3.2%)	-0.02
...Q3 2017; n (%)	10,109 (3.3%)	5,168 (3.6%)	-0.02
...Q4 2017; n (%)	9,261 (3.1%)	4,360 (3.0%)	0.01
...Q1 2018; n (%)	9,242 (3.1%)	4,585 (3.2%)	-0.01
...Q2 2018; n (%)	8,832 (2.9%)	4,683 (3.2%)	-0.02
...Q3 2018; n (%)	10,053 (3.3%)	4,598 (3.2%)	0.01
...Q4 2018; n (%)	9,745 (3.2%)	4,129 (2.9%)	0.02
...Q1 2019; n (%)	10,595 (3.5%)	4,895 (3.4%)	0.01

...Q2 2019; n (%)	9,583 (3.2%)	5,170 (3.6%)	-0.02
...Q3 2019; n (%)	10,815 (3.6%)	4,871 (3.4%)	0.01
...Q4 2019; n (%)	10,667 (3.5%)	4,610 (3.2%)	0.02
...Q1 2020; n (%)	11,306 (3.7%)	5,784 (4.0%)	-0.02
...Q2 2020; n (%)	9,409 (3.1%)	4,240 (2.9%)	0.01
...Q3 2020; n (%)	10,645 (3.5%)	5,665 (3.9%)	-0.02
...Q4 2020; n (%)	11,275 (3.7%)	5,650 (3.9%)	-0.01
...Q1 2021; n (%)	14,012 (4.6%)	6,151 (4.3%)	0.01
...Q2 2021; n (%)	12,116 (4.0%)	6,533 (4.5%)	-0.02
Obesity; n (%)	83,418 (27.6%)	44,312 (30.6%)	-0.07
Burden of comorbidities			
Combined comorbidity score, mean (sd)	1.00 (1.94)	1.14 (1.97)	-0.07
Frailty Score, mean (sd)	0.15 (0.04)	0.15 (0.04)	0.00
Diabetes-related Comorbidities			
Diabetic nephropathy; n (%)	40,797 (13.5%)	24,384 (16.9%)	-0.09
Diabetic retinopathy; n (%)	20,286 (6.7%)	10,786 (7.5%)	-0.03
Lower-limb amputations; n (%)	1,694 (0.6%)	750 (0.5%)	0.01
Diabetic ketoacidosis; n (%)	771 (0.3%)	275 (0.2%)	0.02
Other comorbidities			
Acute MI; n (%)	4,440 (1.5%)	1,536 (1.1%)	0.04
MI sequelae/old MI; n (%)	8,276 (2.7%)	3,507 (2.4%)	0.02
Stable angina; n (%)	9,431 (3.1%)	5,188 (3.6%)	-0.03
Unstable angina; n (%)	4,583 (1.5%)	1,792 (1.2%)	0.03
Coronary atherosclerosis; n (%)	45,856 (15.2%)	20,348 (14.1%)	0.03
Coronary procedure; n (%)	3,705 (1.2%)	1,312 (0.9%)	0.03
History of coronary procedure; n (%)	14,677 (4.9%)	6,000 (4.1%)	0.04
Ischemic stroke; n (%)	13,398 (4.4%)	6,159 (4.3%)	0.00
Congestive heart failure; n (%)	22,228 (7.4%)	9,657 (6.7%)	0.03
Acute Kidney Injury; n (%)	9,246 (3.1%)	3,736 (2.6%)	0.03
CKD Stage 3-4; n (%)	23,446 (7.8%)	14,471 (10.0%)	-0.08
Fractures; n (%)	2,692 (0.9%)	1,163 (0.8%)	0.01
Falls; n (%)	7,905 (2.6%)	3,309 (2.3%)	0.02
Mycotic infections	26,200 (8.7%)	13,222 (9.1%)	-0.01
Diabetes treatment			
Number of glucose-lowering medications at cohort entry, mean (sd)	1.21 (0.85)	1.24 (0.85)	-0.04
No use of glucose-lowering medications at baseline; n (%)	51,028 (16.9%)	21,618 (14.9%)	0.05
Metformin (concurrent use); n (%)	189,252 (62.6%)	93,843 (64.9%)	-0.05
Sulfonylureas - 2nd generation (concurrent use); n (%)	85,125 (28.2%)	42,549 (29.4%)	-0.03
GLP-1 RA (concurrent use); n (%)	24,823 (8.2%)	11,799 (8.2%)	0.00
Insulins (concurrent use); n (%)	47,038 (15.6%)	20,826 (14.4%)	0.03
Other Common treatments			
ACEi and ARBs; n (%)	202,159 (66.9%)	100,112 (69.2%)	-0.05
Beta blockers; n (%)	96,683 (32.0%)	44,899 (31.0%)	0.02
Calcium channel blockers; n (%)	75,576 (25.0%)	36,743 (25.4%)	-0.01
Statins; n (%)	197,579 (65.4%)	99,791 (69.0%)	-0.08
NSAIDs; n (%)	56,940 (18.8%)	27,215 (18.8%)	0.00
Opioids; n (%)	67,322 (22.3%)	29,225 (20.2%)	0.05

Antidepressants; n (%)	74,885 (24.8%)	31,932 (22.1%)	0.06
Health Care Utilization Measures			
Endocrinologist (Number of visits), mean (sd)	0.63 (2.66)	0.46 (1.86)	0.07
Cardiologist (Number of visits), mean (sd)	1.18 (3.80)	1.10 (3.54)	0.02
Electrocardiogram; n (%)	79,541 (26.3%)	40,353 (27.9%)	-0.04
Electrocardiogram (Number of tests), mean (sd)	0.59 (1.55)	0.54 (1.35)	0.03
ECG & Other cardiac imaging; n (%)	35,214 (11.7%)	15,712 (10.9%)	0.03
ECG & Other cardiac imaging (Number of tests), mean (sd)	0.54 (3.27)	0.41 (2.67)	0.04
Number of Hospitalization event, mean (sd)	0.09 (0.37)	0.07 (0.31)	0.06
Number of ED event, mean (sd)	0.19 (0.75)	0.18 (0.76)	0.01
Distinct medications ALL, mean (sd)	9.87 (5.23)	9.85 (5.02)	0.00
Distinct medications all BRAND, mean (sd)	2.19 (1.44)	2.16 (1.41)	0.02
Cost pharmacy out-of-pocket (\$), mean (sd)	388.99 (429.95)	385.28 (428.48)	0.01
Abbreviations. St. Diff., standardized difference; SD, standard deviation; MI, myocardial infarction; CKD, chronic kidney disease; GLP-1 RA, Glucagon-like peptide-1 receptor agonists; ARBs, Angiotensin II Receptor Blockers; ACEis, Angiotensin Converting Enzyme inhibitors; NSAIDs, nonsteroidal anti-inflammatory drugs; ECG, electrocardiogram; ED, emergency department.			

eFigure 1. Study design diagram and definition of the cohort



Abbreviations. MACE, major adverse cardiovascular event; SGLT-2i, Sodium-Glucose Cotransporter-2 Inhibitors; DPP4i, dipeptidyl peptidase 4 Inhibitors.

eTable 2. Definitions of inclusion and exclusion criteria

Inclusion criteria	Codes	Setting/Position
HbA1c laboratory records	<u>Loinc</u> : 17855-8, 17856-6, 71875-9, 41995-2, 43150-2, 4548-4, 4549-2, 55454-3, 74246-0	--
Type 2 diabetes mellitus	<u>ICD 9 diagnosis</u> : 250.00, 250.02, 250.10, 250.12, 250.20, 250.22, 250.30, 250.32, 250.40, 250.42, 250.50, 250.52, 250.60, 250.62, 250.70, 250.72, 250.80, 250.82, 250.90, 250.92 <u>ICD 10 diagnosis</u> : E11.x	Inpatient or outpatient setting, any position
Metformin maintenance therapy*	<u>Generic Name</u> : Metformin	2 fills recorded within 6 months before and including cohort entry
Exclusion criteria	Codes	
End-stage renal disease (dialysis or renal transplant)	<u>ICD-9 diagnosis</u> : 585.5, 585.6, 996.81, V42.0, V45.1x, V56.xx <u>ICD-9 procedure</u> : 39.95, 54.98, 55.6x <u>ICD-10 diagnosis</u> : N18.5, N18.6, R88.0, T82.41x, T82.42x, T82.43x, T82.49x, T85.611x, T85.621x, T85.631x, T85.71x, T86.1x, Y84.1, Z48.22, Z49.xx, Z91.15, Z94.0, Z99.2 <u>ICD-10 procedure</u> : 0TY00Zx, 0TY10Zx, 3E1M39Z, 5A1Dx0Z <u>HCPCS/CPT</u> : 50360, 50365, 90920, 90921, 90924, 90925, 90935, 90937, 90939, 90940, 90945, 90947, 90957, 90958, 90959, 90960, 90961, 90962, 90965, 90966, 90969, 90970, 90989, 90993, 90999, 90997, 99512, 99559, 99512, G0257, G0314, G0315, G0316, G0317, G0318, G0319, G0322, G0323, G0326, G0327, S9335, S9339	Inpatient or outpatient setting, any position
Malignancy (excluding non-melanoma skin cancer)	<u>ICD 9 diagnosis</u> : 140.x-209.x (except 173.x, non-melanoma skin cancer and 209.4x, 209.5x, 209.6x) <u>ICD 10 diagnosis</u> : C00.x-C96, D03.x, D45 (except C44.x, non-melanoma skin cancer)	Inpatient or outpatient setting, any position
Nursing home	<u>Claims in SNF dataset</u> <u>CPT codes</u> : 99301, 99302, 99303, 99311, 99312, 99313, 99315, 99316, 99379, 99380, G0066 <u>Place of service code</u> : 31 (skilled nursing facility), 32 (nursing facility), 33 (custodial care facility)	Inpatient or outpatient setting, any position
Type 1 diabetes mellitus	<u>ICD 9 diagnosis</u> : 250.01, 250.03, 250.11, 250.13, 250.21, 250.23, 250.31, 250.33, 250.41, 250.43, 250.51, 250.53, 250.61, 250.63, 250.71, 250.73, 250.81, 250.83, 250.91, 250.93 <u>ICD 10 diagnosis</u> : E10.x	Inpatient or outpatient setting, any position
Secondary and gestational diabetes	<u>ICD 9 diagnosis</u> : 249.x, 648.8x <u>ICD 10 diagnosis</u> : E08.x, E09.x, O24.4x, O99.81	Inpatient or outpatient setting, any position
Insulin*	<u>Generic name</u> : Insulin	1 fill recorded within 6 months before and including cohort entry
Mycotic infections**	<u>ICD 9 diagnosis</u> : 110.x-118.x <u>ICD 10 diagnosis</u> : B35.x-B49.x	Inpatient or outpatient setting, any position
History of fracture of the hip, pelvis, humerus, radius, or ulna**	Humerus fracture: <u>ICD-9 diagnosis</u> : 812.xx, 733.11 <u>ICD 10 diagnosis</u> : M80.02x, M80.82x, M84.42x, M84.62x, S42.5x <u>ICD-9 procedure</u> : 78.52, 79.01, 79.11, 79.21, 79.31, 79.61 <u>ICD-10 procedure</u> : 0PHCx, 0PHDx, 0PHFx 0PHGx, OPSDx, OPSEx, OPSFx, OPSGx CPT-4: 23600, 23605, 23610, 23615, 23620, 23625, 23630, 23665, 23670, 23680, 24500, 24505, 24510, 24515, 24530, 24531, 24535, 24536, 24538, 24540, 24542, 24545, 24560, 24565, 24575, 24586, 24587, 24588, 24516 Radius/ulna fracture:	Inpatient or outpatient setting, any position

	<u>ICD-9 diagnosis:</u> 813.xx, 733.12 <u>ICD 10 diagnosis:</u> M80.03x, M80.83x, M84.43x, M84.63x, S52.x <u>ICD-9 procedure:</u> 78.53, 79.02, 79.12, 79.22, 79.32, 79.62 <u>ICD-10 procedure:</u> OPHHx, OPHKx, OPHJx, OPHLx, OPSHx, OPSKx, OPSJx, OPSLx CPT-4: 24620, 24635, 24650, 24655, 24660, 24665, 24666, 24670, 24680, 24685, 25500, 25505, 25510, 25515, 25530, 25535, 25540, 25545, 25560, 25565, 25570, 25575, 25600, 25605, 25610, 25611, 25615, 25620, 25650 Hip fracture: <u>ICD-9 diagnosis:</u> 820.x (excl. 820.01, 820.11), 821.x (excl. 821.32, 820.11), 733.14, 733.15, 733.96, 733.97 <u>ICD 10 diagnosis:</u> M80.05x, M80.85x, M84.35x, (excl. M84.350x), M84.45x, (excl. M84.454x), M84.65x (excl. M84.650x), M84.75x, S72.x (excl. S72.02x, S72.44x) Pelvic fracture: <u>ICD-9 diagnosis:</u> 808.xx, 733.98 <u>ICD 10 diagnosis:</u> M84.350x, M84.454x, M84.650x, S32.3x-S32.9x <u>HCPCS/CPT:</u> 27193, 27194, 27200, 27202, 27215, 27216, 27217, 27218, 27220, 27222, 27226, 27227, 27228, G0412, G0413, G0414, G0415	
Diabetic ketoacidosis**	<u>ICD-9 diagnosis:</u> 250.1x <u>ICD-10 diagnosis:</u> E10.1x, E11.1x, E13.1x	Inpatient or outpatient setting, any position
*Inclusion and exclusion criteria applied to the secondary cohort of the comparative effectiveness analysis. ** Exclusion criteria applied only to the secondary cohort of the comparative safety outcomes analysis.		

eTable 3. Outcome definitions

Outcome	Component	Diagnosis and/or Procedure Codes	Setting/Position
Effectiveness outcomes			
Modified MACE	Myocardial Infarction	ICD-9 diagnosis: 410.x ICD-10 diagnosis: I21.x (excluding I21.9, I21.Ax)	Inpatient, primary or secondary position
	Stroke	ICD-9 diagnosis: 430, 431, 433.x1, 434.x1, 436 ICD-10 diagnosis: I60.x, I61.x, I63.x, I67.89	Inpatient, primary position
	All-cause mortality	Information on mortality was available through four sources: Centers for Medicare and Medicaid Services, Social Security Administration Master Death Files, in-hospital deaths, and death as a reason for insurance discontinuation.	
All-cause mortality	--	Same definition provided for the MACE outcome	
Myocardial Infarction	--	Same definition provided for the MACE outcome	
Stroke	--	Same definition provided for the MACE outcome	
Hospitalized Heart Failure	--	ICD-9 diagnosis: 428.xx, 398.91, 402.x1, 404.x1, 404.x3 ICD-10 diagnosis: I09.81, I11.0, I13.0, I13.2, I50.xxx	Inpatient, any position
Safety outcomes			
Major fractures	Humerus	Case qualifying (CQ) = 1 Diagnosis (ICD-9: 812.x, 733.11; ICD-10: M80.02xA, M80.82xA, M84.42xA, M84.62xA, S42.xxxA, S42.xxxB, S42.xxxC) OR CQ = 2 Diagnosis (ICD-9: 812.x, 733.11; ICD-10: M80.02xA, M80.82xA, M84.42xA, M84.62xA, S42.xxxA, S42.xxxB, S42.xxxC) AND (overlapping) Procedure (ICD-9: 78.52, 79.01, 79.11, 79.21, 79.31, 79.61; ICD-10: 0PHCx, 0PHDx, 0PHFx 0PHGx, OPSDx, OPSEx, OPSFx, OPSGx; CPT-4: 23600, 23605, 23610, 23615, 23620, 23625, 23630, 23665, 23670, 23680, 24500, 24505, 24510, 24515, 24530, 24531, 24535, 24536, 24538, 24540, 24542, 24545, 24560, 24565, 24575, 24586, 24587, 24588, 24516)	Inpatient, any position Non-inpatient, any position
	Radius/ulna	CQ = 1 Diagnosis (ICD-9: 813.x, 733.12; ICD-10: M80.03xA, M80.83xA, M84.43xA, M84.63xA, S52.xxxA, S52.xxxB, S52.xxxC) OR CQ = 2 Diagnosis (ICD-9: 813.x, 733.12; ICD-10: M80.03xA, M80.83xA, M84.43xA, M84.63xA, S52.xxxA, S52.xxxB, S52.xxxC) AND (overlapping) Procedure (ICD-9: 78.53, 79.02, 79.12, 79.22, 79.32, 79.62; ICD-10: 0PHHx, 0PHKx, 0PHJx, 0PHLx, OPSHx, OPSKx, OPSJx, OPSLx; CPT-4: 24620, 24635, 24650, 24655, 24660, 24665, 24666, 24670, 24680, 24685, 25500, 25505, 25510, 25515, 25530, 25535, 25540, 25545, 25560, 25565, 25570, 25575, 25600, 25605, 25610, 25611, 25615, 25620, 25650)	Inpatient, any position Non-inpatient, any position
	Hip	CQ = 1 Diagnosis [ICD-9: 820.x (excl. 820.01, 820.11), 821.x (excl. 821.32, 820.11), 733.14, 733.15, 733.96, 733.97; ICD 10: M80.05xA, M80.85xA, M84.35xA (excl. M84.350x), M84.45xA (excl. M84.454x), M84.65xA (excl. M84.650x), M84.75xA, S72.xxxA, S72.xxxB, S72.xxxC (excl. S72.02x, S72.44x)] OR CQ = 2 Diagnosis [ICD-9: 820.x (excl. 820.01, 820.11), 821.x (excl. 821.32, 820.11), 733.14, 733.15, 733.96, 733.97; ICD 10: M80.05xA, M80.85xA, M84.35xA (excl. M84.350x), M84.45xA (excl. M84.454x), M84.65xA (excl. M84.650x), M84.75xA, S72.xxxA, S72.xxxB, S72.xxxC (excl. S72.02x, S72.44x)] AND (overlapping) Procedure (ICD-9: 78.55, 79.05, 79.15, 79.25, 79.35, 79.65; ICD-10: 0QH6x, 0QH7x, 0QH8x, 0QH9x, 0QHBx, 0QHCx, 0QS6x, 0QS7x, 0QS8x, 0QS9x, 0QSBx, 0QSCx; CPT: 27230, 27232, 27235, 27236, 27238, 27240, 27244, 27245, 27246, 27248, 27267, 27268, 27269, 27125, 27130, 27500, 27503, 27508, 27509, 27513, 27501, 27502, 27506, 27507, 27514, 27254)	Inpatient, any position Non-inpatient, any position

	Pelvis	CQ = 1 Diagnosis (ICD-9: 808.x, 733.98; ICD-10: ICD 10 diagnosis: M84.350xA, M84.454xA, M84.650xA, S32.3xxA, S32.3xxB, S32.4xxA, S32.4xxB, S32.5xxA, S32.5xxB, S32.6xxA, S32.6xxB, S32.8xxA, S32.8xxB, S32.9xxA, S32.9xxB) OR CQ = 2 Diagnosis (ICD-9: 808.x, 733.98; ICD-10: ICD 10 diagnosis: M84.350xA, M84.454xA, M84.650xA, S32.3xxA, S32.3xxB, S32.4xxA, S32.4xxB, S32.5xxA, S32.5xxB, S32.6xxA, S32.6xxB, S32.8xxA, S32.8xxB, S32.9xxA, S32.9xxB) AND (overlapping) Procedures (CPT/ HCPCS: 27193, 27194, 27200, 27202, 27215, 27216, 27217, 27218, 27220, 27222, 27226, 27227, 27228, G0412, G0413, G0414, G0415)	Inpatient, any position Non-inpatient, any position
Serious falls injuries	Injury AND Falls	<u>ICD-9 diagnosis:</u> non-pathological fractures = 800.00-806.19, 807.0x-807.2x, 808.0x-808.9x, 810.00-814.19, 818.0x-825.1x, 827.0x-829.1x; Brain injury = 852.00-852.39; Dislocation of the hip, knee, shoulder, elbow, or jaw = 830.0x-832.19, 835.00-835.13, 836.30-836.60 <u>ICD-10 diagnosis:</u> non-pathological fractures = S02.xxxA, S06.xxxA, S14.xxxA, S22.xxxA, S32.xxxA, S42.xxxA, S49.xxxA, S52.xxxA, S62.xxxA, S79.xxxA, S72.xxxA, S82.xxxA, S89.xxxA, S99.xxxA, S02.xxxB, S06.xxxB, S14.xxxB, S22.xxxB, S32.xxxB, S42.xxxB, S49.xxxB, S52.xxxB, S62.xxxB, S79.xxxB, S72.xxxB, S82.xxxB, S89.xxxB, S99.xxxB; Brain injury = S06.5xxA, S06.6xxA; Dislocation of the hip, knee, shoulder, elbow, or jaw = S03.0xxA, S43.0xxA, S43.1xxA, S43.2xxA, S43.3xxA, S53.0xxA, S53.1xxA, S73.0xxA, S83.0xxA, S83.1xxA AND (overlapping) <u>ICD-9 diagnosis:</u> E880.0x-E888.9x <u>ICD-10 diagnosis:</u> V00.xxxA, W00.xxxA-W19.xxxA	Inpatient or ED setting, any position
	Injury NOT Motor vehicle accidents	<u>ICD-9 and ICD-10 diagnosis:</u> See codes for non-pathological; Brain injury; Dislocation of the hip, knee, shoulder, elbow, or jaw reported above NOT (not occurring +/- 15 days) <u>ICD-9 diagnosis:</u> E810.x-E819.x <u>ICD-10 diagnosis:</u> V20-V79	Inpatient or ED setting, any position
Hypovolemia	--	<u>ICD-9 diagnosis:</u> 276.50, 276.52, 276.51 <u>ICD-10 diagnosis:</u> E86.9, E86.1, R57.1, E86.0	Inpatient setting and ED visits, any position
Genital infections^	--	<u>ICD-9 diagnosis:</u> 112.1, 616.1x, 112.2, 607.1, 112.2, 605 <u>ICD-10 diagnosis:</u> B37.3, N77.1, N76.0-N76.3, B37.49, B37.42, N48.1, N47.6, B37.49, N47.x (except N47.0, N47.6)	Any setting, any position
Diabetic ketoacidosis	--	<u>ICD-9 diagnosis:</u> 250.1x <u>ICD-10 diagnosis:</u> E10.1x, E11.1x, E13.1x	Inpatient, primary position
Acute kidney injury	--	<u>ICD-9 diagnosis:</u> 584.x <u>ICD-10 diagnosis:</u> N17.x	Inpatient, any position
Lower-limb amputations	--	<u>ICD-9 procedure:</u> 84.1x (excluding 84.18, 84.19) <u>ICD-10 procedure:</u> 0Y.6x (excluding 0Y.62, 0Y.63, 0Y.64) <u>CPT:</u> 27590, 27591, 27592, 27880, 27881, 27882, 27884, 27886, 27888, 27889, 28800, 28805, 28810, 28820, 28825, 27594, 27596, 27598	Any setting, any position

Abbreviations: MACE, Major Adverse Cardiovascular Events; ICD, International Classification of Diseases; CPT, Current Procedural Terminology.

eTable 4. Baseline characteristics of patients with HbA_{1c} < 7.5% initiating SGLT2 inhibitor vs. DPP4 inhibitor therapy before and after 1:1 PS-matching

Baseline characteristics	DPP-4 inhibitor	SGLT2 inhibitor	St. Diff.	DPP-4 inhibitor	SGLT2 inhibitor	St. Diff.
Number of patients	27,783	16,316	-	12,026	12,026	-
Demographics						
Age						
...mean (sd)	66.68 (11.58)	61.06 (11.54)	0.49	62.34 (11.31)	62.47 (11.40)	-0.01
...median [IQR]	68 [60, 75]	62 [53, 69]	-	65 [55, 70]	64 [55, 71]	-
Age squared						
...mean (sd)	4,580.34 (1,474.32)	3,861.37 (1,367.07)	0.51	4,013.50 (1,355.67)	4,032.10 (1,374.78)	-0.01
...median [IQR]	4,624 [3,600, 5,625]	3,844 [2,809, 4,761]	-	4,225 [3,025, 4,900]	4,096 [3,025, 5,041]	-
Age Categories						
...18 - 39; n (%)	600 (2.2%)	701 (4.3%)	-0.12	424 (3.5%)	403 (3.4%)	0.01
...40 - 44; n (%)	701 (2.5%)	763 (4.7%)	-0.12	490 (4.1%)	485 (4.0%)	0.01
...45 - 49; n (%)	1,201 (4.3%)	1,324 (8.1%)	-0.16	800 (6.7%)	852 (7.1%)	-0.02
...50 - 54; n (%)	1,818 (6.5%)	1,763 (10.8%)	-0.15	1,186 (9.9%)	1,129 (9.4%)	0.02
...55 - 59; n (%)	2,574 (9.3%)	2,224 (13.6%)	-0.14	1,548 (12.9%)	1,522 (12.7%)	0.01
...60 - 64; n (%)	2,867 (10.3%)	2,326 (14.3%)	-0.12	1,513 (12.6%)	1,690 (14.1%)	-0.04
...65 - 69; n (%)	5,760 (20.7%)	3,239 (19.9%)	0.02	2,705 (22.5%)	2,505 (20.8%)	0.04
...70 - 74; n (%)	5,173 (18.6%)	2,261 (13.9%)	0.13	1,920 (16.0%)	1,877 (15.6%)	0.01
...75 - 79; n (%)	3,616 (13.0%)	1,145 (7.0%)	0.20	952 (7.9%)	1,020 (8.5%)	-0.02
...80 - 84; n (%)	2,334 (8.4%)	427 (2.6%)	0.26	365 (3.0%)	401 (3.3%)	-0.02
...≥ 85; n (%)	1,139 (4.1%)	143 (0.9%)	0.21	123 (1.0%)	142 (1.2%)	-0.02
Gender						
...Male; n (%)	12,942 (46.6%)	8,466 (51.9%)	-0.11	6,047 (50.3%)	6,034 (50.2%)	0.00
...Female; n (%)	14,841 (53.4%)	7,850 (48.1%)	0.11	5,979 (49.7%)	5,992 (49.8%)	0.00
Geographic region						
...Northeast; n (%)	3,369 (12.1%)	1,531 (9.4%)	0.09	1,170 (9.7%)	1,172 (9.7%)	0.00
...South; n (%)	15,581 (56.1%)	9,743 (59.7%)	-0.07	7,152 (59.5%)	7,164 (59.6%)	0.00
...Midwest; n (%)	1,874 (6.7%)	1,354 (8.3%)	-0.06	934 (7.8%)	949 (7.9%)	0.00
...West; n (%)	6,959 (25.0%)	3,688 (22.6%)	0.06	2,770 (23.0%)	2,741 (22.8%)	0.00
Race categories						
...White; n (%)	13,584 (48.9%)	9,144 (56.0%)	-0.14	6,436 (53.5%)	6,463 (53.7%)	0.00
...Black; n (%)	3,762 (13.5%)	1,902 (11.7%)	0.05	1,471 (12.2%)	1,483 (12.3%)	0.00
...Asian; n (%)	2,679 (9.6%)	1,098 (6.7%)	0.11	906 (7.5%)	914 (7.6%)	0.00
...Hispanic; n (%)	6,244 (22.5%)	3,252 (19.9%)	0.06	2,513 (20.9%)	2,482 (20.6%)	0.01
...Other or unknown; n (%)	1,514 (5.4%)	920 (5.6%)	-0.01	700 (5.8%)	684 (5.7%)	0.00
Quarter/Year of Cohort Entry Date						
...Q2 2013; n (%)	837 (3.0%)	50 (0.3%)	0.21	35 (0.3%)	50 (0.4%)	-0.02
...Q3 2013; n (%)	951 (3.4%)	70 (0.4%)	0.22	54 (0.4%)	68 (0.6%)	-0.03
...Q4 2013; n (%)	871 (3.1%)	117 (0.7%)	0.18	92 (0.8%)	109 (0.9%)	-0.01
...Q1 2014; n (%)	788 (2.8%)	123 (0.8%)	0.15	96 (0.8%)	115 (1.0%)	-0.02
...Q2 2014; n (%)	700 (2.5%)	181 (1.1%)	0.11	155 (1.3%)	160 (1.3%)	0.00
...Q3 2014; n (%)	817 (2.9%)	258 (1.6%)	0.09	214 (1.8%)	223 (1.9%)	-0.01
...Q4 2014; n (%)	791 (2.8%)	309 (1.9%)	0.06	270 (2.2%)	266 (2.2%)	0.00
...Q1 2015; n (%)	714 (2.6%)	316 (1.9%)	0.05	276 (2.3%)	276 (2.3%)	0.00
...Q2 2015; n (%)	723 (2.6%)	354 (2.2%)	0.03	298 (2.5%)	294 (2.4%)	0.01
...Q3 2015; n (%)	831 (3.0%)	344 (2.1%)	0.06	308 (2.6%)	306 (2.5%)	0.01
...Q4 2015; n (%)	723 (2.6%)	340 (2.1%)	0.03	296 (2.5%)	292 (2.4%)	0.01
...Q1 2016; n (%)	836 (3.0%)	299 (1.8%)	0.08	254 (2.1%)	262 (2.2%)	-0.01

...Q2 2016; n (%)	772 (2.8%)	320 (2.0%)	0.05	295 (2.5%)	287 (2.4%)	0.01
...Q3 2016; n (%)	984 (3.5%)	444 (2.7%)	0.05	377 (3.1%)	389 (3.2%)	-0.01
...Q4 2016; n (%)	854 (3.1%)	400 (2.5%)	0.04	354 (2.9%)	338 (2.8%)	0.01
...Q1 2017; n (%)	905 (3.3%)	442 (2.7%)	0.04	379 (3.2%)	370 (3.1%)	0.01
...Q2 2017; n (%)	864 (3.1%)	449 (2.8%)	0.02	391 (3.3%)	382 (3.2%)	0.01
...Q3 2017; n (%)	1,040 (3.7%)	569 (3.5%)	0.01	470 (3.9%)	467 (3.9%)	0.00
...Q4 2017; n (%)	935 (3.4%)	491 (3.0%)	0.02	427 (3.6%)	409 (3.4%)	0.01
...Q1 2018; n (%)	982 (3.5%)	457 (2.8%)	0.04	382 (3.2%)	375 (3.1%)	0.01
...Q2 2018; n (%)	922 (3.3%)	503 (3.1%)	0.01	409 (3.4%)	396 (3.3%)	0.01
...Q3 2018; n (%)	836 (3.0%)	516 (3.2%)	-0.01	407 (3.4%)	409 (3.4%)	0.00
...Q4 2018; n (%)	863 (3.1%)	478 (2.9%)	0.01	385 (3.2%)	378 (3.1%)	0.01
...Q1 2019; n (%)	929 (3.3%)	576 (3.5%)	-0.01	469 (3.9%)	443 (3.7%)	0.01
...Q2 2019; n (%)	887 (3.2%)	625 (3.8%)	-0.03	479 (4.0%)	483 (4.0%)	0.00
...Q3 2019; n (%)	797 (2.9%)	634 (3.9%)	-0.06	447 (3.7%)	437 (3.6%)	0.01
...Q4 2019; n (%)	743 (2.7%)	734 (4.5%)	-0.10	462 (3.8%)	476 (4.0%)	-0.01
...Q1 2020; n (%)	860 (3.1%)	884 (5.4%)	-0.11	591 (4.9%)	564 (4.7%)	0.01
...Q2 2020; n (%)	707 (2.5%)	567 (3.5%)	-0.06	416 (3.5%)	421 (3.5%)	0.00
...Q3 2020; n (%)	878 (3.2%)	915 (5.6%)	-0.12	585 (4.9%)	600 (5.0%)	0.00
...Q4 2020; n (%)	799 (2.9%)	1,039 (6.4%)	-0.17	620 (5.2%)	601 (5.0%)	0.01
...Q1 2021; n (%)	867 (3.1%)	1,131 (6.9%)	-0.18	656 (5.5%)	691 (5.7%)	-0.01
...Q2 2021; n (%)	777 (2.8%)	1,381 (8.5%)	-0.25	677 (5.6%)	689 (5.7%)	0.00
Burden of comorbidities						
Com. comorbidity score, mean (sd)	1.47 (2.26)	1.12 (1.97)	0.17	1.12 (1.99)	1.12 (2.02)	0.00
Frailty Score, mean (sd)	0.15 (0.05)	0.15 (0.04)	0.00	0.15 (0.04)	0.15 (0.04)	0.00
Frailty Score squared, mean (sd)	0.03 (0.02)	0.02 (0.01)	0.63	0.02 (0.01)	0.02 (0.01)	0.00
Frailty score; n (%)						
...Robust (< 0.15)	15,341 (55.2%)	10,243 (62.8%)	-0.15	7,463 (62.1%)	7,518 (62.5%)	-0.01
...Prefrail (0.15 - 0.25)	11,296 (40.7%)	5,723 (35.1%)	0.12	4,271 (35.5%)	4,241 (35.3%)	0.00
...Frail (>= 0.25)	1,146 (4.1%)	350 (2.1%)	0.12	292 (2.4%)	267 (2.2%)	0.01
Lifestyle factors, n (%)						
Overweight	2,551 (9.2%)	1,490 (9.1%)	0.00	1,162 (9.7%)	1,141 (9.5%)	0.01
Obesity	6,889 (24.8%)	6,254 (38.3%)	-0.29	3,959 (32.9%)	3,995 (33.2%)	-0.01
Smoking	3,498 (12.6%)	2,312 (14.2%)	-0.05	1,664 (13.8%)	1,623 (13.5%)	0.01
Diabetes-related conditions, n (%)						
Diabetic nephropathy	5,948 (21.4%)	2,353 (14.4%)	0.18	1,788 (14.9%)	1,818 (15.1%)	-0.01
Diabetic retinopathy	1,803 (6.5%)	964 (5.9%)	0.02	677 (5.6%)	672 (5.6%)	0.00
Diabetes with other ophthalmic manifestations	1,614 (5.8%)	649 (4.0%)	0.08	538 (4.5%)	526 (4.4%)	0.00
Diabetic neuropathy	5,288 (19.0%)	2,938 (18.0%)	0.03	2,119 (17.6%)	2,130 (17.7%)	0.00
Diabetes with peripheral circulatory disorders	449 (1.6%)	70 (0.4%)	0.12	45 (0.4%)	58 (0.5%)	-0.01
Diabetic foot	398 (1.4%)	208 (1.3%)	0.01	144 (1.2%)	148 (1.2%)	0.00
Infection of lower extremities	566 (2.0%)	325 (2.0%)	0.00	212 (1.8%)	211 (1.8%)	0.00
Lower-limb amputations	120 (0.4%)	66 (0.4%)	0.00	40 (0.3%)	44 (0.4%)	-0.02
Erectile dysfunction	708 (2.5%)	586 (3.6%)	-0.06	390 (3.2%)	386 (3.2%)	0.00
Hypoglycemia	3,814 (13.7%)	2,446 (15.0%)	-0.04	1,741 (14.5%)	1,755 (14.6%)	0.00
Hyperglycemia	7,072 (25.5%)	5,833 (35.8%)	-0.22	3,824 (31.8%)	3,856 (32.1%)	-0.01
Diabetic ketoacidosis	35 (0.1%)	22 (0.1%)	0.00	17 (0.1%)	14 (0.1%)	0.00
Hyperosmolar hyperglycemic nonketotic syndrome	130 (0.5%)	88 (0.5%)	0.00	63 (0.5%)	60 (0.5%)	0.00
Diabetes with other complications	1,655 (6.0%)	1,046 (6.4%)	-0.02	734 (6.1%)	745 (6.2%)	0.00
Diabetes mellitus without mention of complications	22,896 (82.4%)	12,870 (78.9%)	0.09	9,643 (80.2%)	9,571 (79.6%)	0.01

Diabetes treatment						
Number of anti-DM medications on index date						
...mean (sd)	0.98 (0.77)	1.13 (0.88)	-0.18	1.02 (0.79)	1.02 (0.81)	0.00
...median [IQR]	1.00 [0.00, 1.00]	1.00 [1.00, 2.00]	-	1.00 [0.00, 1.00]	1.00 [0.00, 1.00]	-
No use of anti-DM medications in prior 180 days; n (%)	6,053 (21.8%)	2,610 (16.0%)	0.15	2,276 (18.9%)	2,266 (18.8%)	0.00
Metformin (any use); n (%)	19,324 (69.6%)	11,989 (73.5%)	-0.09	8,815 (73.3%)	8,777 (73.0%)	0.01
Metformin (concurrent use); n (%)	16,545 (59.6%)	10,120 (62.0%)	-0.05	7,573 (63.0%)	7,400 (61.5%)	0.03
Sulfonylureas - 2nd gen. (any use); n (%)	7,866 (28.3%)	3,709 (22.7%)	0.13	2,917 (24.3%)	2,910 (24.2%)	0.00
Sulfonylureas - 2nd gen. (concurrent use); n (%)	6,334 (22.8%)	2,863 (17.5%)	0.13	2,311 (19.2%)	2,280 (19.0%)	0.01
Thiazolidinediones (any use); n (%)	2,313 (8.3%)	1,444 (8.9%)	-0.02	1,064 (8.8%)	1,022 (8.5%)	0.01
Thiazolidinediones (concurrent use); n (%)	1,811 (6.5%)	1,113 (6.8%)	-0.01	847 (7.0%)	796 (6.6%)	0.02
GLP-1RA (any use); n (%)	1,011 (3.6%)	3,243 (19.9%)	-0.52	919 (7.6%)	1,023 (8.5%)	-0.03
GLP-1RA (concurrent use); n (%)	580 (2.1%)	2,464 (15.1%)	-0.48	537 (4.5%)	754 (6.3%)	-0.08
Insulins (any use); n (%)	2,233 (8.0%)	2,378 (14.6%)	-0.21	1,215 (10.1%)	1,265 (10.5%)	-0.01
Insulins (concurrent use); n (%)	1,536 (5.5%)	1,750 (10.7%)	-0.19	838 (7.0%)	939 (7.8%)	-0.03
Long term use of insulin; n (%)	1,430 (5.1%)	1,541 (9.4%)	-0.17	774 (6.4%)	800 (6.7%)	-0.01
Miscellaneous anti-DM medications; n (%)	428 (1.5%)	188 (1.2%)	0.03	138 (1.1%)	135 (1.1%)	0.00
Other comorbidities at baseline, n (%)						
Hypertension	22,467 (80.9%)	12,786 (78.4%)	0.06	9,476 (78.8%)	9,425 (78.4%)	0.01
Hyperlipidemia	22,240 (80.0%)	13,276 (81.4%)	-0.04	9,678 (80.5%)	9,699 (80.7%)	-0.01
Acute MI	321 (1.2%)	248 (1.5%)	-0.03	153 (1.3%)	148 (1.2%)	0.01
MI sequelae/old MI	729 (2.6%)	477 (2.9%)	-0.02	311 (2.6%)	304 (2.5%)	0.01
Stable angina	1,152 (4.1%)	795 (4.9%)	-0.04	557 (4.6%)	544 (4.5%)	0.00
ACS unstable angina	413 (1.5%)	275 (1.7%)	-0.02	190 (1.6%)	170 (1.4%)	0.02
Coronary atherosclerosis	4,589 (16.5%)	2,689 (16.5%)	0.00	1,816 (15.1%)	1,875 (15.6%)	-0.01
Coronary procedure	285 (1.0%)	235 (1.4%)	-0.04	147 (1.2%)	143 (1.2%)	0.00
History of coronary procedure	1,275 (4.6%)	870 (5.3%)	-0.03	575 (4.8%)	563 (4.7%)	0.00
Congestive heart failure	2,378 (8.6%)	1,284 (7.9%)	0.03	861 (7.2%)	874 (7.3%)	0.00
Cardiomyopathy	816 (2.9%)	523 (3.2%)	-0.02	335 (2.8%)	335 (2.8%)	0.00
Atrial fibrillation	2,005 (7.2%)	1,005 (6.2%)	0.04	699 (5.8%)	727 (6.0%)	-0.01
Cardiac conduction disorders	770 (2.8%)	489 (3.0%)	-0.01	342 (2.8%)	330 (2.7%)	0.01
Other cardiac dysrhythmia	2,080 (7.5%)	1,141 (7.0%)	0.02	785 (6.5%)	828 (6.9%)	-0.02
Valve disorders	1,982 (7.1%)	1,066 (6.5%)	0.02	708 (5.9%)	784 (6.5%)	-0.02
Other cardiovascular disease	2,494 (9.0%)	1,525 (9.3%)	-0.01	968 (8.0%)	1,078 (9.0%)	-0.04
Ischemic stroke	1,610 (5.8%)	693 (4.2%)	0.07	527 (4.4%)	527 (4.4%)	0.00
TIA	382 (1.4%)	168 (1.0%)	0.04	102 (0.8%)	129 (1.1%)	-0.03
Other cerebrovascular conditions	1,226 (4.4%)	515 (3.2%)	0.06	384 (3.2%)	399 (3.3%)	-0.01
PAD and generalized/unspecified atherosclerosis	2,167 (7.8%)	1,007 (6.2%)	0.06	755 (6.3%)	762 (6.3%)	0.00
Acute Kidney Injury	1,235 (4.4%)	368 (2.3%)	0.12	302 (2.5%)	286 (2.4%)	0.01
CKD	4,930 (17.7%)	1,156 (7.1%)	0.33	1,653 (13.7%)	1,671 (13.9%)	-0.01
CKD Stage 1-2	1,664 (6.0%)	766 (4.7%)	0.06	596 (5.0%)	603 (5.0%)	0.00
CKD Stage 3-4	4,930 (17.7%)	1,156 (7.1%)	0.33	974 (8.1%)	1,009 (8.4%)	-0.01
CKD unspecified	1,672 (6.0%)	425 (2.6%)	0.17	341 (2.8%)	341 (2.8%)	0.00
Miscellaneous renal disease	2,313 (8.3%)	733 (4.5%)	0.16	580 (4.8%)	588 (4.9%)	0.00
Major bleeding	1,646 (5.9%)	834 (5.1%)	0.04	630 (5.2%)	627 (5.2%)	0.00
Urinary tract infections	2,842 (10.2%)	1,137 (7.0%)	0.11	889 (7.4%)	905 (7.5%)	0.00
Mycotic infections	2,638 (9.5%)	1,389 (8.5%)	0.03	975 (8.1%)	1,013 (8.4%)	-0.01
Disorder of Electrolyte	1,883 (6.8%)	856 (5.2%)	0.07	619 (5.1%)	644 (5.4%)	-0.01

Disorders of fluid balance	791 (2.8%)	318 (1.9%)	0.06	246 (2.0%)	243 (2.0%)	0.00
Edema	1,916 (6.9%)	1,009 (6.2%)	0.03	734 (6.1%)	737 (6.1%)	0.00
COPD	2,576 (9.3%)	1,153 (7.1%)	0.08	912 (7.6%)	910 (7.6%)	0.00
Asthma	1,764 (6.3%)	1,067 (6.5%)	-0.01	769 (6.4%)	763 (6.3%)	0.00
Obstructive sleep apnea	3,098 (11.2%)	2,757 (16.9%)	-0.16	1,717 (14.3%)	1,748 (14.5%)	-0.01
Pneumonia	762 (2.7%)	350 (2.1%)	0.04	265 (2.2%)	250 (2.1%)	0.01
Osteoarthritis	4,410 (15.9%)	2,319 (14.2%)	0.05	1,780 (14.8%)	1,756 (14.6%)	0.01
Osteoporosis without fractures	1,442 (5.2%)	511 (3.1%)	0.11	430 (3.6%)	444 (3.7%)	-0.01
Fractures	288 (1.0%)	138 (0.8%)	0.02	99 (0.8%)	105 (0.9%)	-0.01
Falls	802 (2.9%)	353 (2.2%)	0.04	260 (2.2%)	272 (2.3%)	-0.01
NASH/NAFLD	1,113 (4.0%)	949 (5.8%)	-0.08	628 (5.2%)	631 (5.2%)	0.00
Liver disease	987 (3.6%)	535 (3.3%)	0.02	391 (3.3%)	399 (3.3%)	0.00
Depression	3,247 (11.7%)	1,920 (11.8%)	0.00	1,453 (12.1%)	1,413 (11.7%)	0.01
Anxiety and sleep disorders	3,879 (14.0%)	2,699 (16.5%)	-0.07	1,928 (16.0%)	1,904 (15.8%)	0.01
Dementia	906 (3.3%)	213 (1.3%)	0.13	201 (1.7%)	181 (1.5%)	0.02
Psychosis	236 (0.8%)	89 (0.5%)	0.04	77 (0.6%)	70 (0.6%)	0.00
Delirium	194 (0.7%)	67 (0.4%)	0.04	45 (0.4%)	51 (0.4%)	0.00
Other medication use, n (%)						
ACEi and ARBs	19,726 (71.0%)	11,145 (68.3%)	0.06	8,296 (69.0%)	8,248 (68.6%)	0.01
Beta blockers	10,001 (36.0%)	5,387 (33.0%)	0.06	3,897 (32.4%)	3,899 (32.4%)	0.00
Calcium channel blockers	8,406 (30.3%)	4,124 (25.3%)	0.11	3,142 (26.1%)	3,137 (26.1%)	0.00
Nitrates and other antianginal agents	1,328 (4.8%)	712 (4.4%)	0.02	523 (4.3%)	507 (4.2%)	0.00
Thiazide and thiazide-like diuretics	3,442 (12.4%)	1,963 (12.0%)	0.01	1,439 (12.0%)	1,439 (12.0%)	0.00
Loop diuretics	3,387 (12.2%)	1,700 (10.4%)	0.06	1,204 (10.0%)	1,202 (10.0%)	0.00
MRA (potassium-sparing diuretics)	953 (3.4%)	711 (4.4%)	-0.05	432 (3.6%)	460 (3.8%)	-0.01
Other K-sparing diuretics and antihypertensive medications	2,791 (10.0%)	1,116 (6.8%)	0.12	871 (7.2%)	900 (7.5%)	-0.01
Antiarrhythmics	478 (1.7%)	244 (1.5%)	0.02	184 (1.5%)	186 (1.5%)	0.00
Anticoagulants (oral)	1,752 (6.3%)	952 (5.8%)	0.02	674 (5.6%)	669 (5.6%)	0.00
Anticoagulants (injectables)	73 (0.3%)	40 (0.2%)	0.02	21 (0.2%)	30 (0.2%)	0.00
Antiplatelet agents	2,580 (9.3%)	1,476 (9.0%)	0.01	1,039 (8.6%)	1,031 (8.6%)	0.00
Statins	19,655 (70.7%)	11,646 (71.4%)	-0.02	8,490 (70.6%)	8,509 (70.8%)	0.00
PCSK9 inhibitors and other lipid-lowering agents	4,152 (14.9%)	2,441 (15.0%)	0.00	1,753 (14.6%)	1,767 (14.7%)	0.00
COPD & asthma medications	4,009 (14.4%)	2,279 (14.0%)	0.01	1,676 (13.9%)	1,699 (14.1%)	-0.01
Corticosteroids (oral)	3,004 (10.8%)	1,731 (10.6%)	0.01	1,269 (10.6%)	1,292 (10.7%)	0.00
Antiosteoporosis agents	1,263 (4.5%)	408 (2.5%)	0.11	349 (2.9%)	361 (3.0%)	-0.01
NSAIDs	5,324 (19.2%)	3,258 (20.0%)	-0.02	2,394 (19.9%)	2,402 (20.0%)	0.00
Opioids	6,254 (22.5%)	3,227 (19.8%)	0.07	2,449 (20.4%)	2,463 (20.5%)	0.00
Gabapentinoids	3,827 (13.8%)	2,151 (13.2%)	0.02	1,614 (13.4%)	1,606 (13.4%)	0.00
UTI antibiotics	3,759 (13.5%)	1,708 (10.5%)	0.09	1,315 (10.9%)	1,333 (11.1%)	-0.01
Antidepressants	6,588 (23.7%)	4,124 (25.3%)	-0.04	3,023 (25.1%)	2,976 (24.7%)	0.01
Anxiolytics/hypnotics	1,724 (6.2%)	1,060 (6.5%)	-0.01	788 (6.6%)	755 (6.3%)	0.01
Benzodiazepines	3,187 (11.5%)	1,709 (10.5%)	0.03	1,341 (11.2%)	1,326 (11.0%)	0.01
Antipsychotics	793 (2.9%)	429 (2.6%)	0.02	333 (2.8%)	326 (2.7%)	0.01
Antiparkinsonian medications	617 (2.2%)	347 (2.1%)	0.01	260 (2.2%)	238 (2.0%)	0.01
Dementia medications	753 (2.7%)	156 (1.0%)	0.13	177 (1.5%)	129 (1.1%)	0.04
Measures of health care use						
Internist; n (%)	26,008 (93.6%)	14,715 (90.2%)	0.12	11,076 (92.1%)	10,996 (91.4%)	0.03
Internist (-30 days to CED); n (%)	20,309 (73.1%)	11,131 (68.2%)	0.11	8,579 (71.3%)	8,487 (70.6%)	0.02
Internist (-180 days to -31 days before CED); n (%)	23,211 (83.5%)	12,904 (79.1%)	0.11	9,757 (81.1%)	9,615 (80.0%)	0.03

Internist (Number of visits)						
...mean (sd)	12.53 (16.89)	10.15 (15.10)	0.15	10.95 (14.95)	10.79 (15.58)	0.01
Endocrinologist; n (%)	3,041 (10.9%)	3,029 (18.6%)	-0.22	1,598 (13.3%)	1,686 (14.0%)	-0.02
Endocrinologist (-30 days to CED); n (%)	1,961 (7.1%)	2,196 (13.5%)	-0.21	1,122 (9.3%)	1,150 (9.6%)	-0.01
Endocrinologist (-180 days to -31 days before CED); n (%)	2,180 (7.8%)	2,194 (13.4%)	-0.18	1,142 (9.5%)	1,219 (10.1%)	-0.02
Endocrinologist (Number of visits)						
...mean (sd)	0.41 (1.83)	0.70 (2.26)	-0.14	0.50 (2.02)	0.51 (1.90)	-0.01
Cardiologist; n (%)	7,298 (26.3%)	4,181 (25.6%)	0.02	2,934 (24.4%)	2,964 (24.6%)	0.00
Cardiologist (-30 days to CED); n (%)	2,845 (10.2%)	1,749 (10.7%)	-0.02	1,168 (9.7%)	1,201 (10.0%)	-0.01
Cardiologist (-180 days to -31 days before CED); n (%)	6,116 (22.0%)	3,476 (21.3%)	0.02	2,450 (20.4%)	2,457 (20.4%)	0.00
Cardiologist (Number of visits)						
...mean (sd)	1.39 (3.99)	1.44 (4.25)	-0.01	1.31 (3.87)	1.35 (4.17)	-0.01
Electrocardiogram; n (%)	9,104 (32.8%)	4,814 (29.5%)	0.07	3,582 (29.8%)	3,551 (29.5%)	0.01
Electrocardiogram (Number of tests)						
...mean (sd)	0.67 (1.62)	0.60 (1.43)	0.05	0.60 (1.45)	0.59 (1.40)	0.01
ECG & Other cardiac imaging; n (%)	3,745 (13.5%)	2,166 (13.3%)	0.01	1,464 (12.2%)	1,526 (12.7%)	-0.02
ECG & Other cardiac imaging (Number of tests)						
...mean (sd)	0.50 (3.00)	0.57 (3.24)	-0.02	0.49 (2.88)	0.53 (3.18)	-0.01
Cardiovascular stress test; n (%)	1,541 (5.5%)	896 (5.5%)	0.00	667 (5.5%)	645 (5.4%)	0.00
HbA1c test order (Number of tests)						
...mean (sd)	1.59 (0.82)	1.63 (0.81)	-0.05	1.60 (0.81)	1.60 (0.81)	0.00
Glucose test and monitoring; n (%)	6,077 (21.9%)	3,522 (21.6%)	0.01	2,426 (20.2%)	2,506 (20.8%)	-0.01
Glucose test and monitoring (Number of tests)						
...mean (sd)	0.48 (1.38)	0.46 (1.41)	0.01	0.42 (1.23)	0.43 (1.15)	-0.01
Microalbuminuria/proteinuria test order; n (%)	14,749 (53.1%)	8,786 (53.8%)	-0.01	6,376 (53.0%)	6,317 (52.5%)	0.01
Microalbuminuria/proteinuria test order (Number of tests)						
...mean (sd)	0.71 (0.84)	0.71 (0.79)	0.00	0.69 (0.80)	0.69 (0.79)	0.00
Metabolic or renal/creatinine panel test order; n (%)	24,742 (89.1%)	14,001 (85.8%)	0.10	10,475 (87.1%)	10,347 (86.0%)	0.03
Metabolic or renal/creatinine panel test order (Number of tests)						
...mean (sd)	1.87 (1.62)	1.75 (1.52)	0.08	1.73 (1.42)	1.73 (1.49)	0.00
Lipid test order; n (%)	23,838 (85.8%)	14,192 (87.0%)	-0.04	10,454 (86.9%)	10,422 (86.7%)	0.01
Lipid test order (Number of tests)						
...mean (sd)	1.36 (0.97)	1.37 (0.94)	-0.01	1.36 (0.92)	1.36 (0.94)	0.00
Uric acid test order; n (%)	3,684 (13.3%)	1,702 (10.4%)	0.09	1,305 (10.9%)	1,288 (10.7%)	0.01
Vitamin D test order; n (%)	8,855 (31.9%)	4,909 (30.1%)	0.04	3,597 (29.9%)	3,651 (30.4%)	-0.01
PTH test order; n (%)	2,112 (7.6%)	853 (5.2%)	0.10	705 (5.9%)	656 (5.5%)	0.02
Hospitalization event (Number of)						
...mean (sd)	0.10 (0.38)	0.07 (0.31)	0.09	0.07 (0.32)	0.07 (0.31)	0.00
LOS (-180 to -31 days before CED)						
...mean (sd)	0.30 (2.05)	0.25 (1.82)	0.03	0.25 (1.86)	0.24 (1.85)	0.01
LOS (-30 days to CED)						
...mean (sd)	0.17 (2.54)	0.07 (0.73)	0.05	0.06 (0.68)	0.07 (0.78)	-0.01
ED event (Number of)						
...mean (sd)	0.24 (0.88)	0.14 (0.59)	0.13	0.15 (0.64)	0.16 (0.63)	-0.02
Distinct medications ALL						
...mean (sd)	10.22 (5.11)	10.18 (5.23)	0.01	9.95 (5.15)	9.94 (5.10)	0.00

Distinct medications all BRAND						
...mean (sd)	2.12 (1.37)	2.30 (1.47)	-0.13	2.09 (1.35)	2.11 (1.35)	-0.01
Cost pharmacy out-of-pocket (\$)						
...mean (sd)	382.93 (432.92)	442.84 (472.80)	-0.13	397.20 (504.64)	401.41 (410.92)	-0.01
Flu vaccine; n (%)	5,851 (21.1%)	3,254 (19.9%)	0.03	2,480 (20.6%)	2,426 (20.2%)	0.01
Pneumococcal vaccine; n (%)	1,680 (6.0%)	931 (5.7%)	0.01	727 (6.0%)	706 (5.9%)	0.00
Breast mammography or MRI; n (%)	3,808 (13.7%)	2,217 (13.6%)	0.00	1,692 (14.1%)	1,678 (14.0%)	0.00
Prostate DRE or PSA; n (%)	5,094 (18.3%)	3,199 (19.6%)	-0.03	2,428 (20.2%)	2,310 (19.2%)	0.03
Colonoscopy; n (%)	1,404 (5.1%)	790 (4.8%)	0.01	631 (5.2%)	609 (5.1%)	0.00
Pap smear; n (%)	1,137 (4.1%)	835 (5.1%)	-0.05	585 (4.9%)	580 (4.8%)	0.00
Bone mineral density; n (%)	1,410 (5.1%)	615 (3.8%)	0.06	491 (4.1%)	496 (4.1%)	0.00
Laboratory results						
Lab value HbA1c (%)						
...mean (sd)	6.77 (0.59)	6.83 (0.62)	-0.10	6.81 (0.62)	6.82 (0.59)	-0.02
...median [IQR]	6.80 [6.40, 7.20]	6.90 [6.45, 7.20]	-	6.85 [6.40, 7.20]	6.90 [6.45, 7.20]	-
eGFR (w/o race)						
...mean (sd)	67.93 (24.51)	76.11 (24.11)	-0.34	75.14 (23.64)	74.86 (23.64)	0.01
...median [IQR]	69.46 [49.14, 87.77]	79.63 [61.31, 93.96]	-	78.78 [59.69, 92.71]	78.00 [60.06, 92.57]	-
Lab result number - Creatinine						
...mean (sd)	1.18 (1.45)	1.12 (1.30)	0.04	1.10 (1.42)	1.11 (1.28)	-0.01
...median [IQR]	0.98 [0.80, 1.27]	0.92 [0.77, 1.12]	-	0.92 [0.77, 1.14]	0.92 [0.77, 1.13]	-
Lab result number - uACR						
...mean (sd)	135.58 (615.05)	104.82 (497.79)	0.05	101.51 (538.60)	108.41 (523.43)	-0.01
...Missing; n (%)	17,532 (63.1%)	9,997 (61.3%)	0.04	7,453 (62.0%)	7,533 (62.6%)	-0.01
Lab result number - Total cholesterol						
...mean (sd)	171.63 (47.59)	170.89 (50.19)	0.02	170.99 (47.16)	171.89 (50.28)	-0.02
...Missing; n (%)	3,893 (14.0%)	2,291 (14.0%)	0.00	1,563 (13.0%)	1,672 (13.9%)	-0.03
Lab result number - LDL cholesterol						
...mean (sd)	93.42 (41.21)	92.90 (42.81)	0.01	93.41 (40.90)	93.16 (42.52)	0.01
...Missing; n (%)	4,080 (14.7%)	2,453 (15.0%)	-0.01	1,680 (14.0%)	1,805 (15.0%)	-0.03
Lab result number - HDL cholesterol						
...mean (sd)	50.50 (19.54)	49.90 (22.02)	0.03	49.23 (19.33)	50.19 (21.48)	-0.05
...Missing; n (%)	4,246 (15.3%)	2,544 (15.6%)	-0.01	1,741 (14.5%)	1,844 (15.3%)	-0.02
Lab result number - Triglycerides						
...mean (sd)	165.52 (111.66)	181.33 (139.24)	-0.13	170.98 (119.12)	178.78 (133.96)	-0.06
...Missing; n (%)	3,911 (14.1%)	2,222 (13.6%)	0.01	1,563 (13.0%)	1,626 (13.5%)	-0.01
Lab result value - Glucose						
...mean (sd)	141.35 (71.61)	150.01 (98.60)	-0.10	143.99 (75.24)	147.97 (95.56)	-0.05
...Missing; n (%)	816 (2.9%)	441 (2.7%)	0.01	312 (2.6%)	316 (2.6%)	0.00

Abbreviations. St. Diff., standardized difference; SD, standard deviation; GLP-1 RA, Glucagon-like peptide-1 receptor agonists; MI, myocardial infarction; TIA, transient ischemic attack; peripheral artery disease; NASH/NAFLD, Nonalcoholic steatohepatitis/Nonalcoholic fatty liver disease; COPD, chronic obstructive pulmonary disease; CKD, chronic kidney disease; ARBs, Angiotensin II Receptor Blockers; ACEis, Angiotensin Converting Enzyme inhibitors; MRA, mineralocorticoid receptor antagonist; PCSK9, Proprotein convertase subtilisin/kexin type 9; NSAIDs, nonsteroidal anti-inflammatory drugs; MRI, magnetic resonance imaging; DRE, digital rectal examination; PSA, prostate-specific antigen; ED, emergency department, LOS, length of stay; ECG, electrocardiogram; eGFR, estimated glomerular filtration rate; uACR, urine albumin-creatinine ratio; LDL, low-density lipoprotein; HDL, high-density lipoprotein.

eTable 5. Baseline characteristics of patients with HbA_{1c} between 7.5% and 9% initiating SGLT2 inhibitor vs. DPP4 inhibitor therapy before and after 1:1 PS-matching

Baseline characteristics	DPP-4 inhibitor	SGLT2 inhibitor	St. Diff.	DPP-4 inhibitor	SGLT2 inhibitor	St. Diff.
Number of patients	30,674	22,312	-	16,145	16,145	-
Demographics						
Age						
...mean (sd)	64.86 (11.87)	60.80 (11.38)	0.35	61.96 (11.41)	62.03 (11.46)	-0.01
...median [IQR]	67 [57, 73]	62 [53, 69]	-	64 [54, 70]	64 [54, 70]	-
Age squared						
...mean (sd)	4,347.85 (1,480.73)	3,826.14 (1,349.10)	0.37	3,969.46 (1,367.59)	3,979.61 (1,376.03)	-0.01
...median [IQR]	4,489 [3,249, 5,329]	3,844 [2,809, 4,761]	-	4,096 [2,916, 4,900]	4,096 [2,916, 4,900]	-
Age Categories						
...18 - 39; n (%)	843 (2.7%)	899 (4.0%)	-0.07	566 (3.5%)	587 (3.6%)	-0.01
...40 - 44; n (%)	962 (3.1%)	1,142 (5.1%)	-0.10	672 (4.2%)	745 (4.6%)	-0.02
...45 - 49; n (%)	1,817 (5.9%)	1,813 (8.1%)	-0.09	1,256 (7.8%)	1,111 (6.9%)	0.03
...50 - 54; n (%)	2,536 (8.3%)	2,589 (11.6%)	-0.11	1,720 (10.7%)	1,663 (10.3%)	0.01
...55 - 59; n (%)	3,183 (10.4%)	3,129 (14.0%)	-0.11	2,003 (12.4%)	2,078 (12.9%)	-0.02
...60 - 64; n (%)	3,356 (10.9%)	3,165 (14.2%)	-0.10	2,081 (12.9%)	2,220 (13.8%)	-0.03
...65 - 69; n (%)	6,337 (20.7%)	4,354 (19.5%)	0.03	3,494 (21.6%)	3,304 (20.5%)	0.03
...70 - 74; n (%)	5,316 (17.3%)	2,999 (13.4%)	0.11	2,460 (15.2%)	2,436 (15.1%)	0.00
...75 - 79; n (%)	3,376 (11.0%)	1,480 (6.6%)	0.16	1,235 (7.6%)	1,295 (8.0%)	-0.01
...80 - 84; n (%)	2,031 (6.6%)	558 (2.5%)	0.20	483 (3.0%)	524 (3.2%)	-0.01
...≥ 85; n (%)	917 (3.0%)	184 (0.8%)	0.16	175 (1.1%)	182 (1.1%)	0.00
Gender						
...Male; n (%)	15,567 (50.7%)	12,554 (56.3%)	-0.11	8,784 (54.4%)	8,794 (54.5%)	0.00
...Female; n (%)	15,107 (49.3%)	9,758 (43.7%)	0.11	7,361 (45.6%)	7,351 (45.5%)	0.00
Geographic region						
...Northeast; n (%)	3,275 (10.7%)	1,892 (8.5%)	0.07	1,425 (8.8%)	1,430 (8.9%)	0.00
...South; n (%)	16,973 (55.3%)	13,102 (58.7%)	-0.07	9,378 (58.1%)	9,346 (57.9%)	0.00
...Midwest; n (%)	2,445 (8.0%)	2,076 (9.3%)	-0.05	1,459 (9.0%)	1,440 (8.9%)	0.00
...West; n (%)	7,981 (26.0%)	5,242 (23.5%)	0.06	3,883 (24.1%)	3,929 (24.3%)	0.00
Race categories						
...White; n (%)	14,686 (47.9%)	12,186 (54.6%)	-0.13	8,380 (51.9%)	8,358 (51.8%)	0.00
...Black; n (%)	3,851 (12.6%)	2,495 (11.2%)	0.04	1,890 (11.7%)	1,930 (12.0%)	-0.01
...Asian; n (%)	2,548 (8.3%)	1,329 (6.0%)	0.09	1,113 (6.9%)	1,092 (6.8%)	0.00
...Hispanic; n (%)	7,838 (25.6%)	4,970 (22.3%)	0.08	3,768 (23.3%)	3,807 (23.6%)	-0.01
...Other or unknown; n (%)	1,751 (5.7%)	1,332 (6.0%)	-0.01	994 (6.2%)	958 (5.9%)	0.01
Quarter/Year of Cohort Entry Date						
...Q2 2013; n (%)	949 (3.1%)	64 (0.3%)	0.22	37 (0.2%)	64 (0.4%)	-0.04
...Q3 2013; n (%)	942 (3.1%)	155 (0.7%)	0.18	117 (0.7%)	145 (0.9%)	-0.02
...Q4 2013; n (%)	1,000 (3.3%)	167 (0.7%)	0.19	137 (0.8%)	159 (1.0%)	-0.02
...Q1 2014; n (%)	934 (3.0%)	173 (0.8%)	0.16	149 (0.9%)	159 (1.0%)	-0.01
...Q2 2014; n (%)	830 (2.7%)	286 (1.3%)	0.10	237 (1.5%)	244 (1.5%)	0.00
...Q3 2014; n (%)	961 (3.1%)	376 (1.7%)	0.09	307 (1.9%)	323 (2.0%)	-0.01
...Q4 2014; n (%)	992 (3.2%)	475 (2.1%)	0.07	388 (2.4%)	403 (2.5%)	-0.01
...Q1 2015; n (%)	810 (2.6%)	546 (2.4%)	0.01	454 (2.8%)	443 (2.7%)	0.01
...Q2 2015; n (%)	846 (2.8%)	527 (2.4%)	0.03	451 (2.8%)	429 (2.7%)	0.01
...Q3 2015; n (%)	919 (3.0%)	495 (2.2%)	0.05	427 (2.6%)	417 (2.6%)	0.00
...Q4 2015; n (%)	786 (2.6%)	465 (2.1%)	0.03	396 (2.5%)	391 (2.4%)	0.01
...Q1 2016; n (%)	976 (3.2%)	491 (2.2%)	0.06	443 (2.7%)	411 (2.5%)	0.01

...Q2 2016; n (%)	975 (3.2%)	510 (2.3%)	0.06	473 (2.9%)	432 (2.7%)	0.01
...Q3 2016; n (%)	1,103 (3.6%)	631 (2.8%)	0.05	516 (3.2%)	539 (3.3%)	-0.01
...Q4 2016; n (%)	999 (3.3%)	626 (2.8%)	0.03	562 (3.5%)	524 (3.2%)	0.02
...Q1 2017; n (%)	1,092 (3.6%)	654 (2.9%)	0.04	560 (3.5%)	557 (3.4%)	0.01
...Q2 2017; n (%)	1,081 (3.5%)	643 (2.9%)	0.03	557 (3.4%)	536 (3.3%)	0.01
...Q3 2017; n (%)	1,104 (3.6%)	750 (3.4%)	0.01	615 (3.8%)	606 (3.8%)	0.00
...Q4 2017; n (%)	963 (3.1%)	603 (2.7%)	0.02	501 (3.1%)	500 (3.1%)	0.00
...Q1 2018; n (%)	1,008 (3.3%)	658 (2.9%)	0.02	541 (3.4%)	538 (3.3%)	0.01
...Q2 2018; n (%)	1,023 (3.3%)	666 (3.0%)	0.02	549 (3.4%)	530 (3.3%)	0.01
...Q3 2018; n (%)	961 (3.1%)	743 (3.3%)	-0.01	569 (3.5%)	580 (3.6%)	-0.01
...Q4 2018; n (%)	827 (2.7%)	634 (2.8%)	-0.01	509 (3.2%)	498 (3.1%)	0.01
...Q1 2019; n (%)	943 (3.1%)	824 (3.7%)	-0.03	616 (3.8%)	607 (3.8%)	0.00
...Q2 2019; n (%)	955 (3.1%)	904 (4.1%)	-0.05	644 (4.0%)	649 (4.0%)	0.00
...Q3 2019; n (%)	901 (2.9%)	937 (4.2%)	-0.07	638 (4.0%)	638 (4.0%)	0.00
...Q4 2019; n (%)	744 (2.4%)	947 (4.2%)	-0.10	579 (3.6%)	585 (3.6%)	0.00
...Q1 2020; n (%)	906 (3.0%)	1,228 (5.5%)	-0.12	741 (4.6%)	735 (4.6%)	0.00
...Q2 2020; n (%)	760 (2.5%)	865 (3.9%)	-0.08	573 (3.5%)	591 (3.7%)	-0.01
...Q3 2020; n (%)	924 (3.0%)	1,157 (5.2%)	-0.11	713 (4.4%)	700 (4.3%)	0.00
...Q4 2020; n (%)	823 (2.7%)	1,213 (5.4%)	-0.14	679 (4.2%)	700 (4.3%)	0.00
...Q1 2021; n (%)	867 (2.8%)	1,399 (6.3%)	-0.17	761 (4.7%)	772 (4.8%)	0.00
...Q2 2021; n (%)	770 (2.5%)	1,500 (6.7%)	-0.20	706 (4.4%)	740 (4.6%)	-0.01
Burden of comorbidities						
Com. comorbidity score, mean (sd)	1.19 (2.03)	1.01 (1.80)	0.09	1.00 (1.82)	1.01 (1.86)	-0.01
Frailty Score, mean (sd)	0.15 (0.04)	0.14 (0.04)	0.25	0.14 (0.04)	0.14 (0.04)	0.00
Frailty Score squared, mean (sd)	0.02 (0.02)	0.02 (0.01)	0.00	0.02 (0.01)	0.02 (0.01)	0.00
Frailty score; n (%)						
...< 0.15	18,690 (60.9%)	14,686 (65.8%)	-0.10	10,530 (65.2%)	10,575 (65.5%)	-0.01
...0.15 - 0.25	11,163 (36.4%)	7,259 (32.5%)	0.08	5,338 (33.1%)	5,273 (32.7%)	0.01
...≥ 0.25	821 (2.7%)	367 (1.6%)	0.08	277 (1.7%)	297 (1.8%)	-0.01
Lifestyle factors, n (%)						
Overweight	2,485 (8.1%)	1,864 (8.4%)	-0.01	1,351 (8.4%)	1,372 (8.5%)	0.00
Obesity	8,178 (26.7%)	8,107 (36.3%)	-0.21	5,209 (32.3%)	5,198 (32.2%)	0.00
Smoking	3,714 (12.1%)	2,897 (13.0%)	-0.03	2,036 (12.6%)	2,031 (12.6%)	0.00
Diabetes-related conditions, n (%)						
Diabetic nephropathy	5,884 (19.2%)	3,350 (15.0%)	0.11	2,460 (15.2%)	2,477 (15.3%)	0.00
Diabetic retinopathy	2,473 (8.1%)	1,842 (8.3%)	-0.01	1,261 (7.8%)	1,267 (7.8%)	0.00
Diabetes with other ophthalmic manifestations	1,686 (5.5%)	983 (4.4%)	0.05	746 (4.6%)	739 (4.6%)	0.00
Diabetic neuropathy	6,128 (20.0%)	4,494 (20.1%)	0.00	3,141 (19.5%)	3,089 (19.1%)	0.01
Diabetes with peripheral circulatory disorders	534 (1.7%)	133 (0.6%)	0.10	126 (0.8%)	117 (0.7%)	0.01
Diabetic foot	445 (1.5%)	330 (1.5%)	0.00	216 (1.3%)	221 (1.4%)	-0.01
Infection of lower extremities	652 (2.1%)	470 (2.1%)	0.00	315 (2.0%)	320 (2.0%)	0.00
Lower-limb amputations	146 (0.5%)	104 (0.5%)	0.00	76 (0.5%)	73 (0.5%)	0.00
Erectile dysfunction	921 (3.0%)	845 (3.8%)	-0.04	556 (3.4%)	539 (3.3%)	0.01
Hypoglycemia	4,124 (13.4%)	3,420 (15.3%)	-0.05	2,395 (14.8%)	2,375 (14.7%)	0.00
Hyperglycemia	9,957 (32.5%)	9,770 (43.8%)	-0.23	6,318 (39.1%)	6,302 (39.0%)	0.00
Diabetic ketoacidosis	42 (0.1%)	32 (0.1%)	0.00	19 (0.1%)	21 (0.1%)	0.00
Hyperosmolar hyperglycemic nonketotic syndrome	137 (0.4%)	89 (0.4%)	0.00	71 (0.4%)	59 (0.4%)	0.00
Diabetes with other complications	1,734 (5.7%)	1,533 (6.9%)	-0.05	996 (6.2%)	991 (6.1%)	0.00
Diabetes mellitus without mention of complications	24,867 (81.1%)	16,980 (76.1%)	0.12	12,590 (78.0%)	12,600 (78.0%)	0.00

Diabetes treatment						
Number of anti-DM medications on index date						
...mean (sd)	1.24 (0.79)	1.40 (0.92)	-0.19	1.27 (0.80)	1.28 (0.85)	-0.01
...median [IQR]	1.00 [1.00, 2.00]	1.00 [1.00, 2.00]	-	1.00 [1.00, 2.00]	1.00 [1.00, 2.00]	-
No use of anti-DM medications in prior 180 days; n (%)	3,843 (12.5%)	1,898 (8.5%)	0.13	1,687 (10.4%)	1,699 (10.5%)	0.00
Metformin (any use); n (%)	23,323 (76.0%)	17,420 (78.1%)	-0.05	12,657 (78.4%)	12,615 (78.1%)	0.01
Metformin (concurrent use); n (%)	20,337 (66.3%)	14,915 (66.8%)	-0.01	11,062 (68.5%)	10,788 (66.8%)	0.04
Sulfonylureas - 2nd gen. (any use); n (%)	13,498 (44.0%)	8,316 (37.3%)	0.14	6,422 (39.8%)	6,424 (39.8%)	0.00
Sulfonylureas - 2nd gen. (concurrent use); n (%)	11,174 (36.4%)	6,756 (30.3%)	0.13	5,300 (32.8%)	5,269 (32.6%)	0.00
Thiazolidinediones (any use); n (%)	2,386 (7.8%)	2,033 (9.1%)	-0.05	1,369 (8.5%)	1,398 (8.7%)	-0.01
Thiazolidinediones (concurrent use); n (%)	1,886 (6.1%)	1,599 (7.2%)	-0.04	1,096 (6.8%)	1,111 (6.9%)	0.00
GLP-1RA (any use); n (%)	1,313 (4.3%)	4,740 (21.2%)	-0.52	1,234 (7.6%)	1,360 (8.4%)	-0.03
GLP-1RA (concurrent use); n (%)	802 (2.6%)	3,637 (16.3%)	-0.48	760 (4.7%)	1,024 (6.3%)	-0.07
Insulins (any use); n (%)	4,483 (14.6%)	5,421 (24.3%)	-0.25	2,911 (18.0%)	2,951 (18.3%)	-0.01
Insulins (concurrent use); n (%)	3,405 (11.1%)	4,226 (18.9%)	-0.22	2,199 (13.6%)	2,268 (14.0%)	-0.01
Long term use of insulin; n (%)	2,286 (7.5%)	2,847 (12.8%)	-0.18	1,491 (9.2%)	1,498 (9.3%)	0.00
Miscellaneous anti-DM medications; n (%)	548 (1.8%)	297 (1.3%)	0.04	232 (1.4%)	230 (1.4%)	0.00
Other comorbidities at baseline, n (%)						
Hypertension	24,135 (78.7%)	17,258 (77.3%)	0.03	12,454 (77.1%)	12,478 (77.3%)	0.00
Hyperlipidemia	24,139 (78.7%)	17,972 (80.5%)	-0.04	12,829 (79.5%)	12,789 (79.2%)	0.01
Acute MI	330 (1.1%)	229 (1.0%)	0.01	156 (1.0%)	157 (1.0%)	0.00
MI sequelae/old MI	775 (2.5%)	494 (2.2%)	0.02	335 (2.1%)	365 (2.3%)	-0.01
Stable angina	1,053 (3.4%)	828 (3.7%)	-0.02	535 (3.3%)	557 (3.4%)	-0.01
ACS unstable angina	348 (1.1%)	270 (1.2%)	-0.01	185 (1.1%)	177 (1.1%)	0.00
Coronary atherosclerosis	4,539 (14.8%)	3,235 (14.5%)	0.01	2,261 (14.0%)	2,262 (14.0%)	0.00
Coronary procedure	250 (0.8%)	201 (0.9%)	-0.01	132 (0.8%)	126 (0.8%)	0.00
History of coronary procedure	1,303 (4.2%)	1,000 (4.5%)	-0.01	669 (4.1%)	680 (4.2%)	-0.01
Congestive heart failure	2,093 (6.8%)	1,325 (5.9%)	0.04	929 (5.8%)	951 (5.9%)	0.00
Cardiomyopathy	707 (2.3%)	520 (2.3%)	0.00	370 (2.3%)	354 (2.2%)	0.01
Atrial fibrillation	1,725 (5.6%)	1,127 (5.1%)	0.02	780 (4.8%)	794 (4.9%)	0.00
Cardiac conduction disorders	667 (2.2%)	452 (2.0%)	0.01	313 (1.9%)	308 (1.9%)	0.00
Other cardiac dysrhythmia	1,851 (6.0%)	1,273 (5.7%)	0.01	894 (5.5%)	914 (5.7%)	-0.01
Valve disorders	1,675 (5.5%)	1,006 (4.5%)	0.05	774 (4.8%)	760 (4.7%)	0.00
Other cardiovascular disease	2,235 (7.3%)	1,554 (7.0%)	0.01	1,085 (6.7%)	1,110 (6.9%)	-0.01
Ischemic stroke	1,425 (4.6%)	851 (3.8%)	0.04	616 (3.8%)	633 (3.9%)	-0.01
TIA	327 (1.1%)	201 (0.9%)	0.02	130 (0.8%)	154 (1.0%)	-0.02
Other cerebrovascular conditions	1,112 (3.6%)	617 (2.8%)	0.05	456 (2.8%)	466 (2.9%)	-0.01
PAD and generalized/unspecified atherosclerosis	2,250 (7.3%)	1,296 (5.8%)	0.06	977 (6.1%)	991 (6.1%)	0.00
Acute Kidney Injury	841 (2.7%)	368 (1.6%)	0.08	288 (1.8%)	289 (1.8%)	0.00
CKD	3,868 (12.6%)	1,333 (6.0%)	0.23	2,024 (12.5%)	2,029 (12.6%)	0.00
CKD Stage 1-2	1,754 (5.7%)	1,087 (4.9%)	0.04	822 (5.1%)	818 (5.1%)	0.00
CKD Stage 3-4	3,868 (12.6%)	1,333 (6.0%)	0.23	1,121 (6.9%)	1,158 (7.2%)	-0.01
CKD unspecified	1,153 (3.8%)	487 (2.2%)	0.09	368 (2.3%)	386 (2.4%)	-0.01
Miscellaneous renal disease	1,899 (6.2%)	790 (3.5%)	0.13	585 (3.6%)	623 (3.9%)	-0.02
Major bleeding	1,367 (4.5%)	972 (4.4%)	0.00	706 (4.4%)	687 (4.3%)	0.00
UTI	2,470 (8.1%)	1,279 (5.7%)	0.09	1,036 (6.4%)	1,009 (6.2%)	0.01
Mycotic infections	2,912 (9.5%)	1,857 (8.3%)	0.04	1,383 (8.6%)	1,365 (8.5%)	0.00
Disorder of Electrolyte	1,561 (5.1%)	834 (3.7%)	0.07	654 (4.1%)	627 (3.9%)	0.01

Disorders of fluid balance	618 (2.0%)	336 (1.5%)	0.04	243 (1.5%)	249 (1.5%)	0.00
Edema	1,855 (6.0%)	1,176 (5.3%)	0.03	838 (5.2%)	868 (5.4%)	-0.01
COPD	2,353 (7.7%)	1,388 (6.2%)	0.06	1,079 (6.7%)	1,052 (6.5%)	0.01
Asthma	1,715 (5.6%)	1,298 (5.8%)	-0.01	878 (5.4%)	920 (5.7%)	-0.01
Obstructive sleep apnea	3,006 (9.8%)	3,095 (13.9%)	-0.13	1,943 (12.0%)	1,921 (11.9%)	0.00
Pneumonia	696 (2.3%)	400 (1.8%)	0.04	293 (1.8%)	297 (1.8%)	0.00
Osteoarthritis	4,052 (13.2%)	2,726 (12.2%)	0.03	2,041 (12.6%)	2,028 (12.6%)	0.00
Osteoporosis without fractures	1,083 (3.5%)	479 (2.1%)	0.08	404 (2.5%)	398 (2.5%)	0.00
Fractures	258 (0.8%)	144 (0.6%)	0.02	103 (0.6%)	111 (0.7%)	-0.01
Falls	736 (2.4%)	441 (2.0%)	0.03	353 (2.2%)	341 (2.1%)	0.01
NASH/NAFLD	1,118 (3.6%)	1,144 (5.1%)	-0.07	732 (4.5%)	735 (4.6%)	0.00
Liver disease	836 (2.7%)	586 (2.6%)	0.01	440 (2.7%)	433 (2.7%)	0.00
Depression	3,207 (10.5%)	2,444 (11.0%)	-0.02	1,691 (10.5%)	1,731 (10.7%)	-0.01
Anxiety and sleep disorders	3,618 (11.8%)	3,074 (13.8%)	-0.06	2,091 (13.0%)	2,116 (13.1%)	0.00
Dementia	684 (2.2%)	270 (1.2%)	0.08	217 (1.3%)	234 (1.4%)	-0.01
Psychosis	213 (0.7%)	126 (0.6%)	0.01	111 (0.7%)	88 (0.5%)	0.03
Delirium	139 (0.5%)	74 (0.3%)	0.03	51 (0.3%)	64 (0.4%)	-0.02
Other medication use, n (%)						
ACEi and ARBs	22,007 (71.7%)	15,897 (71.2%)	0.01	11,460 (71.0%)	11,469 (71.0%)	0.00
Beta blockers	10,166 (33.1%)	6,950 (31.1%)	0.04	5,029 (31.1%)	5,021 (31.1%)	0.00
Calcium channel blockers - DHP & Non-DHP	8,455 (27.6%)	5,413 (24.3%)	0.08	4,040 (25.0%)	4,112 (25.5%)	-0.01
Nitrates and other antianginal agents	1,243 (4.1%)	829 (3.7%)	0.02	581 (3.6%)	583 (3.6%)	0.00
Thiazide and thiazide-like diuretics	3,604 (11.7%)	2,691 (12.1%)	-0.01	1,950 (12.1%)	1,888 (11.7%)	0.01
Loop diuretics	3,234 (10.5%)	1,912 (8.6%)	0.06	1,383 (8.6%)	1,430 (8.9%)	-0.01
MRA (potassium-sparing diuretics)	837 (2.7%)	660 (3.0%)	-0.02	423 (2.6%)	445 (2.8%)	-0.01
Other K-sparing diuretics and antihypertensive medications	2,411 (7.9%)	1,383 (6.2%)	0.07	1,014 (6.3%)	1,061 (6.6%)	-0.01
Antiarrhythmics	294 (1.0%)	221 (1.0%)	0.00	147 (0.9%)	148 (0.9%)	0.00
Anticoagulants (oral)	1,619 (5.3%)	1,154 (5.2%)	0.00	779 (4.8%)	801 (5.0%)	-0.01
Anticoagulants (injectables)	53 (0.2%)	46 (0.2%)	0.00	28 (0.2%)	29 (0.2%)	0.00
Antiplatelet agents	2,703 (8.8%)	1,944 (8.7%)	0.00	1,321 (8.2%)	1,393 (8.6%)	-0.01
Statins	21,830 (71.2%)	16,174 (72.5%)	-0.03	11,554 (71.6%)	11,573 (71.7%)	0.00
PCSK9 inhibitors and other lipid-lowering agents	3,977 (13.0%)	3,185 (14.3%)	-0.04	2,151 (13.3%)	2,120 (13.1%)	0.01
COPD & asthma medications	3,934 (12.8%)	2,834 (12.7%)	0.00	2,000 (12.4%)	2,019 (12.5%)	0.00
Corticosteroids (oral)	2,963 (9.7%)	2,214 (9.9%)	-0.01	1,555 (9.6%)	1,542 (9.6%)	0.00
Antiosteoporosis agents	1,020 (3.3%)	393 (1.8%)	0.10	319 (2.0%)	354 (2.2%)	-0.01
NSAIDs	5,579 (18.2%)	4,343 (19.5%)	-0.03	3,098 (19.2%)	3,086 (19.1%)	0.00
Opioids	6,290 (20.5%)	4,258 (19.1%)	0.04	3,102 (19.2%)	3,137 (19.4%)	-0.01
Gabapentinoids	4,125 (13.4%)	3,025 (13.6%)	-0.01	2,166 (13.4%)	2,149 (13.3%)	0.00
UTI antibiotics	3,779 (12.3%)	2,241 (10.0%)	0.07	1,670 (10.3%)	1,673 (10.4%)	0.00
Antidepressants	6,502 (21.2%)	5,014 (22.5%)	-0.03	3,471 (21.5%)	3,523 (21.8%)	-0.01
Anxiolytics/hypnotics	1,616 (5.3%)	1,296 (5.8%)	-0.02	898 (5.6%)	880 (5.5%)	0.00
Benzodiazepines	2,827 (9.2%)	1,883 (8.4%)	0.03	1,391 (8.6%)	1,417 (8.8%)	-0.01
Antipsychotics	731 (2.4%)	521 (2.3%)	0.01	385 (2.4%)	372 (2.3%)	0.01
Antiparkinsonian medications	573 (1.9%)	429 (1.9%)	0.00	276 (1.7%)	295 (1.8%)	-0.01
Dementia medications	575 (1.9%)	194 (0.9%)	0.09	197 (1.2%)	165 (1.0%)	0.02
Measures of health care use						
Internist; n (%)	28,619 (93.3%)	20,190 (90.5%)	0.10	14,873 (92.1%)	14,845 (91.9%)	0.01
Internist (-30 days to CED); n (%)	23,960 (78.1%)	16,168 (72.5%)	0.13	12,280 (76.1%)	12,278 (76.0%)	0.00

Internist (-180 days to -31 days before CED); n (%)	24,673 (80.4%)	17,246 (77.3%)	0.08	12,702 (78.7%)	12,609 (78.1%)	0.01
Internist (Number of visits)						
...mean (sd)	11.88 (16.13)	10.02 (14.52)	0.12	10.58 (13.95)	10.63 (14.99)	0.00
Endocrinologist; n (%)	2,609 (8.5%)	3,877 (17.4%)	-0.27	1,731 (10.7%)	1,812 (11.2%)	-0.02
Endocrinologist (-30 days to CED); n (%)	1,826 (6.0%)	3,035 (13.6%)	-0.26	1,302 (8.1%)	1,303 (8.1%)	0.00
Endocrinologist (-180 days to -31 days before CED); n (%)	1,735 (5.7%)	2,739 (12.3%)	-0.23	1,125 (7.0%)	1,272 (7.9%)	-0.03
Endocrinologist (Number of visits)						
...mean (sd)	0.32 (1.55)	0.66 (2.17)	-0.18	0.40 (1.71)	0.40 (1.64)	0.00
Cardiologist; n (%)	6,726 (21.9%)	4,706 (21.1%)	0.02	3,278 (20.3%)	3,348 (20.7%)	-0.01
Cardiologist (-30 days to CED); n (%)	2,492 (8.1%)	1,771 (7.9%)	0.01	1,222 (7.6%)	1,230 (7.6%)	0.00
Cardiologist (-180 days to -31 days before CED); n (%)	5,619 (18.3%)	3,989 (17.9%)	0.01	2,731 (16.9%)	2,814 (17.4%)	-0.01
Cardiologist (Number of visits)						
...mean (sd)	1.10 (3.51)	1.07 (3.48)	0.01	1.02 (3.42)	1.02 (3.38)	0.00
Electrocardiogram; n (%)	8,654 (28.2%)	5,786 (25.9%)	0.05	4,175 (25.9%)	4,238 (26.2%)	-0.01
Electrocardiogram (Number of tests)						
...mean (sd)	0.53 (1.29)	0.49 (1.25)	0.03	0.48 (1.19)	0.49 (1.26)	-0.01
ECG & Other cardiac imaging; n (%)	3,366 (11.0%)	2,317 (10.4%)	0.02	1,604 (9.9%)	1,653 (10.2%)	-0.01
ECG & Other cardiac imaging (Number of tests)						
...mean (sd)	0.38 (2.65)	0.38 (2.54)	0.00	0.36 (2.51)	0.37 (2.49)	0.00
Cardiovascular stress test; n (%)	1,404 (4.6%)	1,064 (4.8%)	-0.01	678 (4.2%)	760 (4.7%)	-0.02
HbA1c test order (Number of tests)						
...mean (sd)	1.60 (0.84)	1.63 (0.81)	-0.04	1.60 (0.81)	1.60 (0.81)	0.00
Glucose test and monitoring; n (%)	6,721 (21.9%)	4,906 (22.0%)	0.00	3,448 (21.4%)	3,319 (20.6%)	0.02
Glucose test and monitoring (Number of tests)						
...mean (sd)	0.47 (1.29)	0.47 (1.26)	0.00	0.44 (1.14)	0.44 (1.25)	0.00
Microalbuminuria/proteinuria test order; n (%)	16,781 (54.7%)	12,635 (56.6%)	-0.04	8,939 (55.4%)	8,954 (55.5%)	0.00
Microalbuminuria/proteinuria test order (Number of tests)						
...mean (sd)	0.71 (0.80)	0.72 (0.76)	-0.01	0.70 (0.77)	0.70 (0.75)	0.00
Metabolic or renal/creatinine panel test order; n (%)	26,802 (87.4%)	19,125 (85.7%)	0.05	13,955 (86.4%)	13,784 (85.4%)	0.03
Metabolic or renal/creatinine panel test order (Number of tests)						
...mean (sd)	1.70 (1.41)	1.63 (1.35)	0.05	1.61 (1.29)	1.62 (1.37)	-0.01
Lipid test order; n (%)	26,104 (85.1%)	19,269 (86.4%)	-0.04	13,895 (86.1%)	13,841 (85.7%)	0.01
Lipid test order (Number of tests)						
...mean (sd)	1.31 (0.93)	1.32 (0.91)	-0.01	1.31 (0.90)	1.30 (0.88)	0.01
Uric acid test order; n (%)	2,869 (9.4%)	1,775 (8.0%)	0.05	1,291 (8.0%)	1,351 (8.4%)	-0.01
Vitamin D test order; n (%)	8,297 (27.0%)	5,548 (24.9%)	0.05	4,110 (25.5%)	4,035 (25.0%)	0.01
PTH test order; n (%)	1,795 (5.9%)	923 (4.1%)	0.08	777 (4.8%)	689 (4.3%)	0.02
Hospitalization event (Number of)						
...mean (sd)	0.07 (0.31)	0.05 (0.27)	0.07	0.06 (0.29)	0.05 (0.28)	0.04
LOS (-180 days to -31 days before CED)						
...mean (sd)	0.20 (1.66)	0.17 (1.39)	0.02	0.18 (1.44)	0.17 (1.43)	0.01
LOS (-30 days to CED)						
...mean (sd)	0.08 (0.87)	0.04 (0.61)	0.05	0.05 (0.66)	0.05 (0.61)	0.00
ED event (Number of)						
...mean (sd)	0.21 (0.87)	0.13 (0.58)	0.11	0.14 (0.58)	0.14 (0.62)	0.00

Distinct medications ALL						
...mean (sd)	9.90 (4.81)	10.13 (5.00)	-0.05	9.77 (4.76)	9.80 (4.89)	-0.01
Distinct medications all BRAND						
...mean (sd)	2.04 (1.33)	2.32 (1.49)	-0.20	2.06 (1.33)	2.08 (1.37)	-0.01
Cost pharmacy OOP (\$)						
...mean (sd)	367.48 (382.64)	447.51 (488.59)	-0.18	387.44 (422.39)	391.10 (399.93)	-0.01
Flu vaccine; n (%)	6,249 (20.4%)	4,537 (20.3%)	0.00	3,192 (19.8%)	3,282 (20.3%)	-0.01
Pneumococcal vaccine; n (%)	1,837 (6.0%)	1,235 (5.5%)	0.02	875 (5.4%)	935 (5.8%)	-0.02
Breast mammography or MRI; n (%)	3,777 (12.3%)	2,660 (11.9%)	0.01	1,995 (12.4%)	1,945 (12.0%)	0.01
Prostate DRE or PSA; n (%)	5,679 (18.5%)	4,391 (19.7%)	-0.03	3,173 (19.7%)	3,098 (19.2%)	0.01
Colonoscopy; n (%)	1,244 (4.1%)	976 (4.4%)	-0.01	684 (4.2%)	694 (4.3%)	0.00
Pap smear; n (%)	1,095 (3.6%)	922 (4.1%)	-0.03	613 (3.8%)	628 (3.9%)	-0.01
Bone mineral density; n (%)	1,141 (3.7%)	625 (2.8%)	0.05	526 (3.3%)	487 (3.0%)	0.02
Laboratory results						
Lab value HbA1c (%)						
...mean (sd)	8.15 (0.57)	8.21 (0.59)	-0.10	8.18 (0.58)	8.18 (0.58)	0.00
...median [IQR]	8.10 [7.70, 8.50]	8.15 [7.80, 8.60]	-	8.10 [7.75, 8.55]	8.10 [7.75, 8.55]	-
eGFR (w/o race)						
...mean (sd)	73.33 (24.32)	78.65 (23.51)	-0.22	77.80 (23.51)	77.44 (23.26)	0.02
...median [IQR]	76.23 [56.03, 92.00]	82.34 [64.23, 95.90]	-	81.90 [62.83, 95.09]	80.51 [62.78, 94.69]	-
Lab result number - Creatinine						
...mean (sd)	1.09 (1.03)	1.07 (1.12)	0.02	1.06 (1.16)	1.06 (1.09)	0.00
...median [IQR]	0.92 [0.77, 1.16]	0.90 [0.76, 1.09]	-	0.90 [0.75, 1.10]	0.91 [0.76, 1.10]	-
Lab result number - UACR						
...mean (sd)	134.23 (550.59)	106.06 (435.57)	0.06	123.14 (517.09)	101.81 (399.81)	0.05
...Missing; n (%)	18,535 (60.4%)	13,099 (58.7%)	0.03	9,551 (59.2%)	9,747 (60.4%)	-0.02
Lab result number - Total cholesterol						
...mean (sd)	174.12 (47.94)	173.72 (51.51)	0.01	173.41 (48.59)	174.65 (51.29)	-0.02
...Missing; n (%)	4,378 (14.3%)	3,236 (14.5%)	-0.01	2,177 (13.5%)	2,330 (14.4%)	-0.03
Lab result number - LDL cholesterol						
...mean (sd)	94.26 (40.99)	93.96 (42.92)	0.01	93.97 (41.25)	94.46 (42.96)	-0.01
...Missing; n (%)	4,914 (16.0%)	3,752 (16.8%)	-0.02	2,526 (15.6%)	2,671 (16.5%)	-0.02
Lab result number - HDL cholesterol						
...mean (sd)	47.82 (18.80)	47.45 (20.75)	0.02	47.10 (19.41)	47.77 (20.16)	-0.03
...Missing; n (%)	4,685 (15.3%)	3,537 (15.9%)	-0.02	2,365 (14.6%)	2,555 (15.8%)	-0.03
Lab result number - Triglycerides						
...mean (sd)	189.85 (136.03)	205.23 (160.48)	-0.10	196.16 (146.87)	201.17 (155.41)	-0.03
...Missing; n (%)	4,412 (14.4%)	3,180 (14.3%)	0.00	2,168 (13.4%)	2,300 (14.2%)	-0.02
Lab result value - Glucose						
...mean (sd)	179.73 (84.21)	186.89 (103.65)	-0.08	182.98 (90.96)	184.65 (96.67)	-0.02
...Missing; n (%)	977 (3.2%)	612 (2.7%)	0.03	472 (2.9%)	435 (2.7%)	0.01

Abbreviations. St. Diff., standardized difference; SD, standard deviation; GLP-1 RA, Glucagon-like peptide-1 receptor agonists; MI, myocardial infarction; TIA, transient ischemic attack; peripheral artery disease; NASH/NAFLD, Nonalcoholic steatohepatitis/Nonalcoholic fatty liver disease; COPD, chronic obstructive pulmonary disease; CKD, chronic kidney disease; ARBs, Angiotensin II Receptor Blockers; ACEis, Angiotensin Converting Enzyme inhibitors; MRA, mineralocorticoid receptor antagonist; PCSK9, Proprotein convertase subtilisin/kexin type 9; NSAIDs, nonsteroidal anti-inflammatory drugs; MRI, magnetic resonance imaging; DRE, digital rectal examination; PSA, prostate-specific antigen; ED, emergency department, LOS, length of stay; ECG, electrocardiogram; eGFR, estimated glomerular filtration rate; uACR, urine albumin-creatinine ratio; LDL, low-density lipoprotein; HDL, high-density lipoprotein.

eTable 6. Baseline characteristics of patients with HbA_{1c} > 9% initiating SGLT2 inhibitor vs. DPP4 inhibitor therapy before and after 1:1 PS-matching

Baseline characteristics	DPP-4 inhibitor	SGLT2 inhibitor	St. Diff.	DPP-4 inhibitor	SGLT2 inhibitor	St. Diff.
Number of patients	25634	21895	-	15,466	15,466	-
Demographics						
Age						
...mean (sd)	59.96 (12.98)	56.68 (11.86)	0.26	57.74 (12.13)	57.64 (12.17)	0.01
...median [IQR]	61 [51, 69]	57 [48, 66]	-	58 [49, 67]	58 [49, 67]	-
Age squared						
...mean (sd)	3,764.17 (1,534.32)	3,353.03 (1,334.61)	0.29	3,481.33 (1,384.16)	3,470.31 (1,383.31)	0.01
...median [IQR]	3,721 [2,601, 4,761]	3,249 [2,304, 4,356]	-	3,364 [2,401, 4,489]	3,364 [2,401, 4,489]	-
Age Categories						
...18 - 39; n (%)	1,707 (6.7%)	1,746 (8.0%)	-0.05	1,170 (7.6%)	1,183 (7.6%)	0.00
...40 - 44; n (%)	1,643 (6.4%)	1,727 (7.9%)	-0.06	1,160 (7.5%)	1,124 (7.3%)	0.01
...45 - 49; n (%)	2,382 (9.3%)	2,630 (12.0%)	-0.09	1,678 (10.8%)	1,683 (10.9%)	0.00
...50 - 54; n (%)	3,032 (11.8%)	3,209 (14.7%)	-0.09	2,101 (13.6%)	2,087 (13.5%)	0.00
...55 - 59; n (%)	3,288 (12.8%)	3,386 (15.5%)	-0.08	2,234 (14.4%)	2,292 (14.8%)	-0.01
...60 - 64; n (%)	2,866 (11.2%)	2,822 (12.9%)	-0.05	1,808 (11.7%)	2,011 (13.0%)	-0.04
...65 - 69; n (%)	4,404 (17.2%)	3,266 (14.9%)	0.06	2,646 (17.1%)	2,449 (15.8%)	0.04
...70 - 74; n (%)	3,090 (12.1%)	1,859 (8.5%)	0.12	1,612 (10.4%)	1,521 (9.8%)	0.02
...75 - 79; n (%)	1,713 (6.7%)	841 (3.8%)	0.13	687 (4.4%)	728 (4.7%)	-0.01
...80 - 84; n (%)	1,001 (3.9%)	308 (1.4%)	0.16	281 (1.8%)	290 (1.9%)	-0.01
...≥ 85; n (%)	508 (2.0%)	101 (0.5%)	0.14	89 (0.6%)	98 (0.6%)	0.00
Gender						
...Male; n (%)	14,047 (54.8%)	12,782 (58.4%)	-0.07	8,859 (57.3%)	8,846 (57.2%)	0.00
...Female; n (%)	11,587 (45.2%)	9,113 (41.6%)	0.07	6,607 (42.7%)	6,620 (42.8%)	0.00
Geographic region						
...Northeast; n (%)	2,491 (9.7%)	1,591 (7.3%)	0.09	1,194 (7.7%)	1,206 (7.8%)	0.00
...South; n (%)	15,000 (58.5%)	13,524 (61.8%)	-0.07	9,378 (60.6%)	9,421 (60.9%)	-0.01
...Midwest; n (%)	1,995 (7.8%)	1,899 (8.7%)	-0.03	1,307 (8.5%)	1,270 (8.2%)	0.01
...West; n (%)	6,148 (24.0%)	4,881 (22.3%)	0.04	3,587 (23.2%)	3,569 (23.1%)	0.00
Race categories						
...White; n (%)	11,060 (43.1%)	10,712 (48.9%)	-0.12	7,141 (46.2%)	7,138 (46.2%)	0.00
...Black; n (%)	3,859 (15.1%)	2,946 (13.5%)	0.05	2,184 (14.1%)	2,193 (14.2%)	0.00
...Asian; n (%)	1,545 (6.0%)	991 (4.5%)	0.07	785 (5.1%)	795 (5.1%)	0.00
...Hispanic; n (%)	7,749 (30.2%)	5,932 (27.1%)	0.07	4,439 (28.7%)	4,418 (28.6%)	0.00
...Other or unknown; n (%)	1,421 (5.5%)	1,314 (6.0%)	-0.02	917 (5.9%)	922 (6.0%)	0.00
Quarter/Year of Cohort Entry Date						
...Q2 2013; n (%)	799 (3.1%)	44 (0.2%)	0.23	31 (0.2%)	44 (0.3%)	-0.02
...Q3 2013; n (%)	825 (3.2%)	141 (0.6%)	0.19	111 (0.7%)	135 (0.9%)	-0.02
...Q4 2013; n (%)	779 (3.0%)	182 (0.8%)	0.16	140 (0.9%)	174 (1.1%)	-0.02
...Q1 2014; n (%)	803 (3.1%)	189 (0.9%)	0.16	165 (1.1%)	179 (1.2%)	-0.01
...Q2 2014; n (%)	736 (2.9%)	273 (1.2%)	0.12	244 (1.6%)	240 (1.6%)	0.00
...Q3 2014; n (%)	814 (3.2%)	421 (1.9%)	0.08	355 (2.3%)	357 (2.3%)	0.00
...Q4 2014; n (%)	810 (3.2%)	488 (2.2%)	0.06	411 (2.7%)	432 (2.8%)	-0.01
...Q1 2015; n (%)	727 (2.8%)	567 (2.6%)	0.01	473 (3.1%)	465 (3.0%)	0.01
...Q2 2015; n (%)	769 (3.0%)	580 (2.6%)	0.02	485 (3.1%)	477 (3.1%)	0.00
...Q3 2015; n (%)	787 (3.1%)	483 (2.2%)	0.06	426 (2.8%)	410 (2.7%)	0.01
...Q4 2015; n (%)	665 (2.6%)	458 (2.1%)	0.03	417 (2.7%)	403 (2.6%)	0.01
...Q1 2016; n (%)	845 (3.3%)	550 (2.5%)	0.05	475 (3.1%)	462 (3.0%)	0.01

...Q2 2016; n (%)	831 (3.2%)	545 (2.5%)	0.04	490 (3.2%)	474 (3.1%)	0.01
...Q3 2016; n (%)	907 (3.5%)	615 (2.8%)	0.04	548 (3.5%)	536 (3.5%)	0.00
...Q4 2016; n (%)	836 (3.3%)	604 (2.8%)	0.03	495 (3.2%)	490 (3.2%)	0.00
...Q1 2017; n (%)	907 (3.5%)	659 (3.0%)	0.03	565 (3.7%)	551 (3.6%)	0.01
...Q2 2017; n (%)	934 (3.6%)	693 (3.2%)	0.02	598 (3.9%)	581 (3.8%)	0.01
...Q3 2017; n (%)	968 (3.8%)	737 (3.4%)	0.02	597 (3.9%)	585 (3.8%)	0.01
...Q4 2017; n (%)	755 (2.9%)	613 (2.8%)	0.01	492 (3.2%)	481 (3.1%)	0.01
...Q1 2018; n (%)	838 (3.3%)	642 (2.9%)	0.02	510 (3.3%)	520 (3.4%)	-0.01
...Q2 2018; n (%)	884 (3.4%)	685 (3.1%)	0.02	546 (3.5%)	538 (3.5%)	0.00
...Q3 2018; n (%)	787 (3.1%)	755 (3.4%)	-0.02	573 (3.7%)	554 (3.6%)	0.01
...Q4 2018; n (%)	670 (2.6%)	657 (3.0%)	-0.02	497 (3.2%)	467 (3.0%)	0.01
...Q1 2019; n (%)	792 (3.1%)	831 (3.8%)	-0.04	589 (3.8%)	590 (3.8%)	0.00
...Q2 2019; n (%)	821 (3.2%)	978 (4.5%)	-0.07	645 (4.2%)	655 (4.2%)	0.00
...Q3 2019; n (%)	693 (2.7%)	909 (4.2%)	-0.08	544 (3.5%)	572 (3.7%)	-0.01
...Q4 2019; n (%)	595 (2.3%)	847 (3.9%)	-0.09	512 (3.3%)	515 (3.3%)	0.00
...Q1 2020; n (%)	755 (2.9%)	1,151 (5.3%)	-0.12	650 (4.2%)	646 (4.2%)	0.00
...Q2 2020; n (%)	580 (2.3%)	761 (3.5%)	-0.07	476 (3.1%)	489 (3.2%)	-0.01
...Q3 2020; n (%)	746 (2.9%)	1,045 (4.8%)	-0.10	617 (4.0%)	630 (4.1%)	-0.01
...Q4 2020; n (%)	652 (2.5%)	1,124 (5.1%)	-0.14	567 (3.7%)	588 (3.8%)	-0.01
...Q1 2021; n (%)	650 (2.5%)	1,237 (5.6%)	-0.16	588 (3.8%)	598 (3.9%)	-0.01
...Q2 2021; n (%)	674 (2.6%)	1,431 (6.5%)	-0.19	634 (4.1%)	628 (4.1%)	0.00
Burden of comorbidities						
Com. comorbidity score, mean (sd)	1.00 (1.87)	0.95 (1.71)	0.03	0.91 (1.70)	0.92 (1.74)	-0.01
Frailty Score, mean (sd)	0.14 (0.04)	0.14 (0.04)	0.00	0.14 (0.04)	0.14 (0.04)	0.00
Frailty Score squared, mean (sd)	0.02 (0.01)	0.02 (0.01)	0.00	0.02 (0.01)	0.02 (0.01)	0.00
Frailty score; n (%)			-			
...< 0.15	17,370 (67.8%)	15,252 (69.7%)	-0.04	10,878 (70.3%)	10,897 (70.5%)	0.00
...0.15 - 0.25	7,728 (30.1%)	6,235 (28.5%)	0.04	4,349 (28.1%)	4,282 (27.7%)	0.01
...≥ 0.25	536 (2.1%)	408 (1.9%)	0.01	239 (1.5%)	287 (1.9%)	-0.03
Lifestyle factors, n (%)						
Overweight	1,989 (7.8%)	1,802 (8.2%)	-0.01	1,283 (8.3%)	1,267 (8.2%)	0.00
Obesity	6,932 (27.0%)	7,952 (36.3%)	-0.20	4,922 (31.8%)	4,941 (31.9%)	0.00
Smoking	3,181 (12.4%)	2,915 (13.3%)	-0.03	1,991 (12.9%)	1,985 (12.8%)	0.00
Diabetes-related conditions, n (%)						
Diabetic nephropathy	4,019 (15.7%)	2,830 (12.9%)	0.08	2,051 (13.3%)	2,042 (13.2%)	0.00
Diabetic retinopathy	1,986 (7.7%)	1,718 (7.8%)	0.00	1,139 (7.4%)	1,134 (7.3%)	0.00
Diabetes with other ophthalmic manifestations	1,065 (4.2%)	768 (3.5%)	0.04	545 (3.5%)	557 (3.6%)	-0.01
Diabetic neuropathy	4,787 (18.7%)	4,459 (20.4%)	-0.04	2,934 (19.0%)	2,945 (19.0%)	0.00
Diabetes with peripheral circulatory disorders	365 (1.4%)	130 (0.6%)	0.08	120 (0.8%)	116 (0.8%)	0.00
Diabetic foot	452 (1.8%)	387 (1.8%)	0.00	261 (1.7%)	263 (1.7%)	0.00
Infection of lower extremities	600 (2.3%)	528 (2.4%)	-0.01	346 (2.2%)	358 (2.3%)	-0.01
Lower-limb amputations	169 (0.7%)	145 (0.7%)	0.00	94 (0.6%)	90 (0.6%)	0.00
Erectile dysfunction	811 (3.2%)	895 (4.1%)	-0.05	540 (3.5%)	556 (3.6%)	-0.01
Hypoglycemia	3,197 (12.5%)	3,137 (14.3%)	-0.05	2,054 (13.3%)	2,060 (13.3%)	0.00
Hyperglycemia	10,196 (39.8%)	11,238 (51.3%)	-0.23	7,272 (47.0%)	7,168 (46.3%)	0.01
Diabetic ketoacidosis	78 (0.3%)	66 (0.3%)	0.00	49 (0.3%)	43 (0.3%)	0.00
Hyperosmolar hyperglycemic nonketotic syndrome	162 (0.6%)	132 (0.6%)	0.00	92 (0.6%)	96 (0.6%)	0.00
Diabetes with other complications	1,480 (5.8%)	1,480 (6.8%)	-0.04	954 (6.2%)	943 (6.1%)	0.00
Diabetes mellitus without mention of complications	19,732 (77.0%)	15,865 (72.5%)	0.10	11,367 (73.5%)	11,366 (73.5%)	0.00

Diabetes treatment						
Number of anti-DM medications on index date						
...mean (sd)	1.32 (0.78)	1.42 (0.91)	-0.12	1.33 (0.80)	1.32 (0.85)	0.01
...median [IQR]	1.00 [1.00, 2.00]	1.00 [1.00, 2.00]	-	1.00 [1.00, 2.00]	1.00 [1.00, 2.00]	-
No use of anti-DM medications in prior 180 days; n (%)	4,630 (18.1%)	2,584 (11.8%)	0.18	2,290 (14.8%)	2,308 (14.9%)	0.00
Metformin (any use); n (%)	19,777 (77.2%)	16,773 (76.6%)	0.01	12,013 (77.7%)	11,957 (77.3%)	0.01
Metformin (concurrent use); n (%)	17,562 (68.5%)	14,364 (65.6%)	0.06	10,584 (68.4%)	10,360 (67.0%)	0.03
Sulfonylureas - 2nd gen. (any use); n (%)	11,041 (43.1%)	7,813 (35.7%)	0.15	6,025 (39.0%)	6,062 (39.2%)	0.00
Sulfonylureas - 2nd gen. (concurrent use); n (%)	9,159 (35.7%)	6,263 (28.6%)	0.15	4,937 (31.9%)	4,937 (31.9%)	0.00
Thiazolidinediones (any use); n (%)	1,883 (7.3%)	1,773 (8.1%)	-0.03	1,191 (7.7%)	1,196 (7.7%)	0.00
Thiazolidinediones (concurrent use); n (%)	1,579 (6.2%)	1,404 (6.4%)	-0.01	994 (6.4%)	962 (6.2%)	0.01
GLP-1RA (any use); n (%)	1,247 (4.9%)	4,544 (20.8%)	-0.49	1,190 (7.7%)	1,252 (8.1%)	-0.01
GLP-1RA (concurrent use); n (%)	806 (3.1%)	3,510 (16.0%)	-0.45	772 (5.0%)	976 (6.3%)	-0.06
Insulins (any use); n (%)	5,683 (22.2%)	6,957 (31.8%)	-0.22	3,957 (25.6%)	3,961 (25.6%)	0.00
Insulins (concurrent use); n (%)	4,476 (17.5%)	5,433 (24.8%)	-0.18	3,086 (20.0%)	3,109 (20.1%)	0.00
Long term use of insulin; n (%)	2,527 (9.9%)	3,448 (15.7%)	-0.17	1,850 (12.0%)	1,836 (11.9%)	0.00
Miscellaneous anti-DM medications; n (%)	373 (1.5%)	251 (1.1%)	0.04	192 (1.2%)	188 (1.2%)	0.00
Other comorbidities at baseline, n (%)						
Hypertension	17,523 (68.4%)	15,251 (69.7%)	-0.03	10,487 (67.8%)	10,525 (68.1%)	-0.01
Hyperlipidemia	18,369 (71.7%)	16,374 (74.8%)	-0.07	11,287 (73.0%)	11,251 (72.7%)	0.01
Acute MI	192 (0.7%)	216 (1.0%)	-0.03	116 (0.8%)	118 (0.8%)	0.00
MI sequelae/old MI	494 (1.9%)	538 (2.5%)	-0.04	302 (2.0%)	321 (2.1%)	-0.01
Stable angina	690 (2.7%)	670 (3.1%)	-0.02	415 (2.7%)	415 (2.7%)	0.00
ACS unstable angina	227 (0.9%)	259 (1.2%)	-0.03	140 (0.9%)	139 (0.9%)	0.00
Coronary atherosclerosis	2,766 (10.8%)	2,530 (11.6%)	-0.03	1,613 (10.4%)	1,647 (10.6%)	-0.01
Coronary procedure	157 (0.6%)	184 (0.8%)	-0.02	104 (0.7%)	104 (0.7%)	0.00
History of coronary procedure	743 (2.9%)	809 (3.7%)	-0.04	463 (3.0%)	471 (3.0%)	0.00
Congestive heart failure	1,415 (5.5%)	1,162 (5.3%)	0.01	731 (4.7%)	767 (5.0%)	-0.01
Cardiomyopathy	494 (1.9%)	490 (2.2%)	-0.02	286 (1.8%)	299 (1.9%)	-0.01
Atrial fibrillation	996 (3.9%)	761 (3.5%)	0.02	509 (3.3%)	523 (3.4%)	-0.01
Cardiac conduction disorders	393 (1.5%)	323 (1.5%)	0.00	217 (1.4%)	221 (1.4%)	0.00
Other cardiac dysrhythmia	1,201 (4.7%)	1,063 (4.9%)	-0.01	683 (4.4%)	685 (4.4%)	0.00
Valve disorders	964 (3.8%)	710 (3.2%)	0.03	491 (3.2%)	474 (3.1%)	0.01
Other cardiovascular disease	1,425 (5.6%)	1,311 (6.0%)	-0.02	837 (5.4%)	870 (5.6%)	-0.01
Ischemic stroke	904 (3.5%)	676 (3.1%)	0.02	467 (3.0%)	470 (3.0%)	0.00
TIA	226 (0.9%)	158 (0.7%)	0.02	118 (0.8%)	119 (0.8%)	0.00
Other cerebrovascular conditions	828 (3.2%)	581 (2.7%)	0.03	411 (2.7%)	412 (2.7%)	0.00
PAD and generalized/unspecified atherosclerosis	1,539 (6.0%)	1,226 (5.6%)	0.02	849 (5.5%)	839 (5.4%)	0.00
Acute Kidney Injury	596 (2.3%)	328 (1.5%)	0.06	250 (1.6%)	254 (1.6%)	0.00
CKD	2,243 (8.8%)	941 (4.3%)	0.18	1,548 (10.0%)	1,570 (10.2%)	-0.01
CKD Stage 1-2	1,296 (5.1%)	930 (4.2%)	0.04	719 (4.6%)	701 (4.5%)	0.00
CKD Stage 3-4	2,243 (8.8%)	941 (4.3%)	0.18	777 (5.0%)	817 (5.3%)	-0.01
CKD unspecified	692 (2.7%)	318 (1.5%)	0.08	240 (1.6%)	256 (1.7%)	-0.01
Miscellaneous renal disease	1,144 (4.5%)	646 (3.0%)	0.08	488 (3.2%)	509 (3.3%)	-0.01
Major bleeding	952 (3.7%)	861 (3.9%)	-0.01	602 (3.9%)	601 (3.9%)	0.00
UTI	1,972 (7.7%)	1,231 (5.6%)	0.08	941 (6.1%)	945 (6.1%)	0.00
Mycotic infections	2,440 (9.5%)	1,986 (9.1%)	0.01	1,421 (9.2%)	1,418 (9.2%)	0.00
Disorder of Electrolyte	1,090 (4.3%)	752 (3.4%)	0.05	547 (3.5%)	507 (3.3%)	0.01

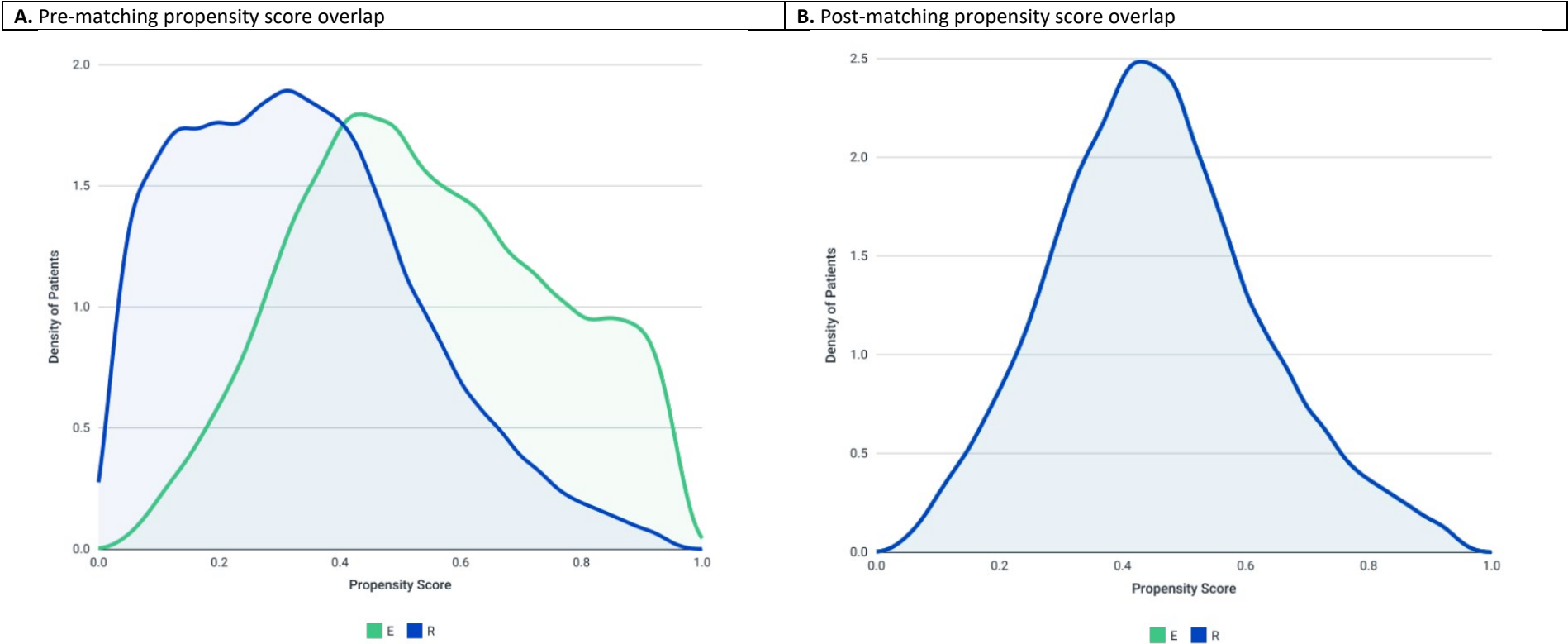
Disorders of fluid balance	575 (2.2%)	391 (1.8%)	0.03	301 (1.9%)	262 (1.7%)	0.02
Edema	1,139 (4.4%)	956 (4.4%)	0.00	628 (4.1%)	634 (4.1%)	0.00
COPD	1,568 (6.1%)	1,245 (5.7%)	0.02	860 (5.6%)	875 (5.7%)	0.00
Asthma	1,208 (4.7%)	1,113 (5.1%)	-0.02	743 (4.8%)	752 (4.9%)	0.00
Obstructive sleep apnea	2,077 (8.1%)	2,423 (11.1%)	-0.10	1,448 (9.4%)	1,452 (9.4%)	0.00
Pneumonia	480 (1.9%)	424 (1.9%)	0.00	265 (1.7%)	273 (1.8%)	-0.01
Osteoarthritis	2,453 (9.6%)	2,156 (9.8%)	-0.01	1,447 (9.4%)	1,468 (9.5%)	0.00
Osteoporosis without fractures	562 (2.2%)	309 (1.4%)	0.06	250 (1.6%)	244 (1.6%)	0.00
Fractures	191 (0.7%)	144 (0.7%)	0.00	102 (0.7%)	108 (0.7%)	0.00
Falls	540 (2.1%)	437 (2.0%)	0.01	296 (1.9%)	306 (2.0%)	-0.01
NASH/NAFLD	903 (3.5%)	999 (4.6%)	-0.06	621 (4.0%)	626 (4.0%)	0.00
Liver disease	674 (2.6%)	511 (2.3%)	0.02	379 (2.5%)	369 (2.4%)	0.01
Depression	2,548 (9.9%)	2,498 (11.4%)	-0.05	1,605 (10.4%)	1,636 (10.6%)	-0.01
Anxiety and sleep disorders	2,824 (11.0%)	2,839 (13.0%)	-0.06	1,853 (12.0%)	1,866 (12.1%)	0.00
Dementia	523 (2.0%)	227 (1.0%)	0.08	199 (1.3%)	185 (1.2%)	0.01
Psychosis	203 (0.8%)	140 (0.6%)	0.02	126 (0.8%)	100 (0.6%)	0.02
Delirium	93 (0.4%)	62 (0.3%)	0.02	42 (0.3%)	43 (0.3%)	0.00
Other medication use, n (%)						
ACEi and ARBs	16,756 (65.4%)	14,581 (66.6%)	-0.03	10,125 (65.5%)	10,151 (65.6%)	0.00
Beta blockers	6,665 (26.0%)	5,730 (26.2%)	0.00	3,852 (24.9%)	3,886 (25.1%)	0.00
Calcium channel blockers - DHP & Non-DHP	5,800 (22.6%)	4,545 (20.8%)	0.04	3,211 (20.8%)	3,262 (21.1%)	-0.01
Nitrates and other antianginal agents	801 (3.1%)	732 (3.3%)	-0.01	443 (2.9%)	488 (3.2%)	-0.02
Thiazide and thiazide-like diuretics	2,552 (10.0%)	2,220 (10.1%)	0.00	1,524 (9.9%)	1,504 (9.7%)	0.01
Loop diuretics	2,090 (8.2%)	1,699 (7.8%)	0.01	1,090 (7.0%)	1,133 (7.3%)	-0.01
MRA (potassium-sparing diuretics)	569 (2.2%)	603 (2.8%)	-0.04	373 (2.4%)	371 (2.4%)	0.00
Other K-sparing diuretics and antihypertensive medications	1,560 (6.1%)	1,136 (5.2%)	0.04	825 (5.3%)	832 (5.4%)	0.00
Antiarrhythmics	181 (0.7%)	130 (0.6%)	0.01	93 (0.6%)	88 (0.6%)	0.00
Anticoagulants (oral)	980 (3.8%)	850 (3.9%)	-0.01	539 (3.5%)	565 (3.7%)	-0.01
Anticoagulants (injectables)	26 (0.1%)	19 (0.1%)	0.00	18 (0.1%)	9 (0.1%)	0.00
Antiplatelet agents	1,979 (7.7%)	1,742 (8.0%)	-0.01	1,162 (7.5%)	1,173 (7.6%)	0.00
Statins	16,126 (62.9%)	14,360 (65.6%)	-0.06	9,907 (64.1%)	9,877 (63.9%)	0.00
PCSK9 inhibitors and other lipid-lowering agents	2,872 (11.2%)	2,776 (12.7%)	-0.05	1,758 (11.4%)	1,784 (11.5%)	0.00
COPD & asthma medications	2,745 (10.7%)	2,356 (10.8%)	0.00	1,607 (10.4%)	1,652 (10.7%)	-0.01
Corticosteroids (oral)	2,068 (8.1%)	1,960 (9.0%)	-0.03	1,311 (8.5%)	1,312 (8.5%)	0.00
Antihypertension agents	497 (1.9%)	261 (1.2%)	0.06	222 (1.4%)	224 (1.4%)	0.00
NSAIDs	4,473 (17.4%)	4,238 (19.4%)	-0.05	2,913 (18.8%)	2,909 (18.8%)	0.00
Opioids	4,986 (19.5%)	4,210 (19.2%)	0.01	2,950 (19.1%)	2,967 (19.2%)	0.00
Gabapentinoids	3,281 (12.8%)	3,036 (13.9%)	-0.03	2,012 (13.0%)	2,036 (13.2%)	-0.01
UTI antibiotics	3,107 (12.1%)	2,279 (10.4%)	0.05	1,659 (10.7%)	1,657 (10.7%)	0.00
Antidepressants	4,901 (19.1%)	4,803 (21.9%)	-0.07	3,110 (20.1%)	3,167 (20.5%)	-0.01
Anxiolytics/hypnotics	1,192 (4.7%)	1,183 (5.4%)	-0.03	770 (5.0%)	786 (5.1%)	0.00
Benzodiazepines	1,898 (7.4%)	1,697 (7.8%)	-0.02	1,193 (7.7%)	1,177 (7.6%)	0.00
Antipsychotics	631 (2.5%)	538 (2.5%)	0.00	377 (2.4%)	381 (2.5%)	-0.01
Antiparkinsonian medications	372 (1.5%)	393 (1.8%)	-0.02	221 (1.4%)	264 (1.7%)	-0.02
Dementia medications	408 (1.6%)	145 (0.7%)	0.08	172 (1.1%)	112 (0.7%)	0.04
Measures of health care use						
Internist; n (%)	23,517 (91.7%)	19,668 (89.8%)	0.07	14,015 (90.6%)	14,050 (90.8%)	-0.01
Internist (-30 days to CED); n (%)	20,170 (78.7%)	16,206 (74.0%)	0.11	11,885 (76.8%)	11,899 (76.9%)	0.00

Internist (-180 days to -31 days before CED); n (%)	17,893 (69.8%)	15,293 (69.8%)	0.00	10,622 (68.7%)	10,732 (69.4%)	-0.02
Internist (Number of visits)						
...mean (sd)	10.55 (15.03)	9.28 (14.05)	0.09	9.61 (13.61)	9.61 (14.26)	0.00
Endocrinologist; n (%)	2,023 (7.9%)	3,385 (15.5%)	-0.24	1,454 (9.4%)	1,527 (9.9%)	-0.02
Endocrinologist (-30 days to CED); n (%)	1,581 (6.2%)	2,809 (12.8%)	-0.23	1,179 (7.6%)	1,183 (7.6%)	0.00
Endocrinologist (-180 days to -31 days before CED); n (%)	1,004 (3.9%)	1,829 (8.4%)	-0.19	710 (4.6%)	830 (5.4%)	-0.04
Endocrinologist (Number of visits)						
...mean (sd)	0.28 (1.45)	0.56 (1.97)	-0.16	0.34 (1.60)	0.34 (1.51)	0.00
Cardiologist; n (%)	4,386 (17.1%)	3,793 (17.3%)	-0.01	2,535 (16.4%)	2,513 (16.2%)	0.01
Cardiologist (-30 days to CED); n (%)	1,716 (6.7%)	1,492 (6.8%)	0.00	970 (6.3%)	956 (6.2%)	0.00
Cardiologist (-180 days to -31 days before CED); n (%)	3,504 (13.7%)	3,085 (14.1%)	-0.01	2,036 (13.2%)	2,045 (13.2%)	0.00
Cardiologist (Number of visits)						
...mean (sd)	0.80 (2.83)	0.86 (3.14)	-0.02	0.76 (2.75)	0.77 (3.00)	0.00
Electrocardiogram; n (%)	6,654 (26.0%)	5,341 (24.4%)	0.04	3,816 (24.7%)	3,714 (24.0%)	0.02
Electrocardiogram (Number of tests)						
...mean (sd)	0.47 (1.23)	0.47 (1.23)	0.00	0.44 (1.07)	0.45 (1.21)	-0.01
ECG & Other cardiac imaging; n (%)	2,210 (8.6%)	1,908 (8.7%)	0.00	1,233 (8.0%)	1,222 (7.9%)	0.00
ECG & Other cardiac imaging (Number of tests)						
...mean (sd)	0.29 (2.19)	0.35 (2.41)	-0.03	0.27 (2.00)	0.29 (2.11)	-0.01
Cardiovascular stress test; n (%)	895 (3.5%)	803 (3.7%)	-0.01	552 (3.6%)	491 (3.2%)	0.02
HbA1c test order (Number of tests)						
...mean (sd)	1.44 (0.81)	1.47 (0.80)	-0.04	1.44 (0.79)	1.44 (0.79)	0.00
Glucose test and monitoring; n (%)	6,517 (25.4%)	5,540 (25.3%)	0.00	3,743 (24.2%)	3,718 (24.0%)	0.00
Glucose test and monitoring (Number of tests)						
...mean (sd)	0.55 (1.39)	0.53 (1.36)	0.01	0.50 (1.21)	0.50 (1.36)	0.00
Microalbuminuria/proteinuria test order; n (%)	13,600 (53.1%)	12,002 (54.8%)	-0.03	8,286 (53.6%)	8,294 (53.6%)	0.00
Microalbuminuria/proteinuria test order (Number of tests)						
...mean (sd)	0.65 (0.74)	0.67 (0.71)	-0.03	0.65 (0.71)	0.65 (0.71)	0.00
Metabolic or renal/creatinine panel test order; n (%)	20,511 (80.0%)	17,229 (78.7%)	0.03	12,213 (79.0%)	12,129 (78.4%)	0.01
Metabolic or renal/creatinine panel test order (Number of tests)						
...mean (sd)	1.44 (1.38)	1.39 (1.28)	0.04	1.36 (1.23)	1.37 (1.27)	-0.01
Lipid test order; n (%)	21,774 (84.9%)	18,864 (86.2%)	-0.04	13,250 (85.7%)	13,278 (85.9%)	-0.01
Lipid test order (Number of tests)						
...mean (sd)	1.21 (0.86)	1.22 (0.83)	-0.01	1.20 (0.82)	1.20 (0.83)	0.00
Uric acid test order; n (%)	2,109 (8.2%)	1,551 (7.1%)	0.04	1,091 (7.1%)	1,131 (7.3%)	-0.01
Vitamin D test order; n (%)	6,789 (26.5%)	5,400 (24.7%)	0.04	3,968 (25.7%)	3,809 (24.6%)	0.03
PTH test order; n (%)	1,194 (4.7%)	762 (3.5%)	0.06	585 (3.8%)	564 (3.6%)	0.01
Hospitalization event (Number of)						
...mean (sd)	0.06 (0.28)	0.05 (0.27)	0.04	0.05 (0.25)	0.05 (0.25)	0.00
LOS (-180 days to -31 days before CED)						
...mean (sd)	0.15 (1.26)	0.18 (1.52)	-0.02	0.15 (1.36)	0.15 (1.26)	0.00
LOS (-30 days to CED)						
...mean (sd)	0.09 (0.86)	0.05 (0.60)	0.05	0.05 (0.54)	0.06 (0.65)	-0.02
ED event (Number of)						
...mean (sd)	0.20 (0.80)	0.14 (0.67)	0.08	0.15 (0.61)	0.15 (0.72)	0.00

Distinct medications ALL						
...mean (sd)	9.13 (4.90)	9.59 (5.07)	-0.09	9.15 (4.90)	9.16 (4.90)	0.00
Distinct medications all BRAND						
...mean (sd)	2.01 (1.33)	2.28 (1.48)	-0.19	2.03 (1.33)	2.05 (1.38)	-0.01
Cost pharmacy OOP (\$)						
...mean (sd)	320.72 (383.46)	382.46 (419.49)	-0.15	334.12 (421.01)	337.07 (356.06)	-0.01
Flu vaccine; n (%)	4,304 (16.8%)	3,810 (17.4%)	-0.02	2,545 (16.5%)	2,635 (17.0%)	-0.01
Pneumococcal vaccine; n (%)	1,442 (5.6%)	1,169 (5.3%)	0.01	875 (5.7%)	869 (5.6%)	0.00
Breast mammography or MRI; n (%)	2,535 (9.9%)	2,172 (9.9%)	0.00	1,531 (9.9%)	1,534 (9.9%)	0.00
Prostate DRE or PSA; n (%)	5,000 (19.5%)	4,272 (19.5%)	0.00	3,055 (19.8%)	3,025 (19.6%)	0.01
Colonoscopy; n (%)	802 (3.1%)	661 (3.0%)	0.01	491 (3.2%)	461 (3.0%)	0.01
Pap smear; n (%)	990 (3.9%)	916 (4.2%)	-0.02	594 (3.8%)	634 (4.1%)	-0.02
Bone mineral density; n (%)	627 (2.4%)	429 (2.0%)	0.03	308 (2.0%)	318 (2.1%)	-0.01
Laboratory results						
Lab value HbA1c (%)						
...mean (sd)	10.63 (1.48)	10.61 (1.41)	0.01	10.63 (1.44)	10.63 (1.42)	0.00
...median [IQR]	10.30 [9.50, 11.50]	10.30 [9.50, 11.40]	-	10.30 [9.50, 11.50]	10.30 [9.50, 11.45]	-
eGFR (w/o race)						
...mean (sd)	80.06 (25.34)	84.03 (24.47)	-0.16	83.16 (24.53)	83.22 (24.44)	0.00
...median [IQR]	84.51 [62.95, 99.03]	88.84 [69.14, 101.8]	-	87.82 [67.75, 100.92]	87.87 [67.97, 101.09]	-
Lab result number - Creatinine						
...mean (sd)	1.05 (1.50)	1.05 (1.62)	0.00	1.04 (1.69)	1.06 (1.79)	-0.01
...median [IQR]	0.89 [0.74, 1.09]	0.87 [0.73, 1.05]	-	0.87 [0.73, 1.05]	0.87 [0.73, 1.05]	-
Lab result number - UACR						
...mean (sd)	183.21 (628.21)	177.96 (691.77)	0.01	165.19 (586.36)	176.54 (716.55)	-0.02
...Missing; n (%)	15,835 (61.8%)	13,269 (60.6%)	0.02	9,406 (60.8%)	9,646 (62.4%)	-0.03
Lab result number - Total cholesterol						
...mean (sd)	191.37 (54.82)	189.79 (57.21)	0.03	191.45 (55.48)	191.29 (56.87)	0.00
...Missing; n (%)	3,550 (13.8%)	3,092 (14.1%)	-0.01	2,068 (13.4%)	2,179 (14.1%)	-0.02
Lab result number - LDL cholesterol						
...mean (sd)	106.16 (45.91)	104.84 (47.12)	0.03	106.32 (45.88)	106.01 (47.30)	0.01
...Missing; n (%)	5,139 (20.0%)	4,555 (20.8%)	-0.02	3,083 (19.9%)	3,207 (20.7%)	-0.02
Lab result number - HDL cholesterol						
...mean (sd)	46.01 (18.35)	45.61 (20.62)	0.02	45.49 (18.69)	45.75 (19.47)	-0.01
...Missing; n (%)	3,818 (14.9%)	3,401 (15.5%)	-0.02	2,261 (14.6%)	2,404 (15.5%)	-0.03
Lab result number - Triglycerides						
...mean (sd)	233.12 (194.16)	250.23 (216.65)	-0.08	239.45 (202.52)	245.76 (211.18)	-0.03
...Missing; n (%)	3,601 (14.0%)	3,022 (13.8%)	0.01	2,099 (13.6%)	2,156 (13.9%)	-0.01
Lab result value - Glucose						
...mean (sd)	256.88 (112.87)	260.92 (135.19)	-0.03	259.05 (117.70)	259.39 (126.65)	0.00
...Missing; n (%)	712 (2.8%)	566 (2.6%)	0.01	431 (2.8%)	396 (2.6%)	0.01

Abbreviations. St. Diff., standardized difference; SD, standard deviation; GLP-1 RA, Glucagon-like peptide-1 receptor agonists; MI, myocardial infarction; TIA, transient ischemic attack; peripheral artery disease; NASH/NAFLD, Nonalcoholic steatohepatitis/Nonalcoholic fatty liver disease; COPD, chronic obstructive pulmonary disease; CKD, chronic kidney disease; ARBs, Angiotensin II Receptor Blockers; ACEis, Angiotensin Converting Enzyme inhibitors; MRA, mineralocorticoid receptor antagonist; PCSK9, Proprotein convertase subtilisin/kexin type 9; NSAIDs, nonsteroidal anti-inflammatory drugs; MRI, magnetic resonance imaging; DRE, digital rectal examination; PSA, prostate-specific antigen; ED, emergency department, LOS, length of stay; ECG, electrocardiogram; eGFR, estimated glomerular filtration rate; uACR, urine albumin-creatinine ratio; LDL, low-density lipoprotein; HDL, high-density lipoprotein.

eFigure 2. Propensity score distributions of SGLT2i and DPP4i initiators in the overall population.



Legend E = SGLT2 inhibitors; R = DPP4 inhibitors.

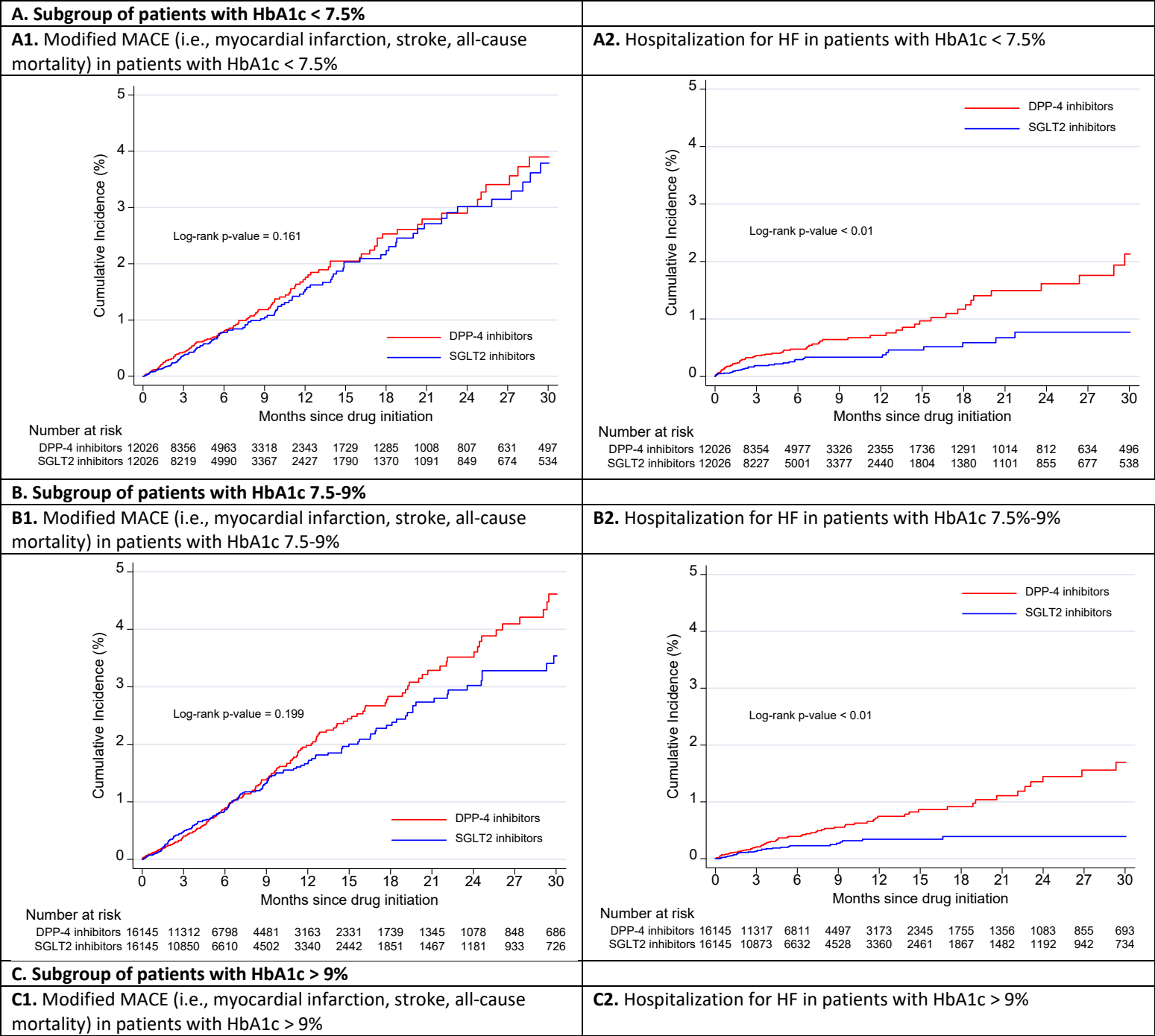
Caption The figure displays the propensity score distribution overlap prior to **(A)** and after **(B)** matching. In both graphs **(A and B)**, the x-axis shows the range of propensity scores (0 to 1), and the y-axis shows the density of patients. Patients in the DPP4i group (blue) have lower propensity scores, while those in the SGLT2i group (green) have higher propensity scores **(A)**. The overlapped proportion of patients in **B** is included in the propensity score matched analysis.

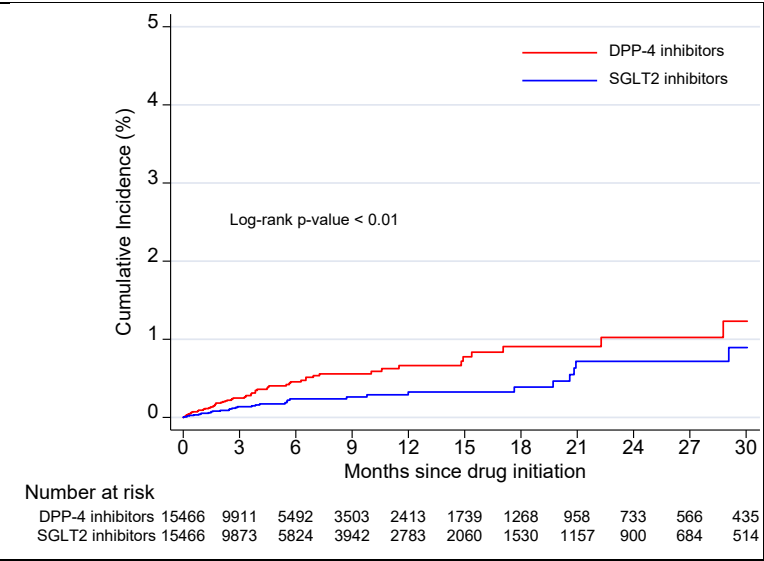
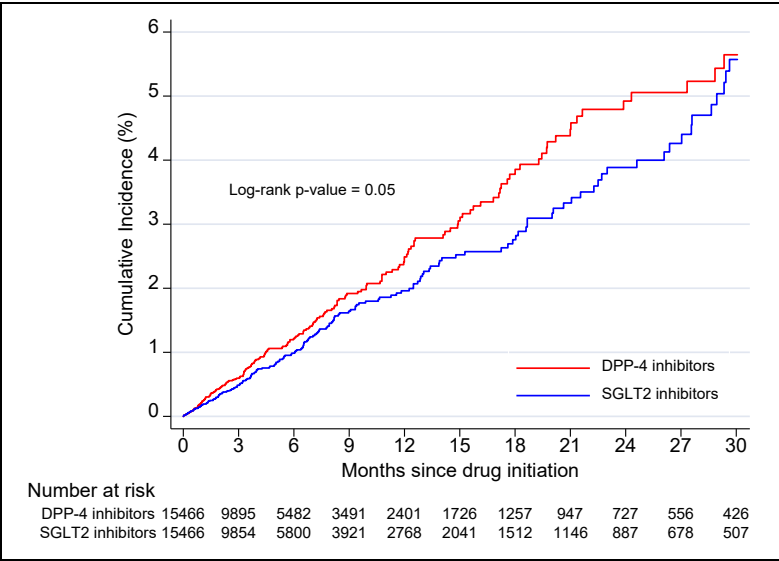
eTable 7. Follow-up and censoring reasons after PS-matching (primary outcomes)

	Patients with HbA1c < 7.5%			Patients with HbA1c 7.5-9%			Patients with HbA1c > 9%		
	Overall N = 24,052	DPP-4 inhibitor N = 12,026	SGLT2 inhibitor N = 12,026	Overall N = 32,290	DPP-4 inhibitor N = 16,145	SGLT2 inhibitor N = 16,145	Overall N = 30,932	DPP-4 inhibitor N = 15,446	SGLT2 inhibitor N = 15,446
Outcome: Modified MACE									
Follow-up, median (IQR), days	133 [68, 300]	131 [70, 298]	136 [64, 303]	134 [66, 302]	136 [77, 299]	133 [58, 305]	118 [58, 262]	118 [58, 248]	119 [58, 277]
Follow-up, mean (SD), days	250 [296.4]	248 [291.6]	252 [301.2]	251 [297.1]	249 [289.7]	252 [304.3]	220 [266.2]	212 [253.0]	229 [278.6]
Censoring reasons, %									
Outcome occurrence	255 (1.06%)	139 (1.16%)	116 (0.96%)	383 (1.19%)	205 (1.27%)	178 (1.10%)	420 (1.36%)	222 (1.44%)	198 (1.28%)
Treatment switching	1,052 (4.37%)	544 (4.52%)	508 (4.22%)	1,960 (6.07%)	1,166 (7.22%)	794 (4.92%)	2,029 (6.56%)	1,272 (8.22%)	757 (4.89%)
Treatment discontinuation	15,061 (62.62%)	7,620 (63.36%)	7,441 (61.87%)	20,365 (63.07%)	10,190 (63.12%)	10,175 (63.02%)	20,044 (64.80%)	10,031 (64.86%)	10,013 (64.74%)
End of available data - 06/30/2021	4,179 (17.37%)	2,041 (16.97%)	2,138 (17.78%)	4,865 (15.07%)	2,342 (14.51%)	2,523 (15.63%)	3,590 (11.61%)	1,715 (11.09%)	1,875 (12.12%)
Disenrollment	3,464 (14.40%)	1,659 (13.80%)	1,805 (15.01%)	4,671 (14.47%)	2,221 (13.76%)	2,450 (15.17%)	4,808 (15.54%)	2,207 (14.27%)	2,601 (16.82%)
Initiation of SGLT-2i/DPP4i combinations	41 (0.17%)	23 (0.19%)	18 (0.15%)	46 (0.14%)	21 (0.13%)	25 (0.15%)	41 (0.13%)	19 (0.12%)	22 (0.14%)
Outcome: Hospitalization for HF									
Follow-up, median (IQR), days	134 [68, 301]	131 [70, 298]	136 [64, 304]	135 [66, 302]	137 [78, 300]	133 [58, 307]	118 [58, 263]	118 [58, 249]	119 [58, 279]
Follow-up, mean (SD), days	251 [297.1]	248 [291.9]	253 [302.2]	252 [297.9]	250 [290.4]	253 [305.1]	222 [267.9]	213 [254.7]	230 [280.1]
Censoring reasons, %									
Outcome occurrence	112 (0.47%)	75 (0.62%)	37 (0.31%)	674 (1.4%)	84 (0.52%)	37 (0.23%)	103 (0.33%)	69 (0.45%)	34 (0.22%)
All-cause mortality	96 (0.40%)	57 (0.47%)	39 (0.32%)	155 (0.48%)	81 (0.50%)	74 (0.46%)	148 (0.48%)	83 (0.54%)	65 (0.42%)
Treatment switching	1,054 (4.38%)	545 (4.53%)	509 (4.23%)	1,963 (6.08%)	1,171 (7.25%)	792 (4.91%)	2,037 (6.59%)	1,273 (8.23%)	764 (4.94%)
Treatment discontinuation	15,092 (62.75%)	7,623 (63.39%)	7,469 (62.11%)	20,432 (63.28%)	10,209 (63.23%)	10,223 (63.32%)	20,165 (65.19%)	10,085 (65.21%)	10,080 (65.18%)
End of available data - 06/30/2021	4,191 (17.42%)	2,047 (17.02%)	2,144 (17.83%)	4,888 (15.14%)	2,356 (14.59%)	2,532 (15.68%)	3,606 (11.66%)	1,721 (11.13%)	1,885 (12.19%)
Disenrollment	3,467 (14.41%)	1,657 (13.78%)	1,810 (15.05%)	4,684 (14.51%)	2,222 (13.76%)	2,462 (15.25%)	4,831 (15.62%)	2,215 (14.32%)	2,616 (16.91%)
Initiation of SGLT-2i/DPP4i combinations	40 (0.17%)	22 (0.18%)	18 (0.15%)	47 (0.15%)	22 (0.15%)	25 (0.15%)	42 (0.14%)	22 (0.14%)	20 (0.13%)

Abbreviations: MACE, major adverse cardiovascular events; IQR, interquartile range; SD, standard deviation; HbA1c, HbA1c, glycated hemoglobin; DPP-4, dipeptidyl peptidase 4; SGLT2, Sodium-Glucose Cotransporter-2. Follow-up and censoring are strictly dependent on the outcome of interest. The table reports follow-up and censoring information specific to the primary outcomes. Follow-up and censoring reasons specific to secondary outcomes may include minor variations.

eFigure 3. Cumulative incidence of modified MACE and HHF comparing 1:1 propensity score–matched patients initiating SGLT2 inhibitor vs. DPP-4 inhibitor therapy stratified by HbA_{1c} levels.



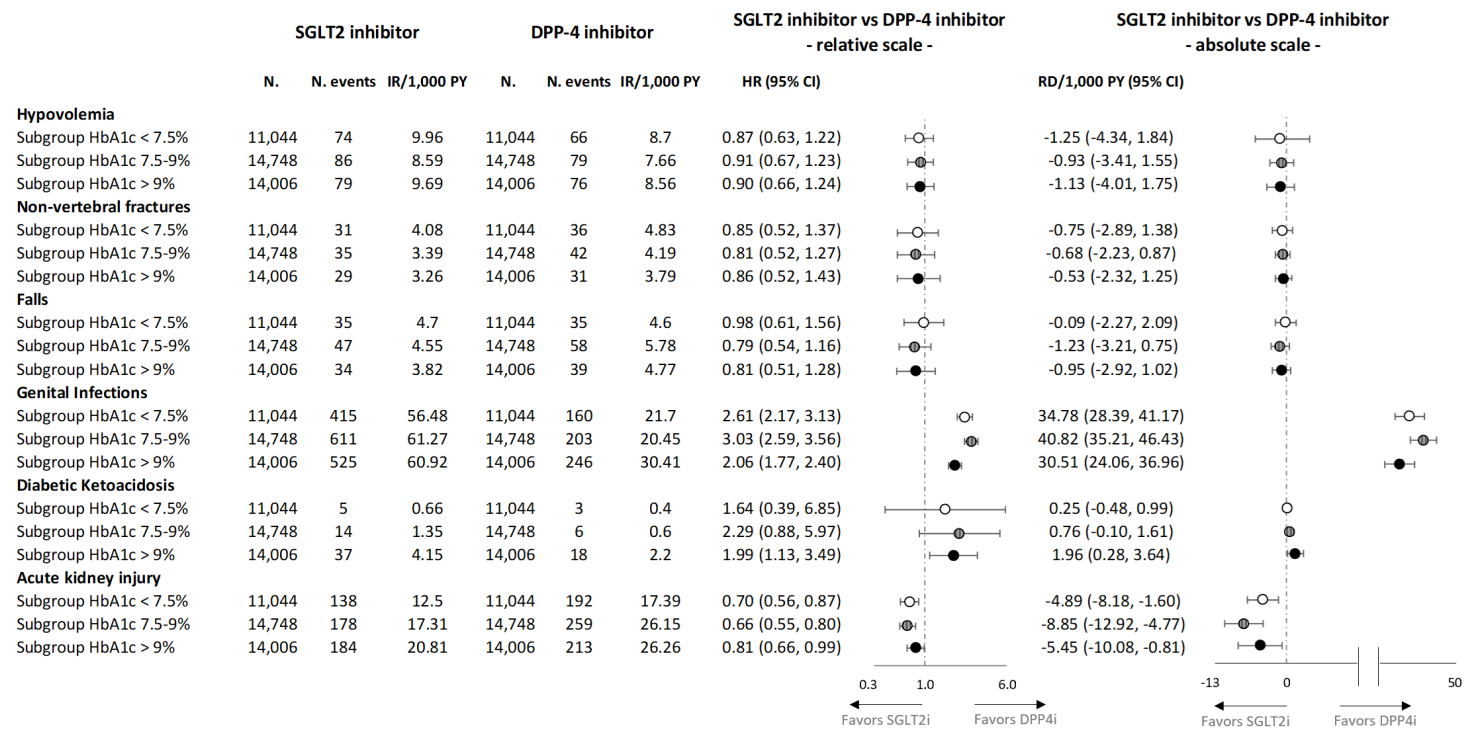


eTable 8. Time-limited “intent-to-treat” analysis and secondary analyses of the primary effectiveness outcomes in 1:1 propensity score-matched patients initiating SGLT2 inhibitor vs. DPP-4 inhibitor therapy and stratified by HbA_{1c} levels.

Sensitivity analyses for effectiveness outcomes	Events, N (IR/1,000 PY)	Events, N (IR/1,000 PY)	HR (95% CI)	RD/1,000 PY (95% CI)
1. Time-limited "intent-to-treat" analysis	SGLT2 inhibitor	DPP-4 inhibitor	SGLT2 inhibitor vs DPP-4 inhibitor	
Modified MACE*				
Subgroup HbA1c < 7.5% (N = 24,078)	150 (15.77)	185 (19.35)	0.82 (0.66, 1.01)	-3.57 (-7.33, 0.19)
Subgroup HbA1c 7.5-9% (N = 32,356)	266 (20.48)	249 (18.94)	1.08 (0.91, 1.29)	1.54 (-1.86, 4.94)
Subgroup HbA1c > 9% (N = 31,052)	278 (22.61)	316 (25.40)	0.89 (0.76, 1.05)	-2.79 (-6.65, 1.08)
Overall population (N = 87,486)	694 (19.95)	750 (21.33)	0.92 (0.82, 1.01)	-1.37 (-3.48, 0.75)
Hospitalization for HF				
Subgroup HbA1c < 7.5% (N = 24,078)	46 (4.82)	92 (9.62)	0.50 (0.35, 0.71)	-4.80 (-7.21, -2.39)
Subgroup HbA1c 7.5-9% (N = 32,356)	58 (4.45)	93 (7.06)	0.63 (0.45, 0.87)	-2.61 (-4.45, -0.78)
Subgroup HbA1c > 9% (N = 31,052)	67 (5.43)	113 (9.06)	0.60 (0.44, 0.81)	-3.63 (-5.74, -1.51)
Overall population (N = 87,486)	171 (4.89)	298 (8.46)	0.57 (0.46, 0.68)	-3.48 (-4.69, -2.28)
2. Secondary analysis restricted to patients with concurrent use of metformin and no use of insulin at baseline	SGLT2 inhibitor	DPP-4 inhibitor	SGLT2 inhibitor vs DPP-4 inhibitor	
Modified MACE*				
Subgroup HbA1c < 7.5% (N = 10,948)	50 (12.16)	60 (14.59)	0.83 (0.57, 1.21)	-2.43 (-7.43, 2.56)
Subgroup HbA1c 7.5-9% (N = 16,066)	74 (12.51)	76 (12.75)	0.99 (0.72, 1.36)	-0.24 (-4.28, 3.80)
Subgroup HbA1c > 9% (N = 11,696)	65 (16.28)	65 (17.16)	0.95 (0.67, 1.33)	-0.88 (-6.63, 4.87)
Overall population (N = 38,710)	189 (13.48)	201 (14.50)	0.92 (0.74, 1.11)	-1.05 (-3.81, 1.70)
Hospitalization for HF				
Subgroup HbA1c < 7.5% (N = 10,948)	8 (1.94)	29 (7.04)	0.27 (0.12, 0.59)	-5.10 (-8.00, -2.21)
Subgroup HbA1c 7.5-9% (N = 16,066)	14 (2.36)	14 (2.34)	1.00 (0.48, 2.11)	0.02 (-1.72, 1.76)
Subgroup HbA1c > 9% (N = 11,696)	4 (0.99)	10 (2.63)	0.39 (0.12, 1.25)	-1.63 (-3.53, 0.27)
Overall population (N = 38,710)	26 (1.85)	53 (3.81)	0.34 (0.13, 0.55)	-1.45 (-2.62, -0.28)
3. Secondary analysis restricted to patients initiating a SGLT2 inhibitor or sitagliptin	SGLT2 inhibitor	Sitagliptin	SGLT2 inhibitor vs Sitagliptin	
Hospitalization for HF				
Subgroup HbA1c < 7.5% (N = 19,512)	37 (5.11)	61 (9.09)	0.56 (0.37, 0.85)	-3.97 (-6.79, -1.16)
Subgroup HbA1c 7.5-9% (N = 25,610)	34 (3.66)	71 (8.09)	0.45 (0.30, 0.68)	-4.43 (-6.68, -2.18)
Subgroup HbA1c > 9% (N = 21,576)	25 (3.53)	73 (11.59)	0.30 (0.19, 0.48)	-8.06 (-11.06, -5.07)
Overall population (N = 66,698)	96 (4.06)	205 (9.41)	0.40 (0.29, 0.50)	-5.23 (-6.74, -3.71)

Abbreviations: DPP-4, dipeptidyl peptidase 4; SGLT2, Sodium-Glucose Cotransporter-2; N, number; IR, incidence rate; PY, person-years; RD, rate difference; HR, hazard ratio; CI, confidence interval; HF, heart failure; MACE, major adverse cardiac events (i.e., myocardial infarction, stroke, and all-cause mortality).

eTable 9. Number of events, incidence rates, relative and absolute estimates for sensitivity analysis of incident safety outcomes in 1:1 PS-matched initiators of SGLT2 inhibitors vs. DPP-4 inhibitors



Abbreviations:DPP-4, dipeptidyl peptidase 4; SGLT2, Sodium-Glucose Cotransporter-2; N, number; IR, incidence rate; PY, person-years; RD, rate difference; HR, hazard ratio; CI, confidence interval; HbA1c, glycated hemoglobin.

P value for homogeneity is > 0.05 for all outcomes except for genital infections where p value for homogeneity is < 0.01.