

## **SUPPLEMENTAL MATERIAL**

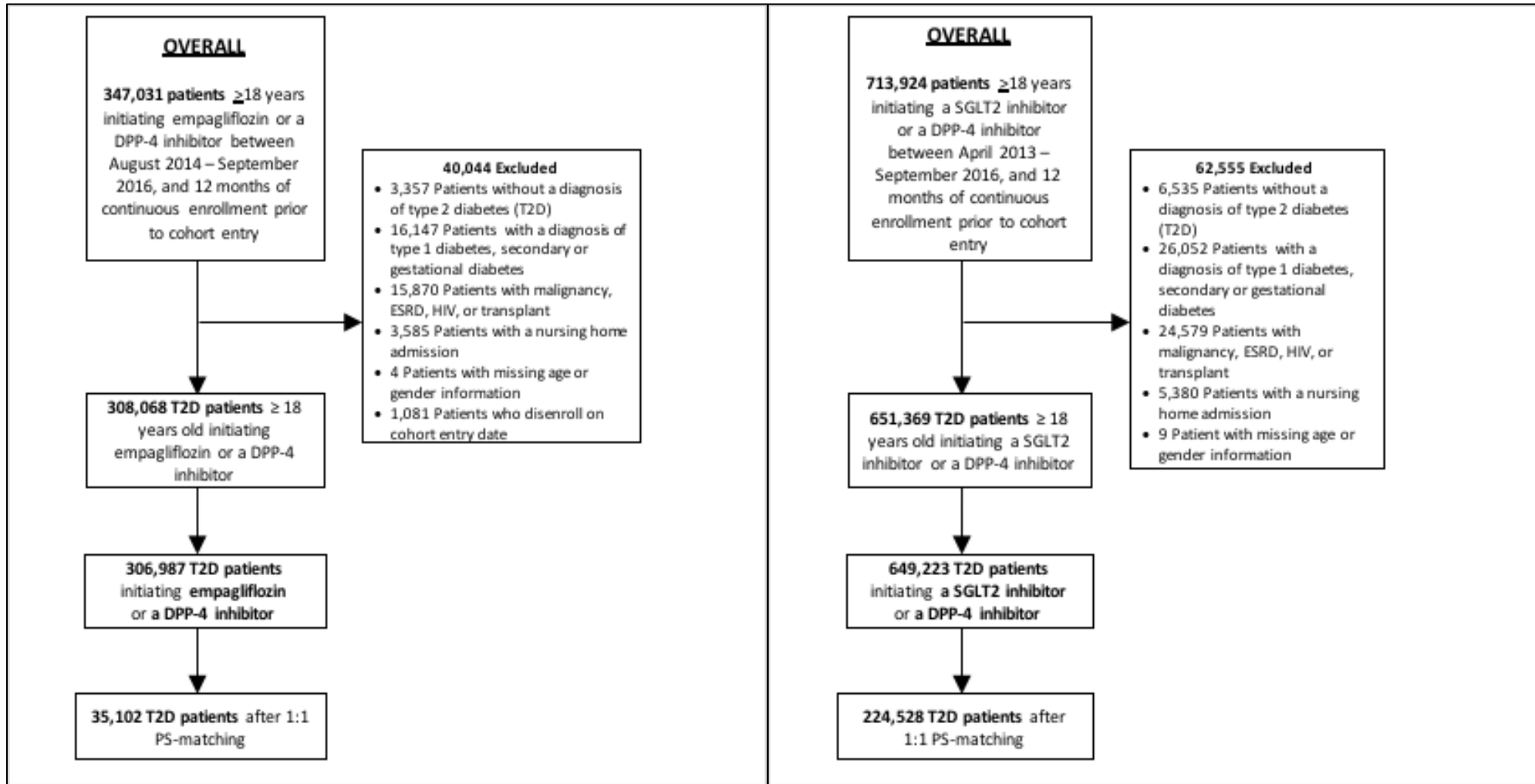
**SUPPLEMENTAL MATERIAL: Empagliflozin and the risk of heart failure hospitalization in routine clinical care: a first analysis from the EMPagliflozin compaRative effectIveness and SafEty (EMPRISE) Study**

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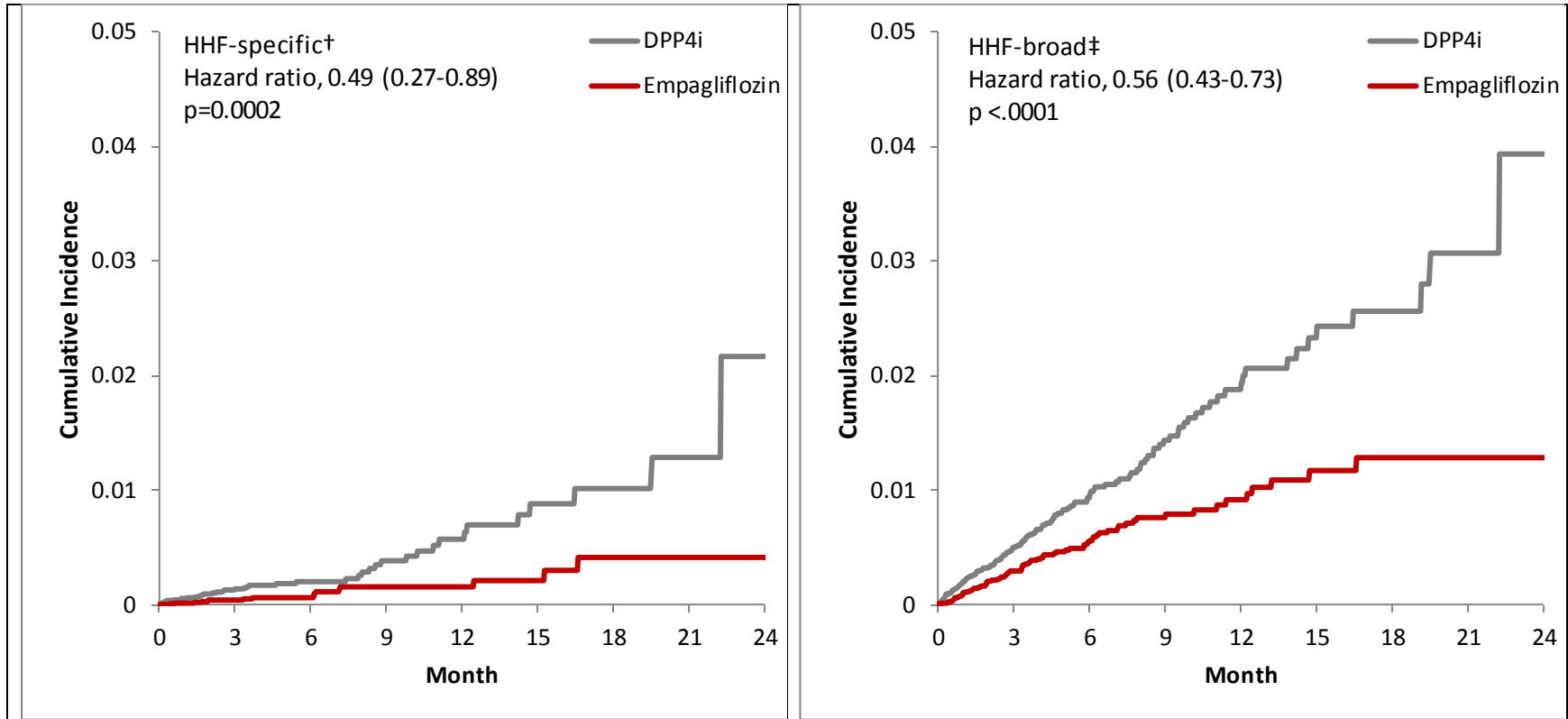
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**Supplemental Figure 1. Flowchart of overall study populations of empagliflozin vs. DPP-4i initiators and SGLT2i vs. DPP-4i initiators.**

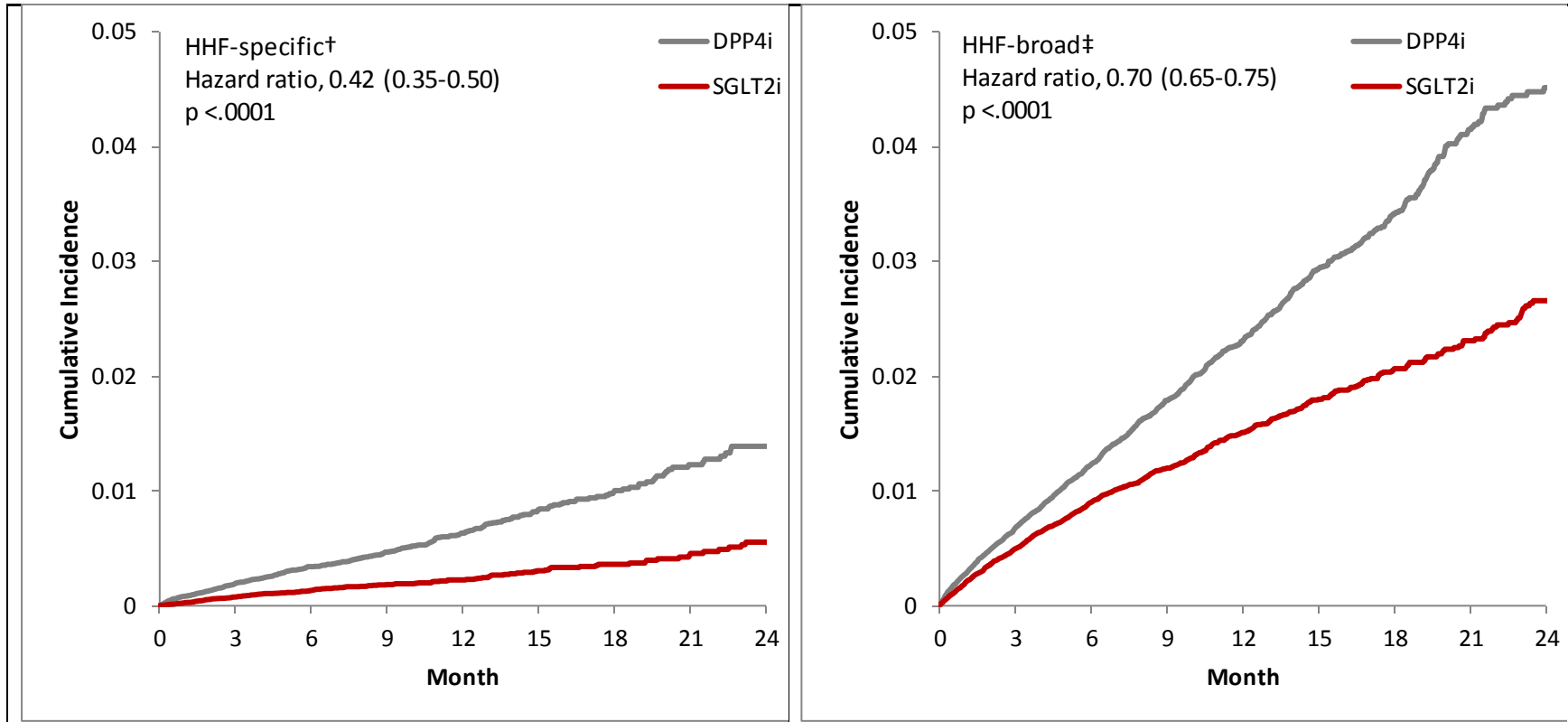


ESRD: end stage renal disease; HIV: human immunodeficiency virus; DPP-4: dipeptidyl peptidase-4; SGLT2i: sodium-glucose co-transporter-2; PS: propensity score

**Supplemental Figure 2. Cumulative incidence of hospitalization for heart failure comparing initiators of empagliflozin vs. DPP-4 inhibitors and SGLT2i vs. DPP-4i\***



Supplemental Fig 2 (continued)



HHF: hospitalization for heart failure; HHF-broad: broad definition of HHF; HHF-specific: narrow definition of HHF; DPP-4: dipeptidyl peptidase-4; SGLT 2i: sodium-glucose co-transporter-2.

\*Analyses were 1:1 propensity score- matched among new users of the study agents.

†Discharge diagnosis of HF in the primary position

‡Discharge diagnosis of HF in any position

**Supplemental Table 1. Baseline characteristics of patients initiating empagliflozin vs. sitagliptin before and after 1:1 PS-matching**

Baseline characteristics	UNMATCHED			PROPENSITY-SCORE MATCHED		
	Sitagliptin (N = 201,839)	Empagliflozin (N = 18,880)	St. Diff.	Sitagliptin (N = 16,443)	Empagliflozin (N = 16,443)	St. Diff.
<b>Demographics</b>						
Age; mean (sd)	67.54 (9.46)	58.41 (8.93)	0.99	59.11 (9.11)	59.09 (8.94)	0.00
Age categories						
18 - 54; n (%)	31,709 (15.7%)	6,923 (36.7%)	-0.49	5,729 (34.8%)	5,700 (34.7%)	0.00
55 - 64; n (%)	30,781 (15.3%)	5,877 (31.1%)	-0.38	4,834 (29.4%)	4,954 (30.1%)	-0.02
65 - 74; n (%)	82,809 (41.0%)	4,742 (25.1%)	0.34	4,587 (27.9%)	4,475 (27.2%)	0.02
>= 75; n (%)	56,540 (28.0%)	1,338 (7.1%)	0.57	1,293 (7.9%)	1,314 (8.0%)	0.00
Male; n (%)	96,641 (47.9%)	10,168 (53.9%)	-0.12	8,777 (53.4%)	8,816 (53.6%)	0.00
Race*						
White; n (%)	86,435 (76.6%)	3,796 (84.7%)	-0.21	3,618 (84.5%)	3,610 (84.3%)	0.01
Black; n (%)	12,007 (10.6%)	299 (6.7%)	0.14	318 (7.4%)	295 (6.9%)	0.02
Asian; n (%)	5,084 (4.5%)	111 (2.5%)	0.11	107 (2.5%)	110 (2.6%)	-0.01
Hispanic; n (%)	4,611 (4.1%)	85 (1.9%)	0.13	71 (1.7%)	85 (2.0%)	-0.02
North American Native; n (%)	487 (0.4%)	18 (0.4%)	0.00	19 (0.4%)	18 (0.4%)	0.00
Other/Unknown; n (%)	4,191 (3.7%)	175 (3.9%)	-0.01	151 (3.5%)	166 (3.9%)	-0.02
Region						
Northeast; n (%)	35,911 (17.8%)	2,627 (13.9%)	0.11	2,361 (14.4%)	2,350 (14.3%)	0.00
South; n (%)	72,783 (36.1%)	5,966 (31.6%)	0.10	5,113 (31.1%)	5,158 (31.4%)	-0.01
Midwest; n (%)	59,604 (29.5%)	7,576 (40.1%)	-0.22	6,534 (39.7%)	6,546 (39.8%)	0.00
West; n (%)	33,002 (16.4%)	2,651 (14.0%)	0.07	2,377 (14.5%)	2,336 (14.2%)	0.01
Calendar time						
Quarter and year of cohort entry						
Q3 2014; n (%)	17,936 (8.9%)	323 (1.7%)	0.33	318 (1.9%)	329 (2.0%)	0.01
Q4 2014; n (%)	25,852 (12.8%)	1,548 (8.2%)	0.15	1399 (8.5%)	1344 (8.2%)	-0.01
Q1 2015; n (%)	24,048 (11.9%)	1,967 (10.4%)	0.05	1,749 (10.6%)	1,701 (10.3%)	-0.01
Q2 2015; n (%)	25,279 (12.5%)	1,668 (8.8%)	0.12	1511 (9.2%)	1507 (9.2%)	0.00
Q3 2015; n (%)	22,792 (11.3%)	1,449 (7.7%)	0.12	1300 (7.9%)	1253 (7.6%)	-0.01
Q4 2015; n (%)	20,779 (10.3%)	2,359 (12.5%)	-0.07	2,014 (12.2%)	2,062 (12.5%)	0.01
Q1 2016; n (%)	23,298 (11.5%)	3,168 (16.8%)	-0.15	2,777 (16.9%)	2,802 (17.0%)	0.00
Q2 2016; n (%)	22,139 (11.0%)	3,170 (16.8%)	-0.17	2,682 (16.3%)	2,736 (16.6%)	0.01
Q3 2016; n (%)	19,716 (9.8%)	3,228 (17.1%)	-0.22	2,688 (16.3%)	2,704 (16.4%)	0.00
<b>Burden of comorbidities</b>						
Combined comorbidity score; mean (sd)	2.89 (2.22)	2.20 (1.59)	0.36	2.22 (1.66)	2.19 (1.63)	0.02
Frailty score, mean (sd)	1.76 (1.91)	1.03 (1.34)	0.44	1.06 (1.40)	1.06 (1.36)	0.00
No. distinct diagnoses; mean (sd)	6.21 (9.25)	5.39 (7.00)	0.10	5.50 (7.02)	5.36 (7.05)	0.02
<b>Diabetes-related complications</b>						
Diabetic nephropathy; n (%)	20,082 (9.9%)	1,490 (7.9%)	0.07	1,257 (7.6%)	1,247 (7.6%)	0.00
Diabetic retinopathy; n (%)	14,153 (7.0%)	1,122 (5.9%)	0.04	966 (5.9%)	957 (5.8%)	0.00

Diabetes with other ophthalmic conditions or ophthalmic procedures; n (%)	8,288 (4.1%)	685 (3.6%)	0.03	572 (3.5%)	575 (3.5%)	0.00
Diabetic neuropathy; n (%)	36,387 (18.0%)	3,216 (17.0%)	0.03	2,698 (16.4%)	2,694 (16.4%)	0.00
Diabetes with peripheral circulatory disorders; n (%)	12,811 (6.3%)	762 (4.0%)	0.10	701 (4.3%)	674 (4.1%)	0.01
Diabetic Foot; n (%)	4,986 (2.5%)	357 (1.9%)	0.04	329 (2.0%)	298 (1.8%)	0.01
Lower extremity amputation; n (%)	881 (0.4%)	58 (0.3%)	0.02	058 (0.4%)	49 (0.3%)	0.02
Skin infections; n (%)	18,710 (9.3%)	1,653 (8.8%)	0.02	1,430 (8.7%)	1,398 (8.5%)	0.01
Foot ulcer; n (%)	5,013 (2.5%)	355 (1.9%)	0.04	324 (2.0%)	297 (1.8%)	0.01
Erectile dysfunction; n (%)	6,944 (3.4%)	870 (4.6%)	-0.06	732 (4.5%)	737 (4.5%)	0.00
Hypoglycemia; n (%)	9,862 (4.9%)	737 (3.9%)	0.05	582 (3.5%)	624 (3.8%)	-0.02
Hyperglycemia; n (%)	14,631 (7.2%)	1,160 (6.1%)	0.04	1,060 (6.4%)	1,057 (6.4%)	0.00
Disorders of fluid electrolyte and acid-base balance; n (%)	22,601 (11.2%)	1,074 (5.7%)	0.20	997 (6.1%)	952 (5.8%)	0.01
Diabetic ketoacidosis; n (%)	778 (0.4%)	52 (0.3%)	0.02	037 (0.2%)	42 (0.3%)	-0.02
Hyperosmolar hyperglycemic nonketotic syndrome; n (%)	1,256 (0.6%)	94 (0.5%)	0.01	088 (0.5%)	084 (0.5%)	0.00
Diabetes with unspecified complication; n (%)	10,778 (5.3%)	1,181 (6.3%)	-0.04	1,001 (6.1%)	965 (5.9%)	0.01
<b>Features of diabetes medication initiation and baseline diabetes therapy</b>						
No. antidiabetic drugs at cohort entry; mean (sd)	2.16 (0.77)	2.29 (0.95)	-0.15	2.21 (0.85)	2.22 (0.90)	-0.01
Naive new user <sup>†</sup> ; n (%)	27,139 (13.4%)	1,380 (7.3%)	0.20	1,294 (7.9%)	1,363 (8.3%)	-0.01
Monotherapy; n (%)	20,203 (10.0%)	1,130 (6.0%)	0.15	1,061 (6.5%)	1,127 (6.9%)	-0.02
Dual therapy with metformin; n (%)	35,186 (17.4%)	2,715 (14.4%)	0.08	2,741 (16.7%)	2,681 (16.3%)	0.01
Concomitant initiation or current use of metformin; n (%)	131,791 (65.3%)	11,305 (59.9%)	0.11	10,010 (60.9%)	10,092 (61.4%)	-0.01
Concomitant initiation or current use of sulfonylureas; n (%)	67,409 (33.4%)	4,849 (25.7%)	0.17	4,385 (26.7%)	4,378 (26.6%)	0.00
Concomitant initiation or current use of insulin; n (%)	19,559 (9.7%)	3,922 (20.8%)	-0.31	3,010 (18.3%)	2,954 (18.0%)	0.01
Concomitant initiation or current use of GLP-1 RAs; n (%)	2,507 (1.2%)	2,929 (15.5%)	-0.54	1,390 (8.5%)	1,479 (9.0%)	-0.02
Concomitant initiation or current use of glitazones; n (%)	9,485 (4.7%)	1,237 (6.6%)	-0.08	979 (6.0%)	1,002 (6.1%)	0.00
Past use of metformin; n (%)	28,860 (14.3%)	3,356 (17.8%)	-0.10	2,868 (17.4%)	2,855 (17.4%)	0.00
Past use of sulfonylureas; n (%)	19,487 (9.7%)	1,514 (8.0%)	0.06	1,230 (7.5%)	1,182 (7.2%)	0.01
Past use of insulin; n (%)	7,531 (3.7%)	1,549 (8.2%)	-0.19	1,160 (7.1%)	1,153 (7.0%)	0.00
Past use of GLP-1 RAs; n (%)	3,551 (1.8%)	1,593 (8.4%)	-0.30	1,164 (7.1%)	1,136 (6.9%)	0.01
Past use of glitazones; n (%)	4,634 (2.3%)	570 (3.0%)	-0.04	430 (2.6%)	445 (2.7%)	-0.01
Any use of meglitinides; n (%)	1,022 (0.5%)	93 (0.5%)	0.00	082 (0.5%)	77 (0.5%)	0.00
Any use of alpha-glucosidase inhibitors; n (%)	369 (0.2%)	40 (0.2%)	0.00	038 (0.2%)	33 (0.2%)	0.00
<b>Life style factors</b>						
Obesity; n (%)	44,813 (22.2%)	5,946 (31.5%)	-0.21	4,922 (29.9%)	4,862 (29.6%)	0.01
Overweight; n (%)	10,176 (5.0%)	879 (4.7%)	0.01	746 (4.5%)	747 (4.5%)	0.00
Smoking; n (%)	29,398 (14.6%)	1,988 (10.5%)	0.12	1,800 (10.9%)	1,776 (10.8%)	0.00
Alcohol abuse or dependence; n (%)	1,943 (1.0%)	151 (0.8%)	0.02	115 (0.7%)	137 (0.8%)	-0.01
Drug abuse or dependence; n (%)	2,565 (1.3%)	178 (0.9%)	0.04	171 (1.0%)	153 (0.9%)	0.01
<b>Other comorbidities at baseline</b>						
History of CV; n (%)	74,342 (36.8%)	4,608 (24.4%)	0.27	4,115 (25.0%)	4,094 (24.9%)	0.00
Ischemic heart disease; n (%)	51,715 (25.6%)	3,382 (17.9%)	0.19	3,013 (18.3%)	2,980 (18.1%)	0.01
Acute myocardial infarction; n (%)	4,461 (2.2%)	239 (1.3%)	0.07	231 (1.4%)	216 (1.3%)	0.01
Old myocardial infarction; n (%)	4,776 (2.4%)	274 (1.5%)	0.07	263 (1.6%)	247 (1.5%)	0.01
Unstable angina; n (%)	8,051 (4.0%)	436 (2.3%)	0.10	420 (2.6%)	397 (2.4%)	0.01



Stable angina; n (%)	8,675 (4.3%)	564 (3.0%)	0.07	504 (3.1%)	506 (3.1%)	0.00
Other chronic ischemic heart disease; n (%)	48,521 (24.0%)	3,187 (16.9%)	0.18	2,824 (17.2%)	2,805 (17.1%)	0.00
Previous coronary revascularization; n (%)	15,386 (7.6%)	864 (4.6%)	0.13	754 (4.6%)	772 (4.7%)	0.00
Ischemic or hemorrhagic stroke; n (%)	19,753 (9.8%)	997 (5.3%)	0.17	948 (5.8%)	913 (5.6%)	0.01
Ischemic stroke; n (%)	19,557 (9.7%)	989 (5.2%)	0.17	940 (5.7%)	905 (5.5%)	0.01
Transient ischemic attack; n (%)	4,995 (2.5%)	256 (1.4%)	0.08	229 (1.4%)	231 (1.4%)	0.00
Hemorrhagic stroke and other cerebrovascular disease; n (%)	488 (0.2%)	15 (0.1%)	0.03	021 (0.1%)	014 (0.1%)	0.00
Late effects of cerebrovascular disease or procedure; n (%)	4,207 (2.1%)	132 (0.7%)	0.12	134 (0.8%)	126 (0.8%)	0.00
Heart failure; n (%)	21,514 (10.7%)	920 (4.9%)	0.22	884 (5.4%)	834 (5.1%)	0.01
Peripheral arterial disease or surgery; n (%)	20,610 (10.2%)	959 (5.1%)	0.19	863 (5.2%)	872 (5.3%)	0.00
Atrial fibrillation; n (%)	19,834 (9.8%)	913 (4.8%)	0.19	843 (5.1%)	831 (5.1%)	0.00
Other cardiac dysrhythmia; n (%)	25,406 (12.6%)	1,468 (7.8%)	0.16	1,353 (8.2%)	1,307 (7.9%)	0.01
Other cardiovascular disease; n (%)	32,761 (16.2%)	1,831 (9.7%)	0.19	1,692 (10.3%)	1,647 (10.0%)	0.01
Hypertension; n (%)	166,283 (82.4%)	14,422 (76.4%)	0.15	12,565 (76.4%)	12,513 (76.1%)	0.01
Hyperlipidemia; n (%)	164,585 (81.5%)	15,157 (80.3%)	0.03	13,089 (79.6%)	13,112 (79.7%)	0.00
Edema; n (%)	21,273 (10.5%)	1,323 (7.0%)	0.12	1,164 (7.1%)	1,154 (7.0%)	0.00
Non-diabetic renal dysfunction; n (%)	43,386 (21.5%)	1,984 (10.5%)	0.30	1,811 (11.0%)	1,796 (10.9%)	0.00
Acute kidney injury; n (%)	10,296 (5.1%)	282 (1.5%)	0.20	274 (1.7%)	270 (1.6%)	0.01
Chronic kidney disease; n (%)	31,924 (15.8%)	1,268 (6.7%)	0.29	1,203 (7.3%)	1,164 (7.1%)	0.01
Chronic kidney disease stage 1-2; n (%)	6,939 (3.4%)	477 (2.5%)	0.05	420 (2.6%)	418 (2.5%)	0.01
Chronic kidney disease stage 3+ or dialysis; n (%)	21,784 (10.8%)	661 (3.5%)	0.29	643 (3.9%)	628 (3.8%)	0.01
Hypertensive nephropathy; n (%)	15,583 (7.7%)	512 (2.7%)	0.23	525 (3.2%)	476 (2.9%)	0.02
Miscellaneous renal insufficiency; n (%)	16,349 (8.1%)	744 (3.9%)	0.18	668 (4.1%)	665 (4.0%)	0.01
Kidney or bladder stones; n (%)	7,475 (3.7%)	684 (3.6%)	0.01	570 (3.5%)	592 (3.6%)	-0.01
Urinary tract infections; n (%)	30,963 (15.3%)	1,711 (9.1%)	0.19	1,533 (9.3%)	1,517 (9.2%)	0.00
COPD; n (%)	21,979 (10.9%)	1,056 (5.6%)	0.19	1,034 (6.3%)	987 (6.0%)	0.01
Asthma; n (%)	16,974 (8.4%)	1,374 (7.3%)	0.04	1,216 (7.4%)	1,193 (7.3%)	0.00
Obstructive sleep apnea; n (%)	20,948 (10.4%)	2,867 (15.2%)	-0.14	2,353 (14.3%)	2,390 (14.5%)	-0.01
Pneumonia; n (%)	8,710 (4.3%)	459 (2.4%)	0.11	443 (2.7%)	414 (2.5%)	0.01
Liver disease; n (%)	13,943 (6.9%)	1,416 (7.5%)	-0.02	1,218 (7.4%)	1,223 (7.4%)	0.00
Osteoarthritis; n (%)	48,920 (24.2%)	3,163 (16.8%)	0.18	2,899 (17.6%)	2,847 (17.3%)	0.01
Other arthritis, arthropathies and musculoskeletal pain; n (%)	100,337 (49.7%)	8,311 (44.0%)	0.11	7,291 (44.3%)	7,270 (44.2%)	0.00
Dorsopathies; n (%)	63,631 (31.5%)	5,280 (28.0%)	0.08	4,604 (28.0%)	4,623 (28.1%)	0.00
Fractures; n (%)	9,015 (4.5%)	587 (3.1%)	0.07	503 (3.1%)	522 (3.2%)	-0.01
Falls; n (%)	8,920 (4.4%)	388 (2.1%)	0.13	373 (2.3%)	346 (2.1%)	0.01
Osteoporosis; n (%)	13,943 (6.9%)	1,416 (7.5%)	-0.02	1,218 (7.4%)	1,223 (7.4%)	0.00
Disorders of thyroid gland; n (%)	38,065 (18.9%)	3,244 (17.2%)	0.04	2,857 (17.4%)	2,788 (17.0%)	0.01
Depression; n (%)	26,202 (13.0%)	2,130 (11.3%)	0.05	1,893 (11.5%)	1,846 (11.2%)	0.01
Anxiety; n (%)	21,485 (10.6%)	1,864 (9.9%)	0.02	1,701 (10.3%)	1,629 (9.9%)	0.01
Sleep disorders; n (%)	29,267 (14.5%)	3,034 (16.1%)	-0.04	2,609 (15.9%)	2,601 (15.8%)	0.00
Dementia; n (%)	11,214 (5.6%)	266 (1.4%)	0.23	258 (1.6%)	252 (1.5%)	0.01
Delirium; n (%)	3,307 (1.6%)	104 (0.6%)	0.10	111 (0.7%)	098 (0.6%)	0.01
Psychosis; n (%)	3,685 (1.8%)	109 (0.6%)	0.11	095 (0.6%)	096 (0.6%)	0.00
Other Medications						
Angiotensin converting enzyme inhibitors; n (%)	94,923 (47.0%)	8,625 (45.7%)	0.03	7,558 (46.0%)	7,487 (45.5%)	0.01

Angiotensin II receptor blockers; n (%)	62,114 (30.8%)	5,703 (30.2%)	0.01	4,904 (29.8%)	4,943 (30.1%)	-0.01
Beta-blockers; n (%)	84,388 (41.8%)	6,146 (32.6%)	0.19	5,405 (32.9%)	5,414 (32.9%)	0.00
Calcium-channel blockers; n (%)	62,990 (31.2%)	4,401 (23.3%)	0.18	3,912 (23.8%)	3,937 (23.9%)	0.00
Thiazide diuretics; n (%)	28,977 (14.4%)	2,302 (12.2%)	0.06	2,043 (12.4%)	2,015 (12.3%)	0.00
Loop diuretics; n (%)	32,075 (15.9%)	1,805 (9.6%)	0.19	1,668 (10.1%)	1,599 (9.7%)	0.01
Other diuretics; n (%)	7,413 (3.7%)	561 (3.0%)	0.04	491 (3.0%)	479 (2.9%)	0.01
Nitrates; n (%)	15,194 (7.5%)	897 (4.8%)	0.11	832 (5.1%)	805 (4.9%)	0.01
Other hypertension drugs; n (%)	15,264 (7.6%)	907 (4.8%)	0.12	810 (4.9%)	809 (4.9%)	0.00
Digoxin; n (%)	5,112 (2.5%)	233 (1.2%)	0.10	213 (1.3%)	209 (1.3%)	0.00
Anti-arrhythmics; n (%)	4,154 (2.1%)	209 (1.1%)	0.08	212 (1.3%)	189 (1.1%)	0.02
COPD or asthma medications; n (%)	44,456 (22.0%)	3,810 (20.2%)	0.04	3,438 (20.9%)	3,342 (20.3%)	0.01
Statins; n (%)	141,955 (70.3%)	12,673 (67.1%)	0.07	10,925 (66.4%)	10,963 (66.7%)	-0.01
Other lipid-lowering drugs; n (%)	27,330 (13.5%)	2,914 (15.4%)	-0.05	2,439 (14.8%)	2,468 (15.0%)	-0.01
Antiplatelet agents; n (%)	27,928 (13.8%)	1,974 (10.5%)	0.10	1,710 (10.4%)	1,756 (10.7%)	-0.01
Oral anticoagulants; n (%)	16,341 (8.1%)	889 (4.7%)	0.14	807 (4.9%)	795 (4.8%)	0.00
Heparin and other low-molecular weight heparins; n (%)	1,000 (0.5%)	37 (0.2%)	0.05	034 (0.2%)	33 (0.2%)	0.00
Nonsteroidal anti-inflammatory drugs; n (%)	48,513 (24.0%)	4,674 (24.8%)	-0.02	4,008 (24.4%)	4,091 (24.9%)	-0.01
Oral corticosteroids; n (%)	51,411 (25.5%)	4,391 (23.3%)	0.05	3,927 (23.9%)	3,818 (23.2%)	0.02
Bisphosphonates; n (%)	6,128 (3.0%)	165 (0.9%)	0.15	146 (0.9%)	153 (0.9%)	0.00
Opioids; n (%)	65,752 (32.6%)	6,096 (32.3%)	0.01	5,417 (32.9%)	5,311 (32.3%)	0.01
Antidepressants; n (%)	52,146 (25.8%)	4,954 (26.2%)	-0.01	4,285 (26.1%)	4,269 (26.0%)	0.00
Antipsychotics; n (%)	5,884 (2.9%)	385 (2.0%)	0.06	349 (2.1%)	335 (2.0%)	0.01
Anticonvulsants; n (%)	33,841 (16.8%)	2,798 (14.8%)	0.05	2,483 (15.1%)	2,439 (14.8%)	0.01
Benzodiazepines; n (%)	27,324 (13.5%)	2,550 (13.5%)	0.00	2,291 (13.9%)	2,232 (13.6%)	0.01
Other anxiolytics or hypnotics; n (%)	14,987 (7.4%)	1,474 (7.8%)	-0.02	1,262 (7.7%)	1,269 (7.7%)	0.00
Dementia medications; n (%)	6,757 (3.3%)	127 (0.7%)	0.19	119 (0.7%)	125 (0.8%)	-0.01
Antiparkinsonian medications; n (%)	5,816 (2.9%)	408 (2.2%)	0.04	352 (2.1%)	354 (2.2%)	-0.01
<b>Measures of healthcare utilization</b>						
Hospitalization within prior 30 days; n (%)	9,580 (4.7%)	163 (0.9%)	0.23	158 (1.0%)	156 (0.9%)	0.01
Hospitalization during prior 31-365 days; n (%)	21,645 (10.7%)	1,328 (7.0%)	0.13	1,211 (7.4%)	1,173 (7.1%)	0.01
No. hospitalizations; mean (sd)	0.20 (0.60)	0.10 (0.38)	0.20	0.10 (0.45)	0.10 (0.38)	0.00
No. hospital days; mean (sd)	1.16 (4.92)	0.47 (2.41)	0.18	0.51 (2.96)	0.48 (2.43)	0.01
No. emergency department visits; mean (sd)	0.73 (2.09)	0.35 (1.37)	0.22	0.36 (1.52)	0.36 (1.33)	0.00
No. office visits; mean (sd)	9.27 (7.12)	8.82 (6.38)	0.07	8.75 (6.76)	8.68 (6.33)	0.01
Endocrinologist visit within prior 30 days; n (%)	13,729 (6.8%)	3,917 (20.7%)	-0.41	2,504 (15.2%)	2,558 (15.6%)	-0.01
Endocrinologist visit during prior 31-365 days; n (%)	16,269 (8.1%)	3,990 (21.1%)	-0.37	2,658 (16.2%)	2,699 (16.4%)	-0.01
No. endocrinologist visits; mean (sd)	0.78 (4.11)	2.37 (7.23)	-0.27	1.62 (5.65)	1.82 (6.54)	-0.03
Internal medicine visit within prior 30 days; n (%)	136,884 (67.8%)	11,000 (58.3%)	0.20	10,327 (62.8%)	10,123 (61.6%)	0.02
Internal medicine visit during prior 31-365 days; n (%)	170,181 (84.3%)	15,340 (81.3%)	0.08	13,642 (83.0%)	13,578 (82.6%)	0.01
No. internal medicine visits; mean (sd)	14.45 (18.08)	11.72 (14.90)	0.16	12.36 (15.28)	12.13 (15.12)	0.02
Cardiologist visit within prior 30 days; n (%)	64,941 (32.2%)	4,654 (24.7%)	0.17	4,112 (25.0%)	4,074 (24.8%)	0.00
Cardiologist visit during prior 31-365 days; n (%)	64,941 (32.2%)	4,654 (24.7%)	0.17	4,112 (25.0%)	4,074 (24.8%)	0.00
No. cardiologist visits; mean (sd)	2.62 (6.96)	1.65 (5.08)	0.16	1.72 (5.96)	1.67 (5.17)	0.01
Electrocardiogram; n (%)	90,386 (44.8%)	6,937 (36.7%)	0.17	6,218 (37.8%)	6,097 (37.1%)	0.01
No. electrocardiograms, mean (sd)	1.14 (2.13)	0.76 (1.58)	0.20	0.81 (1.59)	0.78 (1.59)	0.02

No. distinct medication prescriptions; mean (sd)	12.13 (5.92)	12.40 (5.99)	-0.05	12.21 (6.08)	12.12 (5.90)	0.02
Use of glucose test strips; n (%)	10,613 (5.3%)	1,103 (5.8%)	-0.02	900 (5.5%)	926 (5.6%)	0.00
No. HbA1c tests ordered; mean (sd)	2.29 (1.37)	2.38 (1.34)	-0.07	2.34 (1.39)	2.34 (1.32)	0.00
No. glucose tests ordered; mean (sd)	0.73 (2.20)	0.79 (1.65)	-0.03	0.74 (1.67)	0.74 (1.60)	0.00
No. microalbuminuria tests ordered; mean (sd)	1.02 (1.36)	1.28 (1.56)	-0.18	1.21 (1.48)	1.22 (1.51)	-0.01
No. creatinine tests ordered; mean (sd)	0.13 (0.54)	0.10 (0.47)	0.06	0.09 (0.45)	0.10 (0.48)	-0.02
No. BUN tests ordered, mean (sd)	0.08 (0.42)	0.05 (0.33)	0.08	0.05 (0.33)	0.05 (0.34)	0.00
No. lipid tests; mean (sd)	1.75 (1.46)	1.87 (1.57)	-0.08	1.85 (1.66)	1.84 (1.50)	0.01
<b>Laboratory test results<sup>‡</sup></b>						
HbA1c (%); mean (sd)	8.33 (1.78)	8.50 (1.77)	-0.10	8.60 (1.86)	8.46 (1.77)	0.08
Patients with HbA1c results available; n (%)	17,214 (19.3%)	2,649 (18.4%)	0.02	2,395 (19.7%)	2,091 (17.2%)	0.06
Creatinine (mg/dl); mean (sd)	0.97 (0.33)	0.88 (0.22)	0.32	0.90 (0.26)	0.89 (0.22)	0.04
Patients with creatinine results available; n (%)	17,436 (19.6%)	2,812 (19.5%)	0.00	2,441 (20.1%)	2,197 (18.1%)	0.05
BUN (mg/dl); mean (sd)	16,923 (19.0%)	2,725 (18.9%)	0.00	2,363 (19.4%)	2,131 (17.5%)	0.05
Patients with BUN results available; n (%)	451.10 (8442.85)	592.11 (9142.14)	-0.02	729.22 (10500.44)	580.13 (8891.51)	0.02
Total cholesterol (mg/dl); mean (sd)	176.96 (45.82)	176.69 (45.22)	0.01	179.36 (47.83)	177.42 (45.80)	0.04
Patients with total cholesterol results available; n (%)	15,478 (17.4%)	2,556 (17.8%)	-0.01	2,195 (18.1%)	2,012 (16.5%)	0.04
LDL level (mg/dl); mean (sd)	89.89 (47.55)	87.41 (39.68)	0.06	91.14 (40.49)	88.07 (39.53)	0.08
Patients with LDL results available; n (%)	16,147 (18.1%)	2,543 (17.7%)	0.01	2,243 (18.4%)	2,003 (16.5%)	0.05
HDL level (mg/dl); mean (sd)	46.32 (44.30)	44.07 (13.07)	0.07	43.98 (12.61)	44.24 (13.16)	-0.02
Patients with HDL results available; n (%)	15,345 (17.2%)	2,516 (17.5%)	-0.01	2,179 (17.9%)	1,978 (16.3%)	0.04
Triglyceride level (mg/dl); mean (sd)	188.93 (155.56)	208.51 (219.01)	-0.10	198.49 (154.47)	208.23 (226.49)	-0.05
Patients with triglyceride results available; n (%)	15,242 (17.1%)	2,532 (17.6%)	-0.01	2,154 (17.7%)	1,992 (16.4%)	0.03

DPP-4: dipeptidyl peptidase-4; St. Diff: standardized differences; sd: standard deviation; Q: quarter; GLP-1 RA: glucagon-like peptide-1 receptor agonists; COPD: Chronic obstructive pulmonary disease; BUN: blood urea nitrogen;

HbA1c: hemoglobin A1c; LDL: low-density lipoprotein; HDL: high-density lipoproteins

\* Only available in Medicare fee-for-service

† Defined as patients without any use of glucose-lowering medications during the 12 months prior to cohort entry

‡ Only available in OptumClinformatics and Truven MarketScan

**Supplemental Table 2. Baseline characteristics of patients initiating empagliflozin vs. DPP-4i and SGLT2i vs. DPP-4i before and after 1:1 PS-matching**

Baseline characteristics	UNMATCHED			PROPENSITY-SCORE MATCHED			UNMATCHED			PROPENSITY-SCORE MATCHED		
	Empagliflozin (N = 18,810)	DPP-4i (N = 288,177)	St. Diff.	Empagliflozin (N = 17,551)	DPP-4i (N = 17,551)	St. Diff.	SGLT2i (N = 164,048)	DPP-4i (N = 485,175)	St. Diff.	SGLT2i (N = 112,264)	DPP-4i (N = 112,264)	St. Diff.
<b>Demographics</b>												
Age; mean (sd)	58.39 (8.93)	67.45 (9.69)	0.97	58.71 (8.96)	58.76 (9.09)	0.01	59.21 (8.78)	67.06 (9.86)	0.84	60.70 (8.91)	60.77 (9.15)	0.01
Age categories												
18 - 54; n (%)	6,902 (36.7%)	46,480 (16.1%)	-0.48	6,276 (35.8%)	6,303 (35.9%)	0.00	56,385 (34.4%)	82,739 (17.1%)	-0.40	34,021 (30.3%)	33,903 (30.2%)	0.00
55 - 64; n (%)	5,860 (31.2%)	44,638 (15.5%)	-0.38	5,387 (30.7%)	5,287 (30.1%)	-0.01	47,339 (28.9%)	79,988 (16.5%)	-0.30	29,684 (26.4%)	29,418 (26.2%)	0.00
65 - 74; n (%)	4,723 (25.1%)	115,854 (40.2%)	0.33	4,579 (26.1%)	4,623 (26.3%)	0.00	47,465 (28.9%)	189,089 (39.0%)	0.21	36,804 (32.8%)	36,820 (32.8%)	0.00
>= 75; n (%)	1,325 (7.0%)	81,205 (28.2%)	0.58	1,309 (7.5%)	1,338 (7.6%)	0.00	12,859 (7.8%)	133,359 (27.5%)	0.53	11,755 (10.5%)	12,123 (10.8%)	0.01
Male; n (%)	10,135 (53.9%)	138,263 (48.0%)	-0.12	9,441 (53.8%)	9,435 (53.8%)	0.00	87,142 (53.1%)	234,014 (48.2%)	-0.10	60,039 (53.5%)	60,336 (53.7%)	0.00
Race*												
White; n (%)	3,777 (84.7%)	121,352 (75.6%)	-0.23	3,676 (84.5%)	3,663 (84.2%)	-0.01	39,081 (83.6%)	196,018 (74.9%)	-0.22	31,107 (82.2%)	31,230 (82.5%)	0.01
Black; n (%)	296 (6.6%)	17,407 (10.8%)	0.15	293 (6.7%)	267 (6.1%)	-0.02	3,334 (7.1%)	28,208 (10.8%)	0.13	2,933 (7.7%)	2,865 (7.6%)	0.00
Asian; n (%)	110 (2.5%)	7,761 (4.8%)	0.12	110 (2.5%)	124 (2.9%)	0.02	1,234 (2.6%)	13,770 (5.3%)	0.14	1,151 (3.0%)	1,134 (3.0%)	0.00
Hispanic; n (%)	83 (1.9%)	7,055 (4.4%)	0.14	83 (1.9%)	92 (2.1%)	0.01	1,224 (2.6%)	12,704 (4.9%)	0.12	1,113 (2.9%)	1,098 (2.9%)	0.00
North American Native; n (%)	18 (0.4%)	1,036 (0.6%)	0.03	18 (0.4%)	24 (0.6%)	0.03	185 (0.4%)	1,709 (0.7%)	0.04	163 (0.4%)	179 (0.5%)	0.01
Other/Unknown; n (%)	175 (3.9%)	5,957 (3.7%)	-0.01	170 (3.9%)	180 (4.1%)	0.01	1,699 (3.6%)	9,262 (3.5%)	-0.01	1,387 (3.7%)	1,348 (3.6%)	-0.01
Region												
Northeast; n (%)	2,620 (13.9%)	49,984 (17.3%)	0.09	2,480 (14.1%)	2,462 (14.0%)	0.00	22,200 (13.5%)	84,071 (17.3%)	0.11	16,065 (14.3%)	16,172 (14.4%)	0.00
South; n (%)	5,937 (31.6%)	107,870 (37.4%)	0.12	5,622 (32.0%)	5,638 (32.1%)	0.00	54,236 (33.1%)	180,024 (37.1%)	0.08	38,224 (34.0%)	38,286 (34.1%)	0.00
Midwest; n (%)	7,552 (40.1%)	82,895 (28.8%)	-0.24	6,941 (39.5%)	6,848 (39.0%)	-0.01	64,648 (39.4%)	137,369 (28.3%)	-0.24	41,349 (36.8%)	41,107 (36.6%)	0.00
West; n (%)	2,641 (14.0%)	46,769 (16.2%)	0.06	2,451 (14.0%)	2,541 (14.5%)	0.01	22,222 (13.5%)	81,830 (16.9%)	0.09	16,158 (14.4%)	16,207 (14.4%)	0.00
<b>Calendar time</b>												
Quarter and year of cohort entry												
...Q2 2013; n (%)	-	-	-	-	-	-	2028 (1.2%)	40,288 (8.3%)	0.34	1801 (1.6%)	1,701 (1.5%)	-0.01
...Q3 2013; n (%)	-	-	-	-	-	-	4,239 (2.6%)	37,805 (7.8%)	0.24	3,363 (3.0%)	3,115 (2.8%)	-0.01
...Q4 2013; n (%)	-	-	-	-	-	-	5,442 (3.3%)	36,356 (7.5%)	0.19	4,184 (3.7%)	3,954 (3.5%)	-0.01
...Q1 2014; n (%)	-	-	-	-	-	-	7,103 (4.3%)	39,056 (8.0%)	0.15	5,429 (4.8%)	5,118 (4.6%)	-0.01
...Q2 2014; n (%)	-	-	-	-	-	-	10,609 (6.5%)	40,492 (8.3%)	0.07	7,298 (6.5%)	7,141 (6.4%)	0.00
...Q3 2014; n (%)	323 (1.7%)	24,919 (8.6%)	0.32	73 (0.4%)	77 (0.4%)	0.00	14,491 (8.8%)	37,532 (7.7%)	-0.04	9,201 (8.2%)	9,261 (8.2%)	0.00
...Q4 2014; n (%)	1,548 (8.2%)	36,126 (12.5%)	0.14	407 (2.3%)	409 (2.3%)	0.00	17,443 (10.6%)	35,455 (7.3%)	-0.12	10,800 (9.6%)	10,903 (9.7%)	0.00
...Q1 2015; n (%)	1,967 (10.5%)	35,331 (12.3%)	0.06	1,069 (6.1%)	1,074 (6.1%)	0.00	17,399 (10.6%)	34,416 (7.1%)	-0.12	11,131 (9.9%)	11,238 (10.0%)	0.00
...Q2 2015; n (%)	1,665 (8.9%)	36,799 (12.8%)	0.13	883 (5.0%)	888 (5.1%)	0.00	18,248 (11.1%)	35,535 (7.3%)	-0.13	11,791 (10.5%)	11,723 (10.4%)	0.00
...Q3 2015; n (%)	1,444 (7.7%)	33,244 (11.5%)	0.13	868 (4.9%)	832 (4.7%)	0.01	13,830 (8.4%)	31,880 (6.6%)	-0.07	9,591 (8.5%)	9,674 (8.6%)	0.00
...Q4 2015; n (%)	2,357 (12.5%)	30,118 (10.5%)	-0.06	1,281 (7.3%)	1,337 (7.6%)	-0.01	13,288 (8.1%)	28,766 (5.9%)	-0.09	9,254 (8.2%)	9,363 (8.3%)	0.00
...Q1 2016; n (%)	3,160 (16.8%)	32,864 (11.4%)	-0.16	1,655 (9.4%)	1,690 (9.6%)	-0.01	14,847 (9.1%)	31,356 (6.5%)	-0.10	10,411 (9.3%)	10,582 (9.4%)	0.00
...Q2 2016; n (%)	3,149 (16.7%)	31,096 (10.8%)	-0.17	1,762 (10.0%)	1,723 (9.8%)	0.01	13,129 (8.0%)	29,767 (6.1%)	-0.07	9,438 (8.4%)	9,697 (8.6%)	0.01
...Q3 2016; n (%)	3,197 (17.0%)	27,680 (9.6%)	-0.22	1,786 (10.2%)	1,754 (10.0%)	0.01	11,952 (7.3%)	26,471 (5.5%)	-0.07	8,572 (7.6%)	8,794 (7.8%)	0.01
<b>Burden of comorbidities</b>												

Combined comorbidity score; mean (sd)	2.20 (1.60)	2.97 (2.26)	0.39	2.19 (1.62)	2.19 (1.60)	0.00	2.08 (1.61)	2.86 (2.24)	0.40	2.15 (1.69)	2.17 (1.70)	0.01
Frailty score, mean (sd)	0.13 (0.04)	0.16 (0.05)	0.66	0.13 (0.04)	0.14 (0.04)	0.03	0.15 (0.04)	0.16 (0.05)	0.22	0.15 (0.04)	0.15 (0.04)	0.00
No. distinct diagnoses; mean (sd)	5.37 (7.00)	6.28 (9.37)	0.11	5.37 (7.03)	5.43 (7.04)	0.01	3.66 (6.33)	4.88 (8.50)	0.16	3.93 (6.69)	3.97 (6.61)	0.01
<b>Diabetes-related complications</b>												
Diabetic nephropathy; n (%)	1,481 (7.9%)	31,640(11.0%)	0.11	1,353 (7.7%)	1,381 (7.9%)	0.01	11,014(6.7%)	47,947(9.9%)	0.12	7,637 (6.8%)	7,777 (6.9%)	0.00
Diabetic retinopathy; n (%)	1,121 (6.0%)	20,973(7.3%)	0.05	1,033 (5.9%)	1,060 (6.0%)	0.00	11,524(7.0%)	36,576(7.5%)	0.02	7,421 (6.6%)	7,417 (6.6%)	0.00
Diabetes with other ophthalmic conditions or ophthalmic procedures; n (%)	683 (3.6%)	12,010(4.2%)	0.03	621 (3.5%)	610 (3.5%)	0.00	7,216(4.4%)	21,806(4.5%)	0.00	4,677 (4.2%)	4,598 (4.1%)	-0.01
Diabetic neuropathy; n (%)	3,206 (17.0%)	52,972(18.4%)	0.04	2,908 (16.6%)	2,942 (16.8%)	0.01	26,976(16.4%)	83,971(17.3%)	0.02	17,638(15.7%)	17,604(15.7%)	0.00
Diabetes with peripheral circulatory disorders; n (%)	756 (4.0%)	18,711(6.5%)	0.11	697 (4.0%)	663 (3.8%)	-0.01	6,756(4.1%)	30,800(6.3%)	0.10	4,894 (4.4%)	4,869 (4.3%)	0.00
Diabetic Foot; n (%)	355 (1.9%)	7,314 (2.5%)	0.04	324 (1.8%)	297 (1.7%)	-0.01	3,120 (1.9%)	12,353(2.5%)	0.04	2,117 (1.9%)	2,074 (1.8%)	-0.01
Lower extremity amputation; n (%)	57 (0.3%)	1,294 (0.4%)	0.02	52 (0.3%)	045 (0.3%)	0.00	449 (0.3%)	2,026 (0.4%)	0.02	321 (0.3%)	323 (0.3%)	0.00
Skin infections; n (%)	1,647 (8.8%)	27,043(9.4%)	0.02	1,525 (8.7%)	1,552 (8.8%)	0.00	14,600(8.9%)	45,707(9.4%)	0.02	9,807 (8.7%)	9,884 (8.8%)	0.00
Foot ulcer; n (%)	353 (1.9%)	7,364 (2.6%)	0.05	323 (1.8%)	294 (1.7%)	-0.01	3,141 (1.9%)	12,521(2.6%)	0.05	2,136 (1.9%)	2,086 (1.9%)	0.00
Erectile dysfunction; n (%)	869 (4.6%)	10,019(3.5%)	-0.06	797 (4.5%)	795 (4.5%)	0.00	7,098(4.3%)	16,375(3.4%)	-0.05	4,592 (4.1%)	4,633 (4.1%)	0.00
Hypoglycemia; n (%)	734 (3.9%)	14,531(5.0%)	0.05	672 (3.8%)	688 (3.9%)	0.01	7,374(4.5%)	25,102(5.2%)	0.03	4,820 (4.3%)	4,868 (4.3%)	0.00
Hyperglycemia; n (%)	1,156 (6.1%)	21,184(7.4%)	0.05	1,102 (6.3%)	1,131 (6.4%)	0.00	9,176(5.6%)	33,278(6.9%)	0.05	6,660 (5.9%)	6,655 (5.9%)	0.00
Disorders of fluid electrolyte and acid-base balance; n (%)	1,070 (5.7%)	33,323(11.6%)	0.21	1,011 (5.8%)	994 (5.7%)	0.00	9,837(6.0%)	55,179(11.4%)	0.19	7,218 (6.4%)	7,269 (6.5%)	0.00
Diabetic ketoacidosis; n (%)	52 (0.3%)	1,113 (0.4%)	0.02	47 (0.3%)	041 (0.2%)	-0.02	550 (0.3%)	2,182 (0.4%)	0.02	377 (0.3%)	368 (0.3%)	0.00
Hyperosmolar hyperglycemic nonketotic syndrome; n (%)	94 (0.5%)	1,811 (0.6%)	0.01	090 (0.5%)	089 (0.5%)	0.00	847 (0.5%)	2,871 (0.6%)	0.01	602 (0.5%)	596 (0.5%)	0.00
Diabetes with unspecified complication; n (%)	1,178 (6.3%)	15,794(5.5%)	-0.03	1,055 (6.0%)	1,036 (5.9%)	0.00	8,363 (5.1%)	23,191(4.8%)	-0.01	5,502 (4.9%)	5,420 (4.8%)	0.00

<b>Features of diabetes medication initiation and baseline diabetes therapy</b>												
No. antidiabetic drugs at cohort entry; mean (sd)	2.29 (0.95)	2.14 (0.78)	-0.17	2.24 (0.92)	2.23 (0.86)	-0.01	2.35 (0.94)	2.15 (0.78)	-0.23	2.39 (0.84)	2.38 (0.69)	-0.01
Naive new user†; n (%)	1,370 (7.3%)	39,682 (13.8%)	0.21	1,363 (7.8%)	1,328 (7.6%)	-0.01	12,303 (7.5%)	74,717 (15.4%)	0.25	7,858 (7.0%)	8,195 (7.3%)	-0.02
Monotherapy; n (%)	1,120 (6.0%)	30,678 (10.6%)	0.17	1,120 (6.4%)	1,087 (6.2%)	-0.01	10,991 (6.7%)	52,693 (10.9%)	0.45	7,522 (6.7%)	7,073 (6.3%)	-0.01
Dual therapy with metformin; n (%)	2,712 (14.4%)	48,445 (16.8%)	0.07	2,712 (15.5%)	2,661 (15.2%)	-0.01	21,297 (13.0%)	78,130 (16.1%)	0.09	20,907 (18.6%)	21,066 (18.8%)	0.01
Concomitant initiation or current use of metformin; n (%)	11,270 (59.9%)	180,569 (62.7%)	0.06	10,636 (60.6%)	10,383 (59.2%)	-0.03	102,797 (62.7%)	304,518 (62.8%)	0.00	83,633 (74.5%)	83,119 (74.0%)	-0.01
Concomitant initiation or current use of sulfonylureas; n (%)	4,830 (25.7%)	94,551 (32.8%)	0.16	4,593 (26.2%)	4,687 (26.7%)	0.01	47,472 (28.9%)	162,758 (33.5%)	0.10	38,400 (34.2%)	38,505 (34.3%)	0.00
Concomitant initiation or current use of insulin; n (%)	3,906 (20.8%)	30,112 (10.4%)	-0.29	3,327 (19.0%)	3,333 (19.0%)	0.00	34,638 (21.1%)	48,263 (9.9%)	-0.31	18,761 (16.7%)	18,672 (16.6%)	0.00
Concomitant initiation or current use of GLP-1 RAs; n (%)	2,923 (15.5%)	3,914 (1.4%)	-0.52	1,938 (11.0%)	1,918 (10.9%)	0.00	23,170 (14.1%)	6,261 (1.3%)	-0.49	5,063 (4.5%)	4,818 (4.3%)	-0.01
Concomitant initiation or current use of glitazones; n (%)	1,232 (6.5%)	15,585 (5.4%)	-0.05	1,117 (6.4%)	1,162 (6.6%)	0.01	11,458 (7.0%)	27,659 (5.7%)	-0.05	8,122 (7.2%)	8,132 (7.2%)	0.00
Past use of metformin; n (%)	3,343 (17.8%)	42,577 (14.8%)	-0.08	3,096 (17.6%)	3,189 (18.2%)	0.02	3,224 (2.0%)	71,012 (14.6%)	0.47	3,143 (2.8%)	3,310 (2.9%)	0.01
Past use of sulfonylureas; n (%)	1,509 (8.0%)	28,018 (9.7%)	0.06	1,356 (7.7%)	1,342 (7.6%)	0.00	1,447 (0.9%)	49,017 (10.1%)	0.41	1,379 (1.2%)	1,568 (1.4%)	0.02
Past use of insulin; n (%)	1,542 (8.2%)	11,402 (4.0%)	-0.18	1,323 (7.5%)	1,322 (7.5%)	0.00	1,477 (0.9%)	18,353 (3.8%)	0.19	1,322 (1.2%)	1,422 (1.3%)	0.01
Past use of GLP-1 RAs; n (%)	1,589 (8.4%)	5,350 (1.9%)	-0.30	1,371 (7.8%)	1,302 (7.4%)	-0.02	1,521 (0.9%)	8,998 (1.9%)	0.09	1,384 (1.2%)	1,584 (1.4%)	0.02
Past use of glitazones; n (%)	565 (3.0%)	6,829 (2.4%)	-0.04	487 (2.8%)	485 (2.8%)	0.00	547 (0.3%)	13,746 (2.8%)	0.20	519 (0.5%)	570 (0.5%)	0.00
Any use of meglitinides; n (%)	224 (1.2%)	4,578 (1.6%)	0.03	208 (1.2%)	224 (1.3%)	0.01	2,372 (1.4%)	8,040 (1.7%)	0.02	1,676 (1.5%)	1,745 (1.6%)	0.01
Any use of alpha-glucosidase inhibitors; n (%)	77 (0.4%)	1,614 (0.6%)	0.03	070 (0.4%)	085 (0.5%)	0.01	914 (0.6%)	2,887 (0.6%)	0.00	641 (0.6%)	668 (0.6%)	0.00
<b>Life style factors</b>												
Obesity; n (%)	5,923 (31.5%)	65,007 (22.6%)	-0.20	5,318 (30.3%)	5,240 (29.9%)	-0.01	47,928 (29.2%)	100,589 (20.7%)	-0.20	29,503 (26.3%)	29,654 (26.4%)	0.00

Overweight; n (%)	876 (4.7%)	14,785 (5.1%)	0.02	814 (4.6%)	819 (4.7%)	0.00	6,241 (3.8%)	20,196 (4.2%)	0.02	4,501 (4.0%)	4,492 (4.0%)	0.00
Smoking; n (%)	1,981 (10.5%)	42,356 (14.7%)	0.13	1,882 (10.7%)	1,937 (11.0%)	0.01	16,860 (10.3%)	64,538 (13.3%)	0.09	12,374 (11.0%)	12,483 (11.1%)	0.00
Alcohol abuse or dependence; n (%)	148 (0.8%)	2,808 (1.0%)	0.02	143 (0.8%)	161 (0.9%)	0.01	1,281 (0.8%)	4,644 (1.0%)	0.02	908 (0.8%)	931 (0.8%)	0.00
Drug abuse or dependence; n (%)	177 (0.9%)	3,706 (1.3%)	0.04	164 (0.9%)	188 (1.1%)	0.02	1,711 (1.0%)	5,535 (1.1%)	0.01	1,185 (1.1%)	1,151 (1.0%)	-0.01
<b>Other comorbidities at baseline</b>												
History of cardiovascular disease; n (%)	4,589 (24.4%)	108,099 (37.5%)	0.29	4,309 (24.6%)	4,330 (24.7%)	0.00	40,273 (24.5%)	181,170 (37.3%)	0.28	29,718 (26.5%)	29,752 (26.5%)	0.00
Ischemic heart disease; n (%)	3,368 (17.9%)	75,326 (26.1%)	0.20	3,146 (17.9%)	3,191 (18.2%)	0.01	29,137 (17.8%)	126,314 (26.0%)	0.20	21,275 (19.0%)	21,408 (19.1%)	0.00
Acute myocardial infarction; n (%)	238 (1.3%)	6,369 (2.2%)	0.07	224 (1.3%)	219 (1.2%)	-0.01	1,856 (1.1%)	10,300 (2.1%)	0.08	1,402 (1.2%)	1,396 (1.2%)	0.00
Old myocardial infarction; n (%)	435 (2.3%)	11,670 (4.0%)	0.10	411 (2.3%)	440 (2.5%)	0.01	3,668 (2.2%)	18,990 (3.9%)	0.10	2,779 (2.5%)	2,754 (2.5%)	0.00
Unstable angina; n (%)	271 (1.4%)	6,959 (2.4%)	0.07	257 (1.5%)	274 (1.6%)	0.01	2,432 (1.5%)	11,645 (2.4%)	0.07	1,764 (1.6%)	1,800 (1.6%)	0.00
Stable angina; n (%)	559 (3.0%)	12,602 (4.4%)	0.07	523 (3.0%)	533 (3.0%)	0.00	4,666 (2.8%)	20,472 (4.2%)	0.08	3,424 (3.0%)	3,447 (3.1%)	0.01
Other chronic ischemic heart disease; n (%)	3,173 (16.9%)	70,714 (24.5%)	0.19	2,962 (16.9%)	2,989 (17.0%)	0.00	27,190 (16.6%)	118,485 (24.4%)	0.19	19,914 (17.7%)	20,067 (17.9%)	0.01
Previous coronary revascularization; n (%)	859 (4.6%)	22,416 (7.8%)	0.13	811 (4.6%)	819 (4.7%)	0.00	7,362 (4.5%)	36,456 (7.5%)	0.13	5,580 (5.0%)	5,614 (5.0%)	0.00
Ischemic or hemorrhagic stroke; n (%)	982 (5.2%)	28,919 (10.0%)	0.18	938 (5.3%)	924 (5.3%)	0.00	8,838 (5.4%)	48,361 (10.0%)	0.17	6,836 (6.1%)	6,818 (6.1%)	0.00
Ischemic stroke; n (%)	982 (5.2%)	28,647 (9.9%)	0.18	930 (5.3%)	913 (5.2%)	0.00	8,755 (5.3%)	47,908 (9.9%)	0.17	6,771 (6.0%)	6,752 (6.0%)	0.00
Transient ischemic attack; n (%)	255 (1.4%)	7,258 (2.5%)	0.08	241 (1.4%)	251 (1.4%)	0.00	2,240 (1.4%)	12,193 (2.5%)	0.08	1,727 (1.5%)	1,684 (1.5%)	0.00
Hemorrhagic stroke and other cerebrovascular disease; n (%)	271 (1.4%)	8,899 (3.1%)	0.11	257 (1.5%)	281 (1.6%)	0.01	2,288 (1.4%)	14,702 (3.0%)	0.11	1,800 (1.6%)	1,848 (1.6%)	0.00
Late effects of cerebrovascular disease or procedure; n (%)	131 (0.7%)	6,107 (2.1%)	0.12	128 (0.7%)	120 (0.7%)	0.00	1,429 (0.9%)	10,460 (2.2%)	0.11	1,139 (1.0%)	1,167 (1.0%)	0.00
Heart failure; n (%)	917 (4.9%)	31,877 (11.1%)	0.23	870 (5.0%)	852 (4.9%)	0.00	8,112 (4.9%)	53,077 (10.9%)	0.22	6,330 (5.6%)	6,364 (5.7%)	0.00
Peripheral arterial disease or surgery; n (%)	954 (5.1%)	30,515 (10.6%)	0.21	913 (5.2%)	941 (5.4%)	0.01	9,406 (5.7%)	51,813 (10.7%)	0.18	7,175 (6.4%)	7,194 (6.4%)	0.00
Atrial fibrillation; n (%)	907 (4.8%)	28,538 (9.9%)	0.20	867 (4.9%)	867 (4.9%)	0.00	8,153 (5.0%)	46,447 (9.6%)	0.18	6,283 (5.6%)	6,304 (5.6%)	0.00

Other cardiac dysrhythmia; n (%)	1,462 (7.8%)	36,588 (12.7%)	0.16	1,372 (7.8%)	1,368 (7.8%)	0.00	11,136 (6.8%)	56,323 (11.6%)	0.17	8,442 (7.5%)	8,506 (7.6%)	0.00
Other cardiovascular disease; n (%)	1,823 (9.7%)	48,045 (16.7%)	0.21	1,728 (9.8%)	1,703 (9.7%)	0.00	15,431 (9.4%)	78,969 (16.3%)	0.21	11,703 (10.4%)	11,651 (10.4%)	0.00
Hypertension; n (%)	14,366 (76.4%)	238,781 (82.9%)	0.16	13,362 (76.1%)	13,373 (76.2%)	0.00	124,501 (75.9%)	394,919 (81.4%)	0.13	85,655 (76.3%)	85,792 (76.4%)	0.00
Hyperlipidemia ; n (%)	15,099 (80.3%)	235,991 (81.9%)	0.04	14,024 (79.9%)	14,031 (79.9%)	0.00						
Edema; n (%)	1,319 (7.0%)	31,618 (11.0%)	0.14	1,232 (7.0%)	1,246 (7.1%)	0.00	130,984 (79.8%)	392,265 (80.9%)	0.03	89,143 (79.4%)	89,264 (79.5%)	0.00
Non-diabetic renal dysfunction; n (%)	1,969 (10.5%)	68,101 (23.6%)	0.35	1,890 (10.8%)	1,900 (10.8%)	0.00	11,820 (7.2%)	51,791 (10.7%)	0.12	8,374 (7.5%)	8,435 (7.5%)	0.00
Acute kidney injury; n (%)	282 (1.5%)	15,943 (5.5%)	0.22	278 (1.6%)	278 (1.6%)	0.00	16,396 (10.0%)	108,974 (22.5%)	0.34	12,826 (11.4%)	13,347 (11.9%)	0.02
Chronic kidney disease; n (%)	1,257 (6.7%)	51,475 (17.9%)	0.35	1,221 (7.0%)	1,270 (7.2%)	0.01	2,445 (1.5%)	25,203 (5.2%)	0.21	2,000 (1.8%)	2,057 (1.8%)	0.00
Chronic kidney disease stage 1-2; n (%)	471 (2.5%)	10,756 (3.7%)	0.07	444 (2.5%)	464 (2.6%)	0.01	10,302 (6.3%)	81,590 (16.8%)	0.33	8,331 (7.4%)	8,825 (7.9%)	0.02
Chronic kidney disease stage 3+ or dialysis; n (%)	655 (3.5%)	36,002 (12.5%)	0.34	648 (3.7%)	631 (3.6%)	-0.01	3,602 (2.2%)	16,998 (3.5%)	0.08	2,634 (2.3%)	2,713 (2.4%)	0.01
Hypertensive nephropathy; n (%)	511 (2.7%)	25,135 (8.7%)	0.26	497 (2.8%)	502 (2.9%)	0.01	5,423 (3.3%)	55,766 (11.5%)	0.32	4,698 (4.2%)	4,813 (4.3%)	0.00
Miscellaneous renal insufficiency ; n (%)	737 (3.9%)	25,517 (8.9%)	0.21	695 (4.0%)	682 (3.9%)	-0.01	4,281 (2.6%)	39,692 (8.2%)	0.25	3,550 (3.2%)	3,622 (3.2%)	0.00
Kidney or bladder stones; n (%)	686 (3.6%)	11,176 (3.9%)	0.02	642 (3.7%)	639 (3.6%)	-0.01	6,460 (3.9%)	42,203 (8.7%)	0.20	5,033 (4.5%)	5,030 (4.5%)	0.00
Urinary tract infections; n (%)	1,703 (9.1%)	45,478 (15.8%)	0.20	1,599 (9.1%)	1,597 (9.1%)	0.00	5,505 (3.4%)	17,822 (3.7%)	0.02	3,871 (3.4%)	3,895 (3.5%)	0.01
COPD; n (%)	1,051 (5.6%)	31,878 (11.1%)	0.20	1,013 (5.8%)	1,065 (6.1%)	0.01	16,284 (9.9%)	76,214 (15.7%)	0.17	11,865 (10.6%)	11,908 (10.6%)	0.00
Asthma; n (%)	1,370 (7.3%)	24,144 (8.4%)	0.04	1,288 (7.3%)	1,278 (7.3%)	0.00	10,194 (6.2%)	53,442 (11.0%)	0.17	7,798 (6.9%)	7,817 (7.0%)	0.00
Obstructive sleep apnea; n (%)	2,862 (15.2%)	29,913 (10.4%)	-0.14	2,568 (14.6%)	2,512 (14.3%)	-0.01	12,197 (7.4%)	39,751 (8.2%)	0.03	8,282 (7.4%)	8,238 (7.3%)	0.00
Pneumonia; n (%)	459 (2.4%)	12,541 (4.4%)	0.11	427 (2.4%)	442 (2.5%)	0.01	23,404 (14.3%)	47,532 (9.8%)	-0.14	14,326 (12.8%)	14,270 (12.7%)	0.00
Liver disease; n (%)	1,410 (7.5%)	20,368 (7.1%)	-0.02	1,317 (7.5%)	1,323 (7.5%)	0.00	4,182 (2.5%)	21,125 (4.4%)	0.10	3,011 (2.7%)	2,964 (2.6%)	-0.01
Osteoarthritis; n (%)	3,150 (16.7%)	70,423 (24.4%)	0.19	2,969 (16.9%)	2,994 (17.1%)	0.01	11,298 (6.9%)	32,850 (6.8%)	0.00	7,630 (6.8%)	7,560 (6.7%)	0.00
Other arthritis, arthropathies and musculoskeletal pain; n (%)	8,276 (44.0%)	144,088 (50.0%)	0.12	7,701 (43.9%)	7,748 (44.1%)	0.00	28,694 (17.5%)	115,846 (23.9%)	0.16	20,752 (18.5%)	20,804 (18.5%)	0.00
Dorsopathies; n (%)	5,266 (28.0%)	91,295 (31.7%)	0.08	4,929 (28.1%)	4,989 (28.4%)	0.01	72,572 (44.2%)	239,233 (49.3%)	0.10	49,724 (44.3%)	49,777 (44.3%)	0.00
Fractures; n (%)	585 (3.1%)	12,785 (4.4%)	0.07	556 (3.2%)	541 (3.1%)	-0.01	46,869 (28.6%)	149,846 (30.9%)	0.05	31,953 (28.5%)	31,833 (28.4%)	0.00
Falls; n (%)	388 (2.1%)	12,675 (4.4%)	0.13	363 (2.1%)	375 (2.1%)	0.00	5,201 (3.2%)	20,891 (4.3%)	0.06	3,688 (3.3%)	3,642 (3.2%)	-0.01
Osteoporosis; n (%)	574 (3.1%)	22,194 (7.7%)	0.20	555 (3.2%)	564 (3.2%)	0.00	3,430 (2.1%)	19,465 (4.0%)	0.11	2,614 (2.3%)	2,625 (2.3%)	0.00
Disorders of thyroid gland; n (%)	1,364 (7.3%)	18,368 (6.4%)	-0.04	1,210 (6.9%)	1,231 (7.0%)	0.00	5,942 (3.6%)	39,053 (8.0%)	0.19	4,745 (4.2%)	4,662 (4.2%)	0.00
Depression; n (%)	2,126 (11.3%)	37,340 (13.0%)	0.05	1,970 (11.2%)	1,957 (11.2%)	0.00	10,305 (6.3%)	29,971 (6.2%)	0.00	6,552 (5.8%)	6,550 (5.8%)	0.00
							19,375 (11.8%)	61,316 (12.6%)	0.02	12,999 (11.6%)	12,876 (11.5%)	0.00



Anxiety; n (%)	1,858 (9.9%)	30,680 (10.6%)	0.02	1,741 (9.9%)	1,764 (10.1%)	0.01	15,070 (9.2%)	47,812 (9.9%)	0.02	10,273 (9.2%)	10,173 (9.1%)	0.00
Sleep disorders; n (%)	3,029 (16.1%)	42,188 (14.6%)	-0.04	2,770 (15.8%)	2,694 (15.3%)	-0.01	29,591 (18.0%)	72,325 (14.9%)	-0.08	18,672 (16.6%)	18,452 (16.4%)	-0.01
Dementia; n (%)	264 (1.4%)	16,212 (5.6%)	0.23	255 (1.5%)	270 (1.5%)	0.00	2,647 (1.6%)	26,336 (5.4%)	0.21	2,237 (2.0%)	2,297 (2.0%)	0.00
Delirium; n (%)	103 (0.5%)	4,794 (1.7%)	0.12	99 (0.6%)	109 (0.6%)	0.00	1,007 (0.6%)	7,653 (1.6%)	0.10	790 (0.7%)	811 (0.7%)	0.00
Psychosis; n (%)	109 (0.6%)	5,336 (1.9%)	0.12	104 (0.6%)	091 (0.5%)	-0.01	1,262 (0.8%)	9,035 (1.9%)	0.10	1,009 (0.9%)	1,014 (0.9%)	0.00
<b>Other Medications</b>												
Angiotensin converting enzyme inhibitors; n (%)	8,595 (45.7%)	134,384 (46.6%)	0.02	8,009 (45.6%)	8,002 (45.6%)	0.00	75,849 (46.2%)	228,628 (47.1%)	0.02	52,852 (47.1%)	52,943 (47.2%)	0.00
Angiotensin II receptor blockers; n (%)	5,680 (30.2%)	90,032 (31.2%)	0.02	5,255 (29.9%)	5,259 (30.0%)	0.00	49,637 (30.3%)	149,457 (30.8%)	0.01	33,455 (29.8%)	33,548 (29.9%)	0.00
Beta-blockers; n (%)	6,122 (32.5%)	121,709 (42.2%)	0.20	5,729 (32.6%)	5,640 (32.1%)	-0.01	53,120 (32.4%)	202,895 (41.8%)	0.20	38,089 (33.9%)	37,996 (33.8%)	0.00
Calcium-channel blockers; n (%)	4,383 (23.3%)	91,041 (31.6%)	0.19	4,137 (23.6%)	4,139 (23.6%)	0.00	39,876 (24.3%)	152,237 (31.4%)	0.16	28,600 (25.5%)	28,564 (25.4%)	0.00
Thiazide diuretics; n (%)	2,298 (12.2%)	41,436 (14.4%)	0.06	2,143 (12.2%)	2,072 (11.8%)	-0.01	20,149 (12.3%)	69,207 (14.3%)	0.06	14,163 (12.6%)	14,108 (12.6%)	0.00
Loop diuretics; n (%)	1,797 (9.6%)	47,777 (16.6%)	0.21	1,682 (9.6%)	1,632 (9.3%)	-0.01	17,361 (10.6%)	80,726 (16.6%)	0.18	12,428 (11.1%)	12,384 (11.0%)	0.00
Other diuretics; n (%)	558 (3.0%)	11,070 (3.8%)	0.04	516 (2.9%)	508 (2.9%)	0.00	4,772 (2.9%)	17,896 (3.7%)	0.04	3,193 (2.8%)	3,176 (2.8%)	0.00
Nitrates; n (%)	893 (4.7%)	22,219 (7.7%)	0.12	850 (4.8%)	873 (5.0%)	0.01	7,963 (4.9%)	37,840 (7.8%)	0.12	5,901 (5.3%)	5,966 (5.3%)	0.00
Other hypertension drugs; n (%)	906 (4.8%)	22,944 (8.0%)	0.13	856 (4.9%)	854 (4.9%)	0.00	8,178 (5.0%)	38,674 (8.0%)	0.12	6,087 (5.4%)	6,135 (5.5%)	0.00
Digoxin; n (%)	233 (1.2%)	7,330 (2.5%)	0.10	220 (1.3%)	213 (1.2%)	-0.01	2,109 (1.3%)	13,343 (2.8%)	0.11	1,682 (1.5%)	1,721 (1.5%)	0.00
Anti-arrhythmics; n (%)	208 (1.1%)	6,171 (2.1%)	0.08	202 (1.2%)	201 (1.1%)	-0.01	1,733 (1.1%)	9,951 (2.1%)	0.08	1,318 (1.2%)	1,277 (1.1%)	-0.01
COPD or asthma medications; n (%)	3,798 (20.2%)	63,713 (22.1%)	0.05	3,526 (20.1%)	3,575 (20.4%)	0.01	34,506 (21.0%)	106,286 (21.9%)	0.02	23,498 (20.9%)	23,383 (20.8%)	0.00
Statins; n (%)	12,632 (67.2%)	202,458 (70.3%)	0.07	11,719 (66.8%)	11,712 (66.7%)	0.00	110,712 (67.5%)	338,752 (69.8%)	0.05	76,290 (68.0%)	76,411 (68.1%)	0.00
Other lipid-lowering drugs; n (%)	2,907 (15.5%)	39,875 (13.8%)	-0.05	2,654 (15.1%)	2,693 (15.3%)	0.01	26,382 (16.1%)	70,597 (14.6%)	-0.04	17,326 (15.4%)	17,258 (15.4%)	0.00
Antiplatelet agents; n (%)	1,966 (10.5%)	41,025 (14.2%)	0.11	1,844 (10.5%)	1,807 (10.3%)	-0.01	17,351 (10.6%)	69,643 (14.4%)	0.12	12,508 (11.1%)	12,415 (11.1%)	0.00
Oral anticoagulants; n (%)	882 (4.7%)	23,413 (8.1%)	0.14	830 (4.7%)	844 (4.8%)	0.00	7,751 (4.7%)	38,224 (7.9%)	0.13	5,806 (5.2%)	5,764 (5.1%)	0.00
Heparin and other low-molecular weight heparins; n (%)	037 (0.2%)	1,415 (0.5%)	0.05	036 (0.2%)	034 (0.2%)	0.00	442 (0.3%)	2,472 (0.5%)	0.03	348 (0.3%)	337 (0.3%)	0.00
Nonsteroidal anti-inflammatory drugs; n (%)	4,660 (24.8%)	69,644 (24.2%)	-0.01	4,344 (24.8%)	4,387 (25.0%)	0.00	41,918 (25.6%)	118,174 (24.4%)	-0.03	28,251 (25.2%)	28,327 (25.2%)	0.00
Oral corticosteroids; n (%)	4,370 (23.2%)	73,762 (25.6%)	0.06	4,074 (23.2%)	4,052 (23.1%)	0.00	38,115 (23.2%)	121,816 (25.1%)	0.04	26,261 (23.4%)	26,206 (23.3%)	0.00
Bisphosphonates; n (%)	164 (0.9%)	9,018 (3.1%)	0.16	161 (0.9%)	154 (0.9%)	0.00	2,242 (1.4%)	16,859 (3.5%)	0.14	1,856 (1.7%)	1,817 (1.6%)	-0.01

Opioids; n (%)	6,081 (32.3%)	94,304(32.7%)	0.01	5,673 (32.3%)	5,698 (32.5%)	0.00	55,942(34.1%)	162,128 (33.4%)	-0.01	37,167(33.1%)	37,075(33.0%)	0.00
Antidepressants; n (%)	4,946 (26.3%)	74,054(25.7%)	-0.01	4,553 (25.9%)	4,580 (26.1%)	0.00	44,514(27.1%)	122,946 (25.3%)	-0.04	29,152(26.0%)	28,871(25.7%)	-0.01
Antipsychotics; n (%)	384 (2.0%)	8,362 (2.9%)	0.06	356 (2.0%)	337 (1.9%)	-0.01	3,502 (2.1%)	14,369(3.0%)	0.06	2,456 (2.2%)	2,420 (2.2%)	0.00
Anticonvulsants; n (%)	2,789 (14.8%)	48,863(17.0%)	0.06	2,592 (14.8%)	2,529 (14.4%)	-0.01	25,723(15.7%)	78,984(16.3%)	0.02	17,210(15.3%)	17,109(15.2%)	0.00
Benzodiazepines; n (%)	2,543 (13.5%)	39,343(13.7%)	0.01	2,373 (13.5%)	2,367 (13.5%)	0.00	21,981(13.4%)	65,640(13.5%)	0.00	14,612(13.0%)	14,499(12.9%)	0.00
Other anxiolytics or hypnotics; n (%)	1,470 (7.8%)	21,687(7.5%)	-0.01	1,349 (7.7%)	1,278 (7.3%)	-0.02	13,587(8.3%)	40,166(8.3%)	0.00	8,970 (8.0%)	8,940 (8.0%)	0.00
Dementia medications; n (%)	127 (0.7%)	9,908 (3.4%)	0.19	125 (0.7%)	122 (0.7%)	0.00	1,471 (0.9%)	16,761 (3.5%)	0.18	1,289 (1.1%)	1,255 (1.1%)	0.00
Antiparkinsonian medications; n (%)	407 (2.2%)	8,435 (2.9%)	0.04	373 (2.1%)	389 (2.2%)	0.01	3,973 (2.4%)	14,091 (2.9%)	0.03	2,741 (2.4%)	2,753 (2.5%)	0.01
<b>Measures of healthcare utilization</b>												
Hospitalization within prior 30 days; n (%)	160 (0.9%)	12,925(4.5%)	0.22	157 (0.9%)	152 (0.9%)	0.00	1,496 (0.9%)	21,899(4.5%)	0.22	1,338 (1.2%)	1,326 (1.2%)	0.00
Hospitalization during prior 31-365 days; n (%)	1,321 (7.0%)	31,597(11.0%)	0.14	1,240 (7.1%)	1,315 (7.5%)	0.02	11,620(7.1%)	53,797(11.1%)	0.14	8,316 (7.4%)	8,465 (7.5%)	0.00
No. hospitalizations; mean (sd)	0.10 (0.38)	0.20 (0.59)	0.20	0.10 (0.38)	0.10 (0.36)	0.00	0.10 (0.38)	0.20 (0.60)	0.20	0.11 (0.40)	0.11 (0.40)	0.00
No. hospital days; mean (sd)	0.47 (2.42)	1.16 (4.92)	0.18	0.47 (2.41)	0.47 (2.18)	0.00	0.48 (2.67)	1.16 (4.97)	0.17	0.52 (2.95)	0.54 (2.70)	0.01
No. emergency department visits; mean (sd)	0.35 (1.37)	0.74 (2.06)	0.22	0.36 (1.31)	0.37 (1.40)	0.01	0.37 (1.45)	0.72 (2.04)	0.20	0.42 (1.52)	0.42 (1.47)	0.00
No. office visits; mean (sd)	8.81 (6.38)	9.45 (7.22)	0.09	8.70 (6.31)	8.75 (6.48)	0.01	8.89 (6.49)	9.59 (7.40)	0.10	8.73 (6.45)	8.72 (6.72)	0.00
Endocrinologist visit within prior 30 days; n (%)	3,898 (20.7%)	22,465(7.8%)	-0.38	3,048 (17.4%)	2,976 (17.0%)	-0.01	25,825(15.7%)	37,132(7.7%)	-0.25	12,164(10.8%)	12,023(10.7%)	0.00
Endocrinologist visit during prior 31-365 days; n (%)	3,971 (21.1%)	25,758(8.9%)	-0.35	3,171 (18.1%)	3,157 (18.0%)	0.00	29,327(17.9%)	42,499(8.8%)	-0.27	13,704(12.2%)	13,749(12.2%)	0.00
No. endocrinologist visits; mean (sd)	2.36 (7.21)	0.89 (4.40)	-0.25	2.02 (6.81)	1.77 (5.95)	-0.04	2.00 (6.75)	0.90 (4.42)	-0.19	1.37 (5.81)	1.20 (4.94)	-0.03
Internal medicine visit within prior 30 days; n (%)	10,960(58.3%)	189,363 (65.7%)	0.15	10,487(59.8%)	10,524(60.0%)	0.00	99,094(60.4%)	319,296 (65.8%)	0.11	71,601(63.8%)	71,634(63.8%)	0.00
Internal medicine visit during prior 31-365 days; n (%)	15,287(81.3%)	239,343 (83.1%)	0.05	14,283(81.4%)	14,334(81.7%)	0.01	134,084 (81.7%)	402,837 (83.0%)	0.03	92,188(82.1%)	92,163(82.1%)	0.00

No. internal medicine visits; mean (sd)	11.72 (14.89)	14.29 (18.37)	0.15	11.86 (15.02)	11.96 (15.51)	0.01	12.48 (15.90)	14.47 (18.33)	0.12	12.94 (16.41)	12.66 (16.15)	-0.02
Cardiologist visit within prior 30 days; n (%)	1,199 (6.4%)	31,149 (10.8%)	0.16	1,117 (6.4%)	1,176 (6.7%)	0.01	9,954 (6.1%)	52,927 (10.9%)	0.17	7,403 (6.6%)	7,382 (6.6%)	0.00
Cardiologist visit during prior 31-365 days; n (%)	4,638 (24.7%)	94,659 (32.8%)	0.18	4,341 (24.7%)	4,337 (24.7%)	0.00	40,439 (24.7%)	157,278 (32.4%)	0.17	28,595 (25.5%)	28,730 (25.6%)	0.00
No. cardiologist visits; mean (sd)	1.65 (5.08)	2.73 (7.07)	0.18	1.66 (5.14)	1.63 (4.89)	-0.01	1.65 (4.91)	2.76 (7.04)	0.18	1.77 (5.19)	1.78 (5.42)	0.00
Electrocardiogram; n (%)	6,915 (36.8%)	130,035 (45.1%)	0.17	6,474 (36.9%)	6,483 (36.9%)	0.00	60,793 (37.1%)	218,733 (45.1%)	0.16	42,560 (37.9%)	42,951 (38.3%)	0.01
No. electrocardiograms; mean (sd)	0.76 (1.58)	1.15 (2.12)	0.21	0.77 (1.59)	0.77 (1.55)	0.00	0.76 (1.51)	1.14 (2.10)	0.21	0.80 (1.60)	0.80 (1.53)	0.00
No. distinct medication prescriptions; mean (sd)	12.40 (6.00)	12.26 (6.00)	-0.02	12.20 (5.92)	12.23 (6.14)	0.00	12.53 (6.01)	12.28 (6.05)	-0.04	12.12 (5.77)	12.09 (6.07)	-0.01
Use of glucose test strips; n (%)	1,100 (5.8%)	15,563 (5.4%)	-0.02	1,012 (5.8%)	973 (5.5%)	-0.01	9,609 (5.9%)	27,300 (5.6%)	-0.01	6,225 (5.5%)	6,224 (5.5%)	0.00
No. HbA1c tests ordered; mean (sd)	2.38 (1.34)	2.30 (1.39)	-0.06	2.35 (1.33)	2.36 (1.39)	0.01	2.37 (1.38)	2.27 (1.41)	-0.07	2.30 (1.35)	2.30 (1.40)	0.00
No. glucose tests ordered; mean (sd)	0.79 (1.66)	0.78 (3.02)	0.00	0.76 (1.63)	0.76 (1.77)	0.00	0.80 (1.78)	0.80 (2.90)	0.00	0.74 (1.75)	0.73 (1.77)	-0.01
No. microalbuminuria tests ordered; mean (sd)	1.28 (1.55)	1.03 (1.38)	-0.17	1.24 (1.52)	1.23 (1.52)	-0.01	1.20 (1.52)	1.01 (1.39)	-0.13	1.13 (1.47)	1.14 (1.47)	0.01
No. creatinine tests ordered; mean (sd)	0.10 (0.47)	0.12 (0.54)	0.04	0.09 (0.47)	0.10 (0.47)	0.02	0.10 (0.47)	0.13 (0.56)	0.06	0.10 (0.47)	0.10 (0.49)	0.00
No. BUN tests ordered; mean (sd)	0.05 (0.33)	0.08 (0.42)	0.08	0.05 (0.33)	0.06 (0.33)	0.03	0.05 (0.35)	0.08 (0.45)	0.07	0.05 (0.35)	0.06 (0.36)	0.03
No. lipid tests; mean (sd)	1.88 (1.57)	1.77 (1.48)	-0.07	1.85 (1.51)	1.87 (1.68)	0.01	1.90 (1.61)	1.79 (1.49)	-0.07	1.84 (1.53)	1.84 (1.60)	0.00
<b>Laboratory test results<sup>‡</sup></b>												
HbA1c (%); mean (sd)	8.50 (1.78)	8.38 (1.82)	-0.07	8.49 (1.78)	8.63 (1.94)	0.08	8.62 (1.80)	8.37 (1.82)	-0.14	8.60 (1.79)	8.57 (1.85)	-0.02
Patients with HbA1c results available; n (%)	2,637 (18.4%)	28,325 (22.2%)	0.09	2,449 (18.6%)	2,704 (20.5%)	0.05	21,349 (18.2%)	45,506 (20.4%)	0.06	13,696 (18.4%)	14,678 (19.7%)	0.03
Creatinine (mg/dl); mean (sd)	0.88 (0.22)	0.97 (0.34)	0.31	0.88 (0.22)	0.91 (0.30)	0.11	0.87 (0.22)	0.96 (0.33)	0.32	0.88 (0.23)	0.91 (0.27)	0.12
Patients with creatinine results available; n (%)	2,799 (19.5%)	29,223 (22.9%)	0.08	2,599 (19.7%)	2,760 (20.9%)	0.03	22,671 (19.3%)	47,505 (21.3%)	0.05	14,364 (19.3%)	15,158 (20.4%)	0.03
BUN (mg/dl); mean (sd)	60.43 (65.34)	198.26 (702.27)	0.28	55.68 (59.72)	120.38 (192.12)	0.45	316.51 (6569.76)	197.05 (5400.38)	-0.02	396.60 (7486.21)	266.24 (5938.97)	-0.02

Patients with BUN results available; n (%)	2,713 (18.9%)	28,471 (22.3%)	0.08	2,524 (19.1%)	2,670 (20.2%)	0.03	22,109 (18.8%)	46,457 (20.8%)	0.05	14,020 (18.8%)	14,755 (19.8%)	0.03
Total cholesterol (mg/dl); mean (sd)	176.70(45.25)	178.78(47.25)	0.04	177.05(45.44)	179.86(48.83)	0.06	177.14(48.23)	177.36(49.33)	0.00	177.06(48.23)	179.28(50.55)	0.04
Patients with total cholesterol results available; n (%)	2,545 (17.7%)	26,076(20.4%)	0.07	2,377 (18.0%)	2,503 (19.0%)	0.03	20,568(17.5%)	42,530(19.0%)	0.04	13,093(17.6%)	13,849(18.6%)	0.03
LDL level (mg/dl); mean (sd)	87.37 (39.70)	90.36 (45.06)	0.07	87.54 (39.78)	90.24 (41.35)	0.07	87.44 (40.41)	89.64 (43.68)	0.05	87.62 (40.19)	89.81 (41.60)	0.05
Patients with LDL results available; n (%)	2,532 (17.6%)	26,800(21.0%)	0.09	2,362 (17.9%)	2,563 (19.4%)	0.04	20,513(17.5%)	43,361(19.4%)	0.05	13,103(17.6%)	14,059(18.9%)	0.03
HDL level (mg/dl); mean (sd)	44.06 (13.06)	45.87 (35.23)	0.07	44.15 (13.15)	44.23 (12.95)	0.01	43.83 (13.15)	45.40 (33.54)	0.06	43.95 (13.09)	44.23 (27.86)	0.01
Patients with HDL results available; n (%)	2,505 (17.5%)	25,737(20.2%)	0.07	2,340 (17.7%)	2,486 (18.8%)	0.03	20,253(17.3%)	42,109(18.8%)	0.04	12,889(17.3%)	13,675(18.4%)	0.03
Triglyceride level (mg/dl); mean (sd)	208.61 (219.43)	195.14(179.16)	-0.07	209.34(223.32)	207.74(220.51)	-0.01	207.98(200.38)	192.77(173.54)	-0.08	205.21(193.85)	204.64(193.80)	0.00
Patients with triglyceride results available; n (%)	2,521 (17.6%)	25,742(20.2%)	0.07	2,356 (17.8%)	2,465 (18.7%)	0.02	20,387(17.4%)	42,117(18.8%)	0.04	12,980(17.4%)	13,705(18.4%)	0.03
<b>SGLT2i/DPP4i agent initiated on the index date</b>												
Canagliflozin; n (%)	-	-	-	-	-	-	112,639 (68.7%)	-	-	77,061 (68.6%)	-	-
Dapagliflozin; n (%)	-	-	-	-	-	-	33,315(20.3%)	-	-	20,875(18.6%)	-	-
Empagliflozin; n (%)	18,810(100.0%)	-	-	17,551(100.0%)	-	-	18,115(11.0%)	-	-	14,342(12.8%)	-	-
Alogliptin; n (%)	-	4,686 (1.6%)	-	-	549 (3.1%)	-	-	7,738 (1.6%)	-	-	3,212 (2.9%)	-
Linagliptin; n (%)	-	54,951 (19.1%)	-	-	3,354 (19.1%)	-	-	86,334 (17.8%)	-	-	18,214 (16.2%)	-
Sitagliptin; n (%)	-	201,705 (70.0%)	-	-	11,663 (66.5%)	-	-	334,920 (69.0%)	-	-	77,664 (69.2%)	-
Saxagliptin; n (%)	-	26,925 (9.3%)	-	-	1,990 (11.3%)	-	-	56,337 (11.6%)	-	-	13,210 (11.8%)	-

DPP-4: dipeptidyl peptidase-4; St. Diff: standardized differences; sd: standard deviation; Q: quarter; GLP-1 RA: glucagon-like peptide-1 receptor agonists

\* Only available in Medicare fee-for-service

† Defined as patients without any use of glucose-lowering medications during the 12 months prior to cohort entry

‡ Only available in OptumClinformatics and Truven MarketScan

**Supplemental Table 3. Database-specific incidence rates and hazard ratios for hospitalization for heart failure in 1:1 PS-matched initiators of empagliflozin vs. sitagliptin, empagliflozin vs. DPP-4i, and SGLT2i vs. DPP-4i**

Patient population		Empagliflozin		Sitagliptin		HR (95% CI)	Empagliflozin		DPP-4i		HR (95% CI)	SGLT2i		DPP-4i		HR (95% CI)
		N patients (Person-years)	N events (IR/1000 PY)	N patients (Person-years)	N events (IR/1000 PY)		N patients (Person-years)	N events (IR/1000 PY)	N patients (Person-years)	N events (IR/1000 PY)		N patients (Person-years)	N events (IR/1000 PY)	N patients (Person-years)	N events (IR/1000 PY)	
HHF-Specific*	Optum	3,193 (1,407)	0 (0.0)	3,193 (1,283)	14 (10.9)	-	3,934 (1720)	0 (-)	3,934 (1580)	9 (5.7)	-	21,514 (11,995)	14 (1.2)	21,514 (10,137)	40 (4.0)	0.37 (0.22, 0.62)
	Truven	8,966 (4,332)	5 (1.2)	8,966 (3,987)	8 (2.0)	0.60 (0.20-1.85)	9,267 (4494)	5 (1.1)	9,267 (4086)	11 (2.7)	0.42 (0.15-1.21)	52,896 (32,456)	33 (1.0)	52,896 (28,339)	89 (3.1)	0.33 (0.22, 0.49)
	Medicare	4,284 (1,726)	11 (6.4)	4,284 (1,872)	26 (13.9)	0.47 (0.23-0.94)	4,350 (1755)	11 (6.3)	4,350 (1817)	22 (12.1)	0.53 (0.25-1.08)	37,854 (20,890)	128 (6.1)	37,854 (21,472)	285 (13.3)	0.46 (0.37, 0.57)
	Pooled	<b>16,443</b> <b>(7,465)</b>	16 (2.1)	<b>16,443</b> <b>(7,142)</b>	48 (6.7)	0.50 (0.28-0.91)	<b>17,551</b> <b>(7,969)</b>	16 (2.0)	<b>17,551</b> <b>(7,483)</b>	42 (5.6)	0.49 (0.27-0.89)	<b>112,264</b> <b>(65,341)</b>	175 (2.7)	<b>112,264</b> <b>(59,948)</b>	414 (6.9)	0.42 (0.35-0.50)
HHF-Broad†	Optum	3,193 (1,405)	7 (5.0)	3,193 (1,280)	29 (22.7)	0.22 (0.10-0.51)	3,934 (1717)	9 (5.2)	3,934 (1578)	20 (12.7)	0.43 (0.19-0.94)	21,514 (11,964)	91 (7.6)	21,514 (10,117)	127 (12.6)	0.63 (0.48, 0.82)
	Truven	8,966 (4,324)	25 (5.8)	8,966 (3,981)	32 (8.0)	0.73 (0.43-1.23)	9,267 (4486)	26 (5.8)	9,267 (4080)	39 (9.6)	0.61 (0.37-1.00)	52,896 (32,386)	219 (6.8)	52,896 (28,249)	328 (11.6)	0.59 (0.49, 0.70)
	Medicare	4,284 (1,718)	46 (26.8)	4,284 (1,859)	97 (52.2)	0.51 (0.36-0.72)	4,350 (1747)	47 (26.9)	4,350 (1801)	87 (48.3)	0.56 (0.39-0.79)	37,854 (20,714)	745 (36.0)	37,854 (21,209)	1,031 (48.6)	0.74 (0.67, 0.81)
	Pooled	<b>16,443</b> <b>(7,447)</b>	78 (10.5)	<b>16,443</b> <b>(7,120)</b>	158 (22.2)	0.51 (0.39-0.68)	<b>17,551</b> <b>(7,950)</b>	82 (10.3)	<b>17,551</b> <b>(7,459)</b>	146 (19.6)	0.56 (0.43-0.73)	<b>112,264</b> <b>(65,064)</b>	1,055 (16.2)	<b>112,264</b> <b>(59,575)</b>	1,486 (24.9)	0.70 (0.65-0.75)

HHF: hospitalization for heart failure; PS: propensity-score; DPP-4i: dipeptidyl peptidase-4 inhibitors; SGLT2i: sodium-glucose co-transporter-2 inhibitors; IR: incidence rate; PY: person-years; HR: hazard ratio; CI: confidence intervals.

\* Discharge diagnosis of HF in the primary position

† Discharge diagnosis of HF in any position

**Supplemental Table 4. 1:1 high-dimensional-PS-matched initiators of empagliflozin vs. sitagliptin.**

	<b>Empagliflozin</b>	<b>Sitagliptin</b>	
<b>Sensitivity Analyses</b>	<b>N events (IR/1000 PY)</b>	<b>N events (IR/1000 PY)</b>	<b>HR (95% CI)</b>
<b>1:1 high-dimensional-PS-matched patients</b>	<b>16,539</b>	<b>16,539</b>	
HHF-Specific*	16 (2.1)	40 (5.6)	0.54 (0.29-0.98)
HHF-Broad†	81 (10.8)	148 (20.9)	0.54 (0.41-0.71)

HHF: hospitalization for heart failure; PS: propensity-score; IR: incidence rate; PY: person-years; HR: hazard ratio; CI: confidence intervals.

\* Discharge diagnosis of HF in the primary position

† Discharge diagnosis of HF in any position

**Supplemental Table 5. Incidence rates and hazard ratios for hospitalization for heart failure (broad definition) in 1:1 PS-matched initiators of empagliflozin vs. sitagliptin stratified by duration of follow-up.**

	Empagliflozin	Sitagliptin	
Stratified analysis	N events (IR/1000 PY)	N events (IR/1000 PY)	HR (95% CI)
<b>Lower than median follow-up*</b>			
Number of patients	16,443	16,443	
HHF-Broad <sup>†</sup>	28 (4.7)	58 (10.5)	0.51 (0.32-0.81)
<b>Greater than or equal to median follow-up<sup>‡</sup></b>			
Number of patients	8,720	8,720	
HHF-Broad <sup>†</sup>	50 (34.2)	100 (63.0)	0.54 (0.38-0.76)

HHF: hospitalization for heart failure; PS: propensity-score; IR: incidence rate; PY: person-years; HR: hazard ratio; CI: confidence intervals.

\* Patients were censored on the day prior to the median follow-up (=112 days)

<sup>†</sup> Discharge diagnosis of HF in any position

<sup>‡</sup> Patients' follow-up started on the day of median follow-up and continued in an "as-treated" approach until the first occurrence of treatment discontinuation or switch to a drug in the comparator class, the occurrence of an outcome, a nursing home admission, death, plan disenrollment, or September 30, 2016. This analysis was restricted to the patients who had not been censored prior to the median follow-up

**Supplemental Table 6. Incidence rates and hazard ratio for the occurrence of flu vaccination during follow-up in 1:1 PS-matched initiators of empagliflozin vs. sitagliptin.**

	<b>Empagliflozin</b> (n=16,443)	<b>Sitagliptin</b> (16,443)	
	<b>N events</b> <b>(IR/1000 PY)</b>	<b>N events</b> <b>(IR/1000 PY)</b>	<b>HR (95% CI)</b>
<b>Control outcome with expected null finding - flu vaccination</b>	1,927 (286.1)	1,939 (303.1)	0.96 (0.90-1.02)

PS: propensity-score; IR: incidence rate; PY: person-years; HR: hazard ratio; CI: confidence intervals.