

Replication of Canagliflozin and Cardiovascular and Renal Events in
Type 2 Diabetes (CANVAS Trial)

NCT03936010

May 27, 2021

1. RCT Details

This section provides a high-level overview of the RCT that the described real-world evidence study is trying to replicate as closely as possible given the remaining limitations inherent in the healthcare databases.

1.1 Title

Canagliflozin and Cardiovascular and Renal Events in Type 2 Diabetes ([CANVAS](#) trial)

1.2 Intended aim(s)

To compare canagliflozin to placebo on cardiovascular (CV) events including CV death, heart attack, and stroke in patients with type 2 diabetes mellitus (T2DM), whose diabetes is not well controlled at the beginning of the study and who have a history of CV events or have a high risk for CV events.

1.3 Primary endpoint for replication and RCT finding

Major Adverse Cardiovascular Events, Including CV Death, Nonfatal Myocardial Infarction (MI), and Nonfatal Stroke

1.4 Required power for primary endpoint and noninferiority margin (if applicable)

With 688 cardiovascular safety events recorded across the trials, there would be at least 90% power, at an alpha level of 0.05, to exclude an upper margin of the 95% confidence interval for the hazard ratio of 1.3.

1.5 Primary trial estimate targeted for replication

HR = 0.86 (95% CI 0.75–0.97) comparing canagliflozin to placebo (Neal et al., 2017)

2. Person responsible for implementation of replication in Aetion

Ajinkya Pawar, Ph.D. implemented the study design in the Aetion Evidence Platform. S/he is not responsible for the validity of the design and analytic choices. All implementation steps are recorded and the implementation history is archived in the platform.

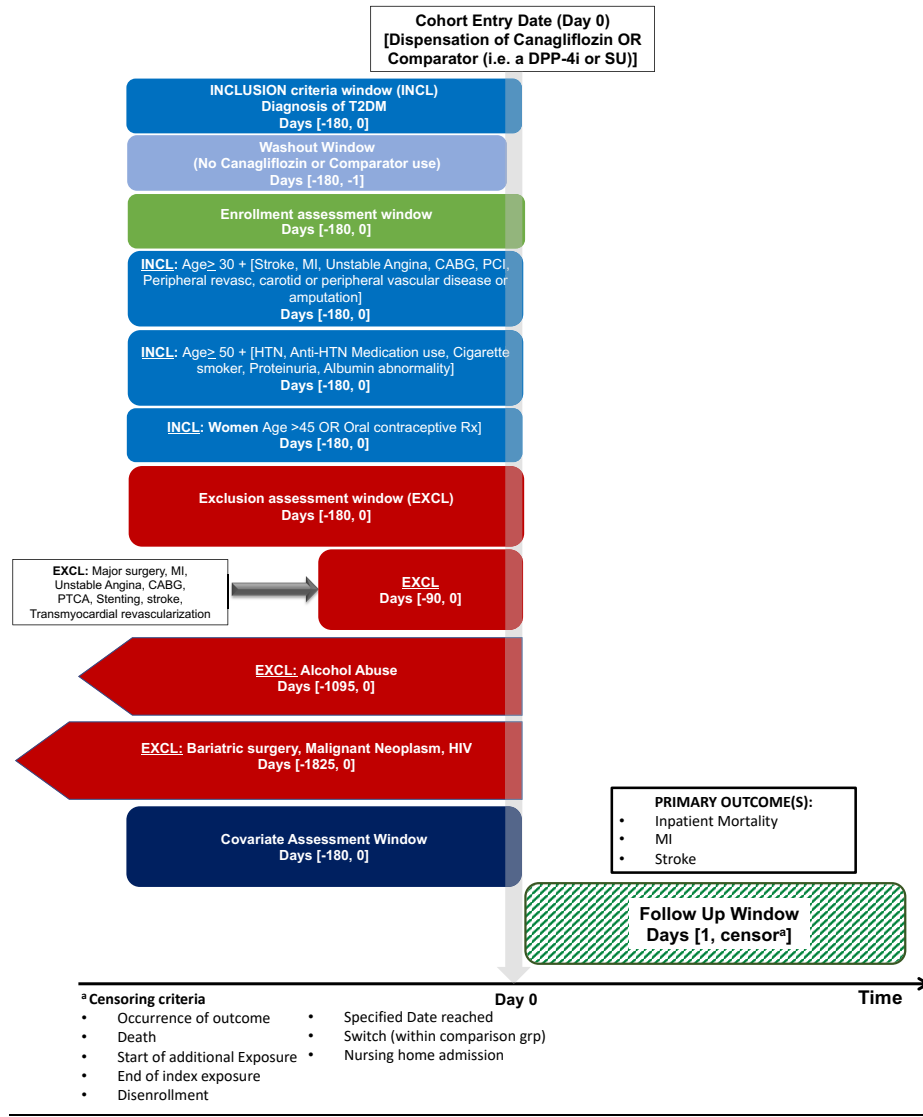
3. Data Source(s)

United/Optum, MarketScan, Medicare

4. Study Design Diagram

The study design diagram visualizes key aspects of the longitudinal study design for expedited review.

Design Diagram – CANVAS TRIAL REPLICATION



5. Cohort Identification

5.1 Cohort Summary

This study will involve a new user, parallel group, cohort study design comparing canagliflozin to the DPP-4 inhibitor (DPP4i) antidiabetic class. DPP4i serve as a proxy for placebo, since this class of antidiabetic drugs is not known to have an impact on the outcome of interest. The comparison against DPP4 inhibitors is the **primary comparison**. Initiators of 2nd generation sulfonylureas are used as a secondary comparator group. The patients will be required to have continuous enrollment during the baseline period of 180 days before initiation of canagliflozin or a comparator drug (cohort entry date). Follow-up for the outcome (3P-MACE), begins the day after drug initiation. As in the trial, patients are allowed to take other antidiabetic medications during the study.

5.2 Important steps for cohort formation

5.2.1 Eligible cohort entry dates

Market availability of canagliflozin in the U.S. started on March 29, 2013.

- For Marketscan and Medicare: April 1, 2013-Dec 31, 2017 (end of data availability).
- For Optum: April 1, 2013-March 31, 2019 (end of data availability).

5.2.2 Specify inclusion/exclusion criteria for cohort entry and define the index date

Inclusion and exclusion criteria were adapted from the trial as closely as possible. Definitions for all inclusion/exclusion are provided in **Appendix A** and are summarized in the flowcharts below.

5.3 Flowchart of the study cohort assembly

For canagliflozin vs. DPP4i

	Optum		Marketscan		Medicare*	
	Less Excluded Patients	Remaining Patients	Less Excluded Patients	Remaining Patients	Less Excluded Patients	Remaining Patients
All patients		74,864,884		191,990,035		23,466,175

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Patients who used exposure or a reference between April 1, 2013 to Dec 2017 (for MarketScan/Medicare)/March 2019 (for Optum)	-74,192,962	671,922	-191,172,811	817,224	-21,718,863	1,747,312
Patients who have continuous 6 months registration in the database	-89,308	582,614	-69,496	747,728	-466,595	1,280,717
Patients without prior use of reference	-339,732	242,882	-464,089	283,639	-810,370	470,347
Patients without prior use of exposure	-75,001	167,881	-89,428	194,211	-71,119	399,228
Excluded because patient qualified in >1 exposure category	-236	167,645	-312	193,899	-301	398,927
Excluded based on Age	-7	167,638	0	193,899	0	398,927
Excluded based on Gender	-8	167,630	0	193,899	0	398,927
Excluded based on Inclusion 1- DM Type 2 with ICD-10	-5,385	162,245	-9,472	184,427	-4,090	394,837
Excluded based on Inclusion 2- History or high risk of cardiovascular disease (with 180 day lookback)	-25,130	137,115	-39,753	144,674	-20,833	374,004
Excluded based on Inclusion 3- Include all males OR Female postmenopausal- >45 years of age OR use of contraceptives	-7	137,108	-9	144,665	0	374,004
Excluded based on Exclusion 1- DM Type I + Secondary DM + Diabetic ketoacidosis with ICD10 CODES	-4,572	132,536	-3,939	140,726	-16,980	357,024
Excluded based on Exclusion 4- History of one or more severe hypoglycemic episode- Severe hypoglycemia (Inpatient, primary)	-109	132,427	-47	140,679	-472	356,552
Excluded based on Exclusion 5- Glucose-galactose malabsorption/Primary Renal glucosuria	-37	132,390	-30	140,649	-173	356,379
Excluded based on Exclusion #7- Renal disease that requires treatment with immunosuppressive therapy	-1,512	130,878	-662	139,987	-6,367	350,012
Excluded based on Exclusion 8- MI, unstable angina, revascularization procedure, or cerebrovascular accident within 3 months	-2,345	128,533	-1,604	138,383	-8,548	341,464
Excluded based on Exclusion 9- Cardiac conduction disorder(inpatient)/Other cardiac dysrhythmia (inpatient)	-167	128,366	-71	138,312	-517	340,947
Excluded based on Exclusion 10- Liver disease	-2,303	126,063	-1,695	136,617	-6,089	334,858
Excluded based on Exclusion 11- Any history of or planned bariatric surgery (prior 5 years)	-22	126,041	-95	136,522	-12	334,846
Excluded based on Exclusion 14- History of Malignant Neoplasm (prior 5 years)	-4,554	121,487	-3,985	132,537	-19,311	315,535
Excluded based on Exclusion 15- HIV/AIDS (dx and meds) -prior 5 years	-64	121,423	-56	132,481	-127	315,408
Excluded based on Exclusion 16- Hematological disorder	-1,540	119,883	-1,633	130,848	-7,624	307,784
Excluded based on Exclusion 17- CCI (180 days) >=10	-177	119,706	-50	130,798	-696	307,088

Effectiveness research with Real World Data to support FDA's regulatory decision making

Excluded based on Exclusion 18 - Major Surgery (90 days prior)	-191	119,515	-212	130,586	-674	306,414
Excluded based on Exclusion 20- Use of SGLT2i (prior 6 months)	-833	118,682	-892	129,694	-817	305,597
Excluded based on Exclusion 22- use of a corticosteroid medication or immunosuppressive agent	-3,235	115,447	-3,085	126,609	-8,985	296,612
Excluded based on Exclusion 23- Use of cana in prior 3 months (although this is already applied as part of cohort creation)	0	115,447	0	126,609	0	296,612
Excluded based on Exclusion 24- Alcohol or Drug abuse (prior 3 years) and Exclusion 25- Pregnancy	-972	114,475	-532	126,077	-1,766	294,846
Final cohort		114,475		126,077		294,846

* Medicare database includes only patients with at least one diagnosis for diabetes, heart failure, or cerebrovascular disease.

**Exclusion 24 and 25 collapsed to adhere to CMS cell suppression guidelines.

For canagliflozin vs. 2nd generation SUs

	Optum		Marketscan		Medicare*	
	Less Excluded Patients	Remaining Patients	Less Excluded Patients	Remaining Patients	Less Excluded Patients	Remaining Patients
All patients		74,864,884		191,990,035		23,466,175
Patients who used exposure or a reference between April 1, 2013 to Dec 2017 (for Marketscan/Medicare)/March 2019 (for Optum)	-73,662,096	1,202,788	-190,768,942	1,221,093	-20,351,733	3,114,442
Patients who have continuous 6 months registration in the database	-165,247	1,037,541	-115,162	1,105,931	-861,454	2,252,988
Patients without prior use of reference	-710,706	326,835	-759,153	346,778	-1,627,827	625,161
Patients without prior use of exposure	-70,933	255,902	-88,833	257,945	-68,783	556,378
Excluded because patient qualified in >1 exposure category	-168	255,734	-149	257,796	-118	556,260
Excluded based on Age	-10	255,724	0	257,796	0	556,260
Excluded based on Gender	-17	255,707	0	257,796	0	556,260
Excluded based on Inclusion 1- DM Type 2 with ICD-10	-14,479	241,228	-23,583	234,213	-8,608	547,652
Excluded based on Inclusion 2- History or high risk of cardiovascular disease (with 180 day lookback)	-38,807	202,421	-54,172	180,041	-30,020	517,632
Excluded based on Inclusion 3- Include all males OR Female postmenopausal- >45 years of age OR use of contraceptives	-21	202,400	-36	180,005	0	517,632

Excluded based on Exclusion 1- DM Type I + Secondary DM + Diabetic ketoacidosis with ICD10 CODES	-5,426	196,974	-4,290	175,715	-19,804	497,828
Excluded based on Exclusion 4- History of one or more severe hypoglycemic episode- Severe hypoglycemia (Inpatient, primary)	-76	196,898	-37	175,678	-332	497,496
Excluded based on Exclusion 5- Glucose-galactose malabsorption/Primary Renal glucosuria	-53	196,845	-55	175,623	-221	497,275
Excluded based on Exclusion #7- Renal disease that requires treatment with immunosuppressive therapy	-2,276	194,569	-976	174,647	-9,763	487,512
Excluded based on Exclusion 8- MI, unstable angina, revascularization procedure, or cerebrovascular accident within 3 months	-3,178	191,391	-2,244	172,403	-11,210	476,302
Excluded based on Exclusion 9- Cardiac conduction disorder(inpatient)/Other cardiac dysrhythmia (inpatient)	-240	191,151	-121	172,282	-837	475,465
Excluded based on Exclusion 10- Liver disease	-3,273	187,878	-2,251	170,031	-8,410	467,055
Excluded based on Exclusion 11- Any history of or planned bariatric surgery (prior 5 years)	-27	187,851	-109	169,922	-16	467,039
Excluded based on Exclusion 14- History of Malignant Neoplasm (prior 5 years)	-6,172	181,679	-5,306	164,616	-25,472	441,567
Excluded based on Exclusion 15- HIV/AIDS (dx and meds) -prior 5 years	-112	181,567	-72	164,544	-198	441,369
Excluded based on Exclusion 16- Hematological disorder	-1,925	179,642	-1,989	162,555	-9,438	431,931
Excluded based on Exclusion 17- CCI (180 days) >=10	-287	179,355	-50	162,505	-993	430,938
Excluded based on Exclusion 18 - Major Surgery (90 days prior)	-317	179,038	-291	162,214	-856	430,082
Excluded based on Exclusion 20- Use of SGLT2i (prior 6 months)	-904	178,134	-984	161,230	-874	429,208
Excluded based on Exclusion 22- use of a corticosteroid medication or immunosuppressive agent	-4,334	173,800	-3,909	157,321	-10,920	418,288
Excluded based on Exclusion 23- Use of cana in prior 3 months (although this is already applied as part of cohort creation)	0	173,800	0	157,321	0	418,288
Excluded based on Exclusion 24- Alcohol or Drug abuse (prior 3 years) and Exclusion 25- Pregnancy	-1566	172,234	-777	156,544	-2,592	415,696
Final cohort		172,234		156,544		415,696

* Medicare database includes only patients with at least one diagnosis for diabetes, heart failure, or cerebrovascular disease.

** Exclusion 24 and 25 collapsed to adhere to CMS cell suppression guidelines.

6. Variables

6.1 Exposure-related variables:

Study drug:

The study exposure of interest is initiation of canagliflozin. Initiation will be defined by no use of any SGLT-2 inhibitor or a comparator in the prior 6 months before treatment initiation (washout period).

Comparator agents:

- Initiators of canagliflozin will be compared to initiators of-
 - DPP4i (**primary**)
 - 2nd generation sulfonylureas

Because canagliflozin and comparators are frequently used as second or third line treatments of T2DM, we expect it to be unlikely that canagliflozin and comparators are initiated in patients with substantially different baseline risk for proposed outcomes.

6.2 Preliminary Covariates:

- Age
- Sex
- Combined Comorbidity Index (CCI), measured over the default baseline covariate assessment period, defined as 180 days prior to and including index date

Covariates listed above represent only a small subset of covariates that will ultimately be controlled for in the design and analysis. We use the covariates above only for initial feasibility analyses to judge whether there is likely to be sufficient overlap between treatment groups to proceed with the study. Remaining covariates are defined only after the study has passed the initial feasibility analysis and the initial power assessment and are listed in Table 1 (**Appendix B**). These covariates are based on those used by Patorno et al. (2019).

6.3 Outcome variables and study follow-up:

6.3.1 Outcome variables

Effectiveness outcomes of interest (definitions provided in **Appendix A**):

- **Primary outcome:** 3-point major adverse cardiovascular events (MACE), i.e., non-fatal myocardial infarction, non-fatal stroke, or CV mortality
- Secondary outcomes: Individual components:
 - Hospital admission for MI (for purposes of this individual component, fatal MI is included)
 - Hospital admission for stroke (for purposes of this individual component, fatal stroke is included)
 - All-cause mortality/CV mortality:
 - All-cause inpatient mortality identified using discharge status codes will be used as a proxy for “CV mortality” in commercial databases
 - Information on CV mortality through data linkage with the National Death Index (NDI) will only become available at a later date for Medicare and will be used in secondary analyses.

Control outcomes of interest (control outcomes only serve to assess aspects of study validity but are not further interpreted):

1. Diabetes Ketoacidosis (we expect to see a positive association; Neal et al., 2017)
2. Heart failure (we expect to see a protective effect; Neal et al., 2017)

Control outcome definitions

Outcome	Definition	Comments
Control Outcomes		
Diabetic Ketoacidosis	Inpatient ICD-9 diagnosis: 250.1x	<u>Note-</u> The corresponding ICD-10 codes will also be used
Heart Failure	Inpatient ICD-9 diagnosis (primary diagnosis): 428.x, 398.91, 402.01, 402.11, 402.91, 404.01, 404.11, 404.91, 404.03, 404.13, 404.93	<u>Note-</u> The corresponding ICD-10 codes will also be used

6.3.2 Study follow-up

Both as-treated (AT) and intention-to-treat (ITT) analyses will be conducted with treatment defined as the index drug on the day of cohort entry. Because adherence in the real world databases is expected to be much worse than in the trial, the AT analysis is the **primary** analysis, as it targets the relative hazard of outcomes on treatment.

For the AT analyses, the follow-up will start the day after initiation of canagliflozin and comparator and will continue until the earliest date of the following events:

- The first occurrence of the outcome of interest, unless otherwise specified for selected outcomes,

- The date of end of continuous registration in the database,
- End of the study period,
- Measured death event occurs,
- Nursing home admission
 - Nursing home admissions are considered a censoring event because the data sources utilized typically provide little to no data on a patient, particularly on drug utilization, after admission. We will utilize this as an exclusion reason for cohorts for the same reason.
- The date of drug discontinuation, defined as the date of the last continuous treatment episode of the index drug (canagliflozin and comparator) plus a defined grace period (i.e., 30 days after the end of the last prescription's days' supply in main analyses).
- The date of augmentation or switching from an exposure to a comparator or any other agent in the comparator class and vice versa (e.g. switching from saxagliptin to linagliptin would be a censoring event);
 - A dosage change on the index treatment does not fulfill this criterion
 - An added treatment that is not part of the exposure or comparator group does not fulfill this criterion (e.g. if a canagliflozin user adds insulin, he or she does not get censored at the time of insulin augmentation)

For the ITT analyses, the censoring based on the augmentation/switching and treatment discontinuation will be replaced with a maximum allowed follow-up time of 365 days.

7. Initial Feasibility Analysis

Action report name:

For canagliflozin vs. DPP4i

Optum- <https://bwh-dope.aetion.com/#/projects/details/660/results/26056/result/0>

Marketscan- <https://bwh-dope.aetion.com/#/projects/details/661/results/26057/result/0>

Medicare- <https://bwh-dope.aetion.com/#/projects/details/662/results/26055/result/0>

For canagliflozin vs. 2nd generation SUs

Optum- <https://bwh-dope.aetion.com/#/projects/details/660/results/26064/result/0>

Marketscan- <https://bwh-dope.aetion.com/#/projects/details/661/results/26065/result/0>

Medicare- <https://bwh-dope.aetion.com/#/projects/details/662/results/26066/result/0>

Date conducted: 09/30/2018

Complete Aetion feasibility analysis using age, sex, and CCI as the only covariates and the primary endpoint (Section 6.3.1) as the outcome. No measures of association will be computed nor will incidence rates stratified by treatment group.

- Report patient characteristics by treatment group
- Report summary parameters of the overall study population
- Report median follow-up time by treatment group
- Report reasons for censoring in the overall study population

8. Initial Power Assessment

Aetion report name:

- For canagliflozin vs. DPP4i
 - Optum- <https://bwh-dope.aetion.com/#/projects/details/660/results/26064/result/0>
 - Marketscan- <https://bwh-dope.aetion.com/#/projects/details/661/results/26065/result/0>
 - Medicare- <https://bwh-dope.aetion.com/#/projects/details/662/results/26066/result/0>
- For canagliflozin vs. 2nd generation Sus
 - Optum- <https://bwh-dope.aetion.com/#/projects/details/660/results/26067/result/0>
 - Marketscan- <https://bwh-dope.aetion.com/#/projects/details/661/results/26068/result/0>
 - Medicare- <https://bwh-dope.aetion.com/#/projects/details/662/results/26069/result/0>

Date conducted: 09/30/2018

In order to complete the initial power analysis, the dummy outcome of a 90-day gap in database enrollment will be used. This outcome is used to ensure that no information on the comparative risks of the outcomes of interest are available at this stage. Complete a 1:1 PS-matched comparative analysis using this outcome. PS should include only 3 covariates: age, sex, and combined comorbidity index. Power calculations are based on the formulas from Chow et al. (2008).

- Stop analyses until feasibility and power are reviewed by primary investigators and FDA. Reviewers evaluate the results of the analyses described above in Sections 7 and 8, including numbers of patients, patient characteristics, follow-up time, and reasons for censoring by treatment group, as well as overall rates of outcomes and study power. These parameters are re-evaluated and reported in the subsequent sections, after incorporating feedback and refining the protocol.

Reviewed by PI:	Jessica M. Franklin	Date reviewed:	10/26/18
Reviewed by FDA:	Ken Quinto	Date reviewed:	12/11/18
Reasons for stopping analysis (if required):			

9. Balance Assessment after PS matching

Action report name:

For canagliflozin vs. DPP4i

- Optum- <https://bwh-dope.aetion.com/projects/details/660/results/44837/result/0>
- Marketscan- <https://bwh-dope.aetion.com/projects/details/661/results/44838/result/0>
- Medicare- <https://bwh-dope.aetion.com/projects/details/662/results/44839/result/0>

For canagliflozin vs. 2nd generation SUs

- Optum- <https://bwh-dope.aetion.com/projects/details/660/results/44834/result/0>
- Marketscan- <https://bwh-dope.aetion.com/projects/details/661/results/44835/result/0>
- Medicare- <https://bwh-dope.aetion.com/projects/details/662/results/44836/result/0>

Date conducted: 11/18/2019

After review of initial feasibility and power analyses, complete creation of the remaining covariates (see Table 1 below for list of covariates). Again, using the dummy outcome of a 90-day gap in database enrollment, complete a 1:1 PS-matched analysis. The PS should include the complete list of covariates (excluding laboratory values, which are missing in some patients).

- Provide plot of PS distributions stratified by treatment group.

Note- Please refer to **Appendix B**.

- Report covariate balance after matching.

Note- For Table 1, please refer to **Appendix B**.

- Report reasons for censoring by treatment group.

- For canagliflozin vs. DPP4i

	Overall	Referent	Exposure
Dummy Outcome	0 (0.00%)	0 (0.00%)	0 (0.00%)
Death	589 (0.39%)	374 (0.49%)	215 (0.28%)
Start of an additional exposure	6,913 (4.54%)	2,413 (3.17%)	4,500 (5.91%)
End of index exposure	98,215 (64.53%)	47,931 (62.98%)	50,284 (66.08%)
Specified date reached	22,353 (14.69%)	12,162 (15.98%)	10,191 (13.39%)
End of patient enrollment	19,170 (12.60%)	9,407 (12.36%)	9,763 (12.83%)
Switch to other DPP4i (for censoring) + nursing home admission	4,962 (3.26%)	3,814 (5.01%)	1,148 (1.51%)

- For canagliflozin vs. 2nd generation SUs

	Overall	Referent	Exposure
Dummy Outcome	0 (0.00%)	0 (0.00%)	0 (0.00%)
Death	548 (0.40%)	364 (0.53%)	184 (0.27%)
Start of an additional exposure	6,001 (4.36%)	1,842 (2.68%)	4,159 (6.04%)
End of index exposure	85,900 (62.38%)	41,024 (59.58%)	44,876 (65.18%)
Specified date reached	22,281 (16.18%)	12,957 (18.82%)	9,324 (13.54%)
End of patient enrollment	18,853 (13.69%)	9,660 (14.03%)	9,193 (13.35%)
Switch to other SUs (for censoring) + nursing home admission	4,117 (2.99%)	3,003 (4.36%)	1,114 (1.62%)

- Report follow-up time by treatment group.

- For canagliflozin vs. DPP4i

Median Follow-Up Time (Days) [IQR]			
Patient Group	Optum	Marketscan	Medicare
Overall Patient Population	127 [58-306]	149 [72-341]	147 [81-318]

Referent	121 [58-297]	153 [87-327]	153 [87-327]
Exposure	134 [58-318]	142 [58-310]	142 [58-310]

- For canagliflozin vs. 2nd generation SUs

Median Follow-Up Time (Days) [IQR]			
Patient Group	Optum	Marketscan	Medicare
Overall Patient Population	141 [63-336]	159 [83-358]	172 [90-373]
Referent	140 [75-330]	200 [118-414]	200 [118-414]
Exposure	141 [58-341]	144 [62-327]	144 [62-327]

- Report risk per 1,000 patients

Action report name:

- For canagliflozin vs. DPP4i
 Optum- <https://bwh-dope.aetion.com/#/projects/details/660/results/34590/result/0>
 Marketscan- <https://bwh-dope.aetion.com/#/projects/details/661/results/34591/result/0>
 Medicare- <https://bwh-dope.aetion.com/#/projects/details/662/results/34592/result/0>
- For canagliflozin vs. 2nd generation SUs
 Optum- <https://bwh-dope.aetion.com/#/projects/details/660/results/34596/result/0>
 Marketscan- <https://bwh-dope.aetion.com/#/projects/details/661/results/34597/result/0>
 Medicare- <https://bwh-dope.aetion.com/#/projects/details/662/results/34598/result/0>

Date conducted: 04/25/2019

For canagliflozin vs. DPP4i

	Optum	Marketscan	Medicare
Risk per 1,000 patients	7.58	7.81	22.56

For canagliflozin vs. 2nd generation SUs

	Optum	Marketscan	Medicare
Risk per 1,000 patients	9.71	9.39	27.67

10. Final Power Assessment

Date conducted: 12/01/2019

- Re-calculate power in the appropriate excel table, using the revised number of matched patients from the PS-match in Section 9. All other parameters in the table should be the same as in Section 8. If the study is to be implemented in more than one database, copy and paste excel sheet to report power for each database separately and for the pooled analysis that uses data from all databases together. Power calculations are based on the formulas from Chow et al. (2008).

- For canagliflozin vs. DPP4i

- Pooled

Superiority Analysis		Non-inferiority Analysis	
Number of patients matched		Number of patients matched	
Reference	76,101	Reference	76,101
Exposed	76,101	Exposed	76,101
Risk per 1,000 patients	12.65	Risk per 1,000 patients	12.65
Desired HR from RCT	0.86	Assumed HR from RCT	1
Alpha (2-sided)	0.05	Alpha (2-sided)	0.05
		Non-inferiority margin	1.3
Number of events expected	1925.3553	Number of events expected	1925.3553
Power	0.911332398	Power	0.999926523

- Optum

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Superiority Analysis		Non-inferiority Analysis	
Number of patients matched		Number of patients matched	
Reference	19,532	Reference	19,532
Exposed	19,532	Exposed	19,532
Risk per 1,000 patients	7.58	Risk per 1,000 patients	7.58
Desired HR from RCT	0.86	Assumed HR from RCT	1
Alpha (2-sided)	0.05	Alpha (2-sided)	0.05
		Non-inferiority margin	1.3
Number of events expected	296.10512	Number of events expected	296.10512
Power	0.254449294	Power	0.616911596

▪ Marketscan

Superiority Analysis		Non-inferiority Analysis	
Number of patients matched		Number of patients matched	
Reference	23,168	Reference	23,168
Exposed	23,168	Exposed	23,168
Risk per 1,000 patients	7.58	Risk per 1,000 patients	7.58
Desired HR from RCT	0.86	Assumed HR from RCT	1
Alpha (2-sided)	0.05	Alpha (2-sided)	0.05
		Non-inferiority margin	1.3
Number of events expected	351.22688	Number of events expected	351.22688
Power	0.292672624	Power	0.690943556

▪ Medicare

Superiority Analysis		Non-inferiority Analysis	
Number of patients matched		Number of patients matched	
Reference	33,401	Reference	33,401
Exposed	33,401	Exposed	33,401
Risk per 1,000 patients	22.56	Risk per 1,000 patients	22.56
Desired HR from RCT	0.86	Assumed HR from RCT	1
Alpha (2-sided)	0.05	Alpha (2-sided)	0.05
		Non-inferiority margin	1.3
Number of events expected	1507.05312	Number of events expected	1507.05312
Power	0.833370249	Power	0.999133759

- For canagliflozin vs. 2nd generation SUs

- Pooled

Superiority Analysis		Non-inferiority Analysis	
Number of patients matched		Number of patients matched	
Reference	68,850	Reference	68,850
Exposed	68,850	Exposed	68,850
Risk per 1,000 patients	15.59	Risk per 1,000 patients	15.59
Desired HR from RCT	0.86	Assumed HR from RCT	1
Alpha (2-sided)	0.05	Alpha (2-sided)	0.05
		Non-inferiority margin	1.3
Number of events expected	2146.743	Number of events expected	2146.743
Power	0.937493971	Power	0.999980899

- Optum

Effectiveness research with Real World Data to support FDA's regulatory decision making

Superiority Analysis		Non-inferiority Analysis	
Number of patients matched		Number of patients matched	
Reference	16,740	Reference	16,740
Exposed	16,740	Exposed	16,740
Risk per 1,000 patients	9.71	Risk per 1,000 patients	9.71
Desired HR from RCT	0.86	Assumed HR from RCT	1
Alpha (2-sided)	0.05	Alpha (2-sided)	0.05
		Non-inferiority margin	1.3
Number of events expected	325.0908	Number of events expected	325.0908
Power	0.274612159	Power	0.657366306

▪ Marketscan

Superiority Analysis		Non-inferiority Analysis	
Number of patients matched		Number of patients matched	
Reference	23,265	Reference	23,265
Exposed	23,265	Exposed	23,265
Risk per 1,000 patients	9.39	Risk per 1,000 patients	9.39
Desired HR from RCT	0.86	Assumed HR from RCT	1
Alpha (2-sided)	0.05	Alpha (2-sided)	0.05
		Non-inferiority margin	1.3
Number of events expected	436.9167	Number of events expected	436.9167
Power	0.350813593	Power	0.782915462

▪ Medicare

Superiority Analysis		Non-inferiority Analysis	
Number of patients matched		Number of patients matched	
Reference	28,845	Reference	28,845
Exposed	28,845	Exposed	28,845
Risk per 1,000 patients	27.67	Risk per 1,000 patients	9.39
Desired HR from RCT	0.86	Assumed HR from RCT	1
Alpha (2-sided)	0.05	Alpha (2-sided)	0.05
		Non-inferiority margin	1.3
Number of events expected	1596.2823	Number of events expected	541.7091
Power	0.853826925	Power	0.86285876

- Stop analyses until balance and final power assessment are reviewed by primary investigators, FDA, and assigned members of advisory board. Reviewers evaluate the results of the analyses described above in Sections 9 and 10, including numbers of patients, balance in patient characteristics, follow-up time, and reasons for censoring by treatment group, as well as overall rates of outcomes and study power.

Reviewed by PI:	Jessica Franklin	Date reviewed:	12/9/19
Reviewed by FDA:	Ken Quinto	Date reviewed:	12/20/19
Reasons for stopping analysis (if required):			

11. Study Confidence and Concerns

Deadline for voting on study confidence and listing concerns: 12/20/19

- If final feasibility and power analyses are reviewed and approved, proceed to the remaining protocol steps.
- All study team and advisory board members that review this protocol should at this stage provide their level of confidence for the success of the RWD study in the [Google Form](#). This form also provides space for reviewers to list any concerns that they feel may

contribute to a failure to replicate the findings of the RCT, including differences in study populations, poor measurement of study variables, or residual confounding. All responses will be kept confidential and individual-level results will only be shared with the individual respondent.

12. Register study protocol on [clinicalTrials.gov](https://clinicaltrials.gov)

Date conducted:

- Register the study on [clinicalTrials.gov](https://clinicaltrials.gov) and upload this document.

13. Comparative Analyses

Action report name:

Date conducted:

13.1 For **primary analysis**:

- In the PS-matched cohort of canagliflozin and DPP4i initiators from Section 9, calculate the HR for each outcome for canagliflozin versus referent patients using a Cox proportional hazards model.

13.2 For secondary analyses:

- In the PS-matched cohort of canagliflozin and 2nd generation SU initiators from Section 9, calculate the HR for canagliflozin versus referent patients using a Cox proportional hazards model.
- In both pre-matched cohorts, perform asymmetrical trimming to remove patients with PS values below the 2.5th percentile of treated patients and above the 97.5th percentile of untreated patients. In the trimmed cohort, calculate the HR for canagliflozin versus referent patients using a Cox proportional hazards model, adjusting for deciles of the PS.

14. Requested Results

14.1 Results from primary and secondary analyses:

Separately for each endpoint and each comparator group:

Analysis	No. exposed events	No. referent events	Exposed rate	Referent rate	HR (95% CI)
Crude					
Primary analysis					
Analysis 2					
...					

HR, Hazard Ratio; CI, Confidence Interval.

15. References

American Diabetes Association. 8. Pharmacologic Approaches to Glycemic Treatment: Standards of Medical Care in Diabetes-2018. Diabetes Care. 2018;41(Suppl 1):S73-S85. doi:10.2337/dc18-S008.

Chow S, Shao J, Wang H. 2008. *Sample Size Calculations in Clinical Research*. 2nd Ed. Chapman & Hall/CRC Biostatistics Series. **page 177**

Neal B, Perkovic V, Mahaffey KW, De Zeeuw D, Fulcher G, Erondur N, Shaw W, Law G, Desai M, Matthews DR. Canagliflozin and cardiovascular and renal events in type 2 diabetes. New England Journal of Medicine. 2017; 377(7):644-57.

Patorno E, Pawar A, Franklin JM, et al. Empagliflozin and the Risk of Heart Failure Hospitalization in Routine Clinical Care: A First Analysis from the Empagliflozin Comparative Effectiveness and Safety (EMPRISE) Study. Circulation. 2019; in press.
(<https://www.ahajournals.org/doi/pdf/10.1161/CIRCULATIONAHA.118.039177>)

Appendix A

#	CANVAS trial definitions	Implementation in routine care	References/Rationale	Color coding
	Trial details- Secondary indication, 4a- unintended superiority with label change		Please see the following Google Drive for further details or any missing information: https://drive.google.com/open?id=1WD618wryw7EaXdtTcuK-VCCnb6b-gV	Criteria
	EXPOSURE vs. COMPARISON		ICD-10 codes are not listed in this document because of excel cell size limitations and excessive number of ICD-10 codes. Full ICD-10 code lists will be available in the above Google Drive Folder (link above). ICD-9 to ICD-10 code conversions were completed using a SAS macro that implements forward/ backward mapping based on the CMS ICD-9 to ICD-10 mapping: https://www.nber.org/data/icd9-icd-10-cm-and-pcs-crosswalk-general-equivalence-mapping.html	Adequate mapping in claims
	Canagliflozin vs. placebo	Canagliflozin vs. DPP4 inhibitors (primary comparison) or vs. 2nd generation sulfonylureas (secondary)	Patorno, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gliiflozin antidiabetic drugs: population based cohort study." BMJ 2018;360:k119 http://dx.doi.org/10.1136/bmj.k119	Intermediate mapping in claims
	PRIMARY OUTCOME			Poor mapping or cannot be measured in claims
	Major Adverse Cardiovascular Events, Including CV Death, Nonfatal Myocardial Infarction (MI), and Nonfatal Stroke HR = 0.86 (95% CI 0.75–0.97)	Measured 1 days after drug initiation in diagnosis position specified below and inpatient care setting: Inpatient mortality/MI/Stroke – For MI Any diagnosis position in inpatient care setting ICD-9 Dx 410.X (acute myocardial infarction) excluding 410.x2 (subsequent episode of care) For stroke Primary diagnosis position in inpatient care setting ICD-9 discharge diagnosis: 430.xx Subarachnoid hemorrhage (SAH) 431.xx Intracerebral hemorrhage (ICH) 433.x1 Occlusion and stenosis of precerebral arteries with cerebral infarction 434.xx (excluding 434.x0) Occlusion and stenosis of cerebral arteries with cerebral infarction 436.x Acute, but ill-defined cerebrovascular events Mortality- See Mortality Sheet.	For MI: →PPV 94% in Medicare claims data [Kiyota Y, Schneeweiss S, Glynn RJ, Cannuscio CC, Avorn J, Solomon DH. Accuracy of Medicare claims-based diagnosis of acute myocardial infarction: estimating positive predictive value on the basis of review of hospital records. American heart journal 2004;148:99-104.] →PPV 88.4% in commercially-insured population [Wahl PM, Rodgers K, Schneeweiss S, et al. Validation of claims-based diagnostic and procedure codes for cardiovascular and gastrointestinal serious adverse events in a commercially-insured population. Pharmacoepidemiology and Drug Safety 2010;19:596-603.] For stroke: PPV of 85% or higher for ischemic stroke PPV ranging from 80% to 98% for hemorrhagic stroke →[Andrade SE, Harold LR, Tjia J, et al. A systematic review of validated methods for identifying cerebrovascular accident or transient ischemic attack using administrative data. Pharmacoepidemiology and Drug Safety 2012;21 Suppl 1:100-28.] →[Tirschwell DL, Longstreth WT, Jr. Validating administrative data in stroke research. Stroke; a journal of cerebral circulation 2002;33:2465-70.] →[Roumie CL, Mitchell E, Gideon PS, Varas-Lorenzo C, Castellsague J, Griffin MR. Validation of ICD-9 codes with a high positive predictive value for incident strokes resulting in hospitalization using Medicaid health data. Pharmacoepidemiology and drug safety 2008;17:20-6.]	Can't be measured in claims but not important for the analysis
	INCLUSION CRITERIA			
1	Man or woman with a diagnosis of type 2 diabetes with glycated hemoglobin level ≥7.0% to ≤10.5% at screening and be either-	Patients with a diagnosis of T2DM (ICD-9 Dx code of 250.x0 or 250.x2) in the 180 days prior to drug initiation in any diagnosis position and inpatient or outpatient care setting.	Patorno, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gliiflozin antidiabetic drugs: population based cohort study." BMJ 2018;360:k119 http://dx.doi.org/10.1136/bmj.k119	
	o (1) not currently on antihyperglycemic agent (AHA) therapy or			
	o (2) on AHA monotherapy or combination therapy with any approved class of agents: e.g., sulfonylurea, metformin, peroxisome proliferator-activated receptor gamma (PPARγ) agonist, alpha-glucosidase inhibitor, glucagon-like peptide-1 (GLP-1) analogue, dipeptidyl peptidase-4 (DPP-4) inhibitor, or insulin.	Depending on the comparison group, we will require new-use (defined as no use 180 days prior to index date) of canagliflozin and a comparator drug	Patorno, Elisabetta et al. "Empagliflozin and the Risk of Heart Failure Hospitalization in Routine Clinical Care: A First Analysis from the Empagliflozin Comparative Effectiveness and Safety (EMPRISE) Study." Circulation. 2019 Apr 8. doi: 10.1161/CIRCULATIONAHA.118.039177	
2	History or high risk of cardiovascular disease defined on the basis of either:			
	- Age ≥30 years with documented symptomatic atherosclerotic cardiovascular disease:	Age ≥30 years at drug initiation		
	o including stroke;	Measured 180 days prior to drug initiation in any diagnosis position and inpatient or outpatient care setting- Any stroke: ICD-9 Dx: 430.xx, 431.xx, 433.xx, 434.xx, 436.xx	Patorno, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gliiflozin antidiabetic drugs: population based cohort study." BMJ 2018;360:k119 http://dx.doi.org/10.1136/bmj.k119	
	o or myocardial infarction (MI);	Measured 180 days prior to drug initiation in any diagnosis position and inpatient or outpatient care setting- Acute MI ICD-9 410.xx, Old MI: 412.xx	Patorno, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gliiflozin antidiabetic drugs: population based cohort study." BMJ 2018;360:k119 http://dx.doi.org/10.1136/bmj.k119	
	o or hospital admission for unstable angina;	Measured 180 days prior to drug initiation in the inpatient care setting with ICD-9 discharge diagnosis 411.xx	Patorno, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gliiflozin antidiabetic drugs: population based cohort study." BMJ 2018;360:k119 http://dx.doi.org/10.1136/bmj.k119	
			Patorno, Elisabetta et al. "Empagliflozin and the Risk of Heart Failure Hospitalization in Routine Clinical Care: A First Analysis from the Empagliflozin Comparative Effectiveness and Safety (EMPRISE) Study." Circulation. 2019 Apr 8. doi: 10.1161/CIRCULATIONAHA.118.039177	

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2a	o or coronary artery bypass graft (CABG);	<p>CABG: Measured 180 days prior to drug initiation in any diagnosis position and inpatient care setting - CPT-4: 33510–33536, 33545, 33572. OR – Measured 180 days prior to drug initiation in any diagnosis position and inpatient or outpatient care setting - ICD-9 procedure: 36.1x, 36.2x</p>	<p>Patorno, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gliiflozin antidiabetic drugs: population based cohort study." <i>BMJ</i> 2018;360:k119 http://dx.doi.org/10.1136/bmj.k119</p> <p>Patorno, Elisabetta et al. "Empagliflozin and the Risk of Heart Failure Hospitalization in Routine Clinical Care: A First Analysis from the Empagliflozin Comparative Effectiveness and Safety (EMPRISE) Study." <i>Circulation</i>. 2019 Apr 8. doi: 10.1161/CIRCULATIONAHA.118.039177</p>
	o or percutaneous coronary intervention (PCI; with or without stenting);	<p>PTCA: Measured 180 days prior to drug initiation in any procedure position and inpatient care setting - CPT-4: 92973, 92982, 92984, 92995, 92996, 92920–92921, 92924–92925, 92937, 92938, 92941, 92943, 92944 OR – Measured 180 days prior to drug initiation in any procedure position and inpatient or outpatient care setting - ICD-9 procedure: 00.66, 36.01, 36.02, 36.03, 36.05, 36.09</p> <p>Stenting: Measured 180 days prior to drug initiation in any procedure position and inpatient care setting- CPT-4: 92980, 92981, 92928–92929, 92933 - 92934 OR – Measured 180 days prior to drug initiation in any procedure position and inpatient or outpatient care setting- ICD-9 procedure: 36.06, 36.07</p>	<p>Patorno, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gliiflozin antidiabetic drugs: population based cohort study." <i>BMJ</i> 2018;360:k119 http://dx.doi.org/10.1136/bmj.k119</p> <p>Patorno, Elisabetta et al. "Empagliflozin and the Risk of Heart Failure Hospitalization in Routine Clinical Care: A First Analysis from the Empagliflozin Comparative Effectiveness and Safety (EMPRISE) Study." <i>Circulation</i>. 2019 Apr 8. doi: 10.1161/CIRCULATIONAHA.118.039177</p>
	o or peripheral revascularization (angioplasty or surgery);	<p>Measured 180 days prior to drug initiation in any diagnosis position and inpatient or outpatient care setting - ICD-9 39.25, 39.50, 39.99.</p>	<p>Patorno, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gliiflozin antidiabetic drugs: population based cohort study." <i>BMJ</i> 2018;360:k119 http://dx.doi.org/10.1136/bmj.k119</p> <p>Patorno, Elisabetta et al. "Empagliflozin and the Risk of Heart Failure Hospitalization in Routine Clinical Care: A First Analysis from the Empagliflozin Comparative Effectiveness and Safety (EMPRISE) Study." <i>Circulation</i>. 2019 Apr 8. doi: 10.1161/CIRCULATIONAHA.118.039177</p>
	o or symptomatic with documented hemodynamically-significant carotid or peripheral vascular disease;	<p>Measured 180 days prior to drug initiation in any diagnosis position and inpatient or outpatient care setting - ICD9 diagnosis: 440.20–440.24, 440.29–440.32, 440.3, 440.4, 443.9</p>	<p>Patorno, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gliiflozin antidiabetic drugs: population based cohort study." <i>BMJ</i> 2018;360:k119 http://dx.doi.org/10.1136/bmj.k119</p> <p>Patorno, Elisabetta et al. "Empagliflozin and the Risk of Heart Failure Hospitalization in Routine Clinical Care: A First Analysis from the Empagliflozin Comparative Effectiveness and Safety (EMPRISE) Study." <i>Circulation</i>. 2019 Apr 8. doi: 10.1161/CIRCULATIONAHA.118.039177</p>
	o or amputation secondary to vascular disease.	<p>Measured 180 days prior to drug initiation in any diagnosis position and inpatient or outpatient care setting - ICD-9 procedure: 84.10-84.18 ICD-9 diagnosis: V49.7x CPT: 27590, 27591, 27592, 27880, 27881, 27882, 27884, 27886, 27888, 27889, 28800, 28805, 28810, 28820, 28825</p>	<p>Patorno, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gliiflozin antidiabetic drugs: population based cohort study." <i>BMJ</i> 2018;360:k119 http://dx.doi.org/10.1136/bmj.k119</p> <p>Patorno, Elisabetta et al. "Empagliflozin and the Risk of Heart Failure Hospitalization in Routine Clinical Care: A First Analysis from the Empagliflozin Comparative Effectiveness and Safety (EMPRISE) Study." <i>Circulation</i>. 2019 Apr 8. doi: 10.1161/CIRCULATIONAHA.118.039177</p>
2b	– Age ≥50 years with 2 or more of the following risk factors determined at the screening visit:	Age ≥50 years at drug initiation	
	o duration of type 2 diabetes of 10 years or more	N/A	We can't capture diabetes duration but will match on number of antidiabetic drugs during baseline
	o or systolic blood pressure >140 mmHg (average of 3 readings) recorded at the screening visit	<p>Measured 180 days prior to drug initiation in any diagnosis position and inpatient or outpatient care setting - Hypertension ICD-9 codes 401.x – 405.x</p>	<p>Patorno, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gliiflozin antidiabetic drugs: population based cohort study." <i>BMJ</i> 2018;360:k119 http://dx.doi.org/10.1136/bmj.k119</p> <p>Patorno, Elisabetta et al. "Empagliflozin and the Risk of Heart Failure Hospitalization in Routine Clinical Care: A First Analysis from the Empagliflozin Comparative Effectiveness and Safety (EMPRISE) Study." <i>Circulation</i>. 2019 Apr 8. doi: 10.1161/CIRCULATIONAHA.118.039177</p>
	o or while the subject is on at least one blood pressure-lowering treatment	<p>Dispensing of at least one of the following medications in the 180 days prior to drug initiation: ACE inhibitor Benazepril, captopril, enalapril, fosinopril, lisinopril, moexipril, perindopril, quinapril, ramipril,trandolapril ARB Azilsartan, candesartan, eprosartan, irbesartan, losartan, olmesartan, telmisartan, valsartan Beta blocker Acebutolol, atenolol, betaxolol, bisoprolol, carteolol, carvedilol, esmolol, labetalol, metoprolol tartrate, metoprolol succinate, propranolol, penbutolol, pindolol, nadolol, nebivolol, sotalol, timolol Calcium channel blocker Diltiazem, mibefradil, verapamil, amlodipine, clevidipine, bepridil, felodipine, isradipine, nicardipine, nifedipine, nimodipine, nisoldipine Loop diuretics Furosemide, bumetanide, torsemide, ethacrynic acid Other diuretics Amiloride, eplerenone, spironolactone, triamterene Other hypertension drugs Doxazosin, eplerenone, prazosin, terazosin, clonidine, guanabenz, guanadrel, guanethidine, guanfacine, hydralazine, methylodopa, metyrosine, reserpine, minoxidil, aliskiren</p>	<p>Patorno, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gliiflozin antidiabetic drugs: population based cohort study." <i>BMJ</i> 2018;360:k119 http://dx.doi.org/10.1136/bmj.k119</p> <p>Patorno, Elisabetta et al. "Empagliflozin and the Risk of Heart Failure Hospitalization in Routine Clinical Care: A First Analysis from the Empagliflozin Comparative Effectiveness and Safety (EMPRISE) Study." <i>Circulation</i>. 2019 Apr 8. doi: 10.1161/CIRCULATIONAHA.118.039177</p>

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	o or current daily cigarette smoker	Measured 180 days prior to drug initiation in any diagnosis/procedure position and inpatient or outpatient care setting- <u>ICD-9 Codes</u> V15.82 305.1x 984.84 <u>CPT codes</u> 99406, 99407, G0436, G0437, G9016, S9453, S4995, G9276, G9458, 1034F, 4004F, 4001F OR dispensing of at least one nicotine or varenicline prescription: nicotine, varenicline	Desai, Rishi J et al. "Identification of smoking using Medicare data—a validation study of claims-based algorithms." <i>Pharmacoepidemiology and drug safety</i> vol. 25,4 (2016): 472-5. doi:10.1002/pds.3953
	o or documented microalbuminuria or macroalbuminuria	Measured 180 days prior to drug initiation in any diagnosis/procedure position and inpatient or outpatient care setting - Proteinuria ICD 9 DX 791.0 ICD10 DX R80.X Albumin abnormality ICD9 Dx- 790.99 ICD10 Dx - R77.0	
	o or documented high-density lipoprotein (HDL) cholesterol of <1 mmol/l (<39 mg/dl).	N/A	
	Women must be: —Postmenopausal, defined as >45 years of age with amenorrhea for at least 18 months, or >45 years of age with amenorrhea for at least 6 months and less than 18 months and a serum follicle stimulating hormone (FSH) level >40 IU/ml, —or Surgically sterile (have had a hysterectomy or bilateral oophorectomy, tubal ligation), or otherwise be incapable of pregnancy.	Women Age >45 years at drug initiation OR N/A	
3	—or Heterosexually active and practicing a highly effective method of birth control, including hormonal prescription oral contraceptives, contraceptive injections, contraceptive patch, intrauterine device, double-barrier method (e.g., condoms, diaphragm, or cervical cap with spermicidal foam, cream, or gel), or male partner sterilization, consistent with local regulations regarding use of birth control methods for subjects participating in clinical trials, for the duration of their participation in the study,	Measured 180 days prior to drug initiation in any diagnosis position and inpatient or outpatient care setting- Encounter for contraceptive management ICD9: V25 OR Non-oral contraceptives (brand names)- Depo-subQ Provera 104 Depo-Provera, generic Mirena Ortho Evra NuvaRing Implanon Oral contraceptives (generic names)- See "oral contraceptives - generic" sheet. Oral contraceptives (brand names)- See "oral contraceptives - generic" sheet.	Krumme, Alexis A, et. al. "Study protocol for the dabigatran, apixaban, rivaroxaban, edoxaban, warfarin comparative effectiveness research study." <i>J. Comp. Eff. Res.</i> (2018):7(1), 57–66. doi: 10.2217/cer-2017-0053.
	—or Not heterosexually active. Note: subjects who are not heterosexually active at screening must agree to utilize a highly effective method of birth control if they become heterosexually active during their participation in the study.	N/A	
4	Women of childbearing potential must have a negative urine β-human chorionic gonadotropin (β-hCG) pregnancy test at screening and baseline (predose, Day 1).	N/A	One of the exclusion criteria is pregnancy, so this can be skipped.
5	Willing and able to adhere to the prohibitions and restrictions specified in this protocol.	N/A	
6	Subjects must have signed an informed consent document indicating that they understand the purpose of and procedures required for the study and are willing to participate in the study.	N/A	
7	To participate in the optional pharmacogenomic component of this study, subjects must have signed the informed consent form for pharmacogenomic research indicating willingness to participate in the pharmacogenomic component of the study (where local regulations permit). Refusal to give consent for this component does not exclude a subject from participation in the clinical study.	N/A	
8	Subjects must have taken ≥80% of their single-blind placebo capsules during the 2-week run-in period at Day 1 to be eligible for randomization.	N/A	
EXCLUSION CRITERIA			
1	History of diabetic ketoacidosis, type 1 diabetes, pancreas or beta-cell transplantation, or diabetes secondary to pancreatitis or pancreatectomy.	Measured 180 days prior to drug initiation in any diagnosis position and inpatient or outpatient care setting- DM type 1- At least 1 ICD-9 Dx code of 250.x1 or 250.x3 or ICD-10 Dx code of E10.x Measured 180 days prior to drug initiation in any procedure position and inpatient or outpatient care setting- Secondary diabetes ICD-9 procedure: 249.xx Secondary diabetes Measured 180 days prior to drug initiation in any diagnosis position and inpatient or outpatient care setting- Ketoacidosis 250.1x Notes: We can't capture pancreas or beta-cell transplantation in claims datasets.	Patorno, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gliiflozin antidiabetic drugs: population based cohort study." <i>BMJ</i> 2018;360:k119 http://dx.doi.org/10.1136/bmj.k119 Patorno, Elisabetta et al. "Empagliflozin and the Risk of Heart Failure Hospitalization in Routine Clinical Care: A First Analysis from the Empagliflozin Comparative Effectiveness and Safety (EMPRISE) Study." <i>Circulation</i> . 2019 Apr 8. doi: 10.1161/CIRCULATIONAHA.118.039177
2	On an AHA and not on a stable regimen (i.e., agents and doses) for at least 8 weeks before the screening visit and through the screening/run-in period. Note: a stable dose of insulin is defined as no change in the insulin regimen (i.e., type[s] of insulin) and ≤15% change in the total daily dose of insulin (averaged over 7 week to account for day-to-day variability).	N/A	

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3	<p>--For patients on a sulfonylurea agent or on insulin: fasting fingerstick glucose at site <110 mg/dl (<6 mmol/l) at Baseline/Day 1.</p> <p>Note: at the investigator's discretion, based upon an assessment of recent self-monitored blood glucose (SMBG) values, subjects meeting either of these fingerstick glucose exclusion criteria may continue the single-blind placebo and return to the investigational site within 14 days and may be randomized if the repeat fasting fingerstick value no longer meets the exclusion criterion. Subjects with fingerstick glucose >270 mg/dl (>15 mmol/l) may have their AHA regimen adjusted and be rescreened once on a stable regimen for at least 8 weeks.</p>	N/A	
4	History of one or more severe hypoglycemic episode within 6 months before screening. Note: a severe hypoglycemic episode is defined as an event that requires the help of another person.	<p>Measured 180 days prior to drug initiation in primary diagnosis position and inpatient care setting- ICD-9 diagnosis: 251.0, 251.1x, 251.2x, or 250.8x.</p> <p>If identified by 250.8x are not included if they co-occur with one of the following diagnoses: 259.8, 272.7, 681.xx, 682.xx, 686.9, 707.1x, 707.2x, 707.8, 707.9, 709.3, 730.0x, 730.1x, 730.2x, 731.8.</p>	<p>PPV 89% (ED component) – Ginde AA, Blanc PG, Lieberman RM, Camargo CA, Jr. Validation of ICD-9-CM coding algorithm for improved identification of hypoglycemia visits. BMC endocrine disorders 2008;8:4.</p> <p>PPV 78% (inpatient component) – Schelleman H, Bilker WB, Brensinger CM, Wan F, Hennessy S. Anti-infectives and the risk of severe hypoglycemia in users of glipizide or glyburide. Clinical pharmacology and therapeutics 2010;88:214-22.</p>
5	History of hereditary glucose-galactose malabsorption or primary renal glucosuria.	<p>Measured 180 days prior to drug initiation in any diagnosis position and inpatient or outpatient care setting- ICD-9 diagnosis codes: 271.3x, 271.4x</p>	Elisabetta suggested these codes
6	Ongoing, inadequately controlled thyroid disorder. Note: subjects on thyroid hormone-replacement therapy must be on a stable dose for at least 6 weeks before Day 1.	N/A	
7	Renal disease that required treatment with immunosuppressive therapy or a history of dialysis or renal transplant. Note: subjects with a history of treated childhood renal disease, without sequelae, may participate.	<p>Measured 180 days prior to drug initiation - 1. Acute renal diseases OR Chronic Renal Insufficiency in any diagnosis position and inpatient or outpatient care setting AND dispensing of an immunosuppressive agent: Acute Renal Disease 572.4x, 580.xx, 584.xx, 791.2x, 791.3x Chronic Renal Insufficiency 582.xx, 583.xx, 585.xx, 586.xx, 587.xx Immunosuppressive therapy: HCPCS codes: "36514", "80420", "C9256", "J0702", "J0704", "J1020", "J1030", "J1040", "J1094", "J1095", "J1100", "J1690", "J1700", "J1710", "J1720", "J2640", "J2650", "J2920", "J2930", "J3300", "J3301", "J3302", "J3303", "J7312", "J7506", "J7509", "J7510", "J7624", "J7637", "J7638", "J7683", "J7684", "J8540", "K0512", "K0513", "K0528", "S0173" with immunosuppressive agents in next tab "Immunosuppressive agents"</p> <p>OR</p> <p>2. Dialysis in any diagnosis position and inpatient care setting OR Renal transplant in any diagnosis position and inpatient or outpatient care setting Codes are in the sheet 'Dialysis and Renal Transplant'</p>	<p>Patorno, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gliiflozin antidiabetic drugs: population based cohort study." BMJ 2018;360:k119 http://dx.doi.org/10.1136/bmj.k119</p> <p>Patorno, Elisabetta et al. "Empagliflozin and the Risk of Heart Failure Hospitalization in Routine Clinical Care: A First Analysis from the Empagliflozin Comparative Effectiveness and Safety (EMPRISE) Study." Circulation. 2019 Apr 8. doi: 10.1161/CIRCULATIONAHA.118.039177</p>
8	MI, unstable angina, revascularization procedure, or cerebrovascular accident within 3 months before screening, or a planned revascularization procedure, or history of New York Heart Association (NYHA) Class IV cardiac disease.	<p>Measured 90 days prior to drug initiation in any diagnosis/procedure position and care setting defined below- Any of the following codes in inpatient or outpatient care setting: MI ICD-9 diagnosis: 410.xx Unstable angina ICD-9 diagnosis: 411.xx Left ventricular assist- CPT-4 33990-33993 Stroke ICD-9 diagnosis: 430.xx, 431.xx, 433.x1, 434.x1, 436.x Carotid bypass: ICD9 procedure: 39.28 TIA 435.xx Peripheral arterial stenting or surgical revascularization ICD-9 39.25, 39.50, 39.99. PTCA: Inpatient CPT-4: 92973, 92982, 92984, 92995, 92996, 92920 – 92921, 92924 – 92925, 92937, 92938, 92941, 92943, 92944 OR – Inpatient or outpatient - ICD-9 procedure: 00.66, 36.01, 36.02, 36.03, 36.05, 36.09 Stenting: Inpatient CPT-4: 92980, 92981, 92928 – 92929, 92933 - 92934 – OR – Inpatient or outpatient - ICD-9 procedure: 36.06, 36.07 CABG: Inpatient CPT-4: 33510 – 33536, 33545, 33572 – OR – Inpatient or outpatient - ICD-9 procedure: 36.1x, 36.2x Transmyocardial revascularization: Inpatient or Outpatient CPT-4: 33140, 33141 OR - Inpatient or outpatient ICD-9 procedure: 36.31-36.34</p>	<p>Patorno, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gliiflozin antidiabetic drugs: population based cohort study." BMJ 2018;360:k119 http://dx.doi.org/10.1136/bmj.k119</p> <p>Patorno, Elisabetta et al. "Empagliflozin and the Risk of Heart Failure Hospitalization in Routine Clinical Care: A First Analysis from the Empagliflozin Comparative Effectiveness and Safety (EMPRISE) Study." Circulation. 2019 Apr 8. doi: 10.1161/CIRCULATIONAHA.118.039177</p> <p>Left Ventricular Assist Codes from- http://www.hcpro.com/HIM-289708-859/Tip-Note-new-codes-for-ventricular-assist-devices.html</p>
9	Findings on 12-lead electrocardiogram (ECG) that would require urgent diagnostic evaluation or intervention (e.g., new clinically important arrhythmia or conduction disturbance).	<p>Measured 180 days prior to drug initiation in primary diagnosis position and inpatient care setting- Cardiac conduction disorders ICD 9: 426.xx Other cardiac dysrhythmia ICD 9: 427.xx, exclude 427.5x (cardiac arrest) and 427.3x And, 427.6x</p>	<p>Patorno, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gliiflozin antidiabetic drugs: population based cohort study." BMJ 2018;360:k119 http://dx.doi.org/10.1136/bmj.k119</p> <p>Patorno, Elisabetta et al. "Empagliflozin and the Risk of Heart Failure Hospitalization in Routine Clinical Care: A First Analysis from the Empagliflozin Comparative Effectiveness and Safety (EMPRISE) Study." Circulation. 2019 Apr 8. doi: 10.1161/CIRCULATIONAHA.118.039177</p>

Appendix A

10	History of hepatitis B surface antigen or hepatitis C antibody positive (unless associated with documented persistently stable/normal range aspartate aminotransferase [AST] and alanine aminotransferase [ALT] levels), or other clinically active liver disease.	Measured 180 days prior to drug initiation in any diagnosis/procedure position and inpatient or outpatient care setting- Liver disease- ICD-9 diagnosis: 070.xx, 570.xx-573.xx 456.0x-456.2x, 576.8x, 782.4x, 789.5x ICD-9 procedure codes: 39.1x, 42.91	Patorno, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gliiflozin antidiabetic drugs: population based cohort study." BMJ 2018;360:k119 http://dx.doi.org/10.1136/bmj.k119 Patorno, Elisabetta et al. "Empagliflozin and the Risk of Heart Failure Hospitalization in Routine Clinical Care: A First Analysis from the Empagliflozin Comparative Effectiveness and Safety (EMPRISE) Study." Circulation. 2019 Apr 8. doi: 10.1161/CIRCULATIONAHA.118.039177
11	Any history of or planned bariatric surgery.	Measured 1825 days prior to drug initiation in any procedure position and inpatient or outpatient care setting- CPT-Code-Abbreviation Procedure 43644 -LRYBG-Laparoscopic Roux-en-Y gastric bypass (Roux limb 150 cm or less) 43645 -LRYGBX- Laparoscopic gastric bypass with small intestine reconstruction to limit absorption 43770 -LAGB-Laparoscopic adjustable gastric band 43846 -ORYGB-Open Roux-en-Y gastric bypass (Roux limb 150 cm or less) 43847 -ORYGBX-Open gastric bypass with small intestine reconstruction to limit absorption	Hatoam, Ida J et al. "Clinical Factors Associated With Remission of Obesity-Related Comorbidities After Bariatric Surgery." JAMA Surg. 2016;151(2):130-137. doi:10.1001/jamasurg.2015.3231
12	Estimated glomerular filtration rate (eGFR) <30 ml/min/1.73 m2 at screening (provided by the central laboratory) —For subjects taking metformin: at screening, serum creatinine ≥1.4 mg/dl (124 µmol/l) for men or ≥1.3 mg/dl (115 µmol/l) for women; no contraindication to the use of metformin (including eGFR) based on the label of the country of investigational site	N/A	
13	ALT levels >2.0 times the upper limit of normal (ULN) or total bilirubin >1.5 times the ULN at screening, unless in the opinion of the investigator and as agreed upon by the sponsor's medical officer, the findings are consistent with Gilbert's disease.	N/A	
14	History of malignancy within 5 years before screening (exceptions: squamous and basal cell carcinomas of the skin and carcinoma of the cervix in situ, or a malignancy that in the opinion of the investigator, with concurrence with the sponsor's medical monitor, is considered cured with minimal risk of recurrence).	Measured 1825 days prior to drug initiation in any diagnosis position and inpatient or outpatient care setting- History of malignant neoplasm 140.xx-208.xx (except 173.xx, non-melanoma skin cancer)	Patorno, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gliiflozin antidiabetic drugs: population based cohort study." BMJ 2018;360:k119 http://dx.doi.org/10.1136/bmj.k119 Patorno, Elisabetta et al. "Empagliflozin and the Risk of Heart Failure Hospitalization in Routine Clinical Care: A First Analysis from the Empagliflozin Comparative Effectiveness and Safety (EMPRISE) Study." Circulation. 2019 Apr 8. doi: 10.1161/CIRCULATIONAHA.118.039177
15	History of human immunodeficiency virus (HIV) antibody positive.	Measured 1825 days prior to drug initiation in any diagnosis position and inpatient or outpatient care setting- 042 Human immunodeficiency virus [HIV] disease 079.53 Human immunodeficiency virus, type 2 [HIV-2] V08 Asymptomatic human immunodeficiency virus [HIV] infection status OR filled prescription for HIV treatment: (Please see HIV Treatment sheet)	Patorno, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gliiflozin antidiabetic drugs: population based cohort study." BMJ 2018;360:k119 http://dx.doi.org/10.1136/bmj.k119 Patorno, Elisabetta et al. "Empagliflozin and the Risk of Heart Failure Hospitalization in Routine Clinical Care: A First Analysis from the Empagliflozin Comparative Effectiveness and Safety (EMPRISE) Study." Circulation. 2019 Apr 8. doi: 10.1161/CIRCULATIONAHA.118.039177
16	Subject has a current clinically important hematological disorder (e.g., symptomatic anemia, proliferative bone marrow disorder, thrombocytopenia).	Measured 180 days prior to drug initiation in any diagnosis position and inpatient or outpatient care setting- ICD-9 Diagnosis Codes: 238.4x, 289.83, 238.71, 280.x-285.x, 287.3x, 287.4x, 287.5x	Expert in this study area advised on the codes used for this inclusion/exclusion criteria.
17	Investigator's assessment that the subject's life expectancy is less than 1 year, or any condition that in the opinion of the investigator would make participation not in the best interest of the subject, or could prevent, limit, or confound the protocol-specified safety or efficacy assessments.	Measured 180 days prior to drug initiation- CCI ≥10	Gagne, Josh J et al. "A combined comorbidity score predicted mortality in elderly patients better than existing scores." J Clin Epidemiol. 2011 Jul;64(7):749-59. doi: 10.1016/j.jclinepi.2010.10.004. Sun, Jenny W et al. "Validation of the Combined Comorbidity Index of Charlson and Elixhauser to Predict 30-Day Mortality Across ICD-9 and ICD-10." Med Care. 2018 Sep;56(9):812. doi: 10.1097/MLR.0000000000000954.
18	Major surgery (i.e., requiring general anesthesia) within 3 months of the screening visit or any surgery planned during the subject's expected participation in the study (except minor surgery, i.e., outpatient surgery under local anesthesia).	Measured 90 days prior to drug initiation in any diagnosis position and inpatient or outpatient care setting- Major surgery selected from codes range 35.x-84.x	
19	Any condition that, in the opinion of the investigator, would compromise the well-being of the subject or prevent the subject from meeting or performing study requirements.	N/A	
20	Current use of other sodium glucose co-transporter 2 (SGLT2) inhibitor.	Measured 180 days prior to drug initiation as a dispensing of one of the following drugs- empagliflozin, dapagliflozin, ertugliflozin	
21	Known allergies, hypersensitivity, or intolerance to canagliflozin or its excipients.	N/A	
22	Current use of a corticosteroid medication or immunosuppressive agent, or likely to require treatment with a corticosteroid medication (for longer than 2 weeks in duration) or an immunosuppressive agent. Note: subjects using inhaled, intranasal, intra-articular, or topical corticosteroids, or corticosteroids in therapeutic replacement doses may participate.	Measured 180 days prior to drug initiation as a dispensing of one of the following drugs- Systemic corticosteroids (With Route of Administration is intravenous): - Cortisone, hydrocortisone, prednisone, prednisolone, methylprednisolone, triamcinolone, dexamethasone, betamethasone. immunosuppressive agents o RA, AS, and PsA: methotrexate, hydroxychloroquine, azathioprine, cyclosporine, leflunomide, minocycline, sulfasalazine. o SLE: hydroxychloroquine, azathioprine, mycophenolate mofetil. o IBD: azathioprine, mercaptopurine	Patorno, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gliiflozin antidiabetic drugs: population based cohort study." BMJ 2018;360:k119 http://dx.doi.org/10.1136/bmj.k119 Patorno, Elisabetta et al. "Empagliflozin and the Risk of Heart Failure Hospitalization in Routine Clinical Care: A First Analysis from the Empagliflozin Comparative Effectiveness and Safety (EMPRISE) Study." Circulation. 2019 Apr 8. doi: 10.1161/CIRCULATIONAHA.118.039177 Desai, Rishi et al. "Risk of serious infections associated with use of immunosuppressive agents in pregnant women with autoimmune inflammatory conditions: cohort study" BMJ 2017; 356 doi: https://doi.org/10.1136/bmj.j895
23	Received an active investigational drug (including vaccines) or used an investigational medical device within 3 months before Day 1/baseline or received at least one dose of canagliflozin in a prior study.	Already applied based on the canagliflozin and comparator washout, but measured again 90 days prior to drug initiation as a dispensing for canagliflozin	

Appendix A

24	History of drug or alcohol abuse within 3 years before screening.	Measured 1095 days prior to drug initiation in any diagnosis position and inpatient or outpatient care setting- Alcohol abuse or dependence 291.xx, 303.xx, 305.0x, 571.0x, 571.1x, 571.2x, 571.3x, 357.5x, 425.5x, E860.0x, V11.3x Drug abuse or dependence 292.xx, 304.xx, 305.2x-305.9x, 648.3x	Patorno, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gliiflozin antidiabetic drugs: population based cohort study." BMJ 2018;360:k1119 http://dx.doi.org/10.1136/bmj.k1119 Patorno, Elisabetta et al. "Empagliflozin and the Risk of Heart Failure Hospitalization in Routine Clinical Care: A First Analysis from the Empagliflozin Comparative Effectiveness and Safety (EMPRISE) Study." Circulation. 2019 Apr 8. doi: 10.1161/CIRCULATIONAHA.118.039177
25	Pregnant or breastfeeding or planning to become pregnant or breastfeed during the study.	Measured 180 days prior to drug initiation in any diagnosis position and inpatient or outpatient care setting- (Please see Pregnancy Sheet for code list)	
26	Employees of the investigator or study center, with direct involvement in the proposed study or other studies under the direction of that investigator or study center, as well as family members of the employees or the investigator.	N/A	

Appendix A

<u>Trial ID</u>	sNDA22
<u>Trial Name (with web links)</u>	CANVAS
<u>NCT</u>	NCT01032629
<u>Trial category</u>	Secondary indication
<u>Therapeutic Area</u>	Endocrinology
<u>RCT Category</u>	4a- Unintended S with label change
<u>Brand Name</u>	Invokana
<u>Generic Name</u>	Canagliflozin
<u>Sponsor</u>	Janssen Research & Development, LLC
<u>Year</u>	2017
<u>Measurable endpoint</u>	Major Adverse Cardiovascular Events, Including CV Death, Nonfatal Myocardial Infarction (MI), and Nonfatal Stroke
<u>Exposure</u>	Canagliflozin
<u>Comparator</u>	Placebo
<u>Population</u>	50% on insulin, 47% using Sulfonylurea, 73% Metformin, 72% statin
<u>Trial finding</u>	HR = 0.86 (95% CI 0.75–0.97)
<u>No. of Patients</u>	4330
<u>Non-inferiority margin</u>	HR = 1.3
<u>Assay Sens. Endpoint</u>	
<u>Assay Sens. Finding</u>	
<u>Power</u>	0.90. With 688 cardiovascular safety events recorded across the trials, there would be at least 90% power, at an alpha level of 0.05, to exclude an upper margin of the 95% confidence interval for the hazard ratio of 1.3.
<u>Blinding</u>	
<u>Statistical Method</u>	Cardiovascular safety was to be shown if the upper boundary of the 95% confidence interval of the hazard ratio with canagliflozin as compared with placebo was less than 1.3, and superiority was to be shown if the upper boundary was less than 1.0.

Appendix A

Mortality- Dependent on data source.

1. All-cause mortality / inpatient mortality

Identified using the vital status file-

Medicare

Identified using the discharge status codes-

Optum-

- 20 = EXPIRED
- 21 = EXPIRED TO BE DEFINED AT STATE LEVEL
- 22 = EXPIRED TO BE DEFINED AT STATE LEVEL
- 23 = EXPIRED TO BE DEFINED AT STATE LEVEL
- 24 = EXPIRED TO BE DEFINED AT STATE LEVEL
- 25 = EXPIRED TO BE DEFINED AT STATE LEVEL
- 26 = EXPIRED TO BE DEFINED AT STATE LEVEL
- 27 = EXPIRED TO BE DEFINED AT STATE LEVEL
- 28 = EXPIRED TO BE DEFINED AT STATE LEVEL
- 29 = EXPIRED TO BE DEFINED AT STATE LEVEL
- 40 = EXPIRED AT HOME (HOSPICE)
- 41 = EXPIRED IN A MEDICAL FACILITY (HOSPICE)
- 42 = EXPIRED - PLACE UNKNOWN (HOSPICE)

Truven-

- 20 - Died
- 22 - Died
- 23 - Died
- 24 - Died
- 25 - Died
- 26 - Died
- 27 - Died
- 28 - Died
- 29 - Died
- 40 - Other died status or Expired at home (Hospice claims only) (depends on year)

Appendix A

- 41 - Other died status or Expired in medical facility (Hospice claims only) (depends on year)
- 42 - Other died status or Expired - place unknown (Hospice claims only) (depends on year)
- 21 - Died or Disch./Transf. to court/law enforcement (depends on year)

2. CV mortality

Information on CV mortality through data linkage with the National Death Index (NDI) will be available for Medicare at a later date. We will conduct secondary analyses using CV mortality at that time.

Appendix A

drug_class	Brand Name
oral contraceptive	Apri;
oral contraceptive	Desogen;
oral contraceptive	Ortho-Cept;
oral contraceptive	Reclipsen
oral contraceptive	Kariva;
oral contraceptive	Mircette
oral contraceptive	Cyclessa;
oral contraceptive	Velivet
oral contraceptive	Yasmin
oral contraceptive	Yaz
oral contraceptive	Demulen 1/35;
oral contraceptive	Kelnor;
oral contraceptive	Zovia 1/25
oral contraceptive	Demulen 1/50;
oral contraceptive	Zovia 1/50
oral contraceptive	Alesse;
oral contraceptive	Aviane;
oral contraceptive	Lessina;
oral contraceptive	Lutera
oral contraceptive	Nordette;
oral contraceptive	Portia;
oral contraceptive	Levora
oral contraceptive	Lybrel
oral contraceptive	Seasonale;
oral contraceptive	Quasense;
oral contraceptive	Jolessa
oral contraceptive	Seasonique
oral contraceptive	Empresse;
oral contraceptive	Triphasil;
oral contraceptive	Trivora
oral contraceptive	Ovcon 35
oral contraceptive	Balziva;

Appendix A

oral contraceptive	Femcon Fe
oral contraceptive	Brevicon;
oral contraceptive	Nortrel 0.5/35;
oral contraceptive	Modicon;
oral contraceptive	Necon 0.5/35
oral contraceptive	Norinyl 1/35;
oral contraceptive	Nortrel 1/35;
oral contraceptive	Ortho-Novum 1/35;
oral contraceptive	Necon 1/35
oral contraceptive	Ovcon 50;
oral contraceptive	Necon 1/50
oral contraceptive	Ortho-Novum 10/11
oral contraceptive	Aranelle;
oral contraceptive	Tri-Norinyl
oral contraceptive	Ortho-Novum 7/7/7;
oral contraceptive	Necon
oral contraceptive	Micronor;
oral contraceptive	Nor-QD;
oral contraceptive	Camila;
oral contraceptive	Errin;
oral contraceptive	Jolivet
oral contraceptive	Junel 21 1/20;
oral contraceptive	Junel 21 Fe 1/20;
oral contraceptive	Loestrin 21 1/20;
oral contraceptive	Loestrin 21 Fe 1/20;
oral contraceptive	Loestrin 24 Fe;
oral contraceptive	Microgestin 1/20
oral contraceptive	Microgestin Fe 1/20
oral contraceptive	Junel 21 1.5/30;
oral contraceptive	Junel 21 Fe 1.5/30;
oral contraceptive	Loestrin 1.5/30;
oral contraceptive	Loestrin Fe 1.5/30
oral contraceptive	Microgestin 1.5/30

Appendix A

oral contraceptive	Microgestin Fe 1.5/30
oral contraceptive	Ethrostep Fe;
oral contraceptive	Tilia Fe;
oral contraceptive	TriLegest Fe
oral contraceptive	Ortho-Cyclen;
oral contraceptive	Sprintec;
oral contraceptive	MonoNessa;
oral contraceptive	Previfem
oral contraceptive	Ortho Tri-Cyclen Lo;
oral contraceptive	Tri-Previfem;
oral contraceptive	TriNessa
oral contraceptive	Ortho Tri-Cyclen;
oral contraceptive	Tri-Sprintec
oral contraceptive	Cryselle;
oral contraceptive	Lo/Ovral;
oral contraceptive	Low-Ogestrel
oral contraceptive	Ovral;
oral contraceptive	Ogestrel
oral contraceptive	Zovia 1/50
oral contraceptive	Alesse;
oral contraceptive	Aviane;
oral contraceptive	Lessina;
oral contraceptive	Lutera
oral contraceptive	Nordette;
oral contraceptive	Portia;
oral contraceptive	Levora
oral contraceptive	Lybrel
oral contraceptive	Seasonale;
oral contraceptive	Quasense;
oral contraceptive	Jolessa
oral contraceptive	Seasonique
oral contraceptive	Empresse;
oral contraceptive	Triphasil;

Appendix A

oral contraceptive	Trivora
oral contraceptive	Ovcon 35
oral contraceptive	Balziva;
oral contraceptive	Femcon Fe
oral contraceptive	Brevicon;
oral contraceptive	Nortrel 0.5/35;
oral contraceptive	Modicon;
oral contraceptive	Necon 0.5/35
oral contraceptive	Norinyl 1/35;
oral contraceptive	Nortrel 1/35;
oral contraceptive	Ortho-Novum 1/35;
oral contraceptive	Necon 1/35
oral contraceptive	Ovcon 50;
oral contraceptive	Necon 1/50
oral contraceptive	Ortho-Novum 10/11
oral contraceptive	Aranelle;
oral contraceptive	Tri-Norinyl
oral contraceptive	Ortho-Novum 7/7/7;
oral contraceptive	Necon
oral contraceptive	Micronor;
oral contraceptive	Nor-QD;
oral contraceptive	Camila;
oral contraceptive	Errin;
oral contraceptive	Jolivette
oral contraceptive	Junel 21 1/20;
oral contraceptive	Junel 21 Fe 1/20;
oral contraceptive	Loestrin 21 1/20;
oral contraceptive	Loestrin 21 Fe 1/20;
oral contraceptive	Loestrin 24 Fe;
oral contraceptive	Microgestin 1/20
oral contraceptive	Microgestin Fe 1/20
oral contraceptive	Junel 21 1.5/30;
oral contraceptive	Junel 21 Fe 1.5/30;

Appendix A

oral contraceptive	Loestrin 1.5/30;
oral contraceptive	Loestrin Fe 1.5/30
oral contraceptive	Microgestin 1.5/30
oral contraceptive	Microgestin Fe 1.5/30
oral contraceptive	Estrostep Fe;
oral contraceptive	Tilia Fe;
oral contraceptive	TriLegest Fe
oral contraceptive	Ortho-Cyclen;
oral contraceptive	Sprintec;
oral contraceptive	MonoNessa;
oral contraceptive	Previfem
oral contraceptive	Ortho Tri-Cyclen Lo;
oral contraceptive	Tri-Previfem;
oral contraceptive	TriNessa
oral contraceptive	Ortho Tri-Cyclen;
oral contraceptive	Tri-Sprintec
oral contraceptive	Cryselle;
oral contraceptive	Lo/Ovral;
oral contraceptive	Low-Ogestrel
oral contraceptive	Ovral;
oral contraceptive	Ogestrel

Appendix A

drug_class	generic	generic_ndc
oral contraceptive	estradiol	desogestrel-ethinyl estradiol
oral contraceptive	estradiol	desogestrel-ethinyl estradiol/ethinyl estradiol
oral contraceptive	estradiol	drospirenone/estradiol
oral contraceptive	estradiol	drospirenone/ethinyl estradiol/levomefolate calcium
oral contraceptive	estradiol	estradiol
oral contraceptive	estradiol	estradiol acetate
oral contraceptive	estradiol	estradiol benzoate
oral contraceptive	estradiol	estradiol cypionate
oral contraceptive	estradiol	estradiol cypionate/medroxyprogesterone acet
oral contraceptive	estradiol	estradiol hemihydrate, micronized
oral contraceptive	estradiol	estradiol micronized
oral contraceptive	estradiol	estradiol valerate
oral contraceptive	estradiol	estradiol valerate/dienogest
oral contraceptive	estradiol	estradiol valerate/sesame oil
oral contraceptive	estradiol	estradiol/estrone
oral contraceptive	estradiol	estradiol/estrone/vit b12
oral contraceptive	estradiol	estradiol/levonorgestrel
oral contraceptive	estradiol	estradiol/norethindrone acetate
oral contraceptive	estradiol	estradiol/norgestimate
oral contraceptive	estradiol	estradiol/progesterone
oral contraceptive	estradiol	ethinyl estradiol
oral contraceptive	estradiol	ethinyl estradiol/drospirenone
oral contraceptive	estradiol	ethinyl estradiol/norethindrone acetate
oral contraceptive	estradiol	ethynodiol d-ethinyl estradiol
oral contraceptive	estradiol	ethynodiol diacetate-ethinyl estradiol
oral contraceptive	estradiol	etonogestrel/ethinyl estradiol
oral contraceptive	estradiol	levonorgestrel-ethinyl estradiol
oral contraceptive	estradiol	levonorgestrel/ethinyl estradiol and ethinyl estradiol
oral contraceptive	estradiol	me-testosterone/eth estradiol
oral contraceptive	estradiol	metttm/estradiol/multivits
oral contraceptive	estradiol	norelgestromin/ethinyl estradiol
oral contraceptive	estradiol	norethindrone a-e estradiol
oral contraceptive	estradiol	norethindrone a-e estradiol/fe

Appendix A

oral contraceptive	estradiol	norethindrone a-e estradiol/ferrous fumarate
oral contraceptive	estradiol	norethindrone acetate-ethinyl estradiol
oral contraceptive	estradiol	norethindrone acetate-ethinyl estradiol/ferrous fumarate
oral contraceptive	estradiol	norethindrone-ethin estradiol
oral contraceptive	estradiol	norethindrone-ethinyl estradiol
oral contraceptive	estradiol	norethindrone-ethinyl estradiol/ferrous fumarate
oral contraceptive	estradiol	norgestimate-ethinyl estradiol
oral contraceptive	estradiol	norgestrel-ethinyl estradiol
oral contraceptive	estradiol	testosterone cypionate/estradiol cypionate
oral contraceptive	estradiol	testosterone enanthate/estradiol valerate
oral contraceptive	estradiol	testosterone/estradiol
oral contraceptive	levonorgestrel	estradiol/levonorgestrel
oral contraceptive	levonorgestrel	levonorgestrel
oral contraceptive	levonorgestrel	levonorgestrel-eth estra
oral contraceptive	levonorgestrel	levonorgestrel-eth estra/pregnancy test kit
oral contraceptive	levonorgestrel	levonorgestrel-ethinyl estradiol
oral contraceptive	levonorgestrel	levonorgestrel/ethinyl estradiol and ethinyl estradiol
oral contraceptive	norethindrone	estradiol/norethindrone acetate
oral contraceptive	norethindrone	ethinyl estradiol/norethindrone acetate
oral contraceptive	norethindrone	leuprolide acetate/norethindrone acetate
oral contraceptive	norethindrone	norethindrone
oral contraceptive	norethindrone	norethindrone a-e estradiol
oral contraceptive	norethindrone	norethindrone a-e estradiol/fe
oral contraceptive	norethindrone	norethindrone a-e estradiol/ferrous fumarate
oral contraceptive	norethindrone	norethindrone acetate
oral contraceptive	norethindrone	norethindrone acetate-ethinyl estradiol
oral contraceptive	norethindrone	norethindrone acetate-ethinyl estradiol/ferrous fumarate
oral contraceptive	norethindrone	norethindrone-ethin estradiol
oral contraceptive	norethindrone	norethindrone-ethinyl estrad
oral contraceptive	norethindrone	norethindrone-ethinyl estradiol
oral contraceptive	norethindrone	norethindrone-ethinyl estradiol/ferrous fumarate
oral contraceptive	norethindrone	norethindrone-mestranol

Appendix A

oral contraceptive	norgestrel	norgestrel
oral contraceptive	norgestrel	norgestrel-ethinyl estradiol
oral contraceptive	polyestradiol phosphate	polyestradiol phosphate

Appendix A

Antidiabetic class	Specific agent	Notes
SGLT2-inhibitors	Canagliflozin	Approved 3/29/2013
	Dapagliflozin	
	Empagliflozin	
	Ertugliflozin	Approved Dec 21, 2017
2 nd generation sulfonylureas	Glimepiride	
	Glipizide	
	Glyburide	
DPP-4 inhibitors	Alogliptin	
	Linagliptin	
	Saxagliptin	
	Sitagliptin	
GLP-1 receptor agonist (GLP1-RA)	Exenatide	
	Liraglutide	
	Albiglutide	Approved April 15, 2014 and discontinued July 26, 2017
	Dulaglutide	Approved Sep 18, 2014
	Lixisenatide	Approved July 28, 2016
	Semaglutide	Approved Dec 5, 2017
Insulin	Insulin Aspart	
	Insulin Aspart/Insulin Aspart Protamine	
	Insulin Degludec	
	Insulin Detemir	
	Insulin Glargine	
	Insulin Glulisine	
	Insulin human isophane (NPH)	
	Insulin human regular (<i>search with NPH, don't want bf-pk</i>)	
	Insulin human regular/ Insulin human isophane (NPH)	
	Insulin Lispro	
	Insulin Lispro/Insulin Lispro Protamine	
Glitazones	Pioglitazone	

Appendix A

Glitazones	Rosiglitazone	
Meglitinides	Nateglinide	
	Repaglinide	
Alpha-glucosidase inhibitors	Acarbose	
	Miglitol	
Pramlintide	Pramlintide	
1 st generation sulfonylureas	Acetohexamide	
	Chlorpropamide	
	Tolazamide	
	Tolbutamide	

Appendix A

Immunosuppressive agents

ALEMTUZUMAB
BETAMETHASONE
BETAMETHASONE ACETATE/BETAMETHASONE SODIUM PHOSPHATE
BETAMETHASONE DIPROPIONATE
BETAMETHASONE DIPROPIONATE/PROPYLENE GLYCOL
BETAMETHASONE SODIUM PHOSPHATE
BETAMETHASONE VALERATE
BUDESONIDE
BUDESONIDE, MICRONIZED
CORTISONE ACETATE
DEXAMETHASONE
DEXAMETHASONE ACETATE
DEXAMETHASONE ACETATE, MICRONIZED
DEXAMETHASONE ISONICOTINATE
DEXAMETHASONE PHOSPHATE
DEXAMETHASONE SOD PHOSPHATE
DEXAMETHASONE SODIUM PHOSPHATE IN 0.9 % SODIUM CHLORIDE
DEXAMETHASONE SODIUM PHOSPHATE/PF
DEXAMETHASONE, MICRONIZED
HYDROCORTISONE
HYDROCORTISONE ACETATE
HYDROCORTISONE CYPIONATE
HYDROCORTISONE SOD PHOSPHATE
HYDROCORTISONE SOD SUCCINATE
IMMUNE GLOBULIN,BOVINE/PLASMA PROTEIN FRACTION, BOVINE
IMMUNE GLOBULIN,GAMM(IGG)/GLYCINE/GLUCOSE/IGA 0 TO 50 MCG/ML
IMMUNE GLOBULIN,GAMM(IGG)/GLYCINE/IGA GREATER THAN 50 MCG/ML
IMMUNE GLOBULIN,GAMM(IGG)/MALTOSE/IGA GREATER THAN 50 MCG/ML
IMMUNE GLOBULIN,GAMM(IGG)/SORBITOL/GLYCIN/IGA 0 TO 50 MCG/ML
IMMUNE GLOBULIN,GAMM(IGG)/SUCROSE/IGA GREATER THAN 50 MCG/ML
IMMUNE GLOBULIN,GAMMA (IGG)/GLYCINE/IGA 0 TO 50 MCG/ML
IMMUNE GLOBULIN,GAMMA (IGG)/PROLINE/IGA 0 TO 50 MCG/ML

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IMMUNE GLOBULIN,GAMMA (IGG)/SORBITOL/IGA 0 TO 50 MCG/ML
LYMPHOCYTE IG,ANTITHYMOCYTE/THIMEROSAL
LYMPHOCYTE IMMUNE GLOBULIN,ANTITHYMOCYTE (EQUINE)
METHYLPREDNISOLONE
METHYLPREDNISOLONE ACETATE
METHYLPREDNISOLONE ACETATE, MICRONIZED
METHYLPREDNISOLONE SODIUM SUCCINATE
METHYLPREDNISOLONE SODIUM SUCCINATE/PF
METHYLPREDNISOLONE, MICRONIZED
PREDNISOLONE
PREDNISOLONE ACETATE
PREDNISOLONE ACETATE, MICRONIZED
PREDNISOLONE SOD PHOSPHATE
PREDNISOLONE, MICRONIZED
PREDNISON
PREDNISON MICRONIZED
RITUXIMAB
RITUXIMAB/HYALURONIDASE, HUMAN RECOMBINANT
TRIAMCINOLONE
TRIAMCINOLONE DIACETATE
TRIAMCINOLONE HEXACETONIDE
TRIAMCINOLONE HEXACETONIDE, MICRONIZED
AZATHIOPRINE
AZATHIOPRINE SODIUM
CYCLOSPORINE
CYCLOSPORINE, MODIFIED
HYDROXYCHLOROQUINE SULFATE
LEFLUNOMIDE
MERCAPTOPURINE
MINOCYCLINE HCL
MINOCYCLINE HCL MICROSPHERES
MINOCYCLINE HCL/EMOL COMB NO.16/SKIN CLNSR L4/TOP AGENT NO.3
MINOCYCLINE HCL/EYELID CLEANSER COMBINATION NO. 1
MINOCYCLINE HCL/WIPES WITH SKIN CLEANSER NO.4
MYCOPHENOLATE MOFETIL
MYCOPHENOLATE MOFETIL HCL

Appendix A

MITOCHONDRIAL MEMBRANE SULFASALAZINE

Appendix A

HIV Treatment
Abacavir
Amprenavir
Atazanavir
Darunavir
Delavirdine
Didanosine
Efavirenz
Emtricitabine
Enfuvirtide
Etravirine
Fosamprenavir
Indinavir
Lamivudine-Zidovudine
Maraviroc
Nelfinavir
Nevirapine
Raltegravir
Rilpivirine
Ritonavir
Ritonavir-Lopinavir
Saquinavir
Stavudine
Tipranavir
Zalcitabine
Zidovudine

Appendix A

Pregnancy

Dx codes

650 NORMAL DELIVERY
660 OBSTRUCTED LABOR
661 ABNORMALITY OF FORCES OF LABOR
662 LONG LABOR
663 UMBILICAL CORD COMPLICATIONS DURING LABOR AND DELIVERY
664 TRAUMA TO PERINEUM AND VULVA DURING DELIVERY
665 OTHER OBSTETRICAL TRAUMA
667 RETAINED PLACENTA OR MEMBRANES WITHOUT HEMORRHAGE
668 COMPLICATIONS OF THE ADMINISTRATION OF ANESTHETIC OR OTHER SEDATION IN LABOR AND DELIVERY
669.94 UNSPECIFIED COMPLICATION OF LABOR AND DELIVERY POSTPARTUM CONDITION OR COMPLICATION
V24 POSTPARTUM CARE AND EXAMINATION
V24.0 POSTPARTUM CARE AND EXAMINATION IMMEDIATELY AFTER DELIVERY
V24.1 POSTPARTUM CARE AND EXAMINATION OF LACTATING MOTHER
V24.2 ROUTINE POSTPARTUM FOLLOW
V27 OUTCOME OF DELIVERY
V27.0 MOTHER WITH SINGLE LIVEBORN
V27.1 MOTHER WITH SINGLE STILLBORN
V27.2 MOTHER WITH TWINS BOTH LIVEBORN
V27.3 MOTHER WITH TWINS ONE LIVEBORN AND ONE STILLBORN
V27.4 MOTHER WITH TWINS BOTH STILLBORN
V27.5 MOTHER WITH OTHER MULTIPLE BIRTH ALL LIVEBORN
V27.6 MOTHER WITH OTHER MULTIPLE BIRTH SOME LIVEBORN
V27.7 MOTHER WITH OTHER MULTIPLE BIRTH ALL STILLBORN
V27.9 MOTHER WITH UNSPECIFIED OUTCOME OF DELIVERY

Procedure codes

72.0 LOW FORCEPS OPERATION
72.1 LOW FORCEPS OPERATION WITH EPISIOTOMY
72.2 MID FORCEPS OPERATION
72.21 MID FORCEPS OPERATION WITH EPISIOTOMY
72.29 OTHER MID FORCEPS OPERATION
72.3 HIGH FORCEPS OPERATION
72.31 HIGH FORCEPS OPERATION WITH EPISIOTOMY
72.39 OTHER HIGH FORCEPS OPERATION

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- 72.4 FORCEPS ROTATION OF FETAL HEAD
- 72.5 BREECH EXTRACTION
 - 72.51 PARTIAL BREECH EXTRACTION WITH FORCEPS TO AFTERCOMING HEAD
 - 72.52 OTHER PARTIAL BREECH EXTRACTION
 - 72.53 TOTAL BREECH EXTRACTION WITH FORCEPS TO AFTERCOMING HEAD
 - 72.54 OTHER TOTAL BREECH EXTRACTION
- 72.6 FORCEPS APPLICATION TO AFTERCOMING HEAD
- 72.7 VACUUM EXTRACTION
 - 72.71 VACUUM EXTRACTION WITH EPISIOTOMY
 - 72.79 OTHER VACUUM EXTRACTION
- 72.8 OTHER SPECIFIED INSTRUMENTAL DELIVERY
- 72.9 UNSPECIFIED INSTRUMENTAL DELIVERY
- 73.0 ARTIFICIAL RUPTURE OF MEMBRANES
 - 73.01 INDUCTION OF LABOR BY ARTIFICIAL RUPTURE OF MEMBRANES
 - 73.09 OTHER ARTIFICIAL RUPTURE OF MEMBRANES
- 73.1 OTHER SURGICAL INDUCTION OF LABOR
- 73.2 INTERNAL AND COMBINED VERSION AND EXTRACTION
 - 73.21 INTERNAL AND COMBINED VERSION WITHOUT EXTRACTION
 - 73.22 INTERNAL AND COMBINED VERSION WITH EXTRACTION
- 73.3 FAILED FORCEPS
- 73.4 MEDICAL INDUCTION OF LABOR
- 73.5 MANUALLY ASSISTED DELIVERY
 - 73.51 MANUAL ROTATION OF FETAL HEAD
 - 73.59 OTHER MANUALLY ASSISTED DELIVERY
- 73.6 EPISIOTOMY
- 73.8 OPERATIONS ON FETUS TO FACILITATE DELIVERY
- 73.9 OTHER OPERATIONS ASSISTING DELIVERY
 - 73.91 EXTERNAL VERSION ASSISTING DELIVERY
 - 73.92 REPLACEMENT OF PROLAPSED UMBILICAL CORD
 - 73.93 INCISION OF CERVIX TO ASSIST DELIVERY
 - 73.94 PUBIOTOMY TO ASSIST DELIVERY
 - 73.99 OTHER OPERATIONS ASSISTING DELIVERY
- 74.0 CLASSICAL CESAREAN SECTION
 - 74.1 LOW CERVICAL CESAREAN SECTION
 - 74.2 EXTRAPERITONEAL CESAREAN SECTION

Appendix A

74.3	REMOVAL OF EXTRATUBAL ECTOPIC PREGNANCY
74.4	CESAREAN SECTION OF OTHER SPECIFIED TYPE
74.9	CESAREAN SECTION OF UNSPECIFIED TYPE
74.91	HYSTEROTOMY TO TERMINATE PREGNANCY
74.99	OTHER CESAREAN SECTION OF UNSPECIFIED TYPE
75.4	MANUAL REMOVAL OF RETAINED PLACENTA
75.5	REPAIR OF CURRENT OBSTETRIC LACERATION OF UTERUS
75.6	REPAIR OF OTHER CURRENT OBSTETRIC LACERATION
75.7	MANUAL EXPLORATION OF UTERINE CAVITY, POSTPARTUM
75.9	OTHER OBSTETRIC OPERATIONS

Appendix A

Dialysis codes

ESRD, defined as 2 codes (either inpatient or outpatient), separated by at least 30 days

Codes include:

- ICD9 prox codes:

39.95, Hemodialysis

54.98, Peritoneal dialysis

- ICD9 dx codes:

585.5x, Chronic kidney disease, Stage V (for ESRD with no mention of dialysis)

585.6x, End stage renal disease (for ESRD with dialysis)

V56.0x, encounter for dialysis NOS

V56.8x, encounter for peritoneal dialysis

V45.1x, renal dialysis status

- CPT4 codes:

90957, 90960, ESRD related services monthly, for patients 12-19 and 20 years of age and older; with 4 or more face-to-face physician visits per month

90958, 90961, ESRD related services monthly, for patients 12-19 and 20 years of age and older; with 2-3 face-to-face physician visits per month

90959, 90962, ESRD related services monthly, for patients 12-19 and 20 years of age and older; with 1 face-to-face physician visit per month

90920, 90921, ESRD related services per full month; for patients 12-19 and twenty years of age and over

90924, 90925, ESRD related services (less than full month), per day; for patients 12-19 and twenty years of age and over

90935, Hemodialysis procedure with single physician evaluation

90937, Hemodialysis procedure requiring repeated evaluation(s) with or without substantial revision of dialysis prescription

90945, Dialysis procedure other than hemodialysis (eg, peritoneal dialysis, hemofiltration, or other continuous renal replacement therapies), with single physician evaluation

90947, Dialysis procedure other than hemodialysis (eg, peritoneal dialysis, hemofiltration, or other continuous renal replacement therapies) requiring repeated physician evaluations, with or without substantial revision of dialysis prescription

90965, 90966, ESRD related services for home dialysis per full month, for patients 12-19 and 20 years of age and older

90969, 90970, ESRD related services for dialysis less than a full month of service, per day; for patients 12-19 and 20 years of age and older

90989, Dialysis training, patient, including helper where applicable, any mode, completed course

90993, Dialysis training, patient, including helper where applicable, any mode, course not completed, per training session

90999, Unlisted dialysis procedure, inpatient or outpatient

99512, Home visit for hemodialysis

- HCPCS codes:

G0257, Unscheduled or emergency dialysis treatment for ESRD patient in a hospital outpatient dept. that is not certified as an ESRD facility

G0314, G0317, ESRD related services during the course of treatment, for patients 12-19 and 20 yrs of age and over to include monitoring for the adequacy of nutrition, etc. w/4 or more physician visit per month

G0315, G0318, ESRD related services during the course of treatment, for patients 12-19 and 20 yrs of age and over to include monitoring for the adequacy of nutrition, etc. w/2 or 3 physician visit per month

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G0316, G0319, ESRD related services during the course of treatment, for patients 12-19 and 20 yrs of age and over to include monitoring for the adequacy of nutrition, etc. w/1 physician visit per month

G0322, G0323, ESRD related services for home dialysis patients per full month: for patients 12-19 and 20 yrs of age and over to include monitoring for adequacy of nutrition and etc.

G0326, G0327, ESRD related services for home dialysis (less than full month), per day; for patients 12-19 and 20 yrs of age and over

S9335, Home therapy, hemodialysis; administrative services, professional pharmacy services, care coordination, and all necessary supplies and equipment (drugs and nursing services coded separately), per diem

S9339, Home therapy, peritoneal dialysis, administrative services, care coordination and all necessary supplies and equipment, per diem

OR

Kidney transplant, defined as either 1 inpatient or 1 outpatient code

Codes include:

-ICD9 dx codes:

V42.0x, Kidney transplant status

996.81 Complications of transplanted kidney

-ICD9 prox codes:

55.6x, Transplant of kidney (Exclude 55.61)

- CPT4 codes:

50360, Renal allotransplantation, implantation, graft, w/o donor & recipient nephrectomy

50365, Renal allotransplantation, implantation, graft, w/ donor & recipient nephrectomy

Appendix B: Canagliflozin vs DPP4i

Optum

MarketScan

Medicare

BEFORE PS MATCHING

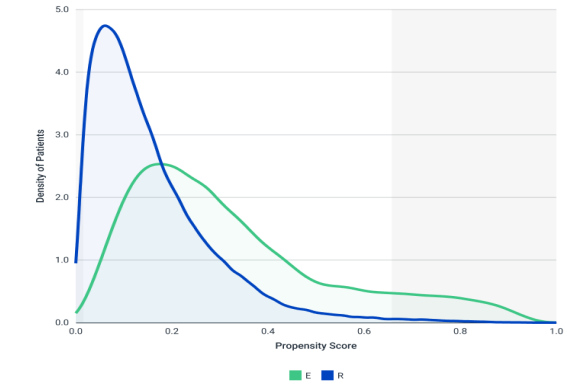


Figure 49: Pre-matching propensity score overlap

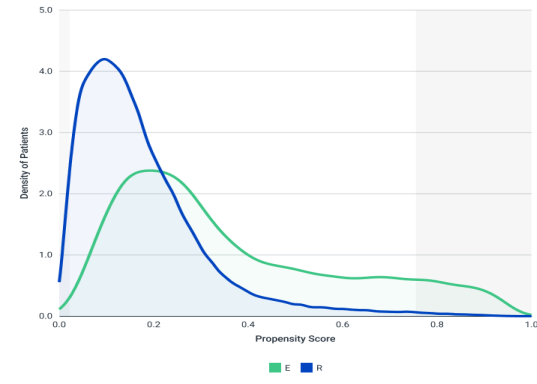


Figure 49: Pre-matching propensity score overlap

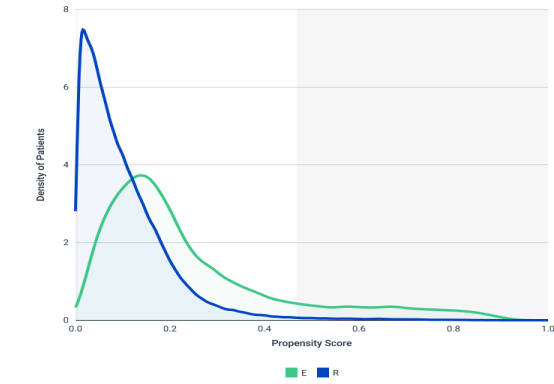


Figure 24: Pre-matching propensity score overlap

The c-statistics for the propensity score model, pre-matching was 0.769. The post-matching c-statistic was 0.523.

The c-statistics for the propensity score model, pre-matching was 0.769. The post-matching c-statistic was 0.521.

The c-statistics for the propensity score model, pre-matching was 0.773. The post-matching c-statistic was 0.519.

AFTER PS MATCHING

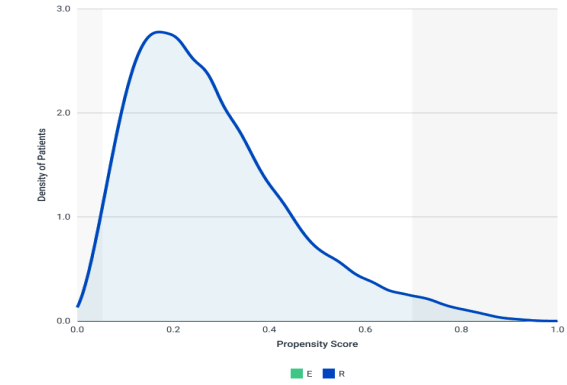


Figure 50: Post-matching propensity score overlap

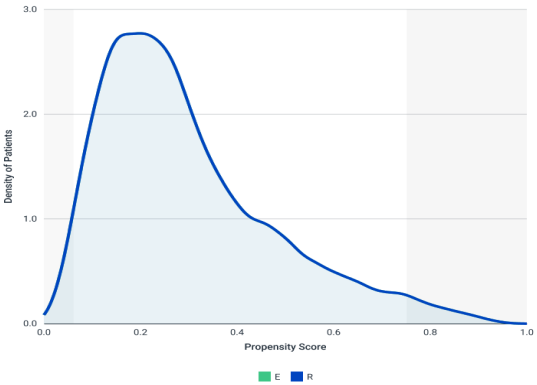


Figure 50: Post-matching propensity score overlap

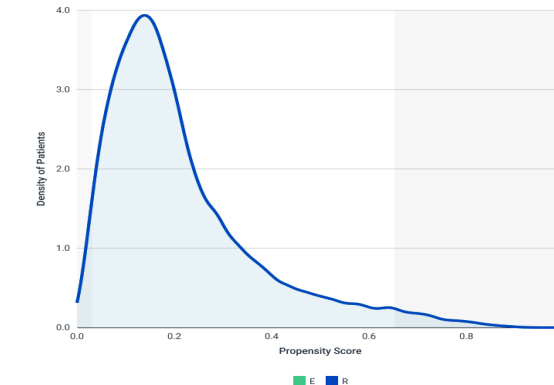


Figure 25: Post-matching propensity score overlap

Table 1

Unmatched									
Variable	Optum		MarketScan		Medicare		POOLED		St. Diff.
	Reference- DPP4i 92,973	Exposure- Canagliflozin 21,346	Reference- DPP4i 98,975	Exposure- Canagliflozin 26,910	Reference- DPP4i 258,794	Exposure- Canagliflozin 35,115	Reference- DPP4i 450,742	Exposure- Canagliflozin 83,371	
Number of patients									
Age									
...mean (sd)	67.55 (9.32)	62.19 (7.89)	62.13 (8.88)	59.26 (6.45)	73.88 (6.99)	70.94 (5.13)	69.99 (7.96)	64.93 (6.36)	0.70
...median [IQR]	68.00 [60.00, 74.00]	61.00 [56.00, 68.00]	61.00 [56.00, 66.00]	59.00 [54.00, 63.00]	72.00 [68.00, 78.00]	70.00 [67.00, 74.00]	68.76 (7.96)	64.15 (6.36)	0.64
Age categories									
...18 - 54; n (%)	9,311 (10.0%)	4,143 (19.4%)	19,542 (19.7%)	6,882 (25.6%)	0 (0.0%)	0 (0.0%)	28,853 (6.4%)	11,025 (13.2%)	-0.23
...55 - 64; n (%)	23,950 (25.8%)	9,021 (42.3%)	50,842 (51.4%)	15,706 (58.4%)	3,273 (1.3%)	396 (1.1%)	78,065 (17.3%)	25,123 (30.1%)	-0.30
...65 - 74; n (%)	38,089 (41.0%)	6,682 (31.3%)	17,664 (17.8%)	3,566 (13.3%)	152,505 (58.9%)	27,352 (77.9%)	208,258 (46.2%)	37,600 (45.1%)	0.02
...>= 75; n (%)	21,623 (23.3%)	1,500 (7.0%)	10,927 (11.0%)	756 (2.8%)	103,016 (39.8%)	7,367 (21.0%)	135,566 (30.1%)	9,623 (11.5%)	0.47
Gender									
...Males; n (%)	46,266 (49.8%)	12,127 (56.8%)	54,577 (55.1%)	15,161 (56.3%)	113,623 (43.9%)	18,052 (51.4%)	214,466 (47.6%)	45,340 (54.4%)	-0.14
...Females; n (%)	46,707 (50.2%)	9,219 (43.2%)	44,398 (44.9%)	11,749 (43.7%)	145,171 (56.1%)	17,063 (48.6%)	236,276 (52.4%)	38,031 (45.6%)	0.14
Race									
...White; n (%)	N/A	N/A	N/A	N/A	191,721 (74.1%)	28,985 (82.5%)	191,721 (74.1%)	28,985 (82.5%)	-0.20
...Black; n (%)	N/A	N/A	N/A	N/A	30,531 (11.8%)	2,789 (7.9%)	30,531 (11.8%)	2,789 (7.9%)	0.13
...Asian; n (%)	N/A	N/A	N/A	N/A	12,516 (4.8%)	906 (2.6%)	12,516 (4.8%)	906 (2.6%)	0.12
...Hispanic; n (%)	N/A	N/A	N/A	N/A	12,026 (4.6%)	951 (2.7%)	12,026 (4.6%)	951 (2.7%)	0.10
...North American Native; n (%)	N/A	N/A	N/A	N/A	1,608 (0.6%)	130 (0.4%)	1,608 (0.6%)	130 (0.4%)	0.03
...Other/Unknown; n (%)	N/A	N/A	N/A	N/A	10,392 (4.0%)	1,354 (3.9%)	10,392 (4.0%)	1,354 (3.9%)	0.01
Region (lumping missing&other category with West)									
...Northeast; n (%)	11,368 (12.2%)	1,714 (8.0%)	19,209 (19.4%)	4,647 (17.3%)	49,085 (19.0%)	5,891 (16.8%)	79,662 (17.7%)	12,252 (14.7%)	0.08
...South; n (%)	46,486 (50.0%)	11,429 (53.5%)	21,785 (22.0%)	4,977 (18.5%)	109,273 (42.2%)	15,802 (45.0%)	177,544 (39.4%)	32,208 (38.6%)	0.02
...Midwest; n (%)	16,955 (18.2%)	4,613 (21.6%)	46,018 (46.5%)	14,463 (53.7%)	55,845 (21.6%)	7,955 (22.7%)	118,818 (26.4%)	27,031 (32.4%)	-0.13
...West; n (%)	18,164 (19.5%)	3,590 (16.8%)	10,722 (10.8%)	2,533 (9.4%)	44,591 (17.2%)	5,467 (15.6%)	73,477 (16.3%)	11,590 (13.9%)	0.07
...Unknown+missing; n (%)	N/A	N/A	1,241 (1.3%)	290 (1.1%)	N/A	N/A	1,241 (1.3%)	290 (1.1%)	0.02
CV Covariates									
Ischemic heart disease; n (%)	17,210 (18.5%)	3,092 (14.5%)	13,876 (14.0%)	3,306 (12.3%)	67,253 (26.0%)	8,851 (25.2%)	98,339 (21.8%)	15,249 (18.3%)	0.09
Acute MI; n (%)	350 (0.4%)	57 (0.3%)	321 (0.3%)	68 (0.3%)	1,182 (0.5%)	123 (0.4%)	1,853 (0.4%)	248 (0.3%)	0.02
ACS/unstable angina; n (%)	438 (0.5%)	95 (0.4%)	398 (0.4%)	103 (0.4%)	1,445 (0.6%)	184 (0.5%)	2,281 (0.5%)	382 (0.5%)	0.00
Old MI; n (%)	2,139 (2.3%)	367 (1.7%)	995 (1.0%)	200 (0.7%)	7,156 (2.8%)	875 (2.5%)	10,290 (2.3%)	1,442 (1.7%)	0.04
Stable angina; n (%)	2,635 (2.8%)	432 (2.0%)	1,655 (1.7%)	351 (1.3%)	7,598 (2.9%)	989 (2.8%)	11,888 (2.6%)	1,772 (2.1%)	0.03
Coronary atherosclerosis and other forms of chronic ischemic heart disease; n (%)	16,133 (17.4%)	2,910 (13.6%)	13,142 (13.3%)	3,136 (11.7%)	64,446 (24.9%)	8,516 (24.3%)	93,721 (20.8%)	14,562 (17.5%)	0.08
Other atherosclerosis with ICD10 ; n (%)	595 (0.6%)	96 (0.4%)	566 (0.6%)	150 (0.6%)	3,406 (1.3%)	400 (1.1%)	4,567 (1.0%)	646 (0.8%)	0.02
Previous cardiac procedure (CABG or PTCA or Stent) ; n (%)	153 (0.2%)	27 (0.1%)	165 (0.2%)	38 (0.1%)	410 (0.2%)	70 (0.2%)	#VALUE!	135 (0.2%)	#VALUE!
History of CABG or PTCA; n (%)	3,786 (4.1%)	645 (3.0%)	1,733 (1.8%)	389 (1.4%)	16,353 (6.3%)	2,097 (6.0%)	21,872 (4.9%)	3,131 (3.8%)	0.05
Any stroke; n (%)	3,557 (3.8%)	526 (2.5%)	2,842 (2.9%)	511 (1.9%)	15,686 (6.1%)	1,822 (5.2%)	22,085 (4.9%)	2,859 (3.4%)	0.08
Ischemic stroke (w and w/o mention of cerebral infarction); n (%)	3,535 (3.8%)	524 (2.5%)	2,824 (2.9%)	508 (1.9%)	15,576 (6.0%)	1,817 (5.2%)	21,935 (4.9%)	2,849 (3.4%)	0.08
Hemorrhagic stroke; n (%)	40 (0.0%)	5 (0.0%)	30 (0.0%)	4 (0.0%)	**	**	**	**	**
TIA; n (%)	406 (0.4%)	63 (0.3%)	318 (0.3%)	55 (0.2%)	1,670 (0.6%)	173 (0.5%)	2,394 (0.5%)	291 (0.3%)	0.03
Other cerebrovascular disease; n (%)	974 (1.0%)	135 (0.6%)	632 (0.6%)	97 (0.4%)	4,269 (1.6%)	353 (1.0%)	5,875 (1.3%)	585 (0.7%)	0.06
Late effects of cerebrovascular disease; n (%)	950 (1.0%)	98 (0.5%)	398 (0.4%)	67 (0.2%)	3,602 (1.4%)	261 (0.7%)	4,950 (1.1%)	426 (0.5%)	0.07
Cerebrovascular procedure; n (%)	34 (0.0%)	7 (0.0%)	41 (0.0%)	4 (0.0%)	133 (0.1%)	18 (0.1%)	208 (0.0%)	29 (0.0%)	#DIV/0!
Heart failure (CHF); n (%)	6,529 (7.0%)	824 (3.9%)	3,776 (3.8%)	566 (2.1%)	25,130 (9.7%)	2,306 (6.6%)	35,435 (7.9%)	3,696 (4.4%)	0.15
Peripheral Vascular Disease (PVD) or PVD Surgery ; n (%)	6,053 (6.5%)	924 (4.3%)	3,642 (3.7%)	717 (2.7%)	25,306 (9.8%)	2,686 (7.6%)	35,001 (7.8%)	4,327 (5.2%)	0.11
Atrial fibrillation; n (%)	5,948 (6.4%)	916 (4.3%)	4,563 (4.6%)	792 (2.9%)	27,072 (10.5%)	3,013 (8.6%)	37,583 (8.3%)	4,721 (5.7%)	0.10
Other cardiac dysrhythmia; n (%)	7,501 (8.1%)	1,129 (5.3%)	5,013 (5.1%)	865 (3.2%)	29,407 (11.4%)	3,368 (9.6%)	41,921 (9.3%)	5,362 (6.4%)	0.11
Cardiac conduction disorders; n (%)	2,036 (2.2%)	285 (1.3%)	1,360 (1.4%)	246 (0.9%)	8,527 (3.3%)	956 (2.7%)	11,923 (2.6%)	1,487 (1.8%)	0.05
Other CVD; n (%)	8,272 (8.9%)	1,281 (6.0%)	6,502 (6.6%)	1,292 (4.8%)	33,542 (13.0%)	3,782 (10.8%)	48,316 (10.7%)	6,355 (7.6%)	0.11
Diabetes-related complications									
Diabetic retinopathy; n (%)	6,055 (6.5%)	1,287 (6.0%)	3,395 (3.4%)	1,172 (4.4%)	17,502 (6.8%)	2,693 (7.7%)	26,952 (6.0%)	5,152 (6.2%)	-0.01
Diabetes with other ophthalmic manifestations; n (%)	808 (0.9%)	139 (0.7%)	2,103 (2.1%)	739 (2.7%)	6,484 (2.5%)	992 (2.8%)	9,395 (2.1%)	1,870 (2.2%)	-0.01
Retinal detachment, vitreous hemorrhage, vitrectomy; n (%)	350 (0.4%)	80 (0.4%)	288 (0.3%)	77 (0.3%)	908 (0.4%)	149 (0.4%)	1,546 (0.3%)	306 (0.4%)	-0.02
Retinal laser coagulation therapy; n (%)	483 (0.5%)	122 (0.6%)	451 (0.5%)	148 (0.5%)	1,384 (0.5%)	225 (0.6%)	2,318 (0.5%)	495 (0.6%)	-0.01
Occurrence of Diabetic Neuropathy ; n (%)	16,540 (17.8%)	3,792 (17.8%)	9,680 (9.8%)	3,123 (11.6%)	44,854 (17.3%)	7,033 (20.0%)	71,074 (15.8%)	13,948 (16.7%)	-0.02

Table 1

Occurrence of diabetic nephropathy with ICD10 ; n (%)	15,236 (16.4%)	2,186 (10.2%)	6,571 (6.6%)	1,538 (5.7%)	28,980 (11.2%)	2,914 (8.3%)	50,787 (11.3%)	6,638 (8.0%)	0.11
Hypoglycemia ; n (%)	1,930 (2.1%)	459 (2.2%)	1,787 (1.8%)	678 (2.5%)	6,000 (2.3%)	829 (2.4%)	9,717 (2.2%)	1,966 (2.4%)	-0.01
Hyperglycemia; n (%)	3,471 (3.7%)	661 (3.1%)	2,989 (3.0%)	672 (2.5%)	10,518 (4.1%)	1,135 (3.2%)	16,978 (3.8%)	2,468 (3.0%)	0.04
Disorders of fluid electrolyte and acid-base balance; n (%)	5,638 (6.1%)	681 (3.2%)	3,600 (3.6%)	582 (2.2%)	18,043 (7.0%)	1,435 (4.1%)	27,281 (6.1%)	2,698 (3.2%)	0.14
Diabetic ketoacidosis; n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	000 (0.0%)	00 (0.0%)	#DIV/0!
Hyperosmolar hyperglycemic nonketotic syndrome (HONK); n (%)	460 (0.5%)	97 (0.5%)	402 (0.4%)	92 (0.3%)	1,230 (0.5%)	172 (0.5%)	2,092 (0.5%)	361 (0.4%)	0.01
Diabetes with peripheral circulatory disorders with ICD-10 ; n (%)	6,454 (6.9%)	1,015 (4.8%)	2,805 (2.8%)	698 (2.6%)	17,985 (6.9%)	2,091 (6.0%)	27,244 (6.0%)	3,804 (4.6%)	0.06
Diabetic Foot; n (%)	1,580 (1.7%)	286 (1.3%)	1,274 (1.3%)	345 (1.3%)	5,641 (2.2%)	715 (2.0%)	8,495 (1.9%)	1,346 (1.6%)	0.02
Gangrene ; n (%)	133 (0.1%)	20 (0.1%)	74 (0.1%)	10 (0.0%)	347 (0.1%)	28 (0.1%)	554 (0.1%)	58 (0.1%)	0.00
Lower extremity amputation; n (%)	492 (0.5%)	63 (0.3%)	134 (0.1%)	32 (0.1%)	1,170 (0.5%)	109 (0.3%)	1,796 (0.4%)	204 (0.2%)	0.04
Osteomyelitis; n (%)	356 (0.4%)	53 (0.2%)	266 (0.3%)	67 (0.2%)	910 (0.4%)	98 (0.3%)	1,532 (0.3%)	218 (0.3%)	0.00
Skin infections ; n (%)	4,261 (4.6%)	989 (4.6%)	4,253 (4.3%)	1,163 (4.3%)	14,883 (5.8%)	1,984 (5.7%)	23,397 (5.2%)	4,136 (5.0%)	0.01
Erectile dysfunction; n (%)	2,518 (2.7%)	767 (3.6%)	2,415 (2.4%)	759 (2.8%)	5,288 (2.0%)	1,093 (3.1%)	10,221 (2.3%)	2,619 (3.1%)	-0.05
Diabetes with unspecified complication; n (%)	4,841 (5.2%)	1,089 (5.1%)	4,301 (4.3%)	1,170 (4.3%)	12,495 (4.8%)	1,873 (5.3%)	21,637 (4.8%)	4,132 (5.0%)	-0.01
Diabetes mellitus without mention of complications; n (%)	79,354 (85.4%)	18,017 (84.4%)	90,348 (91.3%)	24,734 (91.9%)	239,419 (92.5%)	32,095 (91.4%)	409,121 (90.8%)	74,846 (89.8%)	0.03
Hypertension: 1 inpatient or 2 outpatient claims within 365 days; n (%)	86,092 (92.6%)	19,597 (91.8%)	85,616 (86.5%)	23,560 (87.6%)	247,659 (95.7%)	33,591 (95.7%)	419,367 (93.0%)	76,748 (92.1%)	0.03
Hyperlipidemia ; n (%)	69,860 (75.1%)	16,586 (77.7%)	70,415 (71.1%)	20,473 (76.1%)	205,187 (79.3%)	28,928 (82.4%)	345,462 (76.6%)	65,987 (79.1%)	-0.06
Edema; n (%)	5,759 (6.2%)	984 (4.6%)	3,668 (3.7%)	862 (3.2%)	22,340 (8.6%)	2,520 (7.2%)	31,767 (7.0%)	4,366 (5.2%)	0.08
Renal Dysfunction (non-diabetic) ; n (%)	20,147 (21.7%)	2,104 (9.9%)	10,409 (10.5%)	1,423 (5.3%)	56,908 (22.0%)	4,185 (11.9%)	87,464 (19.4%)	7,712 (9.3%)	0.29
Occurrence of acute renal disease ; n (%)	2,464 (2.7%)	173 (0.8%)	1,510 (1.5%)	132 (0.5%)	7,853 (3.0%)	371 (1.1%)	11,827 (2.6%)	676 (0.8%)	0.14
Occurrence of chronic renal insufficiency; n (%)	17,268 (18.6%)	1,743 (8.2%)	7,789 (7.9%)	1,056 (3.9%)	48,344 (18.7%)	3,461 (9.9%)	73,401 (16.3%)	6,260 (7.5%)	0.27
Chronic kidney disease ; n (%)	16,746 (18.0%)	1,620 (7.6%)	7,378 (7.5%)	898 (3.3%)	46,107 (17.8%)	3,184 (9.1%)	70,231 (15.6%)	5,702 (6.8%)	0.28
CKD Stage 3-4; n (%)	11,687 (12.6%)	834 (3.9%)	4,947 (5.0%)	451 (1.7%)	32,580 (12.6%)	1,859 (5.3%)	49,214 (10.9%)	3,144 (3.8%)	0.27
Occurrence of hypertensive nephropathy; n (%)	7,429 (8.0%)	682 (3.2%)	3,128 (3.2%)	368 (1.4%)	19,295 (7.5%)	1,185 (3.4%)	29,852 (6.6%)	2,235 (2.7%)	0.19
Occurrence of miscellaneous renal insufficiency ; n (%)	4,104 (4.4%)	422 (2.0%)	2,795 (2.8%)	398 (1.5%)	15,575 (6.0%)	1,163 (3.3%)	22,474 (5.0%)	1,983 (2.4%)	0.14
Glaucoma or cataracts ; n (%)	18,671 (20.1%)	3,608 (16.9%)	14,922 (15.1%)	3,666 (13.6%)	68,628 (26.5%)	9,616 (27.4%)	102,221 (22.7%)	16,890 (20.3%)	0.06
Cellulitis or abscess of toe; n (%)	1,051 (1.1%)	190 (0.9%)	740 (0.7%)	166 (0.6%)	3,049 (1.2%)	385 (1.1%)	4,840 (1.1%)	741 (0.9%)	0.02
Foot ulcer; n (%)	1,516 (1.6%)	268 (1.3%)	1,254 (1.3%)	347 (1.3%)	5,567 (2.2%)	708 (2.0%)	8,337 (1.8%)	1,323 (1.4%)	0.02
Bladder stones; n (%)	99 (0.1%)	12 (0.1%)	86 (0.1%)	12 (0.0%)	343 (0.1%)	50 (0.1%)	528 (0.1%)	74 (0.1%)	0.00
Kidney stones; n (%)	1,802 (1.9%)	330 (1.5%)	1,911 (1.9%)	471 (1.8%)	5,922 (2.3%)	763 (2.2%)	9,635 (2.1%)	1,564 (1.9%)	0.01
Urinary tract infections (UTIs); n (%)	7,598 (8.2%)	1,041 (4.9%)	5,074 (5.1%)	1,047 (3.9%)	30,499 (11.8%)	2,805 (8.0%)	43,171 (9.6%)	4,893 (5.9%)	0.14
Dipstick urinalysis; n (%)	33,076 (35.6%)	6,473 (30.3%)	30,675 (31.0%)	8,063 (30.0%)	99,731 (38.5%)	12,329 (35.1%)	163,482 (36.3%)	26,865 (32.2%)	0.09
Non-dipstick urinalysis; n (%)	41,645 (44.8%)	9,752 (45.7%)	36,404 (36.8%)	11,482 (42.7%)	111,191 (43.0%)	16,168 (46.0%)	189,240 (42.0%)	37,402 (44.9%)	-0.06
Urine function test; n (%)	1,859 (2.0%)	275 (1.3%)	1,802 (1.8%)	345 (1.3%)	7,703 (3.0%)	906 (2.6%)	11,364 (2.5%)	1,526 (1.8%)	0.05
Cytology; n (%)	537 (0.6%)	88 (0.4%)	639 (0.6%)	126 (0.5%)	2,033 (0.8%)	220 (0.6%)	3,209 (0.7%)	434 (0.5%)	0.03
Cystos; n (%)	820 (0.9%)	135 (0.6%)	855 (0.9%)	185 (0.7%)	2,921 (1.1%)	335 (1.0%)	4,596 (1.0%)	655 (0.8%)	0.02
Other Covariates									
Liver disease; n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	#VALUE!	000 (0.0%)	#VALUE!
Osteoarthritis; n (%)	11,742 (12.6%)	2,168 (10.2%)	7,946 (8.0%)	1,907 (7.1%)	45,826 (17.7%)	5,609 (16.0%)	65,514 (14.5%)	9,684 (11.6%)	0.09
Other arthritis, arthropathies and musculoskeletal pain; n (%)	27,439 (29.5%)	5,725 (26.8%)	24,107 (24.4%)	6,419 (23.9%)	94,733 (36.6%)	11,953 (34.0%)	146,279 (32.5%)	24,097 (28.9%)	0.08
Dorsopathies; n (%)	16,535 (17.8%)	3,757 (17.6%)	14,621 (14.8%)	4,093 (15.2%)	55,400 (21.4%)	7,711 (22.0%)	86,556 (19.2%)	15,561 (18.7%)	0.01
Fractures; n (%)	2,037 (2.2%)	322 (1.5%)	1,777 (1.8%)	385 (1.4%)	7,550 (2.9%)	772 (2.2%)	11,364 (2.5%)	1,479 (1.8%)	0.05
Falls ; n (%)	2,630 (2.8%)	343 (1.6%)	955 (1.0%)	136 (0.5%)	9,355 (3.6%)	716 (2.0%)	12,940 (2.9%)	1,195 (1.4%)	0.10
Osteoporosis; n (%)	4,528 (4.9%)	507 (2.4%)	1,890 (1.9%)	297 (1.1%)	19,484 (7.5%)	1,793 (5.1%)	25,902 (5.7%)	2,597 (3.1%)	0.13
Hyperthyroidism; n (%)	607 (0.7%)	115 (0.5%)	493 (0.5%)	105 (0.4%)	2,277 (0.9%)	255 (0.7%)	3,377 (0.7%)	475 (0.6%)	0.01
Hypothyroidism ; n (%)	14,093 (15.2%)	3,015 (14.1%)	11,014 (11.1%)	3,225 (12.0%)	31,705 (12.3%)	4,238 (12.1%)	56,812 (12.6%)	10,478 (12.6%)	0.00
Other disorders of thyroid gland ; n (%)	3,204 (3.4%)	782 (3.7%)	2,893 (2.9%)	984 (3.7%)	9,716 (3.8%)	1,454 (4.1%)	15,813 (3.5%)	3,220 (3.9%)	-0.02
Depression; n (%)	6,370 (6.9%)	1,494 (7.0%)	5,344 (5.4%)	1,597 (5.9%)	22,933 (8.9%)	2,897 (8.3%)	34,647 (7.7%)	5,988 (7.2%)	0.02
Anxiety; n (%)	6,068 (6.5%)	1,357 (6.4%)	4,637 (4.7%)	1,230 (4.6%)	18,829 (7.3%)	2,345 (6.7%)	29,534 (6.6%)	4,932 (5.9%)	0.03
Sleep_Disorder; n (%)	4,861 (5.2%)	1,601 (7.5%)	7,480 (7.6%)	3,032 (11.3%)	16,931 (6.5%)	2,968 (8.5%)	29,272 (6.5%)	7,601 (9.1%)	-0.10
Dementia; n (%)	3,192 (3.4%)	200 (0.9%)	1,443 (1.5%)	119 (0.4%)	16,772 (6.5%)	910 (2.6%)	21,407 (4.7%)	1,229 (1.5%)	0.19
Delirium; n (%)	725 (0.8%)	57 (0.3%)	410 (0.4%)	31 (0.1%)	3,458 (1.3%)	182 (0.5%)	4,593 (1.0%)	270 (0.3%)	0.09
Psychosis; n (%)	831 (0.9%)	88 (0.4%)	440 (0.4%)	52 (0.2%)	4,373 (1.7%)	258 (0.7%)	5,644 (1.3%)	398 (0.5%)	0.08
Obesity; n (%)	18,832 (20.3%)	5,799 (27.2%)	14,581 (14.7%)	5,276 (19.6%)	34,677 (13.4%)	6,927 (19.7%)	68,090 (15.1%)	18,002 (21.6%)	-0.17
Overweight; n (%)	5,629 (6.1%)	1,083 (5.1%)	2,441 (2.5%)	593 (2.2%)	9,232 (3.6%)	1,237 (3.5%)	17,302 (3.8%)	2,913 (3.5%)	0.02
Smoking; n (%)	8,487 (9.1%)	1,743 (8.2%)	5,746 (5.8%)	1,323 (4.9%)	28,073 (10.8%)	3,758 (10.7%)	42,306 (9.4%)	6,824 (8.2%)	0.04
Alcohol abuse or dependence; n (%)	16 (0.0%)	2 (0.0%)	22 (0.0%)	5 (0.0%)	**	**	**	**	**
Drug abuse or dependence; n (%)	41 (0.0%)	7 (0.0%)	13 (0.0%)	3 (0.0%)	**	**	**	**	**
COPD; n (%)	6,608 (7.1%)	1,038 (4.9%)	3,790 (3.8%)	766 (2.8%)	23,441 (9.1%)	2,714 (7.7%)	33,839 (7.5%)	4,518 (5.4%)	0.09

Table 1

Asthma; n (%)	4,366 (4.7%)	934 (4.4%)	3,552 (3.6%)	957 (3.6%)	13,189 (5.1%)	1,815 (5.2%)	21,107 (4.7%)	3,706 (4.4%)	0.01
Obstructive sleep apnea; n (%)	7,604 (8.2%)	2,530 (11.9%)	8,904 (9.0%)	3,255 (12.1%)	15,485 (6.0%)	3,345 (9.5%)	31,993 (7.1%)	9,130 (11.0%)	-0.14
Pneumonia; n (%)	1,613 (1.7%)	234 (1.1%)	1,356 (1.4%)	241 (0.9%)	6,178 (2.4%)	541 (1.5%)	9,147 (2.0%)	1,016 (1.2%)	0.06
Imaging; n (%)	34 (0.0%)	6 (0.0%)	21 (0.0%)	2 (0.0%)	**	**	**	**	**
Diabetes Medications									
DM Medications - AGIs; n (%)	513 (0.6%)	116 (0.5%)	358 (0.4%)	99 (0.4%)	1,637 (0.6%)	273 (0.8%)	2,508 (0.6%)	488 (0.6%)	0.00
DM Medications - Glitazones; n (%)	7,470 (8.0%)	2,132 (10.0%)	7,539 (7.6%)	2,659 (9.9%)	20,110 (7.8%)	3,517 (10.0%)	35,119 (7.8%)	8,308 (10.0%)	-0.08
DM Medications - Insulin; n (%)	15,209 (16.4%)	5,869 (27.5%)	13,275 (13.4%)	8,133 (30.2%)	44,262 (17.1%)	11,188 (31.9%)	72,746 (16.1%)	25,190 (30.2%)	-0.34
DM Medications - Meglitinides; n (%)	1,069 (1.1%)	220 (1.0%)	346 (1.3%)	346 (1.3%)	4,683 (1.8%)	576 (1.6%)	6,970 (1.5%)	1,142 (1.4%)	0.01
DM Medications - Metformin; n (%)	68,898 (74.1%)	16,690 (78.2%)	78,748 (79.6%)	21,017 (78.1%)	181,431 (70.1%)	26,156 (74.5%)	329,077 (73.0%)	63,863 (76.6%)	-0.08
Concomitant initiation or current use of 2nd Generation SUs; n (%)	33,158 (35.7%)	6,949 (32.6%)	31,388 (31.7%)	8,362 (31.1%)	97,534 (37.7%)	13,082 (37.3%)	162,080 (36.0%)	28,393 (34.1%)	0.04
Concomitant initiation or current use of AGIs; n (%)	378 (0.4%)	82 (0.4%)	250 (0.3%)	54 (0.2%)	1,197 (0.5%)	180 (0.5%)	1,825 (0.4%)	316 (0.4%)	0.00
Concomitant initiation or current use of Glitazones; n (%)	5,771 (6.2%)	1,613 (7.6%)	5,925 (6.0%)	2,013 (7.5%)	15,535 (6.0%)	2,693 (7.7%)	27,231 (6.0%)	6,319 (7.6%)	-0.06
Concomitant initiation or current use of GLP-1 RA; n (%)	1,826 (2.0%)	2,913 (13.6%)	2,187 (2.2%)	4,565 (17.0%)	3,172 (1.2%)	4,049 (11.5%)	7,185 (1.6%)	11,527 (13.8%)	-0.47
Concomitant initiation or current use of Insulin; n (%)	11,555 (12.4%)	4,411 (20.7%)	10,019 (10.1%)	6,296 (23.4%)	34,079 (13.2%)	8,819 (25.1%)	55,653 (12.3%)	19,526 (23.4%)	-0.29
Concomitant initiation or current use of Meglitinides; n (%)	786 (0.8%)	142 (0.7%)	875 (0.9%)	222 (0.8%)	3,410 (1.3%)	402 (1.1%)	5,071 (1.1%)	766 (0.9%)	0.02
Concomitant initiation or current use of Metformin; n (%)	59,526 (64.0%)	14,098 (66.0%)	69,344 (70.1%)	17,788 (66.1%)	156,339 (60.4%)	22,344 (63.6%)	285,209 (63.3%)	54,230 (65.0%)	-0.04
Past use of 2nd Generation SUs; n (%)	6,990 (7.5%)	1,805 (8.5%)	7,050 (7.1%)	2,003 (7.4%)	19,774 (7.6%)	2,765 (7.9%)	33,814 (7.5%)	6,573 (7.9%)	-0.02
Past use of AGIs; n (%)	135 (0.1%)	34 (0.2%)	108 (0.1%)	45 (0.2%)	440 (0.2%)	93 (0.3%)	683 (0.2%)	172 (0.2%)	0.00
Past use of Glitazones; n (%)	1,699 (1.8%)	519 (2.4%)	1,614 (1.6%)	646 (2.4%)	4,575 (1.8%)	824 (2.3%)	7,888 (1.8%)	1,989 (2.4%)	-0.04
Past use of GLP-1 RA; n (%)	1,513 (1.6%)	1,248 (5.8%)	1,750 (1.8%)	1,865 (6.9%)	2,968 (1.1%)	1,792 (5.1%)	6,231 (1.4%)	4,905 (5.9%)	-0.24
Past use of Insulin; n (%)	3,654 (3.9%)	1,458 (6.8%)	3,257 (3.3%)	1,837 (6.8%)	10,185 (3.9%)	2,370 (6.7%)	17,096 (3.8%)	5,665 (6.8%)	-0.13
Past use of Meglitinides; n (%)	283 (0.3%)	78 (0.4%)	343 (0.3%)	124 (0.5%)	1,273 (0.5%)	174 (0.5%)	1,899 (0.4%)	376 (0.5%)	-0.01
Past use of metformin (final); n (%)	9,372 (10.1%)	2,592 (12.1%)	9,405 (9.5%)	3,229 (12.0%)	25,092 (9.7%)	3,812 (10.9%)	43,869 (9.7%)	9,633 (11.6%)	-0.06
Other Medications									
Use of ACE inhibitors; n (%)	48,661 (52.3%)	11,586 (54.3%)	52,091 (52.6%)	14,264 (53.0%)	126,600 (48.9%)	17,572 (50.0%)	227,352 (50.4%)	43,422 (52.1%)	-0.03
Use of ARBs; n (%)	33,271 (35.8%)	7,711 (36.1%)	35,863 (36.2%)	10,233 (38.0%)	92,288 (35.7%)	13,134 (37.4%)	161,422 (35.8%)	31,078 (37.3%)	-0.03
Use of Loop Diuretics; n (%)	11,784 (12.7%)	1,942 (9.1%)	9,018 (9.1%)	2,198 (8.2%)	47,353 (18.3%)	5,440 (15.5%)	68,155 (15.1%)	9,580 (11.5%)	0.11
Use of other diuretics; n (%)	2,738 (2.9%)	549 (2.6%)	2,657 (2.7%)	689 (2.6%)	9,268 (3.6%)	1,194 (3.4%)	14,663 (3.3%)	2,432 (2.9%)	0.02
Use of nitrates-United; n (%)	4,319 (4.6%)	759 (3.6%)	3,623 (3.7%)	874 (3.2%)	18,544 (7.2%)	2,233 (6.4%)	26,486 (5.9%)	3,866 (4.6%)	0.06
Use of other hypertension drugs; n (%)	7,149 (7.7%)	1,137 (5.3%)	5,872 (5.9%)	1,298 (4.8%)	22,836 (8.8%)	2,590 (7.4%)	35,857 (8.0%)	5,025 (6.0%)	0.08
Use of digoxin; n (%)	1,454 (1.6%)	242 (1.1%)	1,364 (1.4%)	236 (0.9%)	7,836 (3.0%)	768 (2.2%)	10,654 (2.4%)	1,246 (1.5%)	0.07
Use of Anti-arrhythmics; n (%)	1,053 (1.1%)	173 (0.8%)	1,025 (1.0%)	190 (0.7%)	4,813 (1.9%)	503 (1.4%)	6,891 (1.5%)	866 (1.0%)	0.05
Use of COPD/asthma meds; n (%)	13,032 (14.0%)	2,801 (13.1%)	13,214 (13.4%)	3,735 (13.9%)	41,359 (16.0%)	5,761 (16.4%)	67,605 (15.0%)	12,297 (14.7%)	0.01
Use of statins; n (%)	67,725 (72.8%)	15,590 (73.0%)	67,262 (68.0%)	18,843 (70.0%)	190,375 (73.6%)	26,610 (75.8%)	325,362 (72.2%)	61,043 (73.2%)	-0.02
Use of other lipid-lowering drugs; n (%)	10,744 (11.6%)	2,824 (13.2%)	13,362 (13.5%)	4,298 (16.0%)	33,537 (13.0%)	5,264 (15.0%)	57,643 (12.8%)	12,386 (14.9%)	-0.06
Use of antiplatelet agents; n (%)	10,807 (11.6%)	2,095 (9.8%)	11,015 (11.1%)	2,709 (10.1%)	37,758 (14.6%)	4,884 (13.9%)	59,580 (13.2%)	9,688 (11.6%)	0.05
Use of oral anticoagulants (Dabigatran, Rivaroxaban, Apixaban, Warfarin); n (%)	5,410 (5.8%)	923 (4.3%)	4,601 (4.6%)	893 (3.3%)	23,012 (8.9%)	2,738 (7.8%)	33,023 (7.3%)	4,554 (5.5%)	0.07
Use of heparin and other low-molecular weight heparins; n (%)	194 (0.2%)	21 (0.1%)	8 (0.0%)	0 (0.0%)	578 (0.2%)	66 (0.2%)	780 (0.2%)	087 (0.1%)	0.03
Use of NSAIDs; n (%)	13,827 (14.9%)	3,495 (16.4%)	15,098 (15.3%)	4,443 (16.5%)	39,001 (15.1%)	5,385 (15.3%)	67,926 (15.1%)	13,323 (16.0%)	-0.02
Use of oral corticosteroids; n (%)	11,453 (12.3%)	2,456 (11.5%)	11,415 (11.5%)	2,993 (11.1%)	36,129 (14.0%)	4,819 (13.7%)	58,997 (13.1%)	10,268 (12.3%)	0.02
Use of bisphosphonate (United); n (%)	2,381 (2.6%)	240 (1.1%)	1,015 (1.0%)	162 (0.6%)	9,128 (3.5%)	777 (2.2%)	12,524 (2.8%)	1,179 (1.4%)	0.10
Use of opioids; n (%)	17,277 (18.6%)	4,109 (19.2%)	18,342 (18.5%)	5,363 (19.9%)	51,367 (19.8%)	7,046 (20.1%)	86,986 (19.3%)	16,518 (19.8%)	-0.01
Use of antidepressants; n (%)	19,561 (21.0%)	4,900 (23.0%)	18,887 (19.1%)	6,026 (22.4%)	59,621 (23.0%)	8,616 (24.5%)	98,069 (21.8%)	19,542 (23.4%)	-0.04
Use of antipsychotics; n (%)	1,969 (2.1%)	365 (1.7%)	1,327 (1.3%)	303 (1.1%)	7,692 (3.0%)	698 (2.0%)	10,988 (2.4%)	1,366 (1.6%)	0.06
Use of anticonvulsants; n (%)	13,269 (14.3%)	2,952 (13.8%)	9,838 (9.9%)	3,006 (11.2%)	38,618 (14.9%)	5,337 (15.2%)	61,725 (13.7%)	11,295 (13.5%)	0.01
Use of lithium; n (%)	105 (0.1%)	21 (0.1%)	107 (0.1%)	20 (0.1%)	245 (0.1%)	29 (0.1%)	457 (0.1%)	070 (0.1%)	0.00
Use of Benzos; n (%)	8,001 (8.6%)	1,860 (8.7%)	7,927 (8.0%)	2,274 (8.5%)	26,120 (10.1%)	3,388 (9.6%)	42,048 (9.3%)	7,522 (9.0%)	0.01
Use of anxiolytics/hypnotics; n (%)	4,283 (4.6%)	1,109 (5.2%)	5,008 (5.1%)	1,439 (5.3%)	13,252 (5.1%)	1,813 (5.2%)	22,543 (5.0%)	4,361 (5.2%)	-0.01
Use of dementia meds; n (%)	2,138 (2.3%)	130 (0.6%)	1,145 (1.2%)	84 (0.3%)	12,186 (4.7%)	724 (2.1%)	15,469 (3.4%)	938 (1.1%)	0.16
Use of antiparkinsonian meds; n (%)	1,865 (2.0%)	401 (1.9%)	1,487 (1.5%)	438 (1.6%)	7,223 (2.8%)	996 (2.8%)	10,575 (2.3%)	1,835 (2.2%)	0.01
Any use of pramlintide; n (%)	6 (0.0%)	27 (0.1%)	14 (0.0%)	51 (0.2%)	26 (0.0%)	36 (0.1%)	046 (0.0%)	114 (0.1%)	-0.04
Any use of 1st generation sulfonylureas; n (%)	6 (0.0%)	0 (0.0%)	11 (0.0%)	0 (0.0%)	**	**	**	**	**
Entresto (sacubitril/valsartan); n (%)	133 (0.1%)	14 (0.1%)	40 (0.0%)	4 (0.0%)	153 (0.1%)	13 (0.0%)	326 (0.1%)	031 (0.0%)	0.00
Initiation as monotherapy; n (%)	8,025 (8.6%)	1,196 (5.6%)	8,499 (8.6%)	1,307 (4.9%)	19,281 (7.5%)	1,217 (3.5%)	35,805 (7.9%)	3,720 (4.5%)	0.14
Labs									
Lab values- HbA1c (%); n (%)	39,394 (42.4%)	9,243 (43.3%)	6,873 (6.9%)	1,671 (6.2%)	N/A	N/A	46,267 (24.1%)	10,914 (22.6%)	0.04
Lab values- HbA1c (%) (within 3 months); n (%)	31,798 (34.2%)	7,578 (35.5%)	5,566 (5.6%)	1,424 (5.3%)	N/A	N/A	37,364 (19.5%)	9,002 (18.7%)	0.02
Lab values- HbA1c (%) (within 6 months); n (%)	39,394 (42.4%)	9,243 (43.3%)	6,873 (6.9%)	1,671 (6.2%)	N/A	N/A	46,267 (24.1%)	10,914 (22.6%)	0.04

Table 1

Lab values- BNP; n (%)	754 (0.8%)	133 (0.6%)	105 (0.1%)	4 (0.0%)	N/A	N/A	859 (0.4%)	137 (0.3%)	0.02
Lab values- BNP (within 3 months); n (%)	469 (0.5%)	82 (0.4%)	73 (0.1%)	3 (0.0%)	N/A	N/A	542 (0.3%)	085 (0.2%)	0.02
Lab values- BNP (within 6 months); n (%)	754 (0.8%)	133 (0.6%)	105 (0.1%)	4 (0.0%)	N/A	N/A	859 (0.4%)	137 (0.3%)	0.02
Lab values- BUN (mg/dl); n (%)	39,324 (42.3%)	9,039 (42.3%)	6,660 (6.7%)	1,583 (5.9%)	N/A	N/A	45,984 (24.0%)	10,622 (22.0%)	0.05
Lab values- BUN (mg/dl) (within 3 months); n (%)	31,041 (33.4%)	7,235 (33.9%)	5,215 (5.3%)	1,301 (4.8%)	N/A	N/A	36,256 (18.9%)	8,536 (17.7%)	0.03
Lab values- BUN (mg/dl) (within 6 months); n (%)	39,324 (42.3%)	9,039 (42.3%)	6,660 (6.7%)	1,583 (5.9%)	N/A	N/A	45,984 (24.0%)	10,622 (22.0%)	0.05
Lab values- Creatinine (mg/dl); n (%)	40,379 (43.4%)	9,338 (43.7%)	7,075 (7.1%)	1,722 (6.4%)	N/A	N/A	47,454 (24.7%)	11,060 (22.9%)	0.04
Lab values- Creatinine (mg/dl) (within 3 months); n (%)	31,911 (34.3%)	7,473 (35.0%)	5,555 (5.6%)	1,428 (5.3%)	N/A	N/A	37,466 (19.5%)	8,901 (18.4%)	0.03
Lab values- Creatinine (mg/dl) (within 6 months); n (%)	40,379 (43.4%)	9,338 (43.7%)	7,075 (7.1%)	1,722 (6.4%)	N/A	N/A	47,454 (24.7%)	11,060 (22.9%)	0.04
Lab values- HDL level (mg/dl); n (%)	33,867 (36.4%)	8,008 (37.5%)	6,271 (6.3%)	1,528 (5.7%)	N/A	N/A	40,138 (20.9%)	9,536 (19.8%)	0.03
Lab values- HDL level (mg/dl) (within 3 months); n (%)	25,297 (27.2%)	6,107 (28.6%)	4,752 (4.8%)	1,206 (4.5%)	N/A	N/A	30,049 (15.7%)	7,313 (15.2%)	0.01
Lab values- HDL level (mg/dl) (within 6 months); n (%)	33,867 (36.4%)	8,008 (37.5%)	6,271 (6.3%)	1,528 (5.7%)	N/A	N/A	40,138 (20.9%)	9,536 (19.8%)	0.03
Lab values- LDL level (mg/dl); n (%)	34,910 (37.5%)	8,251 (38.7%)	6,464 (6.5%)	1,555 (5.8%)	N/A	N/A	41,374 (21.6%)	9,806 (20.3%)	0.03
Lab values- LDL level (mg/dl) (within 3 months); n (%)	26,067 (28.0%)	6,315 (29.6%)	4,889 (4.9%)	1,231 (4.6%)	N/A	N/A	30,956 (16.1%)	7,546 (15.6%)	0.01
Lab values- LDL level (mg/dl) (within 6 months); n (%)	34,910 (37.5%)	8,251 (38.7%)	6,464 (6.5%)	1,555 (5.8%)	N/A	N/A	41,374 (21.6%)	9,806 (20.3%)	0.03
Lab values- NT-proBNP; n (%)	109 (0.1%)	12 (0.1%)	17 (0.0%)	0 (0.0%)	N/A	N/A	126 (0.1%)	12 (0.0%)	0.04
Lab values- NT-proBNP (within 3 months); n (%)	65 (0.1%)	7 (0.0%)	12 (0.0%)	0 (0.0%)	N/A	N/A	77 (0.0%)	7 (0.0%)	-
Lab values- NT-proBNP (within 6 months); n (%)	109 (0.1%)	12 (0.1%)	17 (0.0%)	0 (0.0%)	N/A	N/A	126 (0.1%)	12 (0.0%)	-
Lab values- Total cholesterol (mg/dl); n (%)	34,343 (36.9%)	8,172 (38.3%)	6,281 (6.3%)	1,541 (5.7%)	N/A	N/A	40,624 (21.2%)	9,713 (20.1%)	0.03
Lab values- Total cholesterol (mg/dl) (within 3 months); n (%)	25,693 (27.6%)	6,257 (29.3%)	4,760 (4.8%)	1,222 (4.5%)	N/A	N/A	30,453 (15.9%)	7,479 (15.5%)	0.01
Lab values- Total cholesterol (mg/dl) (within 6 months); n (%)	34,343 (36.9%)	8,172 (38.3%)	6,281 (6.3%)	1,541 (5.7%)	N/A	N/A	40,624 (21.2%)	9,713 (20.1%)	0.03
Lab values- Triglyceride level (mg/dl); n (%)	34,067 (36.6%)	8,123 (38.1%)	6,220 (6.3%)	1,515 (5.6%)	N/A	N/A	40,287 (21.0%)	9,638 (20.0%)	0.02
Lab values- Triglyceride level (mg/dl) (within 3 months); n (%)	25,487 (27.4%)	6,217 (29.1%)	4,718 (4.8%)	1,205 (4.5%)	N/A	N/A	30,205 (15.7%)	7,422 (15.4%)	0.01
Lab values- Triglyceride level (mg/dl) (within 6 months); n (%)	34,067 (36.6%)	8,123 (38.1%)	6,220 (6.3%)	1,515 (5.6%)	N/A	N/A	40,287 (21.0%)	9,638 (20.0%)	0.02
Lab result number- HbA1c (%) mean (only 2 to 20 included)	39,196	9,185	6,611	1,615	N/A	N/A	45,807	10,800	
...mean (sd)	8.25 (1.74)	8.63 (1.75)	8.43 (1.84)	8.63 (1.70)	N/A	N/A	8.28 (1.75)	8.63 (1.74)	-0.20
...median [IQR]	7.90 [7.10, 9.10]	8.30 [7.40, 9.60]	8.00 [7.10, 9.30]	8.30 [7.40, 9.60]	N/A	N/A	7.91 (1.75)	8.30 (1.74)	-0.22
...Missing; n (%)	53,777 (57.8%)	12,161 (57.0%)	92,364 (93.3%)	25,295 (94.0%)	N/A	N/A	146,141 (76.1%)	37,456 (77.6%)	-0.04
Lab result number- BNP mean	754	133	105	4	N/A	N/A	859	137	
...mean (sd)	155.94 (289.65)	91.38 (156.35)	3,194.66 (27,330.33)	335.38 (447.47)	N/A	N/A	527.38 (9530.18)	98.50 (169.01)	0.06
...median [IQR]	66.30 [28.18, 168.20]	42.60 [19.25, 88.20]	103.50 [36.75, 363.17]	192.50 [4.25, 809.38]	N/A	N/A	#VALUE!	46.98 (169.01)	#VALUE!
...Missing; n (%)	92,219 (99.2%)	21,213 (99.4%)	98,870 (99.9%)	26,906 (100.0%)	N/A	N/A	191,089 (99.6%)	48,119 (99.7%)	-0.02
Lab result number- BUN (mg/dl) mean	39,324	9,039	6,660	1,583	N/A	N/A	45,984	10,622	
...mean (sd)	18.81 (7.90)	16.88 (5.75)	870.71 (12,029.05)	2,719.95 (20,223.13)	N/A	N/A	142.19 (4577.70)	419.72 (7805.66)	-0.04
...median [IQR]	17.00 [14.00, 22.00]	16.00 [13.00, 19.50]	16.00 [13.00, 20.00]	16.00 [13.00, 20.00]	N/A	N/A	#VALUE!	#VALUE!	#VALUE!
...Missing; n (%)	53,649 (57.7%)	12,307 (57.7%)	92,315 (93.3%)	25,327 (94.1%)	N/A	N/A	145,964 (76.0%)	37,634 (78.0%)	-0.05
Lab result number- Creatinine (mg/dl) mean (only 0.1 to 15 included)	40,096	9,267	6,197	1,566	N/A	N/A	46,293	10,833	
...mean (sd)	1.04 (0.39)	0.92 (0.24)	1.00 (0.38)	0.93 (0.23)	N/A	N/A	1.03 (0.39)	0.92 (0.24)	0.34
...median [IQR]	0.96 [0.79, 1.19]	0.89 [0.75, 1.04]	0.95 [0.79, 1.09]	0.90 [0.77, 1.05]	N/A	N/A	0.96 (0.39)	0.89 (0.24)	0.22
...Missing; n (%)	52,877 (56.9%)	12,079 (56.6%)	92,778 (93.7%)	25,344 (94.2%)	N/A	N/A	145,655 (75.9%)	37,423 (77.6%)	-0.04
Lab result number- HDL level (mg/dl) mean (only <=5000 included)	33,867	8,008	6,237	1,506	N/A	N/A	40,104	9,514	
...mean (sd)	46.39 (13.51)	44.61 (12.78)	44.36 (39.28)	42.76 (13.63)	N/A	N/A	46.07 (19.85)	44.32 (12.92)	0.10
...median [IQR]	44.00 [37.00, 53.50]	43.00 [36.00, 52.00]	43.00 [35.50, 52.00]	42.00 [35.00, 50.00]	N/A	N/A	43.84 (19.85)	42.84 (12.92)	0.06
...Missing; n (%)	59,106 (63.6%)	13,338 (62.5%)	92,738 (93.7%)	25,404 (94.4%)	N/A	N/A	151,844 (79.1%)	38,742 (80.3%)	-0.03
Lab result number- LDL level (mg/dl) mean (only <=5000 included)	34,168	8,115	5,889	1,378	N/A	N/A	40,057	9,493	
...mean (sd)	85.70 (38.18)	83.53 (38.95)	87.52 (42.90)	85.68 (40.86)	N/A	N/A	85.97 (38.91)	83.84 (39.23)	0.05
...median [IQR]	83.00 [62.00, 107.00]	81.50 [60.50, 105.00]	86.00 [64.00, 112.00]	85.00 [62.00, 109.00]	N/A	N/A	83.44 (38.91)	82.01 (39.23)	0.04
...Missing; n (%)	58,805 (63.2%)	13,231 (62.0%)	93,086 (94.1%)	25,532 (94.9%)	N/A	N/A	151,891 (79.1%)	38,763 (80.3%)	-0.03
Lab result number- Total cholesterol (mg/dl) mean (only <=5000 included)	34,315	8,162	6,246	1,518	N/A	N/A	40,561	9,680	
...mean (sd)	171.23 (44.49)	171.77 (46.18)	171.78 (54.30)	171.14 (48.01)	N/A	N/A	171.31 (46.14)	171.67 (46.47)	-0.01
...median [IQR]	165.00 [141.00, 195.00]	166.00 [141.00, 195.00]	169.29 [143.50, 200.00]	169.00 [143.00, 196.00]	N/A	N/A	165.66 (46.14)	166.47 (46.47)	-0.02
...Missing; n (%)	58,658 (63.1%)	13,184 (61.8%)	92,729 (93.7%)	25,392 (94.4%)	N/A	N/A	151,387 (78.9%)	38,576 (79.9%)	-0.02

Table 1

Lab result number- Triglyceride level (mg/dl) mean (only ≤5000 included)	34,065	8,121	6,184	1,493	N/A	N/A	40,249	9,614	
...mean (sd)	181.59 (137.93)	200.66 (176.08)	183.77 (164.61)	203.24 (187.27)	N/A	N/A	181.92 (142.36)	201.06 (177.87)	-0.12
...median [IQR]	151.00 [108.00, 214.00]	161.00 [114.00, 232.00]	148.00 [103.00, 217.50]	162.50 [112.00, 237.00]	N/A	N/A	150.54 (142.36)	161.23 (177.87)	-0.07
...Missing; n (%)	58,908 (63.4%)	13,225 (62.0%)	92,791 (93.8%)	25,417 (94.5%)	N/A	N/A	151,699 (79.0%)	38,642 (80.1%)	-0.03
Lab result number- Hemoglobin mean (only >0 included)	27,271	5,946	4,588	1,015	N/A	N/A	31,859	6,961	
...mean (sd)	13.46 (1.61)	14.01 (1.56)	12,956.08 (338,258.30)	2,982.84 (19,853.45)	N/A	N/A	1877.32 (128356.31)	446.90 (7579.01)	0.02
...median [IQR]	13.50 [12.40, 14.60]	14.05 [12.90, 15.05]	13.60 [12.50, 14.75]	14.00 [12.90, 15.00]	N/A	N/A	#VALUE!	#VALUE!	#VALUE!
...Missing; n (%)	65,702 (70.7%)	15,400 (72.1%)	94,387 (95.4%)	25,895 (96.2%)	N/A	N/A	160,089 (83.4%)	41,295 (85.6%)	-0.06
Lab result number- Serum sodium mean (only >90 and <190 included)	39,270	9,104	6,401	1,563	N/A	N/A	45,671	10,667	
...mean (sd)	139.43 (2.75)	139.23 (2.68)	138.97 (2.59)	138.92 (2.40)	N/A	N/A	139.37 (2.73)	139.18 (2.64)	0.07
...median [IQR]	139.50 [138.00, 141.00]	139.00 [138.00, 141.00]	139.00 [137.00, 141.00]	139.00 [137.50, 140.25]	N/A	N/A	139.43 (2.73)	139.00 (2.64)	0.16
...Missing; n (%)	53,703 (57.8%)	12,242 (57.4%)	92,574 (93.5%)	25,347 (94.2%)	N/A	N/A	146,277 (76.2%)	37,589 (77.9%)	-0.04
Lab result number- Albumin mean (only >0 and ≤10 included)	36,671	8,549	5,603	1,329	N/A	N/A	42,274	9,878	
...mean (sd)	4.26 (0.31)	4.30 (0.30)	4.09 (0.76)	4.16 (0.66)	N/A	N/A	4.24 (0.40)	4.28 (0.37)	-0.10
...median [IQR]	4.30 [4.10, 4.50]	4.30 [4.10, 4.50]	4.20 [4.00, 4.40]	4.25 [4.00, 4.50]	N/A	N/A	4.29 (0.40)	4.29 (0.37)	0.00
...Missing; n (%)	56,302 (60.6%)	12,797 (60.0%)	93,372 (94.3%)	25,581 (95.1%)	N/A	N/A	149,674 (78.0%)	38,378 (79.5%)	-0.04
Lab result number- Glucose (fasting or random) mean (only 10-1000 included)	39,234	9,095	6,390	1,544	N/A	N/A	45,624	10,639	
...mean (sd)	173.67 (69.39)	181.41 (70.12)	179.40 (72.02)	180.71 (67.24)	N/A	N/A	174.47 (69.77)	181.31 (69.71)	-0.10
...median [IQR]	158.00 [126.67, 203.00]	166.50 [132.00, 216.00]	162.00 [130.00, 211.50]	167.00 [133.00, 216.00]	N/A	N/A	158.56 (69.77)	166.57 (69.71)	-0.11
...Missing; n (%)	53,739 (57.8%)	12,251 (57.4%)	92,585 (93.5%)	25,366 (94.3%)	N/A	N/A	146,324 (76.2%)	37,617 (78.0%)	-0.04
Lab result number- Potassium mean (only 1-7 included)	40,119	9,278	6,414	1,521	N/A	N/A	46,533	10,799	
...mean (sd)	4.47 (0.44)	4.45 (0.41)	4.33 (0.46)	4.36 (0.43)	N/A	N/A	4.45 (0.44)	4.44 (0.41)	0.02
...median [IQR]	4.45 [4.20, 4.70]	4.40 [4.20, 4.70]	4.30 [4.00, 4.60]	4.37 [4.10, 4.60]	N/A	N/A	4.43 (0.44)	4.40 (0.41)	0.07
...Missing; n (%)	52,854 (56.8%)	12,068 (56.5%)	92,561 (93.5%)	25,389 (94.3%)	N/A	N/A	145,415 (75.8%)	37,457 (77.6%)	-0.04
Comorbidity Scores									
CCI (180 days)- ICD9 and ICD10									
...mean (sd)	2.56 (1.72)	2.09 (1.29)	1.87 (1.28)	1.67 (0.99)	2.72 (1.83)	2.35 (1.49)	2.50 (1.70)	2.06 (1.30)	0.29
...median [IQR]	2.00 [1.00, 3.00]	2.00 [1.00, 2.00]	1.00 [1.00, 2.00]	1.00 [1.00, 2.00]	2.00 [1.00, 4.00]	2.00 [1.00, 3.00]	1.78 (1.70)	1.68 (1.30)	0.07
Frailty Score: Qualitative Version 365 days as Categories, v1									
...0; n (%)	57,374 (61.7%)	14,082 (66.0%)	54,311 (54.9%)	14,474 (53.8%)	105,245 (40.7%)	16,251 (46.3%)	216,930 (48.1%)	44,807 (53.7%)	-0.11
...1 to 2; n (%)	26,259 (28.2%)	5,640 (26.4%)	34,281 (34.6%)	10,034 (37.3%)	92,632 (35.8%)	12,243 (34.9%)	153,172 (34.0%)	27,917 (33.5%)	0.01
...3 or more; n (%)	9,340 (10.0%)	1,624 (7.6%)	10,383 (10.5%)	2,402 (8.9%)	60,917 (23.5%)	6,621 (18.9%)	80,640 (17.9%)	10,647 (12.8%)	0.14
Frailty Score: Empirical Version 365 days as Categories,									
...< 0.12908; n (%)	25,893 (27.9%)	7,492 (35.1%)	29,844 (30.2%)	8,892 (33.0%)	33,014 (12.8%)	5,571 (15.9%)	88,751 (19.7%)	21,955 (26.3%)	-0.16
...0.12908 - 0.1631167; n (%)	32,822 (35.3%)	8,051 (37.7%)	37,569 (38.0%)	10,669 (39.6%)	72,707 (28.1%)	11,082 (31.6%)	143,098 (31.7%)	29,802 (35.7%)	-0.08
...>= 0.1631167; n (%)	34,258 (36.8%)	5,803 (27.2%)	31,562 (31.9%)	7,349 (27.3%)	153,073 (59.1%)	18,462 (52.6%)	218,893 (48.6%)	31,614 (37.9%)	0.22
Non-Frailty; n (%)	54,232 (58.3%)	12,377 (58.0%)	51,769 (52.3%)	14,430 (53.6%)	12,308 (4.8%)	1,622 (4.6%)	118,309 (26.2%)	28,429 (34.1%)	-0.17
Frailty Score (mean): Qualitative Version 365 days, v1									
...mean (sd)	0.79 (1.40)	0.64 (1.17)	0.88 (1.36)	0.83 (1.20)	1.54 (1.93)	1.25 (1.64)	1.24 (1.72)	0.96 (1.40)	0.18
...median [IQR]	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	1.00 [0.00, 2.00]	1.00 [0.00, 2.00]	0.57 (1.72)	0.42 (1.40)	0.10
Frailty Score (mean): Empirical Version 365 days,									
...mean (sd)	0.16 (0.05)	0.15 (0.04)	0.15 (0.04)	0.14 (0.04)	0.19 (0.06)	0.18 (0.05)	0.18 (0.05)	0.16 (0.04)	0.44
...median [IQR]	0.15 [0.13, 0.18]	0.14 [0.12, 0.17]	0.14 [0.12, 0.17]	0.14 [0.12, 0.16]	0.17 [0.15, 0.22]	0.17 [0.14, 0.20]	0.16 (0.05)	0.15 (0.04)	0.22
Healthcare Utilization									
Any hospitalization; n (%)	4,363 (4.7%)	515 (2.4%)	4,045 (4.1%)	559 (2.1%)	17,460 (6.7%)	1,265 (3.6%)	25,868 (5.7%)	2,339 (2.8%)	0.14
Any hospitalization within prior 30 days; n (%)	1,461 (1.6%)	85 (0.4%)	1,226 (1.2%)	80 (0.3%)	5,637 (2.2%)	209 (0.6%)	8,324 (1.8%)	374 (0.4%)	0.13
Any hospitalization during prior 31-180 days; n (%)	3,101 (3.3%)	434 (2.0%)	2,913 (2.9%)	482 (1.8%)	12,641 (4.9%)	1,083 (3.1%)	18,655 (4.1%)	1,999 (2.4%)	0.10
Endocrinologist Visit; n (%)	8,305 (8.9%)	3,857 (18.1%)	8,479 (8.6%)	5,166 (19.2%)	28,751 (11.1%)	6,793 (19.3%)	45,535 (10.1%)	15,816 (19.0%)	-0.25
Endocrinologist Visit (30 days prior); n (%)	5,443 (5.9%)	2,835 (13.3%)	5,738 (5.8%)	4,064 (15.1%)	18,611 (7.2%)	4,820 (13.7%)	29,792 (6.6%)	11,719 (14.1%)	-0.25
Endocrinologist Visit (31 to 180 days prior); n (%)	5,625 (6.1%)	2,733 (12.8%)	5,578 (5.6%)	3,673 (13.6%)	20,367 (7.9%)	5,233 (14.9%)	31,570 (7.0%)	11,639 (14.0%)	-0.23
Internal medicine/family medicine visits; n (%)	77,583 (83.4%)	15,326 (71.8%)	87,485 (88.4%)	23,433 (87.1%)	213,115 (82.3%)	28,985 (82.5%)	378,183 (83.9%)	67,744 (81.3%)	0.07
Internal medicine/family medicine visits (30 days prior); n (%)	59,224 (63.7%)	11,193 (52.4%)	66,816 (67.5%)	17,732 (65.9%)	155,670 (60.2%)	21,013 (59.8%)	281,710 (62.5%)	49,938 (59.9%)	0.05
Internal medicine/family medicine visits (31 to 180 days prior); n (%)	66,924 (72.0%)	13,192 (61.8%)	71,698 (72.4%)	19,673 (73.1%)	184,082 (71.1%)	25,511 (72.6%)	322,704 (71.6%)	58,376 (70.0%)	0.04
Cardiologist visit; n (%)	22,028 (23.7%)	4,060 (19.0%)	17,523 (17.7%)	4,413 (16.4%)	79,665 (30.8%)	9,926 (28.3%)	119,216 (26.4%)	18,399 (22.1%)	0.10
Number of Cardiologist visits (30 days prior); n (%)	7,462 (8.0%)	1,253 (5.9%)	5,922 (6.0%)	1,343 (5.0%)	27,234 (10.5%)	3,020 (8.6%)	40,618 (9.0%)	5,616 (6.7%)	0.09

Table 1

Number of Cardiologist visits (31 to 180 days prior); n (%)	18,520 (19.9%)	3,452 (16.2%)	14,636 (14.8%)	3,739 (13.9%)	68,179 (26.3%)	8,616 (24.5%)	101,335 (22.5%)	15,807 (19.0%)	0.09
Electrocardiogram ; n (%)	25,313 (27.2%)	4,791 (22.4%)	25,662 (25.9%)	6,067 (22.5%)	80,490 (31.1%)	9,794 (27.9%)	131,465 (29.2%)	20,652 (24.8%)	0.10
Use of glucose test strips; n (%)	3,407 (3.7%)	762 (3.6%)	3,506 (3.5%)	1,117 (4.2%)	8,264 (3.2%)	1,086 (3.1%)	15,177 (3.4%)	2,965 (3.6%)	-0.01
Dialysis; n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	000 (0.0%)	000 (0.0%)	#DIV/0!
Naive new user v8 ; n (%)	13,385 (14.4%)	1,888 (8.8%)	14,612 (14.8%)	1,995 (7.4%)	32,045 (12.4%)	1,925 (5.5%)	60,042 (13.3%)	5,808 (7.0%)	0.21
N antidiabetic drugs at index date									
...mean (sd)	2.23 (0.81)	2.42 (0.92)	2.23 (0.79)	2.46 (0.96)	2.21 (0.81)	2.47 (0.91)	2.22 (0.81)	2.45 (0.93)	-0.26
...median [IQR]	2.00 [2.00, 3.00]	2.00 [2.00, 3.00]	2.00 [2.00, 3.00]	2.00 [2.00, 3.00]	2.00 [2.00, 3.00]	2.00 [2.00, 3.00]	2.00 (0.81)	2.00 (0.93)	0.00
number of different/distinct medication prescriptions									
...mean (sd)	10.02 (4.35)	10.15 (4.34)	9.12 (4.01)	10.05 (4.19)	9.97 (4.17)	10.43 (4.16)	9.79 (4.17)	10.24 (4.22)	-0.11
...median [IQR]	9.00 [7.00, 12.00]	9.00 [7.00, 12.00]	8.00 [6.00, 11.00]	9.00 [7.00, 12.00]	9.00 [7.00, 12.00]	10.00 [8.00, 13.00]	8.78 (4.17)	9.42 (4.22)	-0.15
Number of Hospitalizations									
...mean (sd)	0.05 (0.26)	0.03 (0.17)	0.04 (0.23)	0.02 (0.16)	0.08 (0.33)	0.04 (0.22)	0.07 (0.30)	0.03 (0.19)	0.16
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 (0.30)	0.00 (0.19)	0.00
Number of hospital days									
...mean (sd)	0.29 (2.21)	0.12 (0.98)	0.23 (1.60)	0.10 (0.85)	0.49 (2.90)	0.21 (1.65)	0.39 (2.53)	0.15 (1.28)	0.12
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 (2.53)	0.00 (1.28)	0.00
Number of Emergency Department (ED) visits									
...mean (sd)	0.31 (0.96)	0.21 (0.75)	0.09 (0.93)	0.05 (0.78)	0.42 (1.19)	0.29 (1.02)	0.32 (1.09)	0.19 (0.88)	0.13
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 (1.09)	0.00 (0.88)	0.00
Number of Office visits									
...mean (sd)	4.32 (3.26)	4.23 (3.02)	4.09 (3.12)	4.26 (3.12)	4.81 (3.63)	4.99 (3.51)	4.55 (3.45)	4.56 (3.27)	0.00
...median [IQR]	4.00 [2.00, 6.00]	3.00 [2.00, 6.00]	3.00 [2.00, 5.00]	3.00 [2.00, 5.00]	4.00 [2.00, 6.00]	4.00 [3.00, 7.00]	3.78 (3.45)	3.42 (3.27)	0.11
Number of Endocrinologist visits									
...mean (sd)	0.40 (2.04)	0.96 (3.30)	0.38 (1.98)	1.03 (3.44)	0.61 (2.93)	1.26 (4.60)	0.52 (2.58)	1.11 (3.94)	-0.18
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 (2.58)	0.00 (3.94)	0.00
Number of internal medicine/family medicine visits									
...mean (sd)	8.97 (12.35)	6.96 (10.66)	6.59 (7.92)	6.45 (7.85)	7.38 (9.52)	7.56 (9.83)	7.53 (9.86)	7.05 (9.47)	0.05
...median [IQR]	5.00 [2.00, 12.00]	4.00 [0.00, 9.00]	4.00 [2.00, 9.00]	4.00 [2.00, 9.00]	4.00 [2.00, 10.00]	5.00 [1.00, 10.00]	4.21 (9.86)	4.42 (9.47)	-0.02
Number of Cardiologist visits									
...mean (sd)	1.01 (2.94)	0.76 (2.48)	0.70 (2.37)	0.62 (2.13)	1.49 (3.91)	1.33 (3.64)	1.22 (3.43)	0.95 (2.94)	0.08
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	0.00 (3.43)	0.00 (2.94)	0.00
Number electrocardiograms received									
...mean (sd)	0.47 (1.08)	0.35 (0.85)	0.42 (0.97)	0.34 (0.79)	0.57 (1.17)	0.48 (1.04)	0.52 (1.11)	0.40 (0.92)	0.12
...median [IQR]	0.00 [0.00, 1.00]	0.00 [0.00, 0.00]	0.00 [0.00, 1.00]	0.00 [0.00, 0.00]	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	0.00 (1.11)	0.00 (0.92)	0.00
Number of HbA1c tests ordered									
...mean (sd)	1.32 (0.89)	1.37 (0.87)	1.08 (0.87)	1.30 (0.87)	1.43 (0.84)	1.57 (0.81)	1.33 (0.86)	1.43 (0.85)	-0.12
...median [IQR]	1.00 [1.00, 2.00]	1.00 [1.00, 2.00]	1.00 [0.00, 2.00]	1.00 [1.00, 2.00]	1.00 [1.00, 2.00]	2.00 [1.00, 2.00]	1.00 (0.86)	1.42 (0.85)	-0.49
Number of glucose tests ordered									
...mean (sd)	0.55 (3.99)	0.43 (1.17)	0.35 (1.05)	0.42 (1.12)	0.42 (1.04)	0.45 (1.08)	0.43 (2.04)	0.44 (1.12)	-0.01
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 (2.04)	0.00 (1.12)	0.00
Number of lipid tests ordered									
...mean (sd)	1.03 (0.93)	1.06 (0.95)	0.91 (1.21)	1.08 (1.23)	1.03 (0.81)	1.11 (0.82)	1.00 (0.94)	1.09 (1.00)	-0.09
...median [IQR]	1.00 [0.00, 1.00]	1.00 [0.00, 2.00]	1.00 [0.00, 1.00]	1.00 [0.00, 2.00]	1.00 [0.00, 1.00]	1.00 [1.00, 2.00]	1.00 (0.94)	1.00 (1.00)	0.00
Number of creatinine tests ordered									
...mean (sd)	0.04 (0.28)	0.03 (0.22)	0.04 (0.26)	0.04 (0.24)	0.07 (0.32)	0.07 (0.33)	0.06 (0.30)	0.05 (0.28)	0.03
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 (0.30)	0.00 (0.28)	0.00
Number of BUN tests ordered									
...mean (sd)	0.03 (0.22)	0.02 (0.17)	0.03 (0.21)	0.02 (0.18)	0.04 (0.26)	0.04 (0.26)	0.04 (0.24)	0.03 (0.22)	0.04
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 (0.24)	0.00 (0.22)	0.00
Number of tests for microalbuminuria									
...mean (sd)	0.85 (1.20)	0.84 (1.16)	0.64 (1.04)	0.76 (1.11)	0.50 (0.72)	0.53 (0.72)	0.60 (0.91)	0.68 (0.98)	-0.08
...median [IQR]	0.00 [0.00, 2.00]	0.00 [0.00, 2.00]	0.00 [0.00, 1.00]	0.00 [0.00, 2.00]	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	0.00 (0.91)	0.00 (0.98)	0.00
Total N distinct ICD9/ICD10 diagnoses at the 3rd digit level									
...mean (sd)	6.16 (6.85)	5.46 (5.86)	2.67 (4.07)	2.01 (3.26)	5.84 (7.61)	5.73 (6.80)	5.21 (6.82)	4.46 (5.63)	0.12
...median [IQR]	5.00 [0.00, 9.00]	5.00 [0.00, 8.00]	0.00 [0.00, 4.00]	0.00 [0.00, 4.00]	4.00 [0.00, 9.00]	4.00 [0.00, 9.00]	3.33 (6.82)	2.96 (5.63)	0.06
Use of thiazide; n (%)	13,054 (14.0%)	2,752 (12.9%)	12,759 (12.9%)	3,416 (12.7%)	39,231 (15.2%)	5,305 (15.1%)	65,044 (14.4%)	11,473 (13.8%)	0.02
Use of beta blockers; n (%)	39,244 (42.2%)	7,904 (37.0%)	37,716 (38.1%)	9,582 (35.6%)	131,430 (50.8%)	17,160 (48.9%)	208,390 (46.2%)	34,646 (41.6%)	0.09
Use of calcium channel blockers; n (%)	32,362 (34.8%)	6,181 (29.0%)	31,378 (31.7%)	7,884 (29.3%)	97,784 (37.8%)	11,964 (34.1%)	161,524 (35.8%)	26,029 (31.2%)	0.10

Table 1

P5-matched									
	Optum		MarketScan		Medicare		POOLED		
Variable	Reference- DPP4I 19532	Exposure- Canagliflozin 19532	Reference- DPP4I 23168	Exposure- Canagliflozin 23168	Reference- DPP4I 33401	Exposure- Canagliflozin 33401	Reference- DPP4I 76,101	Exposure- Canagliflozin 76,101	St. Diff.
Number of patients									
Age									
...mean (sd)	62.47 (8.28)	62.59 (7.93)	59.39 (7.08)	59.50 (6.58)	71.02 (5.32)	71.06 (5.19)	65.28 (6.73)	65.37 (6.41)	-0.01
...median [IQR]	62.00 [55.00, 68.00]	62.00 [56.00, 68.00]	58.00 [54.00, 63.00]	59.00 [55.00, 63.00]	70.00 [67.00, 74.00]	70.00 [67.00, 74.00]	64.29 (6.73)	64.60 (6.41)	-0.05
Age categories									
...18 - 54; n (%)	4,084 (20.9%)	3,519 (18.0%)	6,340 (27.4%)	5,719 (24.7%)	0 (0.0%)	0 (0.0%)	10,424 (13.7%)	9,238 (12.1%)	0.05
...55 - 64; n (%)	7,394 (37.9%)	8,104 (41.5%)	12,899 (55.7%)	13,461 (58.1%)	424 (1.3%)	370 (1.1%)	20,717 (27.2%)	21,935 (28.8%)	-0.04
...65 - 74; n (%)	6,444 (33.0%)	6,418 (32.9%)	2,941 (12.7%)	3,259 (14.1%)	25,613 (76.7%)	25,764 (77.1%)	34,998 (46.0%)	35,441 (46.6%)	-0.01
...≥ 75; n (%)	1,610 (8.2%)	1,491 (7.6%)	988 (4.3%)	729 (3.1%)	7,364 (22.0%)	7,267 (21.8%)	9,962 (13.1%)	9,487 (12.5%)	0.02
Gender									
...Males; n (%)	10,959 (56.1%)	10,973 (56.2%)	12,925 (55.8%)	12,966 (56.0%)	16,977 (50.8%)	17,007 (50.9%)	40,861 (53.7%)	40,946 (53.8%)	0.00
...Females; n (%)	8,573 (43.9%)	8,559 (43.8%)	10,243 (44.2%)	10,202 (44.0%)	16,424 (49.2%)	16,394 (49.1%)	35,240 (46.3%)	35,155 (46.2%)	0.00
Race									
...White; n (%)	N/A	N/A	N/A	N/A	27,463 (82.2%)	27,436 (82.1%)	27,463 (82.2%)	27,436 (82.1%)	0.00
...Black; n (%)	N/A	N/A	N/A	N/A	2,664 (8.0%)	2,721 (8.1%)	2,664 (8.0%)	2,721 (8.1%)	0.00
...Asian; n (%)	N/A	N/A	N/A	N/A	905 (2.7%)	893 (2.7%)	905 (2.7%)	893 (2.7%)	0.00
...Hispanic; n (%)	N/A	N/A	N/A	N/A	970 (2.9%)	935 (2.8%)	970 (2.9%)	935 (2.8%)	0.01
...North American Native; n (%)	N/A	N/A	N/A	N/A	118 (0.4%)	125 (0.4%)	118 (0.4%)	125 (0.4%)	0.00
...Other/Unknown; n (%)	N/A	N/A	N/A	N/A	1,281 (3.8%)	1,291 (3.9%)	1,281 (3.8%)	1,291 (3.9%)	-0.01
Region (lumping missing&other category with West)									
...Northeast; n (%)	1,586 (8.1%)	1,623 (8.3%)	3,890 (16.8%)	3,981 (17.2%)	5,552 (16.6%)	5,609 (16.8%)	11,028 (14.5%)	11,213 (14.7%)	-0.01
...South; n (%)	10,537 (53.9%)	10,459 (53.5%)	4,391 (19.0%)	4,343 (18.7%)	15,091 (45.2%)	15,024 (45.0%)	30,019 (39.4%)	29,826 (39.2%)	0.00
...Midwest; n (%)	4,118 (21.1%)	4,140 (21.2%)	12,382 (53.4%)	12,389 (53.5%)	7,584 (22.7%)	7,572 (22.7%)	24,084 (31.6%)	24,101 (31.7%)	0.00
...West; n (%)	3,291 (16.8%)	3,310 (16.9%)	2,258 (9.7%)	2,209 (9.5%)	5,174 (15.5%)	5,196 (15.6%)	10,723 (14.1%)	10,715 (14.1%)	0.00
...Unknown+missing; n (%)	N/A	N/A	247 (1.1%)	246 (1.1%)	N/A	N/A	247 (1.1%)	246 (1.1%)	0.00
CV Covariates									
Ischemic heart disease; n (%)	2,850 (14.6%)	2,863 (14.7%)	2,777 (12.0%)	2,846 (12.3%)	8,538 (25.6%)	8,401 (25.2%)	14,165 (18.6%)	14,110 (18.5%)	0.00
Acute MI; n (%)	49 (0.3%)	53 (0.3%)	65 (0.3%)	60 (0.3%)	116 (0.3%)	118 (0.4%)	230 (0.3%)	231 (0.3%)	0.00
ACS/unstable angina; n (%)	93 (0.5%)	87 (0.4%)	96 (0.4%)	86 (0.4%)	170 (0.5%)	172 (0.5%)	359 (0.5%)	345 (0.5%)	0.00
Old MI; n (%)	334 (1.7%)	331 (1.7%)	194 (0.8%)	182 (0.8%)	855 (2.6%)	839 (2.5%)	1,383 (1.8%)	1,352 (1.8%)	0.00
Stable angina; n (%)	402 (2.1%)	407 (2.1%)	311 (1.3%)	310 (1.3%)	988 (3.0%)	954 (2.9%)	1,701 (2.2%)	1,671 (2.2%)	0.00
Coronary atherosclerosis and other forms of chronic ischemic heart disease; n (%)	2,663 (13.6%)	2,698 (13.8%)	2,638 (11.4%)	2,695 (11.6%)	8,217 (24.6%)	8,074 (24.2%)	13,518 (17.8%)	13,467 (17.7%)	0.00
Other atherosclerosis with ICD10 ; n (%)	88 (0.5%)	85 (0.4%)	113 (0.5%)	130 (0.6%)	339 (1.0%)	384 (1.1%)	540 (0.7%)	599 (0.8%)	-0.01
Previous cardiac procedure (CABG or PTCA or Stent) ; n (%)	25 (0.1%)	25 (0.1%)	37 (0.2%)	32 (0.1%)	40 (0.1%)	67 (0.2%)	102 (0.1%)	124 (0.2%)	-0.03
History of CABG or PTCA; n (%)	596 (3.1%)	600 (3.1%)	352 (1.5%)	340 (1.5%)	2,019 (6.0%)	1,992 (6.0%)	2,967 (3.9%)	2,932 (3.9%)	0.00
Any stroke; n (%)	462 (2.4%)	489 (2.5%)	450 (1.9%)	451 (1.9%)	1,806 (5.4%)	1,754 (5.3%)	2,718 (3.6%)	2,694 (3.5%)	0.01
Ischemic stroke (w and w/o mention of cerebral infarction); n (%)	460 (2.4%)	487 (2.5%)	448 (1.9%)	448 (1.9%)	1,798 (5.4%)	1,749 (5.2%)	2,706 (3.6%)	2,684 (3.5%)	0.01
Hemorrhagic stroke; n (%)	4 (0.0%)	5 (0.0%)	3 (0.0%)	4 (0.0%)	**	**	**	**	**
TIA; n (%)	48 (0.2%)	59 (0.3%)	46 (0.2%)	50 (0.2%)	171 (0.5%)	170 (0.5%)	265 (0.3%)	279 (0.4%)	-0.02
Other cerebrovascular disease; n (%)	138 (0.7%)	130 (0.7%)	95 (0.4%)	90 (0.4%)	349 (1.0%)	341 (1.0%)	582 (0.8%)	561 (0.7%)	0.01
Late effects of cerebrovascular disease; n (%)	100 (0.5%)	92 (0.5%)	62 (0.3%)	61 (0.3%)	271 (0.8%)	255 (0.8%)	433 (0.6%)	408 (0.5%)	0.01
Cerebrovascular procedure; n (%)	3 (0.0%)	6 (0.0%)	6 (0.0%)	3 (0.0%)	13 (0.0%)	17 (0.1%)	022 (0.0%)	026 (0.0%)	#DIV/0!
Heart failure (CHF); n (%)	756 (3.9%)	780 (4.0%)	482 (2.1%)	496 (2.1%)	2,270 (6.8%)	2,224 (6.7%)	3,508 (4.6%)	3,500 (4.6%)	0.00
Peripheral Vascular Disease (PVD) or PVD Surgery ; n (%)	858 (4.4%)	863 (4.4%)	590 (2.5%)	615 (2.7%)	2,598 (7.8%)	2,579 (7.7%)	4,046 (5.3%)	4,057 (5.3%)	0.00
Atrial fibrillation; n (%)	854 (4.4%)	843 (4.3%)	704 (3.0%)	711 (3.1%)	2,914 (8.7%)	2,860 (8.6%)	4,472 (5.9%)	4,414 (5.8%)	0.00
Other cardiac dysrhythmia; n (%)	1,067 (5.5%)	1,057 (5.4%)	794 (3.4%)	788 (3.4%)	3,293 (9.9%)	3,214 (9.6%)	5,154 (6.8%)	5,059 (6.6%)	0.01
Cardiac conduction disorders; n (%)	270 (1.4%)	270 (1.4%)	227 (1.0%)	220 (0.9%)	864 (2.6%)	912 (2.7%)	1,361 (1.8%)	1,402 (1.8%)	0.00
Other CVD; n (%)	1,212 (6.2%)	1,194 (6.1%)	1,109 (4.8%)	1,153 (5.0%)	3,635 (10.9%)	3,614 (10.8%)	5,956 (7.8%)	5,961 (7.8%)	0.00
Diabetes-related complications									
Diabetic retinopathy; n (%)	1,161 (5.9%)	1,147 (5.9%)	909 (3.9%)	935 (4.0%)	2,514 (7.5%)	2,514 (7.5%)	4,584 (6.0%)	4,596 (6.0%)	0.00
Diabetes with other ophthalmic manifestations; n (%)	120 (0.6%)	136 (0.7%)	561 (2.4%)	567 (2.4%)	879 (2.6%)	924 (2.8%)	1,560 (2.0%)	1,627 (2.1%)	-0.01
Retinal detachment, vitreous hemorrhage, vitrectomy; n (%)	70 (0.4%)	73 (0.4%)	82 (0.4%)	69 (0.3%)	153 (0.5%)	140 (0.4%)	305 (0.4%)	282 (0.4%)	0.00
Retinal laser coagulation therapy; n (%)	115 (0.6%)	103 (0.5%)	145 (0.6%)	122 (0.5%)	222 (0.7%)	209 (0.6%)	482 (0.6%)	434 (0.6%)	0.00
Occurrence of Diabetic Neuropathy ; n (%)	3,305 (16.9%)	3,391 (17.4%)	2,498 (10.8%)	2,503 (10.8%)	6,540 (19.6%)	6,535 (19.6%)	12,343 (16.2%)	12,429 (16.3%)	0.00

Table 1

Occurrence of diabetic nephropathy with ICD10 ; n (%)	1,981 (10.1%)	2,014 (10.3%)	1,299 (5.6%)	1,282 (5.5%)	2,783 (8.3%)	2,769 (8.3%)	6,063 (8.0%)	6,065 (8.0%)	0.00
Hypoglycemia ; n (%)	403 (2.1%)	414 (2.1%)	517 (2.2%)	518 (2.2%)	736 (2.2%)	769 (2.3%)	1,656 (2.2%)	1,701 (2.2%)	0.00
Hyperglycemia; n (%)	650 (3.3%)	631 (3.2%)	659 (2.8%)	626 (2.7%)	1,112 (3.3%)	1,107 (3.3%)	2,421 (3.2%)	2,364 (3.1%)	0.01
Disorders of fluid electrolyte and acid-base balance; n (%)	653 (3.3%)	647 (3.3%)	501 (2.2%)	511 (2.2%)	1,420 (4.3%)	1,381 (4.1%)	2,574 (3.4%)	2,539 (3.3%)	0.01
Diabetic ketoacidosis; n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	000 (0.0%)	000 (0.0%)	#DIV/0!
Hyperosmolar hyperglycemic nonketotic syndrome (HONK); n (%)	86 (0.4%)	88 (0.5%)	80 (0.3%)	81 (0.3%)	163 (0.5%)	158 (0.5%)	329 (0.4%)	327 (0.4%)	0.00
Diabetes with peripheral circulatory disorders with ICD-10 ; n (%)	947 (4.8%)	954 (4.9%)	586 (2.5%)	581 (2.5%)	1,982 (5.9%)	1,982 (5.9%)	3,515 (4.6%)	3,517 (4.6%)	0.00
Diabetic Foot; n (%)	261 (1.3%)	257 (1.3%)	275 (1.2%)	275 (1.2%)	663 (2.0%)	679 (2.0%)	1,199 (1.6%)	1,211 (1.6%)	0.00
Gangrene ; n (%)	19 (0.1%)	19 (0.1%)	8 (0.0%)	9 (0.0%)	36 (0.1%)	27 (0.1%)	063 (0.1%)	055 (0.1%)	0.00
Lower extremity amputation; n (%)	67 (0.3%)	58 (0.3%)	30 (0.1%)	28 (0.1%)	100 (0.3%)	106 (0.3%)	197 (0.3%)	192 (0.3%)	0.00
Osteomyelitis; n (%)	54 (0.3%)	49 (0.3%)	58 (0.3%)	53 (0.2%)	109 (0.3%)	97 (0.3%)	221 (0.3%)	199 (0.3%)	0.00
Skin infections ; n (%)	890 (4.6%)	893 (4.6%)	949 (4.1%)	989 (4.3%)	1,854 (5.6%)	1,877 (5.6%)	3,693 (4.9%)	3,759 (4.9%)	0.00
Erectile dysfunction; n (%)	689 (3.5%)	695 (3.6%)	617 (2.7%)	635 (2.7%)	1,022 (3.1%)	1,015 (3.0%)	2,328 (3.1%)	2,345 (3.1%)	0.00
Diabetes with unspecified complication; n (%)	1,023 (5.2%)	990 (5.1%)	1,050 (4.5%)	991 (4.3%)	1,780 (5.3%)	1,745 (5.2%)	3,853 (5.1%)	3,726 (4.9%)	0.01
Diabetes mellitus without mention of complications; n (%)	16,531 (84.6%)	16,497 (84.5%)	21,189 (91.5%)	21,263 (91.8%)	30,549 (91.5%)	30,535 (91.4%)	68,269 (89.7%)	68,295 (89.7%)	0.00
Hypertension: 1 inpatient or 2 outpatient claims within 365 days; n (%)	17,868 (91.5%)	17,907 (91.7%)	20,220 (87.3%)	20,239 (87.4%)	31,932 (95.6%)	31,930 (95.6%)	70,020 (92.0%)	70,076 (92.1%)	0.00
Hyperlipidemia ; n (%)	14,994 (76.8%)	15,046 (77.0%)	17,333 (74.8%)	17,386 (75.0%)	27,362 (81.9%)	27,400 (82.0%)	59,689 (78.4%)	59,832 (78.6%)	0.00
Edema; n (%)	914 (4.7%)	894 (4.6%)	739 (3.2%)	756 (3.3%)	2,395 (7.2%)	2,412 (7.2%)	4,048 (5.3%)	4,062 (5.3%)	0.00
Renal Dysfunction (non-diabetic) ; n (%)	1,939 (9.9%)	2,024 (10.4%)	1,275 (5.5%)	1,284 (5.4%)	4,135 (12.4%)	4,083 (12.2%)	7,349 (9.7%)	7,391 (9.7%)	0.00
Occurrence of acute renal disease ; n (%)	164 (0.8%)	169 (0.9%)	122 (0.5%)	119 (0.5%)	366 (1.1%)	368 (1.1%)	652 (0.9%)	656 (0.9%)	0.00
Occurrence of chronic renal insufficiency; n (%)	1,542 (7.9%)	1,672 (8.6%)	940 (4.1%)	937 (4.0%)	3,348 (10.0%)	3,378 (10.1%)	5,830 (7.7%)	5,987 (7.9%)	-0.01
Chronic kidney disease ; n (%)	1,464 (7.5%)	1,563 (8.0%)	838 (3.6%)	810 (3.5%)	3,157 (9.5%)	3,109 (9.3%)	5,459 (7.2%)	5,482 (7.2%)	0.00
CKD Stage 3-4; n (%)	753 (3.9%)	822 (4.2%)	430 (1.9%)	420 (1.8%)	1,843 (5.5%)	1,828 (5.5%)	3,026 (4.0%)	3,070 (4.0%)	0.00
Occurrence of hypertensive nephropathy; n (%)	655 (3.4%)	658 (3.4%)	335 (1.4%)	334 (1.4%)	1,133 (3.4%)	1,149 (3.4%)	2,123 (2.8%)	2,141 (2.8%)	0.00
Occurrence of miscellaneous renal insufficiency ; n (%)	390 (2.0%)	404 (2.1%)	337 (1.5%)	368 (1.6%)	1,135 (3.4%)	1,135 (3.4%)	1,862 (2.4%)	1,907 (2.5%)	-0.01
Glaucoma or cataracts ; n (%)	3,316 (17.0%)	3,314 (17.0%)	3,168 (13.7%)	3,115 (13.4%)	9,148 (27.4%)	9,098 (27.2%)	15,632 (20.5%)	15,527 (20.4%)	0.00
Cellulitis or abscess of toe; n (%)	197 (1.0%)	179 (0.9%)	146 (0.6%)	144 (0.6%)	346 (1.0%)	367 (1.1%)	689 (0.9%)	690 (0.9%)	0.00
Foot ulcer; n (%)	253 (1.3%)	241 (1.2%)	271 (1.2%)	275 (1.2%)	657 (2.0%)	672 (2.0%)	1,181 (1.6%)	1,188 (1.6%)	0.00
Bladder stones; n (%)	15 (0.1%)	11 (0.1%)	10 (0.0%)	10 (0.0%)	30 (0.1%)	49 (0.1%)	055 (0.1%)	070 (0.1%)	0.00
Kidney stones; n (%)	312 (1.6%)	305 (1.6%)	406 (1.8%)	406 (1.8%)	692 (2.1%)	721 (2.2%)	1,410 (1.9%)	1,432 (1.9%)	0.00
Urinary tract infections (UTIs); n (%)	978 (5.0%)	975 (5.0%)	961 (4.1%)	933 (4.0%)	2,735 (8.2%)	2,708 (8.1%)	4,674 (6.1%)	4,616 (6.1%)	0.00
Dipstick urinalysis; n (%)	6,234 (31.9%)	5,989 (30.7%)	7,326 (31.6%)	7,016 (30.3%)	11,825 (35.4%)	11,790 (35.3%)	25,385 (33.4%)	24,795 (32.6%)	0.02
Non-dipstick urinalysis; n (%)	8,743 (44.8%)	8,830 (45.2%)	9,618 (41.5%)	9,590 (41.4%)	15,296 (45.8%)	15,274 (45.7%)	33,657 (44.2%)	33,694 (44.3%)	0.00
Urine function test; n (%)	279 (1.4%)	256 (1.3%)	339 (1.5%)	306 (1.3%)	1,002 (3.0%)	850 (2.5%)	1,620 (2.1%)	1,412 (1.9%)	0.01
Cytology; n (%)	79 (0.4%)	80 (0.4%)	129 (0.6%)	116 (0.5%)	229 (0.7%)	206 (0.6%)	437 (0.6%)	402 (0.5%)	0.01
Cystos; n (%)	127 (0.7%)	123 (0.6%)	151 (0.7%)	164 (0.7%)	356 (1.1%)	317 (0.9%)	634 (0.8%)	604 (0.8%)	0.00
Other Covariates									
Liver disease; n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	000 (0.0%)	000 (0.0%)	#DIV/0!
Osteoarthritis; n (%)	1,991 (10.2%)	2,018 (10.3%)	1,579 (6.8%)	1,656 (7.1%)	5,413 (16.2%)	5,337 (16.0%)	8,983 (11.8%)	9,011 (11.8%)	0.00
Other arthritis, arthropathies and musculoskeletal pain; n (%)	5,293 (27.1%)	5,257 (26.9%)	5,487 (23.7%)	5,503 (23.8%)	11,402 (34.1%)	11,358 (34.0%)	22,182 (29.1%)	22,118 (29.1%)	0.00
Dorsopathies; n (%)	3,513 (18.0%)	3,473 (17.8%)	3,457 (14.9%)	3,478 (15.0%)	7,367 (22.1%)	7,314 (21.9%)	14,337 (18.8%)	14,265 (18.7%)	0.00
Fractures; n (%)	313 (1.6%)	304 (1.6%)	351 (1.5%)	323 (1.4%)	758 (2.3%)	740 (2.2%)	1,422 (1.9%)	1,367 (1.8%)	0.01
Falls ; n (%)	325 (1.7%)	329 (1.7%)	125 (0.5%)	121 (0.5%)	729 (2.2%)	691 (2.1%)	1,179 (1.5%)	1,141 (1.5%)	0.00
Osteoporosis; n (%)	484 (2.5%)	496 (2.5%)	262 (1.1%)	266 (1.1%)	1,735 (5.2%)	1,739 (5.2%)	2,481 (3.3%)	2,501 (3.3%)	0.00
Hyperthyroidism; n (%)	132 (0.7%)	102 (0.5%)	131 (0.6%)	90 (0.4%)	270 (0.8%)	238 (0.7%)	533 (0.7%)	430 (0.6%)	0.01
Hypothyroidism ; n (%)	2,755 (14.1%)	2,732 (14.0%)	2,713 (11.7%)	2,686 (11.6%)	4,012 (12.0%)	3,970 (11.9%)	9,480 (12.5%)	9,388 (12.3%)	0.01
Other disorders of thyroid gland ; n (%)	735 (3.8%)	666 (3.4%)	780 (3.4%)	775 (3.3%)	1,483 (4.4%)	1,324 (4.0%)	2,998 (3.9%)	2,765 (3.6%)	0.02
Depression; n (%)	1,318 (6.7%)	1,347 (6.9%)	1,367 (5.9%)	1,317 (5.7%)	2,756 (8.3%)	2,733 (8.2%)	5,441 (7.1%)	5,397 (7.1%)	0.00
Anxiety; n (%)	1,279 (6.5%)	1,247 (6.4%)	1,075 (4.6%)	1,056 (4.6%)	2,282 (6.8%)	2,256 (6.8%)	4,636 (6.1%)	4,559 (6.0%)	0.00
Sleep_Disorder; n (%)	1,356 (6.9%)	1,364 (7.0%)	2,268 (9.8%)	2,344 (10.1%)	2,703 (8.1%)	2,706 (8.1%)	6,327 (8.3%)	6,414 (8.4%)	0.00
Dementia; n (%)	200 (1.0%)	195 (1.0%)	110 (0.5%)	109 (0.5%)	913 (2.7%)	893 (2.7%)	1,123 (1.6%)	1,197 (1.6%)	0.00
Delirium; n (%)	45 (0.2%)	55 (0.3%)	28 (0.1%)	29 (0.1%)	195 (0.6%)	179 (0.5%)	268 (0.4%)	263 (0.3%)	0.02
Psychosis; n (%)	89 (0.5%)	87 (0.4%)	44 (0.2%)	47 (0.2%)	255 (0.8%)	255 (0.8%)	388 (0.5%)	389 (0.5%)	0.00
Obesity; n (%)	5,168 (26.5%)	5,115 (26.2%)	4,206 (18.2%)	4,246 (18.3%)	6,410 (19.2%)	6,322 (18.9%)	15,784 (20.7%)	15,683 (20.6%)	0.00
Overweight; n (%)	1,026 (5.3%)	1,024 (5.2%)	576 (2.5%)	522 (2.3%)	1,239 (3.7%)	1,189 (3.6%)	2,841 (3.7%)	2,735 (3.6%)	0.01
Smoking; n (%)	1,624 (8.3%)	1,622 (8.3%)	1,219 (5.3%)	1,174 (5.1%)	3,528 (10.6%)	3,585 (10.7%)	6,371 (8.4%)	6,381 (8.4%)	0.00
Alcohol abuse or dependence; n (%)	3 (0.0%)	2 (0.0%)	6 (0.0%)	5 (0.0%)	**	**	**	**	**
Drug abuse or dependence; n (%)	6 (0.0%)	7 (0.0%)	2 (0.0%)	2 (0.0%)	**	**	**	**	**
COPD; n (%)	983 (5.0%)	998 (5.1%)	693 (3.0%)	666 (2.9%)	2,671 (8.0%)	2,602 (7.8%)	4,347 (5.7%)	4,266 (5.6%)	0.00

Table 1

Asthma; n (%)	870 (4.5%)	847 (4.3%)	804 (3.5%)	802 (3.5%)	1,756 (5.3%)	1,728 (5.2%)	3,430 (4.5%)	3,377 (4.4%)	0.00
Obstructive sleep apnea; n (%)	2,176 (11.1%)	2,157 (11.0%)	2,591 (11.2%)	2,584 (11.2%)	3,034 (9.1%)	3,034 (9.1%)	7,801 (10.3%)	7,775 (10.2%)	0.00
Pneumonia; n (%)	208 (1.1%)	221 (1.1%)	205 (0.9%)	210 (0.9%)	511 (1.1%)	520 (1.6%)	924 (1.2%)	951 (1.2%)	0.00
Imaging; n (%)	2 (0.0%)	6 (0.0%)	1 (0.0%)	2 (0.0%)	**	**	**	**	**
Diabetes Medications									
DM Medications - AGIs; n (%)	112 (0.6%)	103 (0.5%)	91 (0.4%)	77 (0.3%)	231 (0.7%)	261 (0.8%)	434 (0.6%)	441 (0.6%)	0.00
DM Medications - Glitazones; n (%)	1,856 (9.5%)	1,876 (9.6%)	2,142 (9.2%)	2,148 (9.3%)	3,295 (9.9%)	3,279 (9.8%)	7,293 (9.6%)	7,303 (9.6%)	0.00
DM Medications - Insulin; n (%)	4,810 (24.6%)	4,865 (24.9%)	5,930 (25.6%)	5,958 (25.7%)	10,126 (30.3%)	10,087 (30.2%)	20,866 (27.4%)	20,910 (27.5%)	0.00
DM Medications - Meglitinides; n (%)	203 (1.0%)	194 (1.0%)	294 (1.3%)	272 (1.2%)	583 (1.7%)	542 (1.6%)	1,080 (1.4%)	1,008 (1.3%)	0.01
DM Medications - Metformin; n (%)	15,366 (78.7%)	15,269 (78.2%)	18,243 (78.7%)	18,260 (78.8%)	24,894 (74.5%)	24,848 (74.4%)	58,503 (76.9%)	58,377 (76.7%)	0.00
Concomitant initiation or current use of 2nd Generation SUs; n (%)	6,481 (33.2%)	6,440 (33.0%)	7,299 (31.5%)	7,328 (31.6%)	12,787 (38.3%)	12,548 (37.6%)	26,567 (34.9%)	26,316 (34.6%)	0.01
Concomitant initiation or current use of AGIs; n (%)	50 (0.3%)	77 (0.4%)	33 (0.1%)	50 (0.2%)	154 (0.5%)	175 (0.5%)	237 (0.3%)	302 (0.4%)	-0.02
Concomitant initiation or current use of Glitazones; n (%)	1,422 (7.3%)	1,425 (7.3%)	1,643 (7.1%)	1,624 (7.0%)	2,474 (7.4%)	2,510 (7.5%)	5,539 (7.3%)	5,559 (7.3%)	0.00
Concomitant initiation or current use of GLP-1 RA; n (%)	1,432 (7.3%)	1,544 (7.9%)	1,891 (8.2%)	1,968 (8.5%)	2,410 (7.2%)	2,543 (7.6%)	5,733 (7.5%)	6,055 (8.0%)	-0.02
Concomitant initiation or current use of Insulin; n (%)	3,600 (18.4%)	3,644 (18.7%)	4,552 (19.6%)	4,589 (19.8%)	7,923 (23.7%)	7,913 (23.7%)	16,075 (21.1%)	16,146 (21.2%)	0.00
Concomitant initiation or current use of Meglitinides; n (%)	110 (0.6%)	131 (0.7%)	108 (0.5%)	199 (0.9%)	404 (1.2%)	381 (1.1%)	622 (0.8%)	711 (0.9%)	-0.01
Concomitant initiation or current use of Metformin; n (%)	13,063 (66.9%)	12,913 (66.1%)	15,539 (67.1%)	15,521 (67.0%)	21,246 (63.6%)	21,219 (63.5%)	49,848 (65.5%)	49,653 (65.2%)	0.01
Past use of 2nd Generation SUs ; n (%)	1,625 (8.3%)	1,648 (8.4%)	1,695 (7.3%)	1,732 (7.5%)	2,612 (7.8%)	2,636 (7.9%)	5,932 (7.8%)	6,016 (7.9%)	0.00
Past use of AGIs ; n (%)	62 (0.3%)	26 (0.1%)	58 (0.3%)	27 (0.1%)	77 (0.2%)	86 (0.3%)	197 (0.3%)	139 (0.2%)	0.02
Past use of Glitazones ; n (%)	434 (2.2%)	451 (2.3%)	499 (2.2%)	524 (2.3%)	821 (2.5%)	769 (2.3%)	1,754 (2.3%)	1,744 (2.3%)	0.00
Past use of GLP-1 RA ; n (%)	926 (4.7%)	958 (4.9%)	1,232 (5.3%)	1,223 (5.3%)	1,589 (4.8%)	1,615 (4.8%)	3,747 (4.9%)	3,796 (5.0%)	0.00
Past use of Insulin ; n (%)	1,210 (6.2%)	1,221 (6.3%)	1,379 (6.0%)	1,369 (5.9%)	2,204 (6.6%)	2,175 (6.5%)	4,793 (6.3%)	4,765 (6.3%)	0.00
Past use of Meglitinides ; n (%)	93 (0.5%)	63 (0.3%)	186 (0.8%)	73 (0.3%)	179 (0.5%)	161 (0.5%)	458 (0.6%)	297 (0.4%)	0.03
Past use of metformin (final) ; n (%)	2,303 (11.8%)	2,356 (12.1%)	2,705 (11.7%)	2,739 (11.8%)	3,648 (10.9%)	3,629 (10.9%)	8,656 (11.4%)	8,724 (11.5%)	0.00
Other Medications									
Use of ACE inhibitors; n (%)	10,585 (54.2%)	10,617 (54.4%)	12,359 (53.3%)	12,301 (53.1%)	16,705 (50.0%)	16,765 (50.2%)	39,649 (52.1%)	39,683 (52.1%)	0.00
Use of ARBs; n (%)	7,026 (36.0%)	7,007 (35.9%)	8,593 (37.1%)	8,662 (37.4%)	12,369 (37.0%)	12,384 (37.1%)	27,988 (36.8%)	28,053 (36.9%)	0.00
Use of Loop Diuretics ; n (%)	1,811 (9.3%)	1,788 (9.2%)	1,879 (8.1%)	1,836 (7.9%)	5,110 (15.3%)	5,163 (15.5%)	8,800 (11.6%)	8,787 (11.5%)	0.00
Use of other diuretics; n (%)	505 (2.6%)	487 (2.5%)	581 (2.5%)	573 (2.5%)	1,151 (3.4%)	1,124 (3.4%)	2,237 (2.9%)	2,184 (2.9%)	0.00
Use of nitrates-United; n (%)	696 (3.6%)	705 (3.6%)	742 (3.2%)	742 (3.2%)	2,191 (6.6%)	2,134 (6.4%)	3,629 (4.8%)	3,581 (4.7%)	0.00
Use of other hypertension drugs; n (%)	1,040 (5.3%)	1,072 (5.5%)	1,133 (4.9%)	1,140 (4.9%)	2,470 (7.4%)	2,473 (7.4%)	4,643 (6.1%)	4,685 (6.2%)	0.00
Use of digoxin; n (%)	234 (1.2%)	218 (1.1%)	189 (0.8%)	217 (0.9%)	754 (2.3%)	737 (2.2%)	1,177 (1.5%)	1,172 (1.5%)	0.00
Use of Anti-arrhythmics; n (%)	153 (0.8%)	160 (0.8%)	165 (0.7%)	169 (0.7%)	504 (1.5%)	478 (1.4%)	822 (1.1%)	807 (1.1%)	0.00
Use of COPD/asthma meds; n (%)	2,610 (13.4%)	2,552 (13.1%)	3,182 (13.7%)	3,201 (13.8%)	5,500 (16.5%)	5,455 (16.3%)	11,292 (14.8%)	11,208 (14.7%)	0.00
Use of statins; n (%)	14,115 (72.3%)	14,168 (72.5%)	15,879 (68.5%)	16,013 (69.1%)	25,077 (75.1%)	25,241 (75.6%)	55,071 (72.4%)	55,422 (72.8%)	-0.01
Use of other lipid-lowering drugs; n (%)	2,443 (12.5%)	2,510 (12.9%)	3,546 (15.3%)	3,536 (15.3%)	5,010 (15.0%)	4,896 (14.7%)	10,999 (14.5%)	10,942 (14.4%)	0.00
Use of antiplatelet agents; n (%)	1,985 (10.2%)	1,937 (9.9%)	2,289 (9.9%)	2,327 (10.0%)	4,642 (13.9%)	4,642 (13.9%)	8,916 (11.7%)	8,906 (11.7%)	0.00
Use of oral anticoagulants (Dabigatran, Rivaroxaban, Apixaban, Warfarin); n (%)	833 (4.3%)	855 (4.4%)	799 (3.4%)	791 (3.4%)	2,604 (7.8%)	2,590 (7.8%)	4,236 (5.6%)	4,236 (5.6%)	0.00
Use of heparin and other low-molecular weight heparins; n (%)	18 (0.1%)	19 (0.1%)	0 (0.0%)	0 (0.0%)	61 (0.2%)	62 (0.2%)	079 (0.1%)	081 (0.1%)	0.00
Use of NSAIDs; n (%)	3,256 (16.7%)	3,211 (16.4%)	3,774 (16.3%)	3,788 (16.4%)	5,117 (15.3%)	5,126 (15.3%)	12,147 (16.0%)	12,125 (15.9%)	0.00
Use of oral corticosteroids; n (%)	2,279 (11.7%)	2,243 (11.5%)	2,550 (11.0%)	2,583 (11.1%)	4,680 (14.0%)	4,595 (13.8%)	9,509 (12.5%)	9,421 (12.4%)	0.00
Use of bisphosphonate (United); n (%)	232 (1.2%)	237 (1.2%)	149 (0.6%)	145 (0.6%)	715 (2.1%)	761 (2.3%)	1,096 (1.4%)	1,143 (1.5%)	-0.01
Use of opioids; n (%)	3,797 (19.4%)	3,784 (19.4%)	4,612 (19.9%)	4,603 (19.9%)	6,800 (20.4%)	6,685 (20.0%)	15,209 (20.0%)	15,072 (19.8%)	0.01
Use of antidepressants; n (%)	4,446 (22.8%)	4,408 (22.6%)	5,009 (21.6%)	4,990 (21.5%)	8,171 (24.5%)	8,112 (24.3%)	17,626 (23.2%)	17,510 (23.0%)	0.00
Use of antipsychotics; n (%)	347 (1.8%)	337 (1.7%)	272 (1.2%)	250 (1.1%)	668 (2.0%)	682 (2.0%)	1,287 (1.7%)	1,269 (1.7%)	0.00
Use of anticonvulsants; n (%)	2,716 (13.9%)	2,697 (13.8%)	2,509 (10.8%)	2,513 (10.8%)	5,149 (15.4%)	5,060 (15.1%)	10,374 (13.6%)	10,270 (13.5%)	0.00
Use of lithium; n (%)	29 (0.1%)	18 (0.1%)	27 (0.1%)	14 (0.1%)	48 (0.1%)	29 (0.1%)	104 (0.1%)	061 (0.1%)	0.00
Use of Benzos; n (%)	1,741 (8.9%)	1,703 (8.7%)	1,946 (8.4%)	1,965 (8.5%)	3,284 (9.8%)	3,237 (9.7%)	6,971 (9.2%)	6,905 (9.1%)	0.00
Use of anxiolytics/hypnotics; n (%)	1,016 (5.2%)	1,001 (5.1%)	1,247 (5.4%)	1,234 (5.3%)	1,747 (5.2%)	1,718 (5.1%)	4,010 (5.3%)	3,953 (5.2%)	0.00
Use of dementia meds; n (%)	126 (0.6%)	129 (0.7%)	79 (0.3%)	80 (0.3%)	747 (2.2%)	705 (2.1%)	952 (1.3%)	914 (1.2%)	0.01
Use of antiparkinsonian meds; n (%)	356 (1.8%)	357 (1.8%)	392 (1.7%)	365 (1.6%)	926 (2.8%)	944 (2.8%)	1,674 (2.2%)	1,666 (2.2%)	0.00
Any use of pramlintide; n (%)	3 (0.0%)	24 (0.1%)	6 (0.0%)	43 (0.2%)	**	**	**	**	**
Any use of 1st generation sulfonylureas; n (%)	0 (0.0%)	0 (0.0%)	1 (0.0%)	0 (0.0%)	**	**	**	**	**
Entresto (sacubitril/valsartan); n (%)	24 (0.1%)	14 (0.1%)	3 (0.0%)	4 (0.0%)	14 (0.0%)	13 (0.0%)	041 (0.1%)	031 (0.0%)	0.00
Initiation as monotherapy ; n (%)	1,207 (6.2%)	1,196 (6.1%)	1,314 (5.7%)	1,306 (5.6%)	1,176 (3.5%)	1,217 (3.6%)	3,697 (4.9%)	3,719 (4.9%)	0.00
Labs									
Lab values- HbA1c (%) ; n (%)	8,392 (43.0%)	8,484 (43.4%)	1,674 (7.2%)	1,435 (6.2%)	N/A	N/A	10,066 (23.6%)	9,919 (23.2%)	0.01
Lab values- HbA1c (%) (within 3 months) ; n (%)	6,836 (35.0%)	6,971 (35.7%)	1,370 (5.9%)	1,224 (5.3%)	N/A	N/A	8,206 (19.2%)	8,195 (19.2%)	0.00
Lab values- HbA1c (%) (within 6 months) ; n (%)	8,392 (43.0%)	8,484 (43.4%)	1,674 (7.2%)	1,435 (6.2%)	N/A	N/A	10,066 (23.6%)	9,919 (23.2%)	0.01

Table 1

Lab values- BNP; n (%)	102 (0.5%)	120 (0.6%)	23 (0.1%)	4 (0.0%)	N/A	N/A	125 (0.3%)	124 (0.3%)	0.00
Lab values- BNP (within 3 months); n (%)	62 (0.3%)	76 (0.4%)	18 (0.1%)	3 (0.0%)	N/A	N/A	080 (0.2%)	079 (0.2%)	0.00
Lab values- BNP (within 6 months); n (%)	102 (0.5%)	120 (0.6%)	23 (0.1%)	4 (0.0%)	N/A	N/A	125 (0.3%)	124 (0.3%)	0.00
Lab values- BUN (mg/dl); n (%)	8,334 (42.7%)	8,259 (42.3%)	1,582 (6.8%)	1,359 (5.9%)	N/A	N/A	9,916 (23.2%)	9,618 (22.5%)	0.02
Lab values- BUN (mg/dl) (within 3 months); n (%)	6,579 (33.7%)	6,626 (33.9%)	1,244 (5.4%)	1,116 (4.8%)	N/A	N/A	7,823 (18.3%)	7,742 (18.1%)	0.01
Lab values- BUN (mg/dl) (within 6 months); n (%)	8,334 (42.7%)	8,259 (42.3%)	1,582 (6.8%)	1,359 (5.9%)	N/A	N/A	9,916 (23.2%)	9,618 (22.5%)	0.02
Lab values- Creatinine (mg/dl) ; n (%)	8,573 (43.9%)	8,526 (43.7%)	1,691 (7.3%)	1,486 (6.4%)	N/A	N/A	10,264 (24.0%)	10,012 (23.4%)	0.01
Lab values- Creatinine (mg/dl) (within 3 months); n (%)	6,780 (34.7%)	6,835 (35.0%)	1,337 (5.8%)	1,232 (5.3%)	N/A	N/A	8,117 (19.0%)	8,067 (18.9%)	0.00
Lab values- Creatinine (mg/dl) (within 6 months); n (%)	8,573 (43.9%)	8,526 (43.7%)	1,691 (7.3%)	1,486 (6.4%)	N/A	N/A	10,264 (24.0%)	10,012 (23.4%)	0.01
Lab values- HDL level (mg/dl); n (%)	7,438 (38.1%)	7,329 (37.5%)	1,535 (6.6%)	1,315 (5.7%)	N/A	N/A	8,973 (21.0%)	8,644 (20.2%)	0.02
Lab values- HDL level (mg/dl) (within 3 months); n (%)	5,579 (28.6%)	5,616 (28.8%)	1,181 (5.1%)	1,045 (4.5%)	N/A	N/A	6,760 (15.8%)	6,661 (15.6%)	0.01
Lab values- HDL level (mg/dl) (within 6 months); n (%)	7,438 (38.1%)	7,329 (37.5%)	1,535 (6.6%)	1,315 (5.7%)	N/A	N/A	8,973 (21.0%)	8,644 (20.2%)	0.02
Lab values- LDL level (mg/dl) ; n (%)	7,633 (39.1%)	7,557 (38.7%)	1,599 (6.9%)	1,341 (5.8%)	N/A	N/A	9,232 (21.6%)	8,898 (20.8%)	0.02
Lab values- LDL level (mg/dl) (within 3 months); n (%)	5,723 (29.3%)	5,809 (29.7%)	1,227 (5.3%)	1,068 (4.6%)	N/A	N/A	6,950 (16.3%)	6,877 (16.1%)	0.01
Lab values- LDL level (mg/dl) (within 6 months); n (%)	7,633 (39.1%)	7,557 (38.7%)	1,599 (6.9%)	1,341 (5.8%)	N/A	N/A	9,232 (21.6%)	8,898 (20.8%)	0.02
Lab values- NT-proBNP; n (%)	14 (0.1%)	12 (0.1%)	3 (0.0%)	0 (0.0%)	N/A	N/A	17 (0.0%)	0 (0.0%)	-
Lab values- NT-proBNP (within 3 months); n (%)	9 (0.0%)	7 (0.0%)	3 (0.0%)	0 (0.0%)	N/A	N/A	12 (0.0%)	0 (0.0%)	-
Lab values- NT-proBNP (within 6 months); n (%)	14 (0.1%)	12 (0.1%)	3 (0.0%)	0 (0.0%)	N/A	N/A	17 (0.0%)	12 (0.0%)	-
Lab values- Total cholesterol (mg/dl) ; n (%)	7,546 (38.6%)	7,484 (38.3%)	1,541 (6.7%)	1,326 (5.7%)	N/A	N/A	9,087 (21.3%)	8,810 (20.6%)	0.02
Lab values- Total cholesterol (mg/dl) (within 3 months); n (%)	5,669 (29.0%)	5,759 (29.5%)	1,188 (5.1%)	1,059 (4.6%)	N/A	N/A	6,857 (16.1%)	6,818 (16.0%)	0.00
Lab values- Total cholesterol (mg/dl) (within 6 months); n (%)	7,546 (38.6%)	7,484 (38.3%)	1,541 (6.7%)	1,326 (5.7%)	N/A	N/A	9,087 (21.3%)	8,810 (20.6%)	0.02
Lab values- Triglyceride level (mg/dl); n (%)	7,490 (38.3%)	7,438 (38.1%)	1,519 (6.6%)	1,304 (5.6%)	N/A	N/A	9,009 (21.1%)	8,742 (20.5%)	0.01
Lab values- Triglyceride level (mg/dl) (within 3 months); n (%)	5,623 (28.8%)	5,720 (29.3%)	1,169 (5.0%)	1,046 (4.5%)	N/A	N/A	6,792 (15.9%)	6,766 (15.8%)	0.00
Lab values- Triglyceride level (mg/dl) (within 6 months); n (%)	7,490 (38.3%)	7,438 (38.1%)	1,519 (6.6%)	1,304 (5.6%)	N/A	N/A	9,009 (21.1%)	8,742 (20.5%)	0.01
Lab result number- HbA1c (%) mean (only 2 to 20 included)	8,349	8,430	1,628	1,384	N/A	N/A	9,977	9,814	
...mean (sd)	8.53 (1.83)	8.61 (1.75)	8.63 (1.88)	8.63 (1.72)	N/A	N/A	8.55 (1.84)	8.61 (1.75)	-0.03
...median [IQR]	8.10 [7.30, 9.45]	8.30 [7.40, 9.60]	8.20 [7.30, 9.50]	8.30 [7.40, 9.59]	N/A	N/A	8.12 (1.84)	8.30 (1.75)	-0.10
...Missing; n (%)	11,183 (57.3%)	11,102 (56.8%)	21,540 (93.0%)	21,784 (94.0%)	N/A	N/A	32,723 (76.6%)	32,886 (77.0%)	-0.01
Lab result number- BNP mean	102	120	23	4	N/A	N/A	125	124	
...mean (sd)	119.72 (204.33)	95.52 (162.94)	239.13 (519.14)	335.38 (447.47)	N/A	N/A	141.69 (288.38)	103.26 (176.28)	0.16
...median [IQR]	48.55 [20.27, 141.98]	44.35 [21.32, 88.78]	49.00 [20.00, 214.00]	192.50 [4.25, 809.38]	N/A	N/A	#VALUE!	49.13 (176.28)	#VALUE!
...Missing; n (%)	19,430 (99.5%)	19,412 (99.4%)	23,145 (99.9%)	23,164 (100.0%)	N/A	N/A	42,575 (99.7%)	42,576 (99.7%)	0.00
Lab result number- BUN (mg/dl) mean	8,334	8,259	1,582	1,359	N/A	N/A	9,916	9,618	
...mean (sd)	17.03 (6.43)	16.93 (5.80)	629.58 (9,120.88)	3,069.88 (21,521.68)	N/A	N/A	114.76 (3642.51)	448.30 (8088.19)	-0.05
...median [IQR]	16.00 [13.00, 20.00]	16.00 [13.00, 19.50]	15.50 [12.50, 19.00]	16.00 [13.00, 20.00]	N/A	N/A	#VALUE!	#VALUE!	#VALUE!
...Missing; n (%)	11,198 (57.3%)	11,273 (57.7%)	21,586 (93.2%)	21,809 (94.1%)	N/A	N/A	32,784 (76.8%)	33,082 (77.5%)	-0.02
Lab result number- Creatinine (mg/dl) mean (only 0.1 to 15 included)	8,519	8,459	1,536	1,339	N/A	N/A	10,055	9,798	
...mean (sd)	0.96 (0.31)	0.92 (0.24)	0.96 (0.30)	0.93 (0.23)	N/A	N/A	0.96 (0.31)	0.92 (0.24)	0.14
...median [IQR]	0.90 [0.77, 1.09]	0.89 [0.75, 1.04]	0.92 [0.77, 1.07]	0.90 [0.77, 1.06]	N/A	N/A	0.90 (0.31)	0.89 (0.24)	0.04
...Missing; n (%)	11,013 (56.4%)	11,073 (56.7%)	21,632 (93.4%)	21,829 (94.2%)	N/A	N/A	32,645 (76.5%)	32,902 (77.1%)	-0.01
Lab result number- HDL level (mg/dl) mean (only >=5000 included)	7,438	7,329	1,528	1,294	N/A	N/A	8,966	8,623	
...mean (sd)	44.89 (13.09)	44.78 (12.83)	43.55 (14.91)	43.02 (13.62)	N/A	N/A	44.66 (13.42)	44.52 (12.95)	0.01
...median [IQR]	43.00 [36.00, 51.50]	43.00 [36.00, 52.00]	42.83 [35.00, 51.00]	42.00 [35.00, 50.00]	N/A	N/A	42.97 (13.42)	42.83 (12.95)	0.01
...Missing; n (%)	12,094 (61.9%)	12,203 (62.5%)	21,640 (93.4%)	21,874 (94.4%)	N/A	N/A	33,734 (79.0%)	34,077 (79.8%)	-0.02
Lab result number- LDL level (mg/dl) mean (only >=5000 included)	7,492	7,432	1,416	1,187	N/A	N/A	8,908	8,619	
...mean (sd)	85.61 (39.60)	84.29 (39.26)	87.73 (41.40)	87.33 (40.93)	N/A	N/A	85.95 (39.89)	84.71 (39.50)	0.03
...median [IQR]	83.00 [62.00, 109.00]	82.00 [61.00, 106.00]	87.00 [64.00, 113.00]	88.00 [63.00, 112.00]	N/A	N/A	83.64 (39.89)	82.83 (39.50)	0.02
...Missing; n (%)	12,040 (61.6%)	12,100 (61.9%)	21,752 (93.9%)	21,981 (94.9%)	N/A	N/A	33,792 (79.1%)	34,081 (79.8%)	-0.02
Lab result number- Total cholesterol (mg/dl) mean (only >=5000 included)	7,541	7,474	1,534	1,304	N/A	N/A	9,075	8,778	
...mean (sd)	173.51 (47.47)	172.60 (46.68)	172.33 (52.31)	173.37 (48.27)	N/A	N/A	173.31 (48.32)	172.71 (46.92)	0.01
...median [IQR]	167.00 [142.00, 198.25]	167.00 [142.00, 196.00]	170.00 [143.38, 199.50]	171.00 [147.00, 198.00]	N/A	N/A	167.51 (48.32)	167.59 (46.92)	0.00
...Missing; n (%)	11,991 (61.4%)	12,058 (61.7%)	21,634 (93.4%)	21,864 (94.4%)	N/A	N/A	33,625 (78.7%)	33,922 (79.4%)	-0.02

Table 1

Lab result number- Triglyceride level (mg/dl) mean (only <=5000 included)	7,489	7,436	1,511	1,283	N/A	N/A	9,000	8,719	
...mean (sd)	197.03 (176.04)	200.03 (177.75)	188.47 (180.91)	204.69 (194.45)	N/A	N/A	195.59 (176.88)	200.72 (180.31)	-0.03
...median [IQR]	158.00 [112.00, 228.00]	161.00 [114.00, 230.92]	150.50 [104.50, 223.33]	163.00 [113.00, 237.00]	N/A	N/A	156.74 (176.88)	161.29 (180.31)	-0.03
...Missing; n (%)	12,043 (61.7%)	12,096 (61.9%)	21,657 (93.5%)	21,885 (94.5%)	N/A	N/A	33,700 (78.9%)	33,981 (79.6%)	-0.02
Lab result number- Hemoglobin mean (only >0 included)	5,576	5,481	1,032	879	N/A	N/A	6,608	6,360	
...mean (sd)	13.80 (1.57)	14.00 (1.57)	20,324.36 (440,120.87)	3,301.14 (20,906.38)	N/A	N/A	3185.79 (173886.11)	468.31 (7769.62)	0.02
...median [IQR]	13.80 [12.71, 14.80]	14.00 [12.90, 15.08]	13.70 [12.70, 14.80]	14.00 [12.90, 15.00]	N/A	N/A	#VALUE!	#VALUE!	#VALUE!
...Missing; n (%)	13,956 (71.5%)	14,051 (71.9%)	22,136 (95.5%)	22,289 (96.2%)	N/A	N/A	36,092 (84.5%)	36,340 (85.1%)	-0.02
Lab result number- Serum sodium mean (only >90 and < 190 included)	8,349	8,307	1,543	1,339	N/A	N/A	9,892	9,646	
...mean (sd)	139.33 (2.68)	139.23 (2.69)	138.98 (2.54)	138.92 (2.39)	N/A	N/A	139.22 (2.66)	139.19 (2.65)	0.01
...median [IQR]	139.33 [138.00, 141.00]	139.00 [138.00, 141.00]	139.00 [137.33, 140.62]	139.00 [137.00, 140.33]	N/A	N/A	139.28 (2.66)	139.00 (2.65)	0.11
...Missing; n (%)	11,183 (57.3%)	11,225 (57.5%)	21,625 (93.3%)	21,829 (94.2%)	N/A	N/A	32,808 (76.8%)	33,054 (77.4%)	-0.01
Lab result number- Albumin mean (only >0 and <=10 included)	7,829	7,803	1,323	1,145	N/A	N/A	9,152	8,948	
...mean (sd)	4.29 (0.31)	4.30 (0.30)	4.15 (0.71)	4.17 (0.66)	N/A	N/A	4.27 (0.39)	4.28 (0.37)	-0.03
...median [IQR]	4.30 [4.10, 4.50]	4.30 [4.10, 4.50]	4.25 [4.00, 4.45]	4.25 [4.00, 4.50]	N/A	N/A	4.29 (0.39)	4.29 (0.37)	0.00
...Missing; n (%)	11,703 (59.9%)	11,729 (60.1%)	21,845 (94.3%)	22,023 (95.1%)	N/A	N/A	33,548 (78.6%)	33,752 (79.0%)	-0.01
Lab result number- Glucose (fasting or random) mean (only 10-1000 included)	8,366	8,303	1,537	1,326	N/A	N/A	9,903	9,629	
...mean (sd)	180.41 (72.14)	181.43 (70.42)	181.84 (71.36)	182.28 (68.00)	N/A	N/A	180.63 (72.02)	181.55 (70.10)	-0.01
...median [IQR]	163.50 [130.00, 214.00]	166.50 [132.00, 216.00]	165.00 [132.33, 215.75]	168.25 [134.00, 217.12]	N/A	N/A	163.73 (72.02)	166.74 (70.10)	-0.04
...Missing; n (%)	11,166 (57.2%)	11,229 (57.5%)	21,631 (93.4%)	21,842 (94.3%)	N/A	N/A	32,797 (76.8%)	33,071 (77.4%)	-0.01
Lab result number- Potassium mean (only 1-7 included)	8,517	8,468	1,538	1,307	N/A	N/A	10,055	9,775	
...mean (sd)	4.45 (0.42)	4.45 (0.41)	4.36 (0.44)	4.36 (0.44)	N/A	N/A	4.44 (0.42)	4.44 (0.41)	0.00
...median [IQR]	4.40 [4.20, 4.70]	4.40 [4.20, 4.70]	4.35 [4.00, 4.60]	4.40 [4.10, 4.60]	N/A	N/A	4.39 (0.42)	4.40 (0.41)	-0.02
...Missing; n (%)	11,015 (56.4%)	11,064 (56.6%)	21,630 (93.4%)	21,861 (94.4%)	N/A	N/A	32,645 (76.5%)	32,925 (77.1%)	-0.01
Comorbidity Scores									
CCI (180 days)- ICD9 and ICD10									
...mean (sd)	2.09 (1.28)	2.10 (1.31)	1.67 (1.00)	1.67 (1.00)	2.36 (1.50)	2.35 (1.50)	2.08 (1.31)	2.08 (1.32)	0.00
...median [IQR]	2.00 [1.00, 2.00]	2.00 [1.00, 2.00]	1.00 [1.00, 2.00]	1.00 [1.00, 2.00]	2.00 [1.00, 3.00]	2.00 [1.00, 3.00]	1.70 (1.31)	1.70 (1.32)	0.00
Frailty Score: Qualitative Version 365 days as Categories, v1									
...0; n (%)	13,009 (66.6%)	12,920 (66.1%)	12,672 (54.7%)	12,648 (54.6%)	15,535 (46.5%)	15,495 (46.4%)	41,216 (54.2%)	41,063 (54.0%)	0.00
...1 to 2; n (%)	5,078 (26.0%)	5,112 (26.2%)	8,472 (36.6%)	8,480 (36.6%)	11,515 (34.5%)	11,612 (34.8%)	25,065 (32.9%)	25,204 (33.1%)	0.00
...3 or more; n (%)	1,445 (7.4%)	1,500 (7.7%)	2,024 (8.7%)	2,040 (8.8%)	6,351 (19.0%)	6,294 (18.8%)	9,820 (12.9%)	9,834 (12.9%)	0.00
Frailty Score: Empirical Version 365 days as Categories,									
...< 0.12908; n (%)	6,873 (35.2%)	6,844 (35.0%)	7,705 (33.3%)	7,732 (33.4%)	5,501 (16.5%)	5,302 (15.9%)	20,079 (26.4%)	19,878 (26.1%)	0.01
...0.12908 - 0.1631167; n (%)	7,260 (37.2%)	7,324 (37.5%)	9,157 (39.5%)	9,149 (39.5%)	10,406 (31.2%)	10,542 (31.6%)	26,823 (35.2%)	27,015 (35.5%)	-0.01
...>= 0.1631167; n (%)	5,399 (27.6%)	5,364 (27.5%)	6,306 (27.2%)	6,287 (27.1%)	17,494 (52.4%)	17,557 (52.6%)	29,199 (38.4%)	29,208 (38.4%)	0.00
Non-Frailty; n (%)	11,171 (57.2%)	11,285 (57.8%)	12,238 (52.8%)	12,310 (53.1%)	1,723 (5.2%)	1,549 (4.6%)	25,132 (33.0%)	25,144 (33.0%)	0.00
Frailty Score (mean): Qualitative Version 365 days, v1									
...mean (sd)	0.63 (1.18)	0.64 (1.18)	0.81 (1.19)	0.82 (1.20)	1.26 (1.67)	1.25 (1.64)	0.96 (1.42)	0.96 (1.41)	0.00
...median [IQR]	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	1.00 [0.00, 2.00]	1.00 [0.00, 2.00]	0.44 (1.42)	0.44 (1.41)	0.00
Frailty Score (mean): Empirical Version 365 days,									
...mean (sd)	0.15 (0.04)	0.15 (0.04)	0.14 (0.04)	0.14 (0.04)	0.18 (0.05)	0.18 (0.05)	0.16 (0.04)	0.16 (0.04)	0.00
...median [IQR]	0.14 [0.12, 0.17]	0.14 [0.12, 0.17]	0.14 [0.12, 0.16]	0.14 [0.12, 0.16]	0.17 [0.14, 0.20]	0.17 [0.14, 0.20]	0.15 (0.04)	0.15 (0.04)	0.00
Healthcare Utilization									
Any hospitalization; n (%)	451 (2.3%)	488 (2.5%)	496 (2.1%)	517 (2.2%)	1,265 (3.8%)	1,237 (3.7%)	2,212 (2.9%)	2,242 (2.9%)	0.00
Any hospitalization within prior 30 days; n (%)	62 (0.3%)	83 (0.4%)	64 (0.3%)	79 (0.3%)	198 (0.6%)	207 (0.6%)	324 (0.4%)	369 (0.5%)	-0.01
Any hospitalization during prior 31-180 days; n (%)	394 (2.0%)	409 (2.1%)	436 (1.9%)	441 (1.9%)	1,094 (3.3%)	1,057 (3.2%)	1,924 (2.5%)	1,907 (2.5%)	0.00
Endocrinologist Visit; n (%)	2,773 (14.2%)	2,878 (14.7%)	3,445 (14.9%)	3,370 (14.5%)	5,826 (17.4%)	5,874 (17.6%)	12,044 (15.8%)	12,122 (15.9%)	0.00
Endocrinologist Visit (30 days prior); n (%)	1,974 (10.1%)	2,042 (10.5%)	2,569 (11.1%)	2,555 (11.0%)	4,001 (12.0%)	4,092 (12.3%)	8,544 (11.2%)	8,689 (11.4%)	-0.01
Endocrinologist Visit (31 to 180 days prior); n (%)	1,939 (9.9%)	1,992 (10.2%)	2,311 (10.0%)	2,302 (9.9%)	4,404 (13.2%)	4,479 (13.4%)	8,654 (11.4%)	8,773 (11.5%)	0.00
Internal medicine/family medicine visits; n (%)	14,481 (74.1%)	14,301 (73.2%)	20,561 (88.7%)	20,392 (88.0%)	27,892 (83.5%)	27,600 (82.6%)	62,934 (82.7%)	62,293 (81.9%)	0.02
Internal medicine/family medicine visits (30 days prior); n (%)	10,679 (54.7%)	10,582 (54.2%)	15,756 (68.0%)	15,756 (68.0%)	20,325 (60.9%)	20,166 (60.4%)	46,760 (61.4%)	46,504 (61.1%)	0.01
Internal medicine/family medicine visits (31 to 180 days prior); n (%)	12,286 (62.9%)	12,278 (62.9%)	16,906 (73.0%)	16,939 (73.1%)	24,413 (73.1%)	24,255 (72.6%)	53,605 (70.4%)	53,472 (70.3%)	0.00
Cardiologist visit; n (%)	3,671 (18.8%)	3,733 (19.1%)	3,785 (16.3%)	3,767 (16.3%)	9,403 (28.2%)	9,408 (28.2%)	16,859 (22.2%)	16,908 (22.2%)	0.00
Number of Cardiologist visits (30 days prior); n (%)	1,085 (5.6%)	1,159 (5.9%)	1,191 (5.1%)	1,155 (5.0%)	2,831 (8.5%)	2,875 (8.6%)	5,107 (6.7%)	5,189 (6.8%)	0.00

Table 1

Number of Cardiologist visits (31 to 180 days prior); n (%)	3,120 (16.0%)	3,172 (16.2%)	3,152 (13.6%)	3,189 (13.8%)	8,218 (24.6%)	8,170 (24.5%)	14,490 (19.0%)	14,531 (19.1%)	0.00
Electrocardiogram ; n (%)	4,420 (22.6%)	4,428 (22.7%)	5,282 (22.8%)	5,287 (22.8%)	9,495 (28.4%)	9,314 (27.9%)	19,197 (25.2%)	19,029 (25.0%)	0.00
Use of glucose test strips; n (%)	684 (3.5%)	679 (3.5%)	913 (3.9%)	898 (3.9%)	981 (2.9%)	1,014 (3.0%)	2,578 (3.4%)	2,591 (3.4%)	0.00
Dialysis; n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	000 (0.0%)	000 (0.0%)	#DIV/0!
Naive new user v8 ; n (%)	1,875 (9.6%)	1,885 (9.7%)	1,971 (8.5%)	1,989 (8.6%)	1,878 (5.6%)	1,925 (5.8%)	5,724 (7.5%)	5,799 (7.6%)	0.00
N antidiabetic drugs at index date									
...mean (sd)	2.35 (0.86)	2.35 (0.88)	2.35 (0.87)	2.35 (0.90)	2.42 (0.86)	2.42 (0.87)	2.38 (0.86)	2.38 (0.88)	0.00
...median [IQR]	2.00 [2.00, 3.00]	2.00 [2.00, 3.00]	2.00 [2.00, 3.00]	2.00 [2.00, 3.00]	2.00 [2.00, 3.00]	2.00 [2.00, 3.00]	2.00 (0.86)	2.00 (0.88)	0.00
number of different/distinct medication prescriptions									
...mean (sd)	9.98 (4.40)	9.99 (4.31)	9.72 (4.22)	9.71 (4.07)	10.35 (4.25)	10.32 (4.12)	10.06 (4.28)	10.05 (4.15)	0.00
...median [IQR]	9.00 [7.00, 12.00]	9.00 [7.00, 12.00]	9.00 [7.00, 12.00]	9.00 [7.00, 12.00]	10.00 [7.00, 13.00]	10.00 [7.00, 13.00]	9.44 (4.28)	9.44 (4.15)	0.00
Number of Hospitalizations									
...mean (sd)	0.03 (0.17)	0.03 (0.18)	0.02 (0.16)	0.02 (0.16)	0.04 (0.23)	0.04 (0.23)	0.03 (0.20)	0.03 (0.20)	0.00
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 (0.20)	0.00 (0.20)	0.00
Number of hospital days									
...mean (sd)	0.11 (1.04)	0.12 (1.01)	0.10 (0.84)	0.11 (0.90)	0.22 (1.39)	0.22 (1.68)	0.16 (1.16)	0.16 (1.32)	0.00
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 (1.16)	0.00 (1.32)	0.00
Number of Emergency Department (ED) visits									
...mean (sd)	0.21 (0.70)	0.21 (0.77)	0.05 (0.98)	0.05 (0.79)	0.30 (1.13)	0.30 (1.03)	0.20 (0.99)	0.20 (0.90)	0.00
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 (0.99)	0.00 (0.90)	0.00
Number of Office visits									
...mean (sd)	4.20 (3.19)	4.18 (3.01)	4.16 (3.17)	4.15 (3.01)	4.97 (3.57)	4.95 (3.49)	4.53 (3.36)	4.51 (3.23)	0.01
...median [IQR]	3.00 [2.00, 5.00]	3.00 [2.00, 5.00]	3.00 [2.00, 5.00]	3.00 [2.00, 5.00]	4.00 [2.00, 7.00]	4.00 [3.00, 6.00]	3.44 (3.36)	3.44 (3.23)	0.00
Number of Endocrinologist visits									
...mean (sd)	0.69 (2.71)	0.74 (2.81)	0.71 (2.77)	0.75 (2.94)	1.01 (3.82)	1.13 (4.36)	0.84 (3.26)	0.91 (3.61)	-0.02
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 (3.26)	0.00 (3.61)	0.00
Number of internal medicine/family medicine visits									
...mean (sd)	7.21 (12.35)	7.16 (10.75)	6.39 (7.36)	6.54 (7.69)	7.45 (9.63)	7.60 (9.85)	7.07 (9.82)	7.16 (9.50)	-0.01
...median [IQR]	4.00 [0.00, 9.00]	4.00 [0.00, 9.00]	4.00 [2.00, 8.00]	4.00 [2.00, 9.00]	5.00 [2.00, 10.00]	5.00 [2.00, 10.00]	4.44 (9.82)	4.44 (9.50)	0.00
Number of Cardiologist visits									
...mean (sd)	0.77 (2.66)	0.76 (2.51)	0.64 (2.39)	0.62 (2.14)	1.32 (3.64)	1.33 (3.67)	0.97 (3.06)	0.97 (2.99)	0.00
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	0.00 (3.06)	0.00 (2.99)	0.00
Number electrocardiograms received									
...mean (sd)	0.35 (0.83)	0.35 (0.86)	0.34 (0.82)	0.34 (0.81)	0.49 (1.03)	0.48 (1.05)	0.41 (0.92)	0.40 (0.93)	0.01
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	0.00 (0.92)	0.00 (0.93)	0.00
Number of HbA1c tests ordered									
...mean (sd)	1.35 (0.88)	1.35 (0.86)	1.26 (0.88)	1.26 (0.86)	1.56 (0.86)	1.56 (0.80)	1.41 (0.87)	1.41 (0.83)	0.00
...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]	2.00 [1.00, 2.00]	2.00 [1.00, 2.00]	1.44 (0.87)	1.44 (0.83)	0.00
Number of glucose tests ordered									
...mean (sd)	0.42 (1.48)	0.42 (1.17)	0.39 (0.99)	0.40 (1.12)	0.43 (1.03)	0.43 (1.07)	0.42 (1.15)	0.42 (1.11)	0.00
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 (1.15)	0.00 (1.11)	0.00
Number of lipid tests ordered									
...mean (sd)	1.05 (0.93)	1.05 (0.93)	1.04 (1.21)	1.04 (1.19)	1.11 (0.84)	1.10 (0.82)	1.07 (0.99)	1.07 (0.97)	0.00
...median [IQR]	1.00 [0.00, 2.00]	1.00 [0.00, 2.00]	1.00 [0.00, 1.00]	1.00 [0.00, 1.00]	1.00 [1.00, 2.00]	1.00 [1.00, 2.00]	1.00 (0.99)	1.00 (0.97)	0.00
Number of creatinine tests ordered									
...mean (sd)	0.03 (0.22)	0.03 (0.22)	0.04 (0.24)	0.04 (0.24)	0.06 (0.32)	0.07 (0.33)	0.05 (0.27)	0.05 (0.28)	0.00
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 (0.27)	0.00 (0.28)	0.00
Number of BUN tests ordered									
...mean (sd)	0.02 (0.16)	0.02 (0.16)	0.02 (0.18)	0.02 (0.17)	0.04 (0.25)	0.04 (0.26)	0.03 (0.21)	0.03 (0.21)	0.00
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 (0.21)	0.00 (0.21)	0.00
Number of tests for microalbuminuria									
...mean (sd)	0.83 (1.17)	0.83 (1.15)	0.74 (1.09)	0.73 (1.09)	0.53 (0.72)	0.53 (0.72)	0.67 (0.97)	0.67 (0.96)	0.00
...median [IQR]	0.00 [0.00, 2.00]	0.00 [0.00, 2.00]	0.00 [0.00, 2.00]	0.00 [0.00, 2.00]	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	0.00 (0.97)	0.00 (0.96)	0.00
Total N distinct ICD9/ICD10 diagnoses at the 3rd digit level									
...mean (sd)	5.59 (5.88)	5.54 (5.90)	2.18 (3.30)	2.12 (3.35)	5.83 (6.80)	5.75 (6.82)	4.66 (5.70)	4.59 (5.72)	0.01
...median [IQR]	5.00 [0.00, 8.00]	5.00 [0.00, 8.00]	0.00 [0.00, 4.00]	0.00 [0.00, 4.00]	4.00 [0.00, 9.00]	4.00 [0.00, 9.00]	3.04 (5.70)	3.04 (5.72)	0.00
Use of thiazide; n (%)	2,545 (13.0%)	2,533 (13.0%)	2,933 (12.7%)	2,948 (12.7%)	5,006 (15.0%)	5,024 (15.0%)	10,484 (13.8%)	10,505 (13.8%)	0.00
Use of beta blockers; n (%)	7,182 (36.8%)	7,314 (37.4%)	8,219 (35.5%)	8,226 (35.5%)	16,252 (48.7%)	16,300 (48.8%)	31,653 (41.6%)	31,840 (41.8%)	0.00
Use of calcium channel blockers; n (%)	5,692 (29.1%)	5,762 (29.5%)	6,794 (29.3%)	6,841 (29.5%)	11,246 (33.7%)	11,422 (34.2%)	23,732 (31.2%)	24,025 (31.6%)	-0.01

Appendix B: Canagliflozin vs 2nd Generation Sulfonylureas

Optum

MarketScan

Medicare

BEFORE PS MATCHING

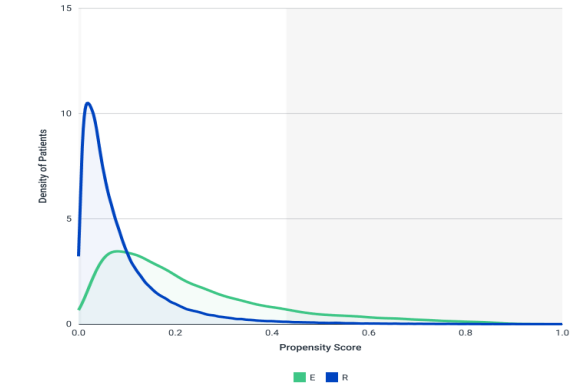


Figure 49: Pre-matching propensity score overlap

The c-statistics for the propensity score model, pre-matching was 0.795. The post-matching c-statistic was 0.524.

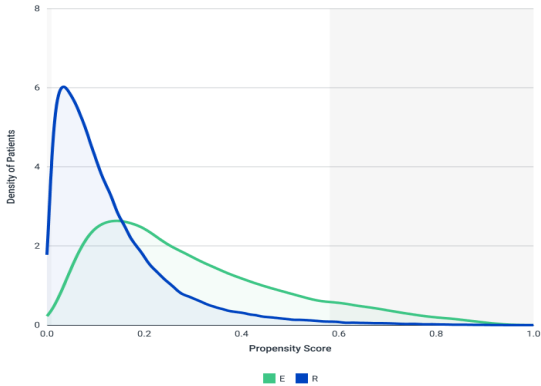


Figure 49: Pre-matching propensity score overlap

The c-statistics for the propensity score model, pre-matching was 0.786. The post-matching c-statistic was 0.52.

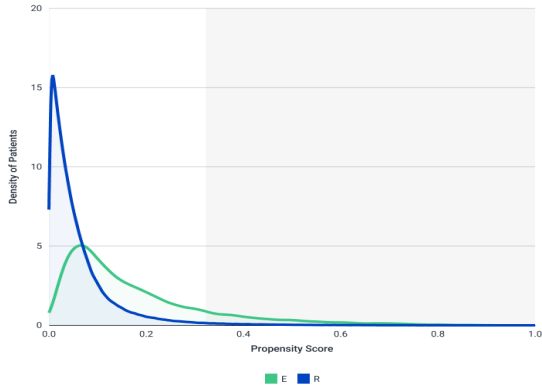


Figure 24: Pre-matching propensity score overlap

The c-statistics for the propensity score model, pre-matching was 0.805. The post-matching c-statistic was 0.525.

AFTER PS MATCHING

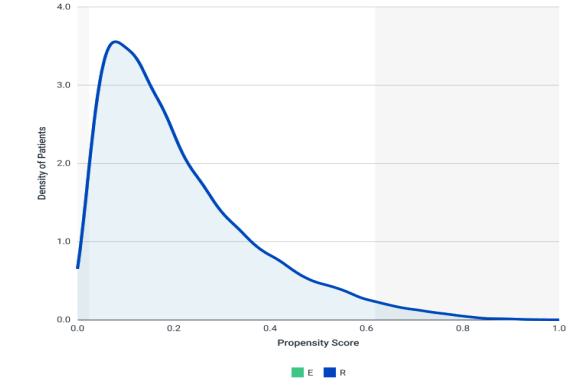


Figure 50: Post-matching propensity score overlap

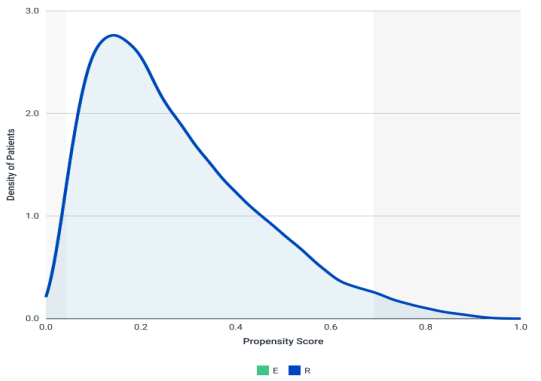


Figure 50: Post-matching propensity score overlap

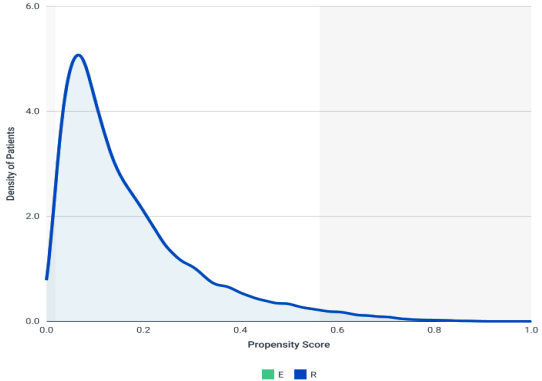


Figure 25: Post-matching propensity score overlap

Table 1

Variable	Unmatched								
	Optum		MarketScan		Medicare		POOLED		St. Diff.
	Reference- 2nd Generation SUs	Exposure- Canagliflozin	Reference- 2nd Generation SUs	Exposure- Canagliflozin	Reference- 2nd Generation SUs	Exposure- Canagliflozin	Reference- 2nd Generation SUs	Exposure- Canagliflozin	
Number of patients	154,886	17,154	132,040	24,318	385,432	28,987	672,358	70,459	
Age									
...mean (sd)	67.76 (9.26)	61.96 (7.84)	62.52 (9.22)	59.18 (6.40)	73.86 (7.06)	71.03 (5.27)	70.23 (8.06)	64.73 (6.37)	0.76
...median [IQR]	68.00 [61.00, 74.00]	61.00 [56.00, 67.00]	61.00 [56.00, 67.00]	59.00 [54.00, 63.00]	72.00 [68.00, 78.00]	70.00 [67.00, 74.00]	68.92 (8.06)	64.01 (6.37)	0.68
Age categories									
...18 - 54; n (%)	14,732 (9.5%)	3,424 (20.0%)	25,558 (19.4%)	6,293 (25.9%)	0 (0.0%)	0 (0.0%)	40,290 (6.0%)	9,717 (13.8%)	-0.26
...55 - 64; n (%)	38,435 (24.8%)	7,427 (43.3%)	66,089 (50.1%)	14,196 (58.4%)	5,075 (1.3%)	329 (1.1%)	109,599 (16.3%)	21,952 (31.2%)	-0.36
...65 - 74; n (%)	65,092 (42.0%)	5,148 (30.0%)	24,049 (18.2%)	3,180 (13.1%)	227,622 (59.1%)	22,378 (77.2%)	316,763 (47.1%)	30,706 (43.6%)	0.07
...≥ 75; n (%)	36,627 (23.6%)	1,155 (6.7%)	16,344 (12.4%)	649 (2.7%)	152,735 (39.6%)	6,280 (21.7%)	205,706 (30.6%)	8,084 (11.5%)	0.48
Gender									
...Males; n (%)	80,936 (52.3%)	9,575 (55.8%)	74,065 (56.1%)	13,608 (56.0%)	176,834 (45.9%)	14,378 (49.6%)	331,835 (49.4%)	37,561 (53.3%)	-0.08
...Females; n (%)	73,950 (47.7%)	7,579 (44.2%)	57,975 (43.9%)	10,710 (44.0%)	208,598 (54.1%)	14,609 (50.4%)	340,523 (50.6%)	32,898 (46.7%)	0.08
Race									
...White; n (%)	N/A	N/A	N/A	N/A	293,566 (76.2%)	23,286 (80.3%)	293,566 (76.2%)	23,286 (80.3%)	-0.10
...Black; n (%)	N/A	N/A	N/A	N/A	46,063 (12.0%)	2,353 (8.1%)	46,063 (12.0%)	2,353 (8.1%)	0.13
...Asian; n (%)	N/A	N/A	N/A	N/A	14,026 (3.6%)	1,041 (3.6%)	14,026 (3.6%)	1,041 (3.6%)	0.00
...Hispanic; n (%)	N/A	N/A	N/A	N/A	15,651 (4.1%)	982 (3.4%)	15,651 (4.1%)	982 (3.4%)	0.04
...North American Native; n (%)	N/A	N/A	N/A	N/A	2,642 (0.7%)	116 (0.4%)	2,642 (0.7%)	116 (0.4%)	0.04
...Other/Unknown; n (%)	N/A	N/A	N/A	N/A	13,484 (3.5%)	1,209 (4.2%)	13,484 (3.5%)	1,209 (4.2%)	-0.04
Region (lumping missing&other category with West)									
...Northeast; n (%)	16,655 (10.8%)	1,468 (8.6%)	21,643 (16.4%)	4,599 (18.9%)	63,475 (16.5%)	5,473 (18.9%)	101,773 (15.1%)	11,540 (16.4%)	-0.04
...South; n (%)	74,258 (47.9%)	9,215 (53.7%)	33,357 (25.3%)	4,231 (17.4%)	162,072 (42.0%)	12,619 (43.5%)	269,687 (40.1%)	26,065 (37.0%)	0.06
...Midwest; n (%)	31,842 (20.6%)	3,552 (20.7%)	57,680 (43.7%)	12,979 (53.4%)	95,692 (24.8%)	5,876 (20.3%)	185,214 (27.5%)	22,407 (31.8%)	-0.09
...West; n (%)	32,131 (20.7%)	2,919 (17.0%)	17,703 (13.4%)	2,224 (9.1%)	64,193 (16.7%)	5,019 (17.3%)	114,027 (17.0%)	10,162 (14.4%)	0.07
...Unknown+missing; n (%)	N/A	N/A	1,657 (1.3%)	285 (1.2%)	N/A	N/A	1,657 (1.3%)	285 (1.2%)	0.01
CV Covariates									
Ischemic heart disease; n (%)	28,161 (18.2%)	2,488 (14.5%)	18,313 (13.9%)	2,973 (12.2%)	100,011 (25.9%)	7,262 (25.1%)	146,485 (21.8%)	12,723 (18.1%)	0.09
Acute MI; n (%)	644 (0.4%)	39 (0.2%)	444 (0.3%)	58 (0.2%)	1,926 (0.5%)	101 (0.3%)	3,014 (0.4%)	198 (0.3%)	0.02
ACS/unstable angina; n (%)	778 (0.5%)	76 (0.4%)	524 (0.4%)	81 (0.3%)	2,195 (0.6%)	149 (0.5%)	3,497 (0.5%)	306 (0.4%)	0.01
Old MI; n (%)	3,799 (2.5%)	290 (1.7%)	1,411 (1.1%)	196 (0.8%)	11,166 (2.9%)	703 (2.4%)	16,376 (2.4%)	1,189 (1.7%)	0.05
Stable angina; n (%)	4,163 (2.7%)	350 (2.0%)	2,056 (1.6%)	318 (1.3%)	10,964 (2.8%)	864 (3.0%)	17,183 (2.6%)	1,532 (2.2%)	0.03
Coronary atherosclerosis and other forms of chronic ischemic heart disease; n (%)	26,304 (17.0%)	2,355 (13.7%)	17,287 (13.1%)	2,811 (11.6%)	96,007 (24.9%)	6,954 (24.0%)	139,598 (20.8%)	12,120 (17.2%)	0.09
Other atherosclerosis with ICD10 Copy; n (%)	962 (0.6%)	74 (0.4%)	670 (0.5%)	132 (0.5%)	4,672 (1.2%)	340 (1.2%)	6,304 (0.9%)	546 (0.8%)	0.01
Previous cardiac procedure (CABG or PTCA or Stent) ; n (%)	256 (0.2%)	18 (0.1%)	227 (0.2%)	32 (0.1%)	734 (0.2%)	53 (0.2%)	1,217 (0.2%)	103 (0.1%)	0.03
History of CABG or PTCA; n (%)	6,458 (4.2%)	505 (2.9%)	2,302 (1.7%)	345 (1.4%)	24,925 (6.5%)	1,676 (5.8%)	33,685 (5.0%)	2,526 (3.6%)	0.07
Any stroke; n (%)	5,514 (3.6%)	452 (2.6%)	3,637 (2.8%)	480 (2.0%)	22,740 (5.9%)	1,588 (5.5%)	31,891 (4.7%)	2,520 (3.6%)	0.06
Ischemic stroke (w and w/o mention of cerebral infarction); n (%)	5,460 (3.5%)	449 (2.6%)	3,611 (2.7%)	475 (2.0%)	22,597 (5.9%)	1,580 (5.5%)	31,668 (4.7%)	2,504 (3.6%)	0.06
Hemorrhagic stroke; n (%)	72 (0.0%)	5 (0.0%)	44 (0.0%)	6 (0.0%)	231 (0.1%)	11 (0.0%)	347 (0.1%)	22 (0.0%)	0.04
TIA; n (%)	654 (0.4%)	52 (0.3%)	432 (0.3%)	47 (0.2%)	2,582 (0.7%)	152 (0.5%)	3,668 (0.5%)	251 (0.4%)	0.01
Other cerebrovascular disease; n (%)	1,586 (1.0%)	109 (0.6%)	842 (0.6%)	98 (0.4%)	6,208 (1.6%)	332 (1.1%)	8,636 (1.3%)	539 (0.8%)	0.05
Late effects of cerebrovascular disease; n (%)	1,489 (1.0%)	77 (0.4%)	610 (0.5%)	50 (0.2%)	5,373 (1.4%)	244 (0.8%)	7,472 (1.1%)	371 (0.5%)	0.07
Cerebrovascular procedure; n (%)	71 (0.0%)	5 (0.0%)	44 (0.0%)	4 (0.0%)	239 (0.1%)	17 (0.1%)	354 (0.1%)	26 (0.0%)	0.04
Heart failure (CHF); n (%)	10,952 (7.1%)	634 (3.7%)	5,273 (4.0%)	480 (2.0%)	36,922 (9.6%)	2,004 (6.9%)	53,147 (7.9%)	3,118 (4.4%)	0.15
Peripheral Vascular Disease (PVD) or PVD Surgery ; n (%)	9,275 (6.0%)	729 (4.2%)	4,752 (3.6%)	643 (2.6%)	34,887 (9.1%)	2,314 (8.0%)	48,914 (7.3%)	3,686 (5.2%)	0.09
Atrial fibrillation; n (%)	10,323 (6.7%)	740 (4.3%)	6,297 (4.8%)	765 (3.1%)	41,954 (10.9%)	2,419 (8.3%)	58,574 (8.7%)	3,924 (5.6%)	0.12
Other cardiac dysrhythmia; n (%)	12,809 (8.3%)	896 (5.2%)	6,775 (5.1%)	799 (3.3%)	43,918 (11.4%)	2,772 (9.6%)	63,502 (9.4%)	4,467 (6.3%)	0.12
Cardiac conduction disorders; n (%)	3,451 (2.2%)	225 (1.3%)	1,828 (1.4%)	211 (0.9%)	12,984 (3.4%)	758 (2.6%)	18,263 (2.7%)	1,194 (1.7%)	0.07
Other CVD; n (%)	13,518 (8.7%)	1,010 (5.9%)	8,464 (6.4%)	1,176 (4.8%)	48,376 (12.6%)	3,167 (10.9%)	70,358 (10.5%)	5,353 (7.6%)	0.10
Diabetes-related complications									
Diabetic retinopathy; n (%)	8,707 (5.6%)	978 (5.7%)	4,265 (3.2%)	1,010 (4.2%)	22,583 (5.9%)	2,188 (7.5%)	35,555 (5.3%)	4,176 (5.9%)	-0.03
Diabetes with other ophthalmic manifestations; n (%)	1,194 (0.8%)	100 (0.6%)	2,603 (2.0%)	618 (2.5%)	8,498 (2.2%)	828 (2.9%)	12,295 (1.8%)	1,546 (2.2%)	-0.03
Retinal detachment, vitreous hemorrhage, vitrectomy; n (%)	541 (0.3%)	61 (0.4%)	305 (0.2%)	64 (0.3%)	1,186 (0.3%)	119 (0.4%)	2,032 (0.3%)	244 (0.3%)	0.00
Retinal laser coagulation therapy; n (%)	711 (0.5%)	104 (0.6%)	514 (0.4%)	115 (0.5%)	1,635 (0.4%)	205 (0.7%)	2,860 (0.4%)	424 (0.6%)	-0.03
Occurrence of Diabetic Neuropathy Copy; n (%)	25,944 (16.8%)	2,962 (17.3%)	12,232 (9.3%)	2,705 (11.1%)	61,265 (15.9%)	5,766 (19.9%)	99,441 (14.8%)	11,433 (16.2%)	-0.04

Table 1

Occurrence of diabetic nephropathy with ICD10 Copy; n (%)	23,516 (15.2%)	1,648 (9.6%)	8,598 (6.5%)	1,283 (5.3%)	37,114 (9.6%)	2,340 (8.1%)	69,228 (10.3%)	5,271 (7.5%)	0.10
Hypoglycemia ; n (%)	2,683 (1.7%)	357 (2.1%)	2,848 (2.2%)	594 (2.4%)	7,156 (1.9%)	660 (2.3%)	12,687 (1.9%)	1,611 (2.3%)	-0.03
Hyperglycemia; n (%)	5,729 (3.7%)	582 (3.4%)	3,944 (3.0%)	627 (2.6%)	15,025 (3.9%)	1,020 (3.5%)	24,698 (3.7%)	2,229 (3.2%)	0.03
Disorders of fluid electrolyte and acid-base balance; n (%)	8,950 (5.8%)	552 (3.2%)	4,904 (3.7%)	534 (2.2%)	25,824 (6.7%)	1,227 (4.2%)	39,678 (5.9%)	2,313 (3.3%)	0.12
Diabetic ketoacidosis; n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	000 (0.0%)	00 (0.0%)	#DIV/0!
Hyperosmolar hyperglycemic nonketotic syndrome (HONK); n (%)	677 (0.4%)	76 (0.4%)	472 (0.4%)	73 (0.3%)	1,573 (0.4%)	144 (0.5%)	2,722 (0.4%)	293 (0.4%)	0.00
Diabetes with peripheral circulatory disorders with ICD-10 Copy; n (%)	10,012 (6.5%)	787 (4.6%)	3,656 (2.8%)	613 (2.5%)	24,561 (6.4%)	1,804 (6.2%)	38,229 (5.7%)	3,204 (4.5%)	0.05
Diabetic Foot; n (%)	2,746 (1.8%)	225 (1.3%)	1,770 (1.3%)	267 (1.1%)	8,551 (2.2%)	561 (1.9%)	13,067 (1.9%)	1,053 (1.5%)	0.03
Gangrene ; n (%)	196 (0.1%)	21 (0.1%)	140 (0.1%)	5 (0.0%)	528 (0.1%)	19 (0.1%)	864 (0.1%)	45 (0.1%)	0.00
Lower extremity amputation; n (%)	771 (0.5%)	46 (0.3%)	205 (0.2%)	24 (0.1%)	1,708 (0.4%)	84 (0.3%)	2,684 (0.4%)	154 (0.2%)	0.04
Osteomyelitis; n (%)	575 (0.4%)	43 (0.3%)	368 (0.3%)	45 (0.2%)	1,347 (0.3%)	74 (0.3%)	2,290 (0.3%)	162 (0.2%)	0.02
Skin infections ; n (%)	7,163 (4.6%)	798 (4.7%)	5,853 (4.4%)	994 (4.1%)	21,559 (5.6%)	1,617 (5.6%)	34,575 (5.1%)	3,409 (4.8%)	0.01
Erectile dysfunction; n (%)	4,013 (2.6%)	591 (3.4%)	3,090 (2.3%)	691 (2.8%)	7,642 (2.0%)	868 (3.0%)	14,745 (2.2%)	2,150 (3.1%)	-0.06
Diabetes with unspecified complication; n (%)	7,328 (4.7%)	839 (4.9%)	4,931 (3.7%)	1,046 (4.3%)	16,772 (4.4%)	1,530 (5.3%)	29,031 (4.3%)	3,415 (4.8%)	-0.02
Diabetes mellitus without mention of complications; n (%)	131,414 (84.8%)	14,605 (85.1%)	120,351 (91.1%)	22,432 (92.2%)	355,860 (92.3%)	26,575 (91.7%)	607,625 (90.4%)	63,612 (90.3%)	0.00
Hypertension: 1 inpatient or 2 outpatient claims within 365 days; n (%)	140,329 (90.6%)	15,738 (91.7%)	111,054 (84.1%)	21,293 (87.6%)	364,169 (94.5%)	27,766 (95.8%)	615,552 (91.6%)	64,797 (92.0%)	-0.01
Hyperlipidemia ; n (%)	111,115 (71.7%)	13,329 (77.7%)	89,589 (67.8%)	18,477 (76.0%)	293,228 (76.1%)	23,958 (82.7%)	493,932 (73.5%)	55,764 (79.1%)	-0.13
Edema; n (%)	8,922 (5.8%)	767 (4.5%)	4,785 (3.6%)	772 (3.2%)	31,716 (8.2%)	2,111 (7.3%)	45,423 (6.8%)	3,650 (5.2%)	0.07
Renal Dysfunction (non-diabetic) ; n (%)	31,030 (20.0%)	1,617 (9.4%)	13,265 (10.0%)	1,233 (5.1%)	75,670 (19.6%)	3,535 (12.2%)	119,965 (17.8%)	6,385 (9.1%)	0.26
Occurrence of acute renal disease ; n (%)	3,885 (2.5%)	136 (0.8%)	1,944 (1.5%)	95 (0.4%)	10,543 (2.7%)	322 (1.1%)	16,372 (2.4%)	553 (0.8%)	0.13
Occurrence of chronic renal insufficiency; n (%)	26,302 (17.0%)	1,333 (7.8%)	9,757 (7.4%)	892 (3.7%)	63,348 (16.4%)	2,891 (10.0%)	99,407 (14.8%)	5,116 (7.3%)	0.24
Chronic kidney disease ; n (%)	25,400 (16.4%)	1,244 (7.3%)	9,238 (7.0%)	765 (3.1%)	60,327 (15.7%)	2,654 (9.2%)	94,965 (14.1%)	4,663 (6.6%)	0.25
CKD Stage 3-4; n (%)	17,724 (11.4%)	638 (3.7%)	6,019 (4.6%)	375 (1.5%)	42,095 (10.9%)	1,536 (5.3%)	65,838 (9.8%)	2,549 (3.6%)	0.25
Occurrence of hypertensive nephropathy; n (%)	11,901 (7.7%)	539 (3.1%)	4,074 (3.1%)	305 (1.3%)	25,957 (6.7%)	1,009 (3.5%)	41,932 (6.2%)	1,853 (2.6%)	0.18
Occurrence of miscellaneous renal insufficiency ; n (%)	6,270 (4.0%)	315 (1.8%)	3,464 (2.6%)	373 (1.5%)	20,943 (5.4%)	1,032 (3.6%)	30,677 (4.6%)	1,720 (2.4%)	0.12
Glaucoma or cataracts ; n (%)	29,202 (18.9%)	2,865 (16.7%)	18,976 (14.4%)	3,293 (13.5%)	96,718 (25.1%)	7,893 (27.2%)	144,896 (21.6%)	14,051 (19.9%)	0.04
Cellulitis or abscess of toe; n (%)	1,798 (1.2%)	152 (0.9%)	980 (0.7%)	137 (0.6%)	4,579 (1.2%)	308 (1.1%)	7,357 (1.1%)	597 (0.8%)	0.03
Foot ulcer; n (%)	2,634 (1.7%)	213 (1.2%)	1,736 (1.3%)	264 (1.1%)	8,482 (2.2%)	558 (1.9%)	12,852 (1.9%)	1,035 (1.5%)	0.03
Bladder stones; n (%)	170 (0.1%)	13 (0.1%)	132 (0.1%)	16 (0.1%)	548 (0.1%)	37 (0.1%)	850 (0.1%)	66 (0.1%)	0.00
Kidney stones; n (%)	2,807 (1.8%)	261 (1.5%)	2,375 (1.8%)	433 (1.8%)	8,275 (2.1%)	659 (2.3%)	13,457 (2.0%)	1,353 (1.9%)	0.01
Urinary tract infections (UTIs); n (%)	11,361 (7.3%)	883 (5.1%)	6,545 (5.0%)	963 (4.0%)	41,611 (10.8%)	2,560 (8.8%)	59,517 (8.9%)	4,406 (6.3%)	0.10
Dipstick urinalysis; n (%)	49,794 (32.1%)	5,364 (31.3%)	37,552 (28.4%)	7,447 (30.6%)	135,533 (35.2%)	10,690 (36.9%)	222,879 (33.1%)	23,501 (33.4%)	-0.01
Non-dipstick urinalysis; n (%)	64,593 (41.7%)	7,874 (45.9%)	44,790 (33.9%)	10,311 (42.4%)	151,194 (39.2%)	13,426 (46.3%)	260,577 (38.8%)	31,611 (44.9%)	-0.12
Urine function test; n (%)	2,926 (1.9%)	230 (1.3%)	2,192 (1.7%)	317 (1.3%)	10,601 (2.8%)	809 (2.8%)	15,719 (2.3%)	1,356 (1.9%)	0.03
Cytology; n (%)	733 (0.5%)	74 (0.4%)	752 (0.6%)	124 (0.5%)	2,588 (0.7%)	202 (0.7%)	4,073 (0.6%)	400 (0.6%)	0.00
Cystoscopy; n (%)	1,397 (0.9%)	110 (0.6%)	1,137 (0.9%)	161 (0.7%)	4,335 (1.1%)	295 (1.0%)	6,869 (1.0%)	566 (0.8%)	0.02
Other Covariates									
Liver disease; n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	#VALUE!	000 (0.0%)	#VALUE!
Osteoarthritis; n (%)	18,548 (12.0%)	1,772 (10.3%)	10,553 (8.0%)	1,694 (7.0%)	64,696 (16.8%)	4,889 (16.9%)	93,797 (14.0%)	8,355 (11.9%)	0.06
Other arthritis, arthropathies and musculoskeletal pain; n (%)	43,333 (28.0%)	4,698 (27.4%)	31,686 (24.0%)	5,758 (23.7%)	134,642 (34.9%)	10,271 (35.4%)	209,661 (31.2%)	20,727 (29.4%)	0.04
Dorsopathies; n (%)	27,300 (17.6%)	3,034 (17.7%)	19,269 (14.6%)	3,723 (15.3%)	80,976 (21.0%)	6,590 (22.7%)	127,545 (19.0%)	13,347 (18.9%)	0.00
Fractures; n (%)	3,317 (2.1%)	299 (1.7%)	2,317 (1.8%)	355 (1.5%)	11,160 (2.9%)	681 (2.3%)	16,794 (2.5%)	1,335 (1.9%)	0.04
Falls ; n (%)	4,393 (2.8%)	292 (1.7%)	1,273 (1.0%)	126 (0.5%)	13,534 (3.5%)	651 (2.2%)	19,200 (2.9%)	1,069 (1.5%)	0.10
Osteoporosis; n (%)	6,177 (4.0%)	446 (2.6%)	2,182 (1.7%)	323 (1.3%)	23,320 (6.1%)	1,802 (6.2%)	31,679 (4.7%)	2,571 (3.6%)	0.06
Hyperthyroidism; n (%)	881 (0.6%)	92 (0.5%)	541 (0.4%)	104 (0.4%)	2,984 (0.8%)	244 (0.8%)	4,406 (0.7%)	440 (0.6%)	0.01
Hypothyroidism ; n (%)	21,624 (14.0%)	2,517 (14.7%)	13,319 (10.1%)	2,893 (11.9%)	44,004 (11.4%)	3,638 (12.6%)	78,947 (11.7%)	9,048 (12.8%)	-0.03
Other disorders of thyroid gland ; n (%)	4,419 (2.9%)	666 (3.9%)	3,264 (2.5%)	897 (3.7%)	12,341 (3.2%)	1,310 (4.5%)	20,024 (3.0%)	2,873 (4.1%)	-0.06
Depression; n (%)	10,169 (6.6%)	1,264 (7.4%)	7,134 (5.4%)	1,503 (6.2%)	32,440 (8.4%)	2,562 (8.8%)	49,743 (7.4%)	5,329 (7.6%)	-0.01
Anxiety; n (%)	9,789 (6.3%)	1,176 (6.9%)	5,860 (4.4%)	1,146 (4.7%)	26,959 (7.0%)	2,045 (7.1%)	42,608 (6.3%)	4,367 (6.2%)	0.00
Sleep_Disorder; n (%)	7,808 (5.0%)	1,334 (7.8%)	9,758 (7.4%)	2,822 (11.6%)	24,586 (6.4%)	2,463 (8.5%)	42,152 (6.3%)	6,619 (9.4%)	-0.12
Dementia; n (%)	4,899 (3.2%)	163 (1.0%)	2,106 (1.6%)	124 (0.5%)	23,566 (6.1%)	942 (3.2%)	30,571 (4.5%)	1,229 (1.7%)	0.16
Delirium; n (%)	1,146 (0.7%)	47 (0.3%)	567 (0.4%)	36 (0.1%)	4,774 (1.2%)	187 (0.6%)	6,487 (1.0%)	270 (0.4%)	0.07
Psychosis; n (%)	1,233 (0.8%)	77 (0.4%)	619 (0.5%)	46 (0.2%)	5,761 (1.5%)	258 (0.9%)	7,613 (1.1%)	381 (0.5%)	0.07
Obesity; n (%)	29,896 (19.3%)	4,631 (27.0%)	18,364 (13.9%)	4,643 (19.1%)	48,909 (12.7%)	5,747 (19.8%)	97,169 (14.5%)	15,021 (21.3%)	-0.18
Overweight; n (%)	8,442 (5.5%)	854 (5.0%)	2,983 (2.3%)	553 (2.3%)	12,502 (3.2%)	1,070 (3.7%)	23,927 (3.6%)	2,477 (3.5%)	0.01
Smoking; n (%)	14,958 (9.7%)	1,412 (8.2%)	7,989 (6.1%)	1,213 (5.0%)	44,623 (11.6%)	3,182 (11.0%)	67,570 (10.0%)	5,807 (8.2%)	0.06
Alcohol abuse or dependence; n (%)	56 (0.0%)	0 (0.0%)	37 (0.0%)	6 (0.0%)	**	**	**	**	**
Drug abuse or dependence; n (%)	63 (0.0%)	7 (0.0%)	25 (0.0%)	4 (0.0%)	**	**	**	**	**
COPD; n (%)	11,438 (7.4%)	842 (4.9%)	5,445 (4.1%)	667 (2.7%)	35,836 (9.3%)	2,375 (8.2%)	52,719 (7.8%)	3,884 (5.5%)	0.09

Table 1

Asthma; n (%)	6,705 (4.3%)	826 (4.8%)	4,598 (3.5%)	883 (3.6%)	18,875 (4.9%)	1,554 (5.4%)	30,178 (4.5%)	3,263 (4.6%)	0.00
Obstructive sleep apnea; n (%)	12,320 (8.0%)	2,043 (11.9%)	11,112 (8.4%)	3,033 (12.5%)	23,357 (6.1%)	2,710 (9.3%)	46,789 (7.0%)	7,786 (11.1%)	-0.14
Pneumonia; n (%)	2,800 (1.8%)	193 (1.1%)	1,979 (1.5%)	213 (0.9%)	9,582 (2.5%)	478 (1.6%)	14,361 (2.1%)	884 (1.3%)	0.06
Imaging; n (%)	70 (0.0%)	3 (0.0%)	3 (0.0%)	3 (0.0%)	173 (0.0%)	12 (0.0%)	277 (0.0%)	18 (0.0%)	#DIV/0!
Diabetes Medications									
DM Medications - AGIs; n (%)	589 (0.4%)	64 (0.4%)	395 (0.3%)	78 (0.3%)	1,594 (0.4%)	198 (0.7%)	2,578 (0.4%)	340 (0.5%)	-0.01
DM Medications - Glitazones; n (%)	10,422 (6.7%)	1,544 (9.0%)	8,718 (6.6%)	2,208 (9.1%)	24,517 (6.4%)	2,742 (9.5%)	43,657 (6.5%)	6,494 (9.2%)	-0.10
DM Medications - Insulin; n (%)	19,589 (12.6%)	5,087 (29.7%)	15,413 (11.7%)	7,310 (30.1%)	53,691 (13.9%)	10,058 (34.7%)	88,693 (13.2%)	22,455 (31.9%)	-0.46
DM Medications - Meglitinides; n (%)	924 (0.6%)	247 (1.4%)	1,054 (0.8%)	491 (2.0%)	3,952 (1.0%)	817 (2.8%)	5,930 (0.9%)	1,555 (2.2%)	-0.11
DM Medications - Metformin; n (%)	108,309 (69.9%)	13,385 (78.0%)	96,831 (73.3%)	19,082 (78.5%)	254,527 (66.0%)	21,505 (74.2%)	459,667 (68.4%)	53,972 (76.6%)	-0.18
Concomitant initiation or current use of DPP4i Copy; n (%)	17,486 (11.3%)	3,345 (19.5%)	21,174 (16.0%)	5,938 (24.4%)	51,735 (13.4%)	7,439 (25.7%)	90,395 (13.4%)	16,722 (23.7%)	-0.27
Concomitant initiation or current use of AGIs; n (%)	425 (0.3%)	45 (0.3%)	286 (0.2%)	39 (0.2%)	1,174 (0.3%)	139 (0.5%)	1,885 (0.3%)	223 (0.3%)	0.00
Concomitant initiation or current use of Glitazones; n (%)	8,576 (5.5%)	1,175 (6.8%)	7,176 (5.4%)	1,639 (6.7%)	20,067 (5.2%)	2,075 (7.2%)	35,819 (5.3%)	4,889 (6.9%)	-0.07
Concomitant initiation or current use of GLP-1 RA; n (%)	4,299 (2.8%)	2,107 (12.3%)	4,901 (3.7%)	3,223 (13.3%)	7,426 (1.9%)	2,835 (9.8%)	16,626 (2.5%)	8,165 (11.6%)	-0.36
Concomitant initiation or current use of Insulin; n (%)	13,776 (8.9%)	3,869 (22.6%)	11,356 (8.6%)	5,709 (23.5%)	39,091 (10.1%)	8,072 (27.8%)	64,223 (9.6%)	17,650 (25.1%)	-0.42
Concomitant initiation or current use of Meglitinides; n (%)	613 (0.4%)	171 (1.0%)	711 (0.5%)	321 (1.3%)	2,576 (0.7%)	581 (2.0%)	3,900 (0.6%)	1,073 (1.5%)	-0.09
Concomitant initiation or current use of Metformin; n (%)	92,596 (59.8%)	11,270 (65.7%)	83,076 (62.9%)	16,009 (65.8%)	217,493 (56.4%)	18,170 (62.7%)	393,165 (58.5%)	45,449 (64.5%)	-0.12
Past use of DPP4i Copy; n (%)	6,565 (4.2%)	1,159 (6.8%)	5,963 (4.5%)	1,809 (7.4%)	17,310 (4.5%)	2,138 (7.4%)	29,838 (4.4%)	5,106 (7.2%)	-0.12
Past use of AGIs Copy; n (%)	164 (0.1%)	19 (0.1%)	109 (0.1%)	39 (0.2%)	420 (0.1%)	59 (0.2%)	693 (0.1%)	117 (0.2%)	-0.03
Past use of Glitazones Copy; n (%)	1,846 (1.2%)	369 (2.2%)	1,543 (1.2%)	569 (2.3%)	4,450 (1.2%)	667 (2.3%)	7,839 (1.2%)	1,605 (2.3%)	-0.08
Past use of GLP-1 RA Copy; n (%)	2,375 (1.5%)	888 (5.2%)	2,076 (1.6%)	1,436 (5.9%)	4,256 (1.1%)	1,234 (4.3%)	8,707 (1.3%)	3,558 (5.0%)	-0.21
Past use of Insulin Copy; n (%)	5,813 (3.8%)	1,218 (7.1%)	4,057 (3.1%)	1,601 (6.6%)	14,604 (3.8%)	1,987 (6.9%)	24,474 (3.6%)	4,806 (6.8%)	-0.14
Past use of Meglitinides Copy; n (%)	311 (0.2%)	76 (0.4%)	343 (0.3%)	170 (0.7%)	1,376 (0.4%)	236 (0.8%)	2,030 (0.3%)	482 (0.7%)	-0.06
Past use of metformin (final) Copy; n (%)	15,713 (10.1%)	2,115 (12.3%)	13,756 (10.4%)	3,073 (12.6%)	37,034 (9.6%)	3,335 (11.5%)	66,503 (9.9%)	8,523 (12.1%)	-0.07
Other Medications									
Use of ACE inhibitors; n (%)	84,706 (54.7%)	8,925 (52.0%)	72,224 (54.7%)	12,297 (50.6%)	197,008 (51.1%)	13,650 (47.1%)	353,938 (52.6%)	34,872 (49.5%)	0.06
Use of ARBs; n (%)	47,885 (30.9%)	6,552 (38.2%)	42,148 (31.9%)	9,717 (40.0%)	119,221 (30.9%)	11,500 (39.7%)	209,254 (31.1%)	27,769 (39.4%)	-0.17
Use of Loop Diuretics ; n (%)	19,348 (12.5%)	1,498 (8.7%)	12,373 (9.4%)	1,847 (7.6%)	68,480 (17.8%)	4,431 (15.3%)	100,201 (14.9%)	7,776 (11.0%)	0.12
Use of other diuretics; n (%)	4,344 (2.8%)	466 (2.7%)	3,400 (2.6%)	615 (2.5%)	13,410 (3.5%)	985 (3.4%)	21,154 (3.1%)	2,066 (2.9%)	0.01
Use of nitrates-United; n (%)	7,132 (4.6%)	547 (3.2%)	4,935 (3.7%)	735 (3.0%)	27,238 (7.1%)	1,788 (6.2%)	39,305 (5.8%)	3,070 (4.4%)	0.06
Use of other hypertension drugs; n (%)	11,822 (7.6%)	853 (5.0%)	8,348 (6.3%)	1,083 (4.5%)	34,116 (8.9%)	2,082 (7.2%)	54,286 (8.1%)	4,018 (5.7%)	0.09
Use of digoxin; n (%)	2,388 (1.5%)	178 (1.0%)	1,809 (1.4%)	225 (0.9%)	11,438 (3.0%)	609 (2.1%)	15,635 (2.3%)	1,012 (1.4%)	0.07
Use of Anti-arrhythmics; n (%)	1,811 (1.2%)	148 (0.9%)	1,428 (1.1%)	195 (0.8%)	7,241 (1.9%)	442 (1.5%)	10,480 (1.6%)	785 (1.1%)	0.04
Use of COPD/asthma meds; n (%)	18,661 (12.0%)	2,398 (14.0%)	16,481 (12.5%)	3,563 (14.7%)	54,930 (14.3%)	5,018 (17.3%)	90,072 (13.4%)	10,979 (15.6%)	-0.06
Use of statins; n (%)	106,155 (68.5%)	12,492 (72.8%)	85,402 (64.7%)	17,004 (69.9%)	267,482 (69.4%)	22,004 (75.9%)	459,039 (68.3%)	51,500 (73.1%)	-0.11
Use of other lipid-lowering drugs; n (%)	14,959 (9.7%)	2,353 (13.7%)	15,699 (11.9%)	3,931 (16.2%)	42,819 (11.1%)	4,445 (15.3%)	73,477 (10.9%)	10,729 (15.2%)	-0.13
Use of antiplatelet agents; n (%)	16,208 (10.5%)	1,683 (9.8%)	13,697 (10.4%)	2,526 (10.4%)	50,943 (13.2%)	4,302 (14.8%)	80,848 (12.0%)	8,511 (12.1%)	0.00
Use of oral anticoagulants (Dabigatran, Rivaroxaban, Apixaban, Warfarin); n (%)	9,071 (5.9%)	726 (4.2%)	6,372 (4.8%)	810 (3.3%)	35,017 (9.1%)	2,235 (7.7%)	50,460 (7.5%)	3,771 (5.4%)	0.09
Use of heparin and other low-molecular weight heparins; n (%)	309 (0.2%)	16 (0.1%)	7 (0.0%)	0 (0.0%)	1,042 (0.3%)	70 (0.2%)	1,358 (0.2%)	086 (0.1%)	0.03
Use of NSAIDs; n (%)	21,661 (14.0%)	2,844 (16.6%)	19,311 (14.6%)	3,992 (16.4%)	53,840 (14.0%)	4,711 (16.3%)	94,812 (14.1%)	11,547 (16.4%)	-0.06
Use of oral corticosteroids; n (%)	18,506 (11.9%)	2,069 (12.1%)	15,049 (11.4%)	2,725 (11.2%)	53,287 (13.8%)	4,148 (14.3%)	86,842 (12.9%)	8,942 (12.7%)	0.01
Use of bisphosphonate (United); n (%)	3,267 (2.1%)	202 (1.2%)	1,232 (0.9%)	166 (0.7%)	10,720 (2.8%)	820 (2.8%)	15,219 (2.3%)	1,188 (1.7%)	0.04
Use of opioids; n (%)	28,673 (18.5%)	3,296 (19.2%)	25,050 (19.0%)	4,773 (19.6%)	77,313 (20.1%)	5,898 (20.3%)	131,036 (19.5%)	13,967 (19.8%)	-0.01
Use of antidepressants; n (%)	30,934 (20.0%)	4,117 (24.0%)	24,343 (18.4%)	5,483 (22.5%)	84,498 (21.9%)	7,501 (25.9%)	139,775 (20.8%)	17,101 (24.3%)	-0.08
Use of antipsychotics; n (%)	2,865 (1.8%)	313 (1.8%)	1,708 (1.3%)	306 (1.3%)	10,029 (2.6%)	710 (2.4%)	14,602 (2.2%)	1,329 (1.9%)	0.02
Use of anticonvulsants; n (%)	20,628 (13.3%)	2,395 (14.0%)	12,316 (9.3%)	2,631 (10.8%)	53,496 (13.9%)	4,560 (15.7%)	86,440 (12.9%)	9,586 (13.6%)	-0.02
Use of lithium; n (%)	183 (0.1%)	23 (0.1%)	171 (0.1%)	13 (0.1%)	395 (0.1%)	27 (0.1%)	749 (0.1%)	063 (0.1%)	0.00
Use of Benzos; n (%)	12,618 (8.1%)	1,545 (9.0%)	10,457 (7.9%)	2,066 (8.5%)	37,940 (9.8%)	2,876 (9.9%)	61,015 (9.1%)	6,487 (9.2%)	0.00
Use of anxiolytics/hypnotics; n (%)	6,385 (4.1%)	938 (5.5%)	6,064 (4.6%)	1,394 (5.7%)	17,827 (4.6%)	1,653 (5.7%)	30,276 (4.5%)	3,985 (5.7%)	-0.05
Use of dementia meds; n (%)	3,210 (2.1%)	113 (0.7%)	1,591 (1.2%)	88 (0.4%)	15,947 (4.1%)	791 (2.7%)	20,748 (3.1%)	992 (1.4%)	0.11
Use of antiparkinsonian meds; n (%)	2,966 (1.9%)	338 (2.0%)	1,934 (1.5%)	385 (1.6%)	10,222 (2.7%)	859 (3.0%)	15,122 (2.2%)	1,582 (2.2%)	0.00
Any use of pramlintide; n (%)	3 (0.0%)	28 (0.2%)	22 (0.0%)	43 (0.2%)	22 (0.0%)	35 (0.1%)	047 (0.0%)	106 (0.2%)	-0.06
Any use of 1st generation sulfonylureas; n (%)	18 (0.0%)	2 (0.0%)	57 (0.0%)	1 (0.0%)	**	**	**	**	**
Entresto (sacubitril/valsartan); n (%)	182 (0.1%)	8 (0.0%)	45 (0.0%)	6 (0.0%)	**	**	**	**	**
Initiation as monotherapy Copy; n (%)	16,688 (10.8%)	1,198 (7.0%)	12,296 (9.3%)	1,306 (5.4%)	39,187 (10.2%)	1,233 (4.3%)	68,171 (10.1%)	3,737 (5.3%)	0.18
Labs									
Lab values- HbA1c (%) ; n (%)	60,079 (38.8%)	7,406 (43.2%)	8,994 (6.8%)	1,531 (6.3%)	N/A	N/A	69,073 (24.1%)	8,937 (21.5%)	0.06
Lab values- HbA1c (%) (within 3 months) ; n (%)	46,986 (30.3%)	6,068 (35.4%)	7,101 (5.4%)	1,306 (5.4%)	N/A	N/A	54,087 (18.9%)	7,374 (17.8%)	0.03
Lab values- HbA1c (%) (within 6 months) ; n (%)	60,079 (38.8%)	7,406 (43.2%)	8,994 (6.8%)	1,531 (6.3%)	N/A	N/A	69,073 (24.1%)	8,937 (21.5%)	0.06

Table 1

Lab values- BNP; n (%)	984 (0.6%)	101 (0.6%)	131 (0.1%)	14 (0.1%)	N/A	N/A	1,115 (0.4%)	115 (0.3%)	0.02
Lab values- BNP (within 3 months); n (%)	593 (0.4%)	65 (0.4%)	79 (0.1%)	9 (0.0%)	N/A	N/A	672 (0.2%)	074 (0.2%)	0.00
Lab values- BNP (within 6 months); n (%)	984 (0.6%)	101 (0.6%)	131 (0.1%)	14 (0.1%)	N/A	N/A	1,115 (0.4%)	115 (0.3%)	0.02
Lab values- BUN (mg/dl); n (%)	59,127 (38.2%)	7,320 (42.7%)	7,741 (5.9%)	1,426 (5.9%)	N/A	N/A	66,868 (23.3%)	8,746 (21.1%)	0.05
Lab values- BUN (mg/dl) (within 3 months); n (%)	45,566 (29.4%)	5,834 (34.0%)	5,886 (4.5%)	1,167 (4.8%)	N/A	N/A	51,452 (17.9%)	7,001 (16.9%)	0.03
Lab values- BUN (mg/dl) (within 6 months); n (%)	59,127 (38.2%)	7,320 (42.7%)	7,741 (5.9%)	1,426 (5.9%)	N/A	N/A	66,868 (23.3%)	8,746 (21.1%)	0.05
Lab values- Creatinine (mg/dl) ; n (%)	60,630 (39.1%)	7,582 (44.2%)	8,186 (6.2%)	1,576 (6.5%)	N/A	N/A	68,816 (24.0%)	9,158 (22.1%)	0.05
Lab values- Creatinine (mg/dl) (within 3 months); n (%)	46,724 (30.2%)	6,043 (35.2%)	6,236 (4.7%)	1,301 (5.3%)	N/A	N/A	52,960 (18.5%)	7,344 (17.7%)	0.02
Lab values- Creatinine (mg/dl) (within 6 months); n (%)	60,630 (39.1%)	7,582 (44.2%)	8,186 (6.2%)	1,576 (6.5%)	N/A	N/A	68,816 (24.0%)	9,158 (22.1%)	0.05
Lab values- HDL level (mg/dl); n (%)	50,020 (32.3%)	6,461 (37.7%)	7,994 (6.1%)	1,439 (5.9%)	N/A	N/A	58,014 (20.2%)	7,900 (19.0%)	0.03
Lab values- HDL level (mg/dl) (within 3 months); n (%)	36,675 (23.7%)	4,910 (28.6%)	5,881 (4.5%)	1,126 (4.6%)	N/A	N/A	42,556 (14.8%)	6,036 (14.6%)	0.01
Lab values- HDL level (mg/dl) (within 6 months); n (%)	50,020 (32.3%)	6,461 (37.7%)	7,994 (6.1%)	1,439 (5.9%)	N/A	N/A	58,014 (20.2%)	7,900 (19.0%)	0.03
Lab values- LDL level (mg/dl) ; n (%)	51,820 (33.5%)	6,667 (38.9%)	8,382 (6.3%)	1,463 (6.0%)	N/A	N/A	60,202 (21.0%)	8,130 (19.6%)	0.03
Lab values- LDL level (mg/dl) (within 3 months); n (%)	37,965 (24.5%)	5,085 (29.6%)	6,157 (4.7%)	1,149 (4.7%)	N/A	N/A	44,122 (15.4%)	6,234 (15.0%)	0.01
Lab values- LDL level (mg/dl) (within 6 months) ; n (%)	51,820 (33.5%)	6,667 (38.9%)	8,382 (6.3%)	1,463 (6.0%)	N/A	N/A	60,202 (21.0%)	8,130 (19.6%)	0.03
Lab values- NT-proBNP; n (%)	153 (0.1%)	9 (0.1%)	12 (0.0%)	0 (0.0%)	N/A	N/A	165 (0.1%)	9 (0.0%)	0.04
Lab values- NT-proBNP (within 3 months); n (%)	95 (0.1%)	5 (0.0%)	6 (0.0%)	0 (0.0%)	N/A	N/A	101 (0.0%)	5 (0.0%)	-
Lab values- NT-proBNP (within 6 months); n (%)	153 (0.1%)	9 (0.1%)	12 (0.0%)	0 (0.0%)	N/A	N/A	165 (0.1%)	9 (0.0%)	-
Lab values- Total cholesterol (mg/dl) ; n (%)	50,792 (32.8%)	6,592 (38.4%)	7,701 (5.8%)	1,444 (5.9%)	N/A	N/A	58,493 (20.4%)	8,036 (19.4%)	0.03
Lab values- Total cholesterol (mg/dl) (within 3 months) ; n (%)	37,250 (24.0%)	5,024 (29.3%)	5,639 (4.3%)	1,134 (4.7%)	N/A	N/A	42,889 (14.9%)	6,158 (14.8%)	0.00
Lab values- Total cholesterol (mg/dl) (within 6 months) ; n (%)	50,792 (32.8%)	6,592 (38.4%)	7,701 (5.8%)	1,444 (5.9%)	N/A	N/A	58,493 (20.4%)	8,036 (19.4%)	0.03
Lab values- Triglyceride level (mg/dl); n (%)	50,177 (32.4%)	6,549 (38.2%)	7,861 (6.0%)	1,423 (5.9%)	N/A	N/A	58,038 (20.2%)	7,972 (19.2%)	0.03
Lab values- Triglyceride level (mg/dl) (within 3 months); n (%)	36,827 (23.8%)	4,987 (29.1%)	5,788 (4.4%)	1,120 (4.6%)	N/A	N/A	42,615 (14.9%)	6,107 (14.7%)	0.01
Lab values- Triglyceride level (mg/dl) (within 6 months); n (%)	50,177 (32.4%)	6,549 (38.2%)	7,861 (6.0%)	1,423 (5.9%)	N/A	N/A	58,038 (20.2%)	7,972 (19.2%)	0.03
Lab result number- HbA1c (%) mean (only 2 to 20 included)	59,675	7,362	8,091	1,482	N/A	N/A	67,766	8,844	
...mean (sd)	8.19 (1.84)	8.51 (1.76)	8.39 (1.91)	8.53 (1.75)	N/A	N/A	8.21 (1.85)	8.51 (1.76)	-0.17
...median [IQR]	7.75 [6.93, 9.00]	8.10 [7.25, 9.47]	7.95 [7.00, 9.30]	8.10 [7.30, 9.40]	N/A	N/A	7.77 (1.85)	8.10 (1.76)	-0.18
...Missing; n (%)	95,211 (61.5%)	9,792 (57.1%)	123,949 (93.9%)	22,836 (93.9%)	N/A	N/A	219,160 (76.4%)	32,628 (78.7%)	-0.06
Lab result number- BNP mean	984	101	131	14	N/A	N/A	1,115	115	
...mean (sd)	184.36 (301.56)	69.43 (79.37)	262.73 (698.20)	535.59 (1,297.93)	N/A	N/A	193.57 (370.65)	126.18 (448.51)	0.16
...median [IQR]	77.10 [29.92, 204.97]	41.30 [18.65, 86.70]	61.00 [30.00, 216.00]	55.50 [16.65, 170.65]	N/A	N/A	#VALUE!	#VALUE!	#VALUE!
...Missing; n (%)	153,902 (99.4%)	17,053 (99.4%)	131,909 (99.9%)	24,304 (99.9%)	N/A	N/A	285,811 (99.6%)	41,357 (99.7%)	-0.02
Lab result number- BUN (mg/dl) mean	59,127	7,320	7,741	1,426	N/A	N/A	66,868	8,746	
...mean (sd)	18.65 (8.00)	16.63 (5.60)	1,108.21 (12,786.12)	2,280.99 (18,384.49)	N/A	N/A	144.78 (4350.21)	385.82 (7422.14)	-0.04
...median [IQR]	17.00 [13.50, 22.00]	16.00 [13.00, 19.00]	16.00 [13.00, 20.00]	16.00 [13.00, 19.00]	N/A	N/A	#VALUE!	#VALUE!	#VALUE!
...Missing; n (%)	95,759 (61.8%)	9,834 (57.3%)	124,299 (94.1%)	22,892 (94.1%)	N/A	N/A	220,058 (76.7%)	32,726 (78.9%)	-0.05
Lab result number- Creatinine (mg/dl) mean (only 0.1 to 15 included)	60,232	7,531	7,231	1,439	N/A	N/A	67,463	8,970	
...mean (sd)	1.04 (0.40)	0.92 (0.24)	1.00 (0.36)	0.93 (0.23)	N/A	N/A	1.04 (0.40)	0.92 (0.24)	0.36
...median [IQR]	0.95 [0.79, 1.18]	0.89 [0.76, 1.04]	0.95 [0.79, 1.10]	0.90 [0.76, 1.05]	N/A	N/A	0.95 (0.40)	0.89 (0.24)	0.18
...Missing; n (%)	94,654 (61.1%)	9,623 (56.1%)	124,809 (94.5%)	22,879 (94.1%)	N/A	N/A	219,463 (76.5%)	32,502 (78.4%)	-0.05
Lab result number- HDL level (mg/dl) mean (only <=5000 included)	50,020	6,461	7,944	1,422	N/A	N/A	57,964	7,883	
...mean (sd)	46.42 (13.62)	45.25 (13.20)	44.50 (14.95)	46.24 (105.86)	N/A	N/A	46.16 (13.81)	45.43 (46.52)	0.02
...median [IQR]	44.50 [37.00, 54.00]	43.00 [36.00, 52.00]	43.00 [36.00, 52.00]	42.50 [35.00, 50.06]	N/A	N/A	44.29 (13.81)	42.91 (46.52)	0.04
...Missing; n (%)	104,866 (67.7%)	10,693 (62.3%)	124,096 (94.0%)	22,896 (94.2%)	N/A	N/A	228,962 (79.8%)	33,589 (81.0%)	-0.03
Lab result number- LDL level (mg/dl) mean (only <=5000 included)	50,646	6,539	7,492	1,290	N/A	N/A	58,138	7,829	
...mean (sd)	87.95 (39.92)	84.31 (39.29)	90.16 (42.99)	86.14 (40.59)	N/A	N/A	88.23 (40.33)	84.61 (39.51)	0.09
...median [IQR]	85.00 [64.00, 111.00]	82.00 [61.00, 106.00]	89.00 [66.00, 115.00]	85.00 [62.50, 110.50]	N/A	N/A	85.52 (40.33)	82.49 (39.51)	0.08
...Missing; n (%)	104,240 (67.3%)	10,615 (61.9%)	124,548 (94.3%)	23,028 (94.7%)	N/A	N/A	228,788 (79.7%)	33,643 (81.1%)	-0.04
Lab result number- Total cholesterol (mg/dl) mean (only <=5000 included)	50,753	6,586	7,649	1,425	N/A	N/A	58,402	8,011	
...mean (sd)	174.22 (46.76)	172.48 (46.71)	175.10 (52.79)	171.47 (55.16)	N/A	N/A	174.34 (47.59)	172.30 (48.32)	0.04
...median [IQR]	168.00 [143.00, 199.00]	166.50 [142.00, 195.50]	172.00 [146.00, 204.00]	169.00 [143.00, 196.00]	N/A	N/A	168.52 (47.59)	166.94 (48.32)	0.03
...Missing; n (%)	104,133 (67.2%)	10,568 (61.6%)	124,391 (94.2%)	22,893 (94.1%)	N/A	N/A	228,524 (79.6%)	33,461 (80.7%)	-0.03

Table 1

Lab result number- Triglyceride level (mg/dl) mean (only =<5000 included)	50,170	6,548	7,808	1,404	N/A	N/A	57,978	7,952	
...mean (sd)	184.72 (150.34)	197.99 (180.75)	187.17 (163.73)	195.06 (186.08)	N/A	N/A	185.05 (152.21)	197.47 (181.71)	-0.07
...median [IQR]	151.00 [108.00, 216.00]	157.75 [112.00, 227.00]	150.00 [105.00, 219.25]	158.75 [111.00, 227.00]	N/A	N/A	150.87 (152.21)	157.93 (181.71)	-0.04
...Missing; n (%)	104,716 (67.6%)	10,606 (61.8%)	124,232 (94.1%)	22,914 (94.2%)	N/A	N/A	228,948 (79.8%)	33,520 (80.8%)	-0.03
Lab result number- Hemoglobin mean (only >0 included)	40,207	4,846	5,256	907	N/A	N/A	45,463	5,753	
...mean (sd)	13.52 (1.64)	14.06 (1.55)	9,789.51 (284,520.72)	13,220.12 (332,411.46)	N/A	N/A	1143.73 (96735.42)	2096.09 (131949.02)	-0.01
...median [IQR]	13.55 [12.45, 14.60]	14.10 [13.00, 15.10]	13.70 [12.60, 14.80]	13.95 [12.90, 15.00]	N/A	N/A	#VALUE!	#VALUE!	#VALUE!
...Missing; n (%)	114,679 (74.0%)	12,308 (71.8%)	126,784 (96.0%)	23,411 (96.3%)	N/A	N/A	241,463 (84.2%)	35,719 (86.1%)	-0.05
Lab result number- Serum sodium mean (only >90 and < 190 included)	58,728	7,403	7,402	1,411	N/A	N/A	66,130	8,814	
...mean (sd)	139.42 (2.80)	139.27 (2.61)	138.86 (2.72)	139.05 (2.40)	N/A	N/A	139.36 (2.79)	139.23 (2.58)	0.05
...median [IQR]	139.67 [138.00, 141.00]	139.00 [138.00, 141.00]	139.00 [137.00, 141.00]	139.00 [138.00, 140.67]	N/A	N/A	139.60 (2.79)	139.00 (2.58)	0.22
...Missing; n (%)	96,158 (62.1%)	9,751 (56.8%)	124,638 (94.4%)	22,907 (94.2%)	N/A	N/A	220,796 (77.0%)	32,658 (78.7%)	-0.04
Lab result number- Albumin mean (only >0 and <=10 included)	54,335	6,987	6,383	1,182	N/A	N/A	60,718	8,169	
...mean (sd)	4.26 (0.31)	4.31 (0.30)	4.10 (0.73)	4.17 (0.69)	N/A	N/A	4.24 (0.38)	4.29 (0.38)	-0.13
...median [IQR]	4.30 [4.10, 4.50]	4.30 [4.10, 4.50]	4.20 [4.00, 4.40]	4.30 [4.00, 4.50]	N/A	N/A	4.29 (0.38)	4.30 (0.38)	-0.03
...Missing; n (%)	100,551 (64.9%)	10,167 (59.3%)	125,657 (95.2%)	23,136 (95.1%)	N/A	N/A	226,208 (78.8%)	33,303 (80.3%)	-0.04
Lab result number- Glucose (fasting or random) mean (only 10-1000 included)	58,552	7,391	7,387	1,393	N/A	N/A	65,939	8,784	
...mean (sd)	174.40 (73.35)	178.35 (69.83)	182.10 (77.32)	175.89 (63.14)	N/A	N/A	175.26 (73.81)	177.96 (68.82)	-0.04
...median [IQR]	156.00 [126.00, 203.00]	162.00 [130.00, 211.00]	162.00 [130.00, 215.00]	163.00 [131.50, 208.00]	N/A	N/A	156.67 (73.81)	162.16 (68.82)	-0.08
...Missing; n (%)	96,334 (62.2%)	9,763 (56.9%)	124,653 (94.4%)	22,925 (94.3%)	N/A	N/A	220,987 (77.0%)	32,688 (78.8%)	-0.04
Lab result number- Potassium mean (only 1-7 included)	60,268	7,541	7,444	1,371	N/A	N/A	67,712	8,912	
...mean (sd)	4.46 (0.44)	4.44 (0.40)	4.32 (0.46)	4.36 (0.41)	N/A	N/A	4.44 (0.44)	4.43 (0.40)	0.02
...median [IQR]	4.45 [4.20, 4.70]	4.40 [4.20, 4.70]	4.30 [4.00, 4.60]	4.38 [4.10, 4.60]	N/A	N/A	4.43 (0.44)	4.40 (0.40)	0.07
...Missing; n (%)	94,618 (61.1%)	9,613 (56.0%)	124,596 (94.4%)	22,947 (94.4%)	N/A	N/A	219,214 (76.4%)	32,560 (78.5%)	-0.05
Comorbidity Scores									
CCI (180 days)- ICD9 and ICD10									
...mean (sd)	2.48 (1.68)	2.06 (1.28)	1.84 (1.27)	1.65 (0.97)	2.61 (1.79)	2.37 (1.51)	2.43 (1.67)	2.05 (1.29)	0.25
...median [IQR]	2.00 [1.00, 3.00]	2.00 [1.00, 2.00]	1.00 [1.00, 2.00]	1.00 [1.00, 2.00]	2.00 [1.00, 4.00]	2.00 [1.00, 3.00]	1.80 (1.67)	1.65 (1.29)	0.10
Frailty Score: Qualitative Version 365 days as Categories,									
...0; n (%)	97,586 (63.0%)	11,069 (64.5%)	71,771 (54.4%)	12,999 (53.5%)	159,513 (41.4%)	13,058 (45.0%)	328,870 (48.9%)	37,126 (52.7%)	-0.08
...1 to 2; n (%)	42,109 (27.2%)	4,734 (27.6%)	45,704 (34.6%)	9,121 (37.5%)	136,252 (35.4%)	10,120 (34.9%)	224,065 (33.3%)	23,975 (34.0%)	-0.01
...3 or more; n (%)	15,191 (9.8%)	1,351 (7.9%)	14,565 (11.0%)	2,198 (9.0%)	89,667 (23.3%)	5,809 (20.0%)	119,423 (17.8%)	9,358 (13.3%)	0.12
Frailty Score: Empirical Version 365 days as Categories,									
...< 0.12908; n (%)	43,729 (28.2%)	5,999 (35.0%)	38,804 (29.4%)	8,113 (33.4%)	51,925 (13.5%)	4,669 (16.1%)	134,458 (20.0%)	18,781 (26.7%)	-0.16
...0.12908 - 0.1631167; n (%)	55,491 (35.8%)	6,402 (37.3%)	50,669 (38.4%)	9,645 (39.7%)	111,334 (28.9%)	8,922 (30.8%)	217,494 (32.3%)	24,969 (35.4%)	-0.07
...>= 0.1631167; n (%)	55,666 (35.9%)	4,753 (27.7%)	42,567 (32.2%)	6,560 (27.0%)	222,173 (57.6%)	15,396 (53.1%)	320,406 (47.7%)	26,709 (37.9%)	0.20
Non-Frailty; n (%)	86,446 (55.8%)	9,990 (58.2%)	65,874 (49.9%)	13,103 (53.9%)	20,611 (5.3%)	1,336 (4.6%)	172,931 (25.7%)	24,429 (34.7%)	-0.20
Frailty Score (mean): Qualitative Version 365 days,									
...mean (sd)	0.78 (1.42)	0.67 (1.20)	0.91 (1.42)	0.83 (1.20)	1.53 (1.95)	1.32 (1.69)	1.24 (1.74)	0.99 (1.42)	0.16
...median [IQR]	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	1.00 [0.00, 2.00]	1.00 [0.00, 2.00]	0.57 (1.74)	0.41 (1.42)	0.10
Frailty Score (mean): Empirical Version 365 days,									
...mean (sd)	0.16 (0.05)	0.15 (0.04)	0.15 (0.04)	0.14 (0.04)	0.19 (0.06)	0.18 (0.05)	0.18 (0.05)	0.16 (0.04)	0.44
...median [IQR]	0.15 [0.13, 0.18]	0.14 [0.12, 0.17]	0.14 [0.12, 0.17]	0.14 [0.12, 0.16]	0.17 [0.14, 0.21]	0.17 [0.14, 0.20]	0.16 (0.05)	0.15 (0.04)	0.22
Healthcare Utilization									
Any hospitalization; n (%)	7,615 (4.9%)	403 (2.3%)	6,017 (4.6%)	501 (2.1%)	27,334 (7.1%)	1,128 (3.9%)	40,966 (6.1%)	2,032 (2.9%)	0.15
Any hospitalization within prior 30 days; n (%)	2,663 (1.7%)	63 (0.4%)	2,107 (1.6%)	77 (0.3%)	9,168 (2.4%)	186 (0.6%)	13,938 (2.1%)	326 (0.5%)	0.14
Any hospitalization during prior 31-180 days; n (%)	5,232 (3.4%)	341 (2.0%)	4,082 (3.1%)	428 (1.8%)	19,390 (5.0%)	964 (3.3%)	28,704 (4.3%)	1,733 (2.5%)	0.10
Endocrinologist Visit; n (%)	10,283 (6.6%)	2,944 (17.2%)	9,029 (6.8%)	4,320 (17.8%)	32,210 (8.4%)	5,395 (18.6%)	51,522 (7.7%)	12,659 (18.0%)	-0.31
Endocrinologist Visit (30 days prior); n (%)	6,054 (3.9%)	2,159 (12.6%)	5,613 (4.3%)	3,385 (13.9%)	18,533 (4.8%)	3,825 (13.2%)	30,200 (4.5%)	9,369 (13.3%)	-0.31
Endocrinologist Visit (31 to 180 days prior); n (%)	7,255 (4.7%)	2,095 (12.2%)	6,203 (4.7%)	3,089 (12.7%)	24,236 (6.3%)	4,125 (14.2%)	37,694 (5.6%)	9,309 (13.2%)	-0.26
Internal medicine/family medicine visits; n (%)	129,232 (83.4%)	12,121 (70.7%)	113,946 (86.3%)	21,262 (87.4%)	316,729 (82.2%)	23,915 (82.5%)	559,907 (83.3%)	57,298 (81.3%)	0.05
Internal medicine/family medicine visits (30 days prior); n (%)	95,398 (61.6%)	8,775 (51.2%)	85,543 (64.8%)	16,208 (66.7%)	220,852 (57.3%)	17,395 (60.0%)	401,793 (59.8%)	42,378 (60.1%)	-0.01
Internal medicine/family medicine visits (31 to 180 days prior); n (%)	107,756 (69.6%)	10,414 (60.7%)	89,803 (68.0%)	17,894 (73.6%)	266,263 (69.1%)	21,172 (73.0%)	463,822 (69.0%)	49,480 (70.2%)	-0.03
Cardiologist visit; n (%)	35,417 (22.9%)	3,293 (19.2%)	21,785 (16.5%)	4,133 (17.0%)	114,927 (29.8%)	8,307 (28.7%)	172,129 (25.6%)	15,733 (22.3%)	0.08
Number of Cardiologist visits (30 days prior); n (%)	12,163 (7.9%)	1,041 (6.1%)	7,375 (5.6%)	1,236 (5.1%)	38,495 (10.0%)	2,576 (8.9%)	58,033 (8.6%)	4,853 (6.9%)	0.06

Table 1

Number of Cardiologist visits (31 to 180 days prior); n (%)	29,585 (19.1%)	2,777 (16.2%)	18,012 (13.6%)	3,495 (14.4%)	98,325 (25.5%)	7,192 (24.8%)	145,922 (21.7%)	13,464 (19.1%)	0.06
Electrocardiogram ; n (%)	39,699 (25.6%)	3,920 (22.9%)	32,047 (24.3%)	5,731 (23.6%)	114,568 (29.7%)	8,455 (29.2%)	186,314 (27.7%)	18,106 (25.7%)	0.05
Use of glucose test strips; n (%)	4,705 (3.0%)	608 (3.5%)	4,168 (3.2%)	1,037 (4.3%)	11,116 (2.9%)	960 (3.3%)	19,989 (3.0%)	2,605 (3.7%)	-0.04
Dialysis; n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	000 (0.0%)	000 (0.0%)	#DIV/0!
Naive new user v8 Copy; n (%)	33,568 (21.7%)	1,869 (10.9%)	27,156 (20.6%)	2,032 (8.4%)	74,547 (19.3%)	1,975 (6.8%)	135,271 (20.1%)	5,876 (8.3%)	0.34
N antidiabetic drugs at index date Copy									
...mean (sd)	1.89 (0.73)	2.29 (0.88)	1.98 (0.76)	2.35 (0.90)	1.88 (0.74)	2.36 (0.89)	1.90 (0.74)	2.34 (0.89)	-0.54
...median [IQR]	2.00 [1.00, 2.00]	2.00 [2.00, 3.00]	2.00 [1.00, 2.00]	2.00 [2.00, 3.00]	2.00 [1.00, 2.00]	2.00 [2.00, 3.00]	2.00 (0.74)	2.00 (0.89)	0.00
number of different/distinct medication prescriptions									
...mean (sd)	9.15 (4.15)	10.03 (4.47)	8.64 (3.92)	9.85 (4.23)	9.16 (3.98)	10.48 (4.44)	9.06 (4.01)	10.15 (4.38)	-0.26
...median [IQR]	8.00 [6.00, 11.00]	9.00 [7.00, 12.00]	8.00 [6.00, 11.00]	9.00 [7.00, 12.00]	9.00 [6.00, 11.00]	10.00 [7.00, 13.00]	8.57 (4.01)	9.41 (4.38)	-0.20
Number of Hospitalizations									
...mean (sd)	0.06 (0.27)	0.03 (0.17)	0.05 (0.24)	0.02 (0.16)	0.08 (0.34)	0.04 (0.23)	0.07 (0.31)	0.03 (0.19)	0.16
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 (0.31)	0.00 (0.19)	0.00
Number of hospital days									
...mean (sd)	0.29 (2.03)	0.11 (0.96)	0.26 (1.78)	0.10 (0.87)	0.51 (3.04)	0.23 (1.86)	0.41 (2.62)	0.16 (1.38)	0.12
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 (2.62)	0.00 (1.38)	0.00
Number of Emergency Department (ED) visits									
...mean (sd)	0.32 (0.96)	0.21 (0.76)	0.10 (0.93)	0.04 (0.54)	0.43 (1.16)	0.31 (1.07)	0.34 (1.07)	0.19 (0.84)	0.16
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 (1.07)	0.00 (0.84)	0.00
Number of Office visits									
...mean (sd)	3.95 (3.11)	4.28 (3.09)	3.80 (3.07)	4.27 (3.11)	4.45 (3.52)	5.10 (3.63)	4.21 (3.34)	4.61 (3.33)	-0.12
...median [IQR]	3.00 [2.00, 5.00]	3.00 [2.00, 5.00]	3.00 [2.00, 5.00]	3.00 [2.00, 5.00]	4.00 [2.00, 6.00]	4.00 [3.00, 7.00]	3.57 (3.34)	3.41 (3.33)	0.05
Number of Endocrinologist visits									
...mean (sd)	0.29 (1.68)	0.94 (3.31)	0.28 (1.62)	0.98 (3.45)	0.44 (2.45)	1.25 (4.77)	0.37 (2.15)	1.08 (4.02)	-0.22
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 (2.15)	0.00 (4.02)	0.00
Number of internal medicine/family medicine visits									
...mean (sd)	8.28 (11.20)	6.97 (10.95)	5.99 (7.55)	6.47 (7.65)	6.87 (9.22)	7.76 (10.04)	7.02 (9.42)	7.12 (9.53)	-0.01
...median [IQR]	5.00 [2.00, 11.00]	4.00 [0.00, 9.00]	4.00 [2.00, 8.00]	4.00 [2.00, 9.00]	4.00 [1.00, 9.00]	5.00 [2.00, 10.00]	4.23 (9.42)	4.41 (9.53)	-0.02
Number of Cardiologist visits									
...mean (sd)	0.96 (2.84)	0.76 (2.44)	0.63 (2.23)	0.63 (2.15)	1.40 (3.79)	1.35 (3.65)	1.15 (3.33)	0.96 (2.92)	0.06
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	0.00 (3.33)	0.00 (2.92)	0.00
Number electrocardiograms received									
...mean (sd)	0.45 (1.12)	0.35 (0.86)	0.40 (0.93)	0.35 (0.83)	0.55 (1.15)	0.50 (1.07)	0.50 (1.10)	0.41 (0.94)	0.09
...median [IQR]	0.00 [0.00, 1.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	0.00 (1.10)	0.00 (0.94)	0.00
Number of HbA1c tests ordered									
...mean (sd)	1.20 (0.86)	1.36 (0.88)	1.00 (0.85)	1.30 (0.86)	1.30 (0.82)	1.56 (0.82)	1.22 (0.84)	1.42 (0.85)	-0.24
...median [IQR]	1.00 [1.00, 2.00]	1.00 [1.00, 2.00]	1.00 [0.00, 2.00]	1.00 [1.00, 2.00]	1.00 [1.00, 2.00]	2.00 [1.00, 2.00]	1.00 (0.84)	1.41 (0.85)	-0.49
Number of glucose tests ordered									
...mean (sd)	0.39 (2.19)	0.44 (1.71)	0.32 (1.15)	0.40 (1.03)	0.34 (0.93)	0.48 (1.14)	0.35 (1.36)	0.44 (1.27)	-0.07
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 (1.36)	0.00 (1.27)	0.00
Number of lipid tests ordered									
...mean (sd)	0.92 (0.89)	1.07 (0.96)	0.83 (1.13)	1.07 (1.14)	0.93 (0.78)	1.13 (0.84)	0.91 (0.88)	1.09 (0.98)	-0.19
...median [IQR]	1.00 [0.00, 1.00]	1.00 [0.00, 2.00]	1.00 [0.00, 1.00]	1.00 [0.00, 2.00]	1.00 [0.00, 1.00]	1.00 [1.00, 2.00]	1.00 (0.88)	1.00 (0.98)	0.00
Number of creatinine tests ordered									
...mean (sd)	0.04 (0.27)	0.03 (0.21)	0.06 (0.33)	0.04 (0.23)	0.07 (0.34)	0.07 (0.32)	0.06 (0.32)	0.05 (0.27)	0.03
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 (0.32)	0.00 (0.27)	0.00
Number of BUN tests ordered									
...mean (sd)	0.02 (0.20)	0.02 (0.16)	0.03 (0.23)	0.02 (0.17)	0.04 (0.28)	0.04 (0.26)	0.03 (0.25)	0.03 (0.21)	0.00
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 (0.25)	0.00 (0.21)	0.00
Number of tests for microalbuminuria									
...mean (sd)	0.77 (1.14)	0.85 (1.19)	0.58 (0.99)	0.76 (1.12)	0.44 (0.67)	0.54 (0.73)	0.54 (0.87)	0.69 (1.00)	-0.16
...median [IQR]	0.00 [0.00, 2.00]	0.00 [0.00, 2.00]	0.00 [0.00, 1.00]	0.00 [0.00, 2.00]	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	0.00 (0.87)	0.00 (1.00)	0.00
Total N distinct ICD9/ICD10 diagnoses at the 3rd digit level Copy									
...mean (sd)	6.00 (6.67)	5.41 (6.00)	2.52 (4.05)	2.02 (3.24)	5.62 (7.42)	5.82 (6.93)	5.10 (6.71)	4.41 (5.67)	0.11
...median [IQR]	5.00 [0.00, 9.00]	5.00 [0.00, 8.00]	0.00 [0.00, 4.00]	0.00 [0.00, 4.00]	4.00 [0.00, 9.00]	4.00 [0.00, 9.00]	3.44 (6.71)	2.86 (5.67)	0.09
Use of thiazide; n (%)	21,636 (14.0%)	2,104 (12.3%)	17,561 (13.3%)	2,846 (11.7%)	59,136 (15.3%)	4,124 (14.2%)	98,333 (14.6%)	9,074 (12.9%)	0.05
Use of beta blockers; n (%)	64,047 (41.4%)	6,162 (35.9%)	49,659 (37.6%)	8,563 (35.2%)	190,922 (49.5%)	13,995 (48.3%)	304,628 (45.3%)	28,720 (40.8%)	0.09
Use of calcium channel blockers; n (%)	51,925 (33.5%)	4,913 (28.6%)	41,303 (31.3%)	6,991 (28.7%)	139,264 (36.1%)	9,858 (34.0%)	232,492 (34.6%)	21,762 (30.9%)	0.08

Table 1

PS-matched									
	Optum		MarketScan		Medicare		POOLED		
Variable	Reference- 2nd Generation SUs	Exposure- Canagliflozin	Reference- 2nd Generation SUs	Exposure- Canagliflozin	Reference- 2nd Generation SUs	Exposure- Canagliflozin	Reference- 2nd Generation SUs	Exposure- Canagliflozin	St. Diff.
Number of patients	16740	16740	23265	23265	28845	28845	68,850	68,850	
Age									
...mean (sd)	62.01 (8.13)	62.11 (7.84)	59.18 (6.78)	59.28 (6.44)	70.96 (5.29)	71.04 (5.27)	64.80 (6.58)	64.89 (6.37)	-0.01
...median [IQR]	61.00 [55.00, 68.00]	61.00 [56.00, 68.00]	58.00 [54.00, 63.00]	59.00 [54.00, 63.00]	70.00 [67.00, 74.00]	70.00 [67.00, 74.00]	63.76 (6.58)	64.09 (6.37)	-0.05
Age categories									
...18 - 54; n (%)	3,698 (22.1%)	3,224 (19.3%)	6,341 (27.3%)	5,909 (25.4%)	0 (0.0%)	0 (0.0%)	10,039 (14.6%)	9,133 (13.3%)	0.04
...55 - 64; n (%)	6,485 (38.7%)	7,238 (43.2%)	13,228 (56.9%)	13,588 (58.4%)	355 (1.2%)	326 (1.1%)	20,068 (29.1%)	21,152 (30.7%)	-0.03
...65 - 74; n (%)	5,339 (31.9%)	5,124 (30.6%)	2,904 (12.5%)	3,121 (13.4%)	22,248 (77.1%)	22,245 (77.1%)	30,491 (44.3%)	30,490 (44.3%)	0.00
...≥ 75; n (%)	1,218 (7.3%)	1,154 (6.9%)	792 (3.4%)	647 (2.8%)	6,242 (21.6%)	6,274 (21.8%)	8,252 (12.0%)	8,075 (11.7%)	0.01
Gender									
...Males; n (%)	9,326 (55.7%)	9,329 (55.7%)	12,867 (55.3%)	12,977 (55.8%)	14,338 (49.7%)	14,294 (49.6%)	36,531 (53.1%)	36,600 (53.2%)	0.00
...Females; n (%)	7,414 (44.3%)	7,411 (44.3%)	10,398 (44.7%)	10,288 (44.2%)	14,507 (50.3%)	14,551 (50.4%)	32,319 (46.9%)	32,250 (46.8%)	0.00
Race									
...White; n (%)	N/A	N/A	N/A	N/A	23,182 (80.4%)	23,167 (80.3%)	23,182 (80.4%)	23,167 (80.3%)	0.00
...Black; n (%)	N/A	N/A	N/A	N/A	2,305 (8.0%)	2,349 (8.1%)	2,305 (8.0%)	2,349 (8.1%)	0.00
...Asian; n (%)	N/A	N/A	N/A	N/A	1,028 (3.6%)	1,033 (3.6%)	1,028 (3.6%)	1,033 (3.6%)	0.00
...Hispanic; n (%)	N/A	N/A	N/A	N/A	989 (3.4%)	979 (3.4%)	989 (3.4%)	979 (3.4%)	0.00
...North American Native; n (%)	N/A	N/A	N/A	N/A	117 (0.4%)	116 (0.4%)	117 (0.4%)	116 (0.4%)	0.00
...Other/Unknown; n (%)	N/A	N/A	N/A	N/A	1,224 (4.2%)	1,201 (4.2%)	1,224 (4.2%)	1,201 (4.2%)	0.00
Region (lumping missing&other category with West)									
...Northeast; n (%)	1,493 (8.9%)	1,442 (8.6%)	4,400 (18.9%)	4,366 (18.8%)	5,438 (18.9%)	5,436 (18.8%)	11,331 (16.5%)	11,244 (16.3%)	0.01
...South; n (%)	8,914 (53.2%)	8,950 (53.5%)	4,094 (17.6%)	4,131 (17.8%)	12,680 (44.0%)	12,557 (43.5%)	25,688 (37.3%)	25,638 (37.2%)	0.00
...Midwest; n (%)	3,472 (20.7%)	3,479 (20.8%)	12,357 (53.1%)	12,331 (53.0%)	5,681 (19.7%)	5,860 (20.3%)	21,510 (31.2%)	21,670 (31.5%)	-0.01
...West; n (%)	2,861 (17.1%)	2,869 (17.1%)	2,142 (9.2%)	2,164 (9.3%)	5,046 (17.5%)	4,992 (17.3%)	10,049 (14.6%)	10,025 (14.6%)	0.00
...Unknown+missing; n (%)	N/A	N/A	272 (1.2%)	273 (1.2%)	N/A	N/A	272 (1.2%)	273 (1.2%)	0.00
CV Covariates									
Ischemic heart disease; n (%)	2,400 (14.3%)	2,439 (14.6%)	2,833 (12.2%)	2,838 (12.2%)	7,091 (24.6%)	7,225 (25.0%)	12,324 (17.9%)	12,502 (18.2%)	-0.01
Acute MI; n (%)	46 (0.3%)	38 (0.2%)	62 (0.3%)	56 (0.2%)	111 (0.4%)	100 (0.3%)	219 (0.3%)	194 (0.3%)	0.00
ACS/unstable angina; n (%)	75 (0.4%)	74 (0.4%)	84 (0.4%)	78 (0.3%)	146 (0.5%)	147 (0.5%)	305 (0.4%)	299 (0.4%)	0.00
Old MI; n (%)	266 (1.6%)	282 (1.7%)	167 (0.7%)	191 (0.8%)	701 (2.4%)	697 (2.4%)	1,134 (1.6%)	1,170 (1.7%)	-0.01
Stable angina; n (%)	331 (2.0%)	344 (2.1%)	327 (1.4%)	308 (1.3%)	849 (2.9%)	855 (3.0%)	1,507 (2.2%)	1,507 (2.2%)	0.00
Coronary atherosclerosis and other forms of chronic ischemic heart disease; n (%)	2,260 (13.5%)	2,311 (13.8%)	2,679 (11.5%)	2,680 (11.5%)	6,812 (23.6%)	6,919 (24.0%)	11,751 (17.1%)	11,910 (17.3%)	-0.01
Other atherosclerosis with ICD10 Copy; n (%)	66 (0.4%)	71 (0.4%)	89 (0.4%)	130 (0.6%)	271 (0.9%)	336 (1.2%)	426 (0.6%)	537 (0.8%)	-0.02
Previous cardiac procedure (CABG or PTCA or Stent) ; n (%)	26 (0.2%)	17 (0.1%)	27 (0.1%)	31 (0.1%)	51 (0.2%)	52 (0.2%)	104 (0.2%)	100 (0.1%)	0.03
History of CABG or PTCA; n (%)	502 (3.0%)	496 (3.0%)	344 (1.5%)	326 (1.4%)	1,690 (5.9%)	1,666 (5.8%)	2,536 (3.7%)	2,488 (3.6%)	0.01
Any stroke; n (%)	447 (2.7%)	446 (2.7%)	432 (1.9%)	464 (2.0%)	1,546 (5.4%)	1,579 (5.5%)	2,425 (3.5%)	2,489 (3.6%)	-0.01
Ischemic stroke (w and w/o mention of cerebral infarction); n (%)	441 (2.6%)	443 (2.6%)	432 (1.9%)	459 (2.0%)	1,544 (5.4%)	1,571 (5.4%)	2,417 (3.5%)	2,473 (3.6%)	-0.01
Hemorrhagic stroke; n (%)	6 (0.0%)	5 (0.0%)	1 (0.0%)	6 (0.0%)	**	**	**	**	**
TIA; n (%)	55 (0.3%)	52 (0.3%)	51 (0.2%)	44 (0.2%)	171 (0.6%)	152 (0.5%)	277 (0.4%)	248 (0.4%)	0.00
Other cerebrovascular disease; n (%)	121 (0.7%)	109 (0.7%)	104 (0.4%)	96 (0.4%)	314 (1.1%)	331 (1.1%)	539 (0.8%)	536 (0.8%)	0.00
Late effects of cerebrovascular disease; n (%)	95 (0.6%)	75 (0.4%)	39 (0.2%)	49 (0.2%)	224 (0.8%)	244 (0.8%)	358 (0.5%)	368 (0.5%)	0.00
Cerebrovascular procedure; n (%)	6 (0.0%)	5 (0.0%)	2 (0.0%)	4 (0.0%)	13 (0.0%)	17 (0.1%)	021 (0.0%)	026 (0.0%)	#DIV/0!
Heart failure (CHF); n (%)	626 (3.7%)	624 (3.7%)	463 (2.0%)	463 (2.0%)	1,993 (6.9%)	1,994 (6.9%)	3,082 (4.5%)	3,081 (4.5%)	0.00
Peripheral Vascular Disease (PVD) or PVD Surgery ; n (%)	705 (4.2%)	715 (4.3%)	610 (2.6%)	610 (2.6%)	2,231 (7.7%)	2,292 (7.9%)	3,546 (5.2%)	3,617 (5.3%)	0.00
Atrial fibrillation; n (%)	703 (4.2%)	724 (4.3%)	745 (3.2%)	745 (3.2%)	2,434 (8.4%)	2,409 (8.4%)	3,882 (5.6%)	3,878 (5.6%)	0.00
Other cardiac dysrhythmia; n (%)	873 (5.2%)	880 (5.3%)	744 (3.2%)	784 (3.4%)	2,760 (9.6%)	2,761 (9.6%)	4,377 (6.4%)	4,425 (6.4%)	0.00
Cardiac conduction disorders; n (%)	231 (1.4%)	224 (1.3%)	223 (1.0%)	206 (0.9%)	815 (2.8%)	751 (2.6%)	1,269 (1.8%)	1,181 (1.7%)	0.01
Other CVD; n (%)	975 (5.8%)	995 (5.9%)	1,144 (4.9%)	1,136 (4.9%)	3,065 (10.6%)	3,147 (10.9%)	5,184 (7.5%)	5,278 (7.7%)	-0.01
Diabetes-related complications									
Diabetic retinopathy; n (%)	893 (5.3%)	950 (5.7%)	894 (3.8%)	931 (4.0%)	2,088 (7.2%)	2,176 (7.5%)	3,875 (5.6%)	4,057 (5.9%)	-0.01
Diabetes with other ophthalmic manifestations; n (%)	89 (0.5%)	98 (0.6%)	544 (2.3%)	556 (2.4%)	829 (2.9%)	817 (2.8%)	1,462 (2.1%)	1,471 (2.1%)	0.00
Retinal detachment, vitreous hemorrhage, vitrectomy; n (%)	65 (0.4%)	60 (0.4%)	62 (0.3%)	60 (0.3%)	133 (0.5%)	118 (0.4%)	260 (0.4%)	238 (0.3%)	0.02
Retinal laser coagulation therapy; n (%)	102 (0.6%)	102 (0.6%)	106 (0.5%)	109 (0.5%)	182 (0.6%)	202 (0.7%)	390 (0.6%)	413 (0.6%)	0.00
Occurrence of Diabetic Neuropathy Copy; n (%)	2,833 (16.9%)	2,850 (17.0%)	2,441 (10.5%)	2,499 (10.7%)	5,678 (19.7%)	5,713 (19.8%)	10,952 (15.9%)	11,062 (16.1%)	-0.01

Table 1

Occurrence of diabetic nephropathy with ICD10									
Copy; n (%)	1,592 (9.5%)	1,610 (9.6%)	1,235 (5.3%)	1,208 (5.2%)	2,370 (8.2%)	2,334 (8.1%)	5,197 (7.5%)	5,152 (7.5%)	0.00
Hypoglycemia ; n (%)	359 (2.1%)	342 (2.0%)	487 (2.1%)	533 (2.3%)	633 (2.2%)	656 (2.3%)	1,479 (2.1%)	1,531 (2.2%)	-0.01
Hyperglycemia; n (%)	581 (3.5%)	578 (3.5%)	638 (2.7%)	616 (2.6%)	1,019 (3.5%)	1,016 (3.5%)	2,238 (3.3%)	2,210 (3.2%)	0.01
Disorders of fluid electrolyte and acid-base balance; n (%)	569 (3.4%)	541 (3.2%)	496 (2.1%)	515 (2.2%)	1,213 (4.2%)	1,221 (4.2%)	2,278 (3.3%)	2,277 (3.3%)	0.00
Diabetic ketoacidosis; n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	000 (0.0%)	000 (0.0%)	#DIV/0!
Hyperosmolar hyperglycemic nonketotic syndrome (HONK); n (%)	89 (0.5%)	74 (0.4%)	74 (0.3%)	71 (0.3%)	149 (0.5%)	141 (0.5%)	312 (0.5%)	286 (0.4%)	0.01
Diabetes with peripheral circulatory disorders with ICD-10 Copy; n (%)	789 (4.7%)	773 (4.6%)	548 (2.4%)	565 (2.4%)	1,805 (6.3%)	1,788 (6.2%)	3,142 (4.6%)	3,126 (4.5%)	0.00
Diabetic Foot; n (%)	230 (1.4%)	217 (1.3%)	237 (1.0%)	258 (1.1%)	555 (1.9%)	559 (1.9%)	1,022 (1.5%)	1,034 (1.5%)	0.00
Gangrene ; n (%)	14 (0.1%)	20 (0.1%)	17 (0.1%)	5 (0.0%)	28 (0.1%)	19 (0.1%)	059 (0.1%)	044 (0.1%)	0.00
Lower extremity amputation; n (%)	40 (0.2%)	46 (0.3%)	21 (0.1%)	24 (0.1%)	87 (0.3%)	84 (0.3%)	148 (0.2%)	154 (0.2%)	0.00
Osteomyelitis; n (%)	50 (0.3%)	41 (0.2%)	56 (0.2%)	45 (0.2%)	77 (0.3%)	74 (0.3%)	183 (0.3%)	160 (0.2%)	0.02
Skin infections ; n (%)	812 (4.9%)	778 (4.6%)	925 (4.0%)	943 (4.1%)	1,598 (5.5%)	1,605 (5.6%)	3,335 (4.8%)	3,326 (4.8%)	0.00
Erectile dysfunction; n (%)	587 (3.5%)	575 (3.4%)	686 (2.9%)	655 (2.9%)	830 (2.9%)	860 (3.0%)	2,103 (3.1%)	2,090 (3.0%)	0.01
Diabetes with unspecified complication; n (%)	836 (5.0%)	814 (4.9%)	988 (4.2%)	990 (4.3%)	1,526 (5.3%)	1,517 (5.3%)	3,350 (4.9%)	3,321 (4.8%)	0.00
Diabetes mellitus without mention of complications; n (%)	14,237 (85.0%)	14,249 (85.1%)	21,402 (92.0%)	21,452 (92.2%)	26,407 (91.5%)	26,443 (91.7%)	62,046 (90.1%)	62,144 (90.3%)	-0.01
Hypertension: 1 inpatient or 2 outpatient claims within 365 days; n (%)	15,348 (91.7%)	15,341 (91.6%)	20,375 (87.6%)	20,341 (87.4%)	27,592 (95.7%)	27,624 (95.8%)	63,315 (92.0%)	63,306 (91.9%)	0.00
Hyperlipidemia ; n (%)	12,921 (77.2%)	12,951 (77.4%)	17,546 (75.4%)	17,573 (75.5%)	23,820 (82.6%)	23,824 (82.6%)	54,287 (78.8%)	54,348 (78.9%)	0.00
Edema; n (%)	721 (4.3%)	741 (4.4%)	728 (3.1%)	727 (3.1%)	2,166 (7.5%)	2,095 (7.3%)	3,615 (5.3%)	3,563 (5.2%)	0.00
Renal Dysfunction (non-diabetic) ; n (%)	1,611 (9.6%)	1,605 (9.6%)	1,291 (5.5%)	1,199 (5.2%)	3,614 (12.5%)	3,519 (12.2%)	6,516 (9.5%)	6,323 (9.2%)	0.01
Occurrence of acute renal disease ; n (%)	146 (0.9%)	135 (0.8%)	89 (0.4%)	92 (0.4%)	300 (1.0%)	320 (1.1%)	535 (0.8%)	547 (0.8%)	0.00
Occurrence of chronic renal insufficiency; n (%)	1,286 (7.7%)	1,321 (7.9%)	910 (3.9%)	861 (3.7%)	2,943 (10.2%)	2,882 (10.0%)	5,139 (7.5%)	5,064 (7.4%)	0.00
Chronic kidney disease ; n (%)	1,211 (7.2%)	1,235 (7.4%)	834 (3.6%)	743 (3.2%)	2,753 (9.5%)	2,646 (9.2%)	4,798 (7.0%)	4,624 (6.7%)	0.01
CKD Stage 3-4; n (%)	628 (3.8%)	635 (3.8%)	398 (1.7%)	370 (1.6%)	1,538 (5.3%)	1,534 (5.3%)	2,564 (3.7%)	2,539 (3.7%)	0.00
Occurrence of hypertensive nephropathy; n (%)	553 (3.3%)	537 (3.2%)	283 (1.2%)	295 (1.3%)	990 (3.4%)	1,006 (3.5%)	1,826 (2.7%)	1,838 (2.7%)	0.00
Occurrence of miscellaneous renal insufficiency ; n (%)	318 (1.9%)	314 (1.9%)	375 (1.6%)	368 (1.6%)	1,003 (3.5%)	1,026 (3.6%)	1,696 (2.5%)	1,708 (2.5%)	0.00
Glaucoma or cataracts ; n (%)	2,814 (16.8%)	2,806 (16.8%)	3,187 (13.7%)	3,120 (13.4%)	7,913 (27.4%)	7,842 (27.2%)	13,914 (20.2%)	13,768 (20.0%)	0.00
Cellulitis or abscess of toe; n (%)	176 (1.1%)	146 (0.9%)	129 (0.6%)	132 (0.6%)	332 (1.2%)	306 (1.1%)	637 (0.9%)	584 (0.8%)	0.01
Foot ulcer; n (%)	217 (1.3%)	205 (1.2%)	233 (1.0%)	255 (1.1%)	542 (1.9%)	556 (1.9%)	992 (1.4%)	1,016 (1.5%)	-0.01
Bladder stones; n (%)	11 (0.1%)	12 (0.1%)	24 (0.1%)	16 (0.1%)	41 (0.1%)	37 (0.1%)	076 (0.1%)	065 (0.1%)	0.00
Kidney stones; n (%)	267 (1.6%)	256 (1.5%)	428 (1.8%)	414 (1.8%)	667 (2.3%)	653 (2.3%)	1,362 (2.0%)	1,323 (1.9%)	0.01
Urinary tract infections (UTIs); n (%)	850 (5.1%)	871 (5.2%)	926 (4.0%)	923 (4.0%)	2,574 (8.9%)	2,543 (8.8%)	4,350 (6.3%)	4,337 (6.3%)	0.00
Dipstick urinalysis; n (%)	5,198 (31.1%)	5,250 (31.4%)	7,224 (31.1%)	7,104 (30.5%)	10,370 (36.0%)	10,618 (36.8%)	22,792 (33.1%)	22,972 (33.4%)	-0.01
Non-dipstick urinalysis; n (%)	7,491 (44.7%)	7,645 (45.7%)	9,491 (40.8%)	9,736 (41.8%)	13,163 (45.6%)	13,338 (46.2%)	30,145 (43.8%)	30,719 (44.6%)	-0.02
Urine function test; n (%)	275 (1.6%)	224 (1.3%)	362 (1.6%)	304 (1.3%)	893 (3.1%)	797 (2.8%)	1,530 (2.2%)	1,325 (1.9%)	0.02
Cytology; n (%)	76 (0.5%)	72 (0.4%)	136 (0.6%)	118 (0.5%)	208 (0.7%)	200 (0.7%)	420 (0.6%)	390 (0.6%)	0.00
Cystoscopy; n (%)	120 (0.7%)	107 (0.6%)	202 (0.9%)	156 (0.7%)	298 (1.0%)	292 (1.0%)	620 (0.9%)	555 (0.8%)	0.01
Other Covariates									
Liver disease; n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	000 (0.0%)	000 (0.0%)	#DIV/0!
Osteoarthritis; n (%)	1,728 (10.3%)	1,733 (10.4%)	1,617 (7.0%)	1,622 (7.0%)	4,923 (17.1%)	4,854 (16.8%)	8,268 (12.0%)	8,209 (11.9%)	0.00
Other arthritis, arthropathies and musculoskeletal pain; n (%)	4,582 (27.4%)	4,572 (27.3%)	5,474 (23.5%)	5,476 (23.5%)	10,139 (35.1%)	10,202 (35.4%)	20,195 (29.3%)	20,250 (29.4%)	0.00
Dorsopathies; n (%)	3,062 (18.3%)	2,956 (17.7%)	3,524 (15.1%)	3,554 (15.3%)	6,484 (22.5%)	6,550 (22.7%)	13,070 (19.0%)	13,060 (19.0%)	0.00
Fractures; n (%)	284 (1.7%)	289 (1.7%)	333 (1.4%)	333 (1.4%)	677 (2.3%)	677 (2.3%)	1,294 (1.9%)	1,299 (1.9%)	0.00
Falls ; n (%)	318 (1.9%)	286 (1.7%)	106 (0.5%)	120 (0.5%)	630 (2.2%)	648 (2.2%)	1,054 (1.5%)	1,054 (1.5%)	0.00
Osteoporosis; n (%)	453 (2.7%)	444 (2.7%)	326 (1.4%)	303 (1.3%)	1,765 (6.1%)	1,786 (6.2%)	2,544 (3.7%)	2,533 (3.7%)	0.00
Hyperthyroidism; n (%)	121 (0.7%)	87 (0.5%)	117 (0.5%)	97 (0.4%)	251 (0.9%)	242 (0.8%)	489 (0.7%)	426 (0.6%)	0.01
Hypothyroidism ; n (%)	2,426 (14.5%)	2,438 (14.6%)	2,825 (12.1%)	2,723 (11.7%)	3,638 (12.6%)	3,615 (12.5%)	8,889 (12.9%)	8,776 (12.7%)	0.01
Other disorders of thyroid gland ; n (%)	664 (4.0%)	631 (3.8%)	840 (3.6%)	824 (3.5%)	1,287 (4.5%)	1,291 (4.5%)	2,791 (4.1%)	2,746 (4.0%)	0.01
Depression; n (%)	1,229 (7.3%)	1,217 (7.3%)	1,471 (6.3%)	1,423 (6.1%)	2,574 (8.9%)	2,543 (8.8%)	5,274 (7.7%)	5,183 (7.5%)	0.01
Anxiety; n (%)	1,167 (7.0%)	1,136 (6.8%)	1,084 (4.7%)	1,088 (4.7%)	2,123 (7.4%)	2,036 (7.1%)	4,374 (6.4%)	4,260 (6.2%)	0.01
Sleep_Disorder; n (%)	1,227 (7.3%)	1,260 (7.5%)	2,580 (11.1%)	2,582 (11.1%)	2,379 (8.2%)	2,430 (8.4%)	6,186 (9.0%)	6,272 (9.1%)	0.00
Dementia; n (%)	155 (0.9%)	162 (1.0%)	112 (0.5%)	120 (0.5%)	902 (3.1%)	938 (3.3%)	1,169 (1.7%)	1,220 (1.8%)	-0.01
Delirium; n (%)	39 (0.2%)	46 (0.3%)	36 (0.2%)	35 (0.2%)	179 (0.6%)	186 (0.6%)	254 (0.4%)	267 (0.4%)	0.00
Psychosis; n (%)	65 (0.4%)	77 (0.5%)	32 (0.1%)	44 (0.2%)	223 (0.8%)	257 (0.9%)	320 (0.5%)	378 (0.5%)	0.00
Obesity; n (%)	4,419 (26.4%)	4,456 (26.6%)	4,267 (18.3%)	4,308 (18.5%)	5,666 (19.6%)	5,680 (19.7%)	14,352 (20.8%)	14,444 (21.0%)	0.00
Overweight; n (%)	838 (5.0%)	841 (5.0%)	537 (2.3%)	530 (2.3%)	1,065 (3.7%)	1,063 (3.7%)	2,440 (3.5%)	2,434 (3.5%)	0.00
Smoking; n (%)	1,399 (8.4%)	1,383 (8.3%)	1,206 (5.2%)	1,169 (5.0%)	3,129 (10.8%)	3,165 (11.0%)	5,734 (8.3%)	5,717 (8.3%)	0.00
Alcohol abuse or dependence; n (%)	5 (0.0%)	0 (0.0%)	7 (0.0%)	6 (0.0%)	**	**	**	**	**
Drug abuse or dependence; n (%)	3 (0.0%)	7 (0.0%)	4 (0.0%)	4 (0.0%)	**	**	**	**	**
COPD; n (%)	851 (5.1%)	834 (5.0%)	633 (2.7%)	643 (2.8%)	2,322 (8.0%)	2,360 (8.2%)	3,806 (5.5%)	3,837 (5.6%)	0.00

Table 1

Asthma; n (%)	846 (5.1%)	794 (4.7%)	817 (3.5%)	834 (3.6%)	1,494 (5.2%)	1,542 (5.3%)	3,157 (4.6%)	3,170 (4.6%)	0.00
Obstructive sleep apnea; n (%)	1,899 (11.3%)	1,960 (11.7%)	2,788 (12.0%)	2,804 (12.1%)	2,661 (9.2%)	2,680 (9.3%)	7,348 (10.7%)	7,444 (10.8%)	0.00
Pneumonia; n (%)	181 (1.1%)	190 (1.1%)	187 (0.8%)	208 (0.9%)	471 (1.6%)	474 (1.6%)	839 (1.2%)	872 (1.3%)	-0.01
Imaging; n (%)	2 (0.0%)	3 (0.0%)	3 (0.0%)	3 (0.0%)	15 (0.1%)	12 (0.0%)	20 (0.0%)	18 (0.0%)	#DIV/0!
Diabetes Medications									
DM Medications - AGIs; n (%)	61 (0.4%)	63 (0.4%)	72 (0.3%)	73 (0.3%)	180 (0.6%)	197 (0.7%)	313 (0.5%)	333 (0.5%)	0.00
DM Medications - Glitazones; n (%)	1,570 (9.4%)	1,478 (8.8%)	2,106 (9.1%)	2,058 (8.8%)	2,732 (9.5%)	2,715 (9.4%)	6,408 (9.3%)	6,251 (9.1%)	0.01
DM Medications - Insulin; n (%)	4,643 (27.7%)	4,731 (28.3%)	6,185 (26.6%)	6,447 (27.7%)	9,686 (33.6%)	9,923 (34.4%)	20,514 (29.8%)	21,101 (30.6%)	-0.02
DM Medications - Meglitinides; n (%)	227 (1.4%)	223 (1.3%)	418 (1.8%)	421 (1.8%)	744 (2.6%)	791 (2.7%)	1,389 (2.0%)	1,435 (2.1%)	-0.01
DM Medications - Metformin; n (%)	13,035 (77.9%)	13,035 (77.9%)	18,359 (78.9%)	18,245 (78.4%)	21,390 (74.2%)	21,384 (74.1%)	52,784 (76.7%)	52,664 (76.5%)	0.00
Concomitant initiation or current use of DPP4i Copy; n (%)	3,291 (19.7%)	3,255 (19.4%)	5,946 (25.6%)	5,704 (24.5%)	7,563 (26.2%)	7,384 (25.6%)	16,800 (24.4%)	16,343 (23.7%)	0.02
Concomitant initiation or current use of AGIs; n (%)	40 (0.2%)	45 (0.3%)	44 (0.2%)	36 (0.2%)	124 (0.4%)	139 (0.5%)	208 (0.3%)	220 (0.3%)	0.00
Concomitant initiation or current use of Glitazones; n (%)	1,230 (7.3%)	1,133 (6.8%)	1,583 (6.8%)	1,544 (6.6%)	2,061 (7.1%)	2,060 (7.1%)	4,874 (7.1%)	4,737 (6.9%)	0.01
Concomitant initiation or current use of GLP-1 RA; n (%)	1,791 (10.7%)	1,857 (11.1%)	2,706 (11.6%)	2,734 (11.8%)	2,458 (8.5%)	2,727 (9.5%)	6,955 (10.1%)	7,318 (10.6%)	-0.02
Concomitant initiation or current use of Insulin; n (%)	3,487 (20.8%)	3,579 (21.4%)	4,765 (20.5%)	4,982 (21.4%)	7,619 (26.4%)	7,943 (27.5%)	15,871 (23.1%)	16,504 (24.0%)	-0.02
Concomitant initiation or current use of Meglitinides; n (%)	130 (0.8%)	155 (0.9%)	241 (1.0%)	289 (1.2%)	526 (1.8%)	563 (2.0%)	897 (1.3%)	1,007 (1.5%)	-0.02
Concomitant initiation or current use of Metformin; n (%)	10,980 (65.6%)	10,982 (65.6%)	15,378 (66.1%)	15,321 (65.9%)	18,049 (62.6%)	18,065 (62.6%)	44,407 (64.5%)	44,368 (64.4%)	0.00
Past use of DPP4i Copy; n (%)	1,151 (6.9%)	1,121 (6.7%)	1,783 (7.7%)	1,697 (7.3%)	2,213 (7.7%)	2,127 (7.4%)	5,147 (7.5%)	4,945 (7.2%)	0.01
Past use of AGIs Copy; n (%)	21 (0.1%)	18 (0.1%)	28 (0.1%)	37 (0.2%)	56 (0.2%)	58 (0.2%)	105 (0.2%)	113 (0.2%)	0.00
Past use of Glitazones Copy; n (%)	340 (2.0%)	345 (2.1%)	523 (2.2%)	514 (2.2%)	671 (2.3%)	655 (2.3%)	1,534 (2.2%)	1,514 (2.2%)	0.00
Past use of GLP-1 RA Copy; n (%)	823 (4.9%)	826 (4.9%)	1,206 (5.2%)	1,219 (5.2%)	1,172 (4.1%)	1,224 (4.2%)	3,201 (4.6%)	3,269 (4.7%)	0.00
Past use of Insulin Copy; n (%)	1,156 (6.9%)	1,152 (6.9%)	1,420 (6.1%)	1,465 (6.3%)	2,067 (7.2%)	1,981 (6.9%)	4,643 (6.7%)	4,598 (6.7%)	0.00
Past use of Meglitinides Copy; n (%)	97 (0.6%)	68 (0.4%)	177 (0.8%)	132 (0.6%)	218 (0.8%)	228 (0.8%)	492 (0.7%)	428 (0.6%)	0.01
Past use of metformin (final) Copy; n (%)	2,055 (12.3%)	2,053 (12.3%)	2,981 (12.8%)	2,924 (12.6%)	3,341 (11.6%)	3,319 (11.5%)	8,377 (12.2%)	8,296 (12.0%)	0.01
Other Medications									
Use of ACE inhibitors; n (%)	8,762 (52.3%)	8,727 (52.1%)	11,715 (50.4%)	11,848 (50.9%)	13,662 (47.4%)	13,602 (47.2%)	34,139 (49.6%)	34,177 (49.6%)	0.00
Use of ARBs; n (%)	6,316 (37.7%)	6,365 (38.0%)	9,235 (39.7%)	9,169 (39.4%)	11,406 (39.5%)	11,415 (39.6%)	26,957 (39.2%)	26,949 (39.1%)	0.00
Use of Loop Diuretics ; n (%)	1,436 (8.6%)	1,463 (8.7%)	1,706 (7.3%)	1,750 (7.5%)	4,396 (15.2%)	4,395 (15.2%)	7,538 (10.9%)	7,608 (11.1%)	-0.01
Use of other diuretics; n (%)	460 (2.7%)	456 (2.7%)	595 (2.6%)	579 (2.5%)	975 (3.4%)	981 (3.4%)	2,030 (2.9%)	2,016 (2.9%)	0.00
Use of nitrates-United; n (%)	570 (3.4%)	543 (3.2%)	673 (2.9%)	696 (3.0%)	1,759 (6.1%)	1,776 (6.2%)	3,002 (4.4%)	3,015 (4.4%)	0.00
Use of other hypertension drugs; n (%)	836 (5.0%)	841 (5.0%)	1,023 (4.4%)	1,042 (4.5%)	2,103 (7.3%)	2,069 (7.2%)	3,962 (5.8%)	3,952 (5.7%)	0.00
Use of digoxin; n (%)	160 (1.0%)	175 (1.0%)	214 (0.9%)	221 (0.9%)	654 (2.3%)	606 (2.1%)	1,028 (1.5%)	1,002 (1.5%)	0.00
Use of Anti-arrhythmics; n (%)	147 (0.9%)	146 (0.9%)	189 (0.8%)	190 (0.8%)	433 (1.5%)	440 (1.5%)	769 (1.1%)	776 (1.1%)	0.00
Use of COPD/asthma meds; n (%)	2,395 (14.3%)	2,326 (13.9%)	3,399 (14.6%)	3,371 (14.5%)	4,932 (17.1%)	4,962 (17.2%)	10,726 (15.6%)	10,659 (15.5%)	0.00
Use of statins; n (%)	12,032 (71.9%)	12,150 (72.6%)	16,087 (69.1%)	16,153 (69.4%)	21,847 (75.7%)	21,876 (75.8%)	49,966 (72.6%)	50,179 (72.9%)	-0.01
Use of other lipid-lowering drugs; n (%)	2,203 (13.2%)	2,259 (13.5%)	3,621 (15.6%)	3,669 (15.8%)	4,378 (15.2%)	4,409 (15.3%)	10,202 (14.8%)	10,337 (15.0%)	-0.01
Use of antiplatelet agents; n (%)	1,646 (9.8%)	1,642 (9.8%)	2,383 (10.2%)	2,401 (10.3%)	4,209 (14.6%)	4,265 (14.8%)	8,238 (12.0%)	8,308 (12.1%)	0.00
Use of oral anticoagulants (Dabigatran, Rivaroxaban, Apixaban, Warfarin); n (%)	711 (4.2%)	713 (4.3%)	774 (3.3%)	785 (3.4%)	2,191 (7.6%)	2,225 (7.7%)	3,676 (5.3%)	3,723 (5.4%)	0.00
Use of heparin and other low-molecular weight heparins; n (%)	17 (0.1%)	16 (0.1%)	0 (0.0%)	0 (0.0%)	63 (0.2%)	69 (0.2%)	080 (0.1%)	085 (0.1%)	0.00
Use of NSAIDs; n (%)	2,804 (16.8%)	2,766 (16.5%)	3,777 (16.2%)	3,810 (16.4%)	4,635 (16.1%)	4,674 (16.2%)	11,216 (16.3%)	11,250 (16.3%)	0.00
Use of oral corticosteroids; n (%)	2,110 (12.6%)	2,010 (12.0%)	2,618 (11.3%)	2,588 (11.1%)	4,136 (14.3%)	4,125 (14.3%)	8,864 (12.9%)	8,723 (12.7%)	0.01
Use of bisphosphonate (United); n (%)	209 (1.2%)	202 (1.2%)	164 (0.7%)	155 (0.7%)	811 (2.8%)	819 (2.8%)	1,184 (1.7%)	1,176 (1.7%)	0.00
Use of opioids; n (%)	3,250 (19.4%)	3,204 (19.1%)	4,506 (19.4%)	4,557 (19.6%)	5,860 (20.3%)	5,864 (20.3%)	13,616 (19.8%)	13,625 (19.8%)	0.00
Use of antidepressants; n (%)	3,994 (23.9%)	3,963 (23.7%)	5,150 (22.1%)	5,158 (22.2%)	7,507 (26.0%)	7,437 (25.8%)	16,651 (24.2%)	16,558 (24.0%)	0.00
Use of antipsychotics; n (%)	300 (1.8%)	303 (1.8%)	281 (1.2%)	287 (1.2%)	678 (2.4%)	701 (2.4%)	1,259 (1.8%)	1,291 (1.9%)	-0.01
Use of anticonvulsants; n (%)	2,436 (14.6%)	2,322 (13.9%)	2,448 (10.5%)	2,480 (10.7%)	4,502 (15.6%)	4,524 (15.7%)	9,386 (13.6%)	9,326 (13.5%)	0.00
Use of lithium; n (%)	15 (0.1%)	20 (0.1%)	33 (0.1%)	11 (0.0%)	38 (0.1%)	27 (0.1%)	086 (0.1%)	058 (0.1%)	0.00
Use of Benzos; n (%)	1,504 (9.0%)	1,501 (9.0%)	1,957 (8.4%)	1,972 (8.5%)	2,903 (10.1%)	2,856 (9.9%)	6,364 (9.2%)	6,329 (9.2%)	0.00
Use of anxiolytics/hypnotics; n (%)	932 (5.6%)	906 (5.4%)	1,304 (5.6%)	1,324 (5.7%)	1,707 (5.9%)	1,632 (5.7%)	3,943 (5.7%)	3,862 (5.6%)	0.00
Use of dementia meds; n (%)	104 (0.6%)	112 (0.7%)	82 (0.4%)	88 (0.4%)	760 (2.6%)	785 (2.7%)	946 (1.4%)	985 (1.4%)	0.00
Use of antiparkinsonian meds; n (%)	322 (1.9%)	325 (1.9%)	374 (1.6%)	362 (1.6%)	830 (2.9%)	852 (3.0%)	1,526 (2.2%)	1,539 (2.2%)	0.00
Any use of pramlintide; n (%)	0 (0.0%)	28 (0.2%)	10 (0.0%)	41 (0.2%)	**	**	**	**	**
Any use of 1st generation sulfonylureas; n (%)	1 (0.0%)	2 (0.0%)	6 (0.0%)	1 (0.0%)	**	**	**	**	**
Entresto (sacubitril/valsartan); n (%)	15 (0.1%)	8 (0.0%)	10 (0.0%)	6 (0.0%)	**	**	**	**	**
Initiation as monotherapy Copy; n (%)	1,194 (7.1%)	1,198 (7.2%)	1,283 (5.5%)	1,306 (5.6%)	1,205 (4.2%)	1,233 (4.3%)	3,682 (5.3%)	3,737 (5.4%)	0.00
Labs									
Lab values- HbA1c (%) ; n (%)	7,105 (42.4%)	7,211 (43.1%)	1,740 (7.5%)	1,440 (6.2%)	N/A	N/A	8,845 (22.1%)	8,651 (21.6%)	0.01
Lab values- HbA1c (%) (within 3 months) ; n (%)	5,645 (33.7%)	5,910 (35.3%)	1,376 (5.9%)	1,224 (5.3%)	N/A	N/A	7,021 (17.6%)	7,134 (17.8%)	-0.01
Lab values- HbA1c (%) (within 6 months) ; n (%)	7,105 (42.4%)	7,211 (43.1%)	1,740 (7.5%)	1,440 (6.2%)	N/A	N/A	8,845 (22.1%)	8,651 (21.6%)	0.01

Table 1

Lab values- BNP; n (%)	73 (0.4%)	99 (0.6%)	14 (0.1%)	13 (0.1%)	N/A	N/A	087 (0.2%)	112 (0.3%)	-0.02
Lab values- BNP (within 3 months); n (%)	42 (0.3%)	64 (0.4%)	8 (0.0%)	9 (0.0%)	N/A	N/A	050 (0.1%)	073 (0.2%)	-0.03
Lab values- BNP (within 6 months); n (%)	73 (0.4%)	99 (0.6%)	14 (0.1%)	13 (0.1%)	N/A	N/A	087 (0.2%)	112 (0.3%)	-0.02
Lab values- BUN (mg/dl); n (%)	6,923 (41.4%)	7,113 (42.5%)	1,610 (6.9%)	1,347 (5.8%)	N/A	N/A	8,533 (21.3%)	8,460 (21.1%)	0.00
Lab values- BUN (mg/dl) (within 3 months); n (%)	5,349 (32.0%)	5,668 (33.9%)	1,229 (5.3%)	1,095 (4.7%)	N/A	N/A	6,578 (16.4%)	6,763 (16.9%)	-0.01
Lab values- BUN (mg/dl) (within 6 months); n (%)	6,923 (41.4%)	7,113 (42.5%)	1,610 (6.9%)	1,347 (5.8%)	N/A	N/A	8,533 (21.3%)	8,460 (21.1%)	0.00
Lab values- Creatinine (mg/dl) ; n (%)	7,103 (42.4%)	7,370 (44.0%)	1,719 (7.4%)	1,488 (6.4%)	N/A	N/A	8,822 (22.1%)	8,858 (22.1%)	0.00
Lab values- Creatinine (mg/dl) (within 3 months); n (%)	5,484 (32.8%)	5,872 (35.1%)	1,321 (5.7%)	1,221 (5.2%)	N/A	N/A	6,805 (17.0%)	7,093 (17.7%)	-0.02
Lab values- Creatinine (mg/dl) (within 6 months); n (%)	7,103 (42.4%)	7,370 (44.0%)	1,719 (7.4%)	1,488 (6.4%)	N/A	N/A	8,822 (22.1%)	8,858 (22.1%)	0.00
Lab values- HDL level (mg/dl); n (%)	6,063 (36.2%)	6,278 (37.5%)	1,611 (6.9%)	1,358 (5.8%)	N/A	N/A	7,674 (19.2%)	7,636 (19.1%)	0.00
Lab values- HDL level (mg/dl) (within 3 months); n (%)	4,499 (26.9%)	4,780 (28.6%)	1,182 (5.1%)	1,058 (4.5%)	N/A	N/A	5,681 (14.2%)	5,838 (14.6%)	-0.01
Lab values- HDL level (mg/dl) (within 6 months); n (%)	6,063 (36.2%)	6,278 (37.5%)	1,611 (6.9%)	1,358 (5.8%)	N/A	N/A	7,674 (19.2%)	7,636 (19.1%)	0.00
Lab values- LDL level (mg/dl) ; n (%)	6,280 (37.5%)	6,482 (38.7%)	1,663 (7.1%)	1,379 (5.9%)	N/A	N/A	7,943 (19.9%)	7,861 (19.7%)	0.01
Lab values- LDL level (mg/dl) (within 3 months); n (%)	4,650 (27.8%)	4,954 (29.6%)	1,216 (5.2%)	1,078 (4.6%)	N/A	N/A	5,866 (14.7%)	6,032 (15.1%)	-0.01
Lab values- LDL level (mg/dl) (within 6 months); n (%)	6,280 (37.5%)	6,482 (38.7%)	1,663 (7.1%)	1,379 (5.9%)	N/A	N/A	7,943 (19.9%)	7,861 (19.7%)	0.01
Lab values- NT-proBNP; n (%)	13 (0.1%)	9 (0.1%)	4 (0.0%)	0 (0.0%)	N/A	N/A	17 (0.0%)	0 (0.0%)	-
Lab values- NT-proBNP (within 3 months); n (%)	9 (0.1%)	5 (0.0%)	2 (0.0%)	0 (0.0%)	N/A	N/A	11 (0.0%)	0 (0.0%)	-
Lab values- NT-proBNP (within 6 months); n (%)	13 (0.1%)	9 (0.1%)	4 (0.0%)	0 (0.0%)	N/A	N/A	17 (0.0%)	9 (0.0%)	-
Lab values- Total cholesterol (mg/dl) ; n (%)	6,193 (37.0%)	6,409 (38.3%)	1,610 (6.9%)	1,363 (5.9%)	N/A	N/A	7,803 (19.5%)	7,772 (19.4%)	0.00
Lab values- Total cholesterol (mg/dl) (within 3 months); n (%)	4,591 (27.4%)	4,894 (29.2%)	1,183 (5.1%)	1,066 (4.6%)	N/A	N/A	5,774 (14.4%)	5,960 (14.9%)	-0.01
Lab values- Total cholesterol (mg/dl) (within 6 months); n (%)	6,193 (37.0%)	6,409 (38.3%)	1,610 (6.9%)	1,363 (5.9%)	N/A	N/A	7,803 (19.5%)	7,772 (19.4%)	0.00
Lab values- Triglyceride level (mg/dl); n (%)	6,139 (36.7%)	6,366 (38.0%)	1,598 (6.9%)	1,343 (5.8%)	N/A	N/A	7,737 (19.3%)	7,709 (19.3%)	0.00
Lab values- Triglyceride level (mg/dl) (within 3 months); n (%)	4,554 (27.2%)	4,857 (29.0%)	1,177 (5.1%)	1,053 (4.5%)	N/A	N/A	5,731 (14.3%)	5,910 (14.8%)	-0.01
Lab values- Triglyceride level (mg/dl) (within 6 months); n (%)	6,139 (36.7%)	6,366 (38.0%)	1,598 (6.9%)	1,343 (5.8%)	N/A	N/A	7,737 (19.3%)	7,709 (19.3%)	0.00
Lab result number- HbA1c (%) mean (only 2 to 20 included)	7,067	7,168	1,685	1,391	N/A	N/A	8,752	8,559	
...mean (sd)	8.55 (1.87)	8.50 (1.76)	8.59 (1.89)	8.53 (1.77)	N/A	N/A	8.56 (1.87)	8.50 (1.76)	0.03
...median [IQR]	8.10 [7.20, 9.60]	8.10 [7.25, 9.43]	8.10 [7.30, 9.50]	8.10 [7.25, 9.40]	N/A	N/A	8.10 (1.87)	8.10 (1.76)	0.00
...Missing; n (%)	9,673 (57.8%)	9,572 (57.2%)	21,580 (92.8%)	21,874 (94.0%)	N/A	N/A	31,253 (78.1%)	31,446 (78.6%)	-0.01
Lab result number- BNP mean	73	99	14	13	N/A	N/A	87	112	
...mean (sd)	105.60 (266.26)	68.61 (79.50)	110.61 (177.08)	575.59 (1,341.91)	N/A	N/A	106.41 (256.16)	127.46 (451.58)	-0.06
...median [IQR]	43.00 [18.05, 97.15]	40.40 [17.00, 86.10]	45.00 [17.75, 119.62]	56.00 [20.00, 194.30]	N/A	N/A	#VALUE!	#VALUE!	#VALUE!
...Missing; n (%)	16,667 (99.6%)	16,641 (99.4%)	23,251 (99.9%)	23,252 (99.9%)	N/A	N/A	39,918 (99.8%)	39,893 (99.7%)	0.02
Lab result number- BUN (mg/dl) mean	6,923	7,113	1,610	1,347	N/A	N/A	8,533	8,460	
...mean (sd)	16.86 (6.32)	16.65 (5.62)	988.41 (11,243.54)	2,413.80 (18,907.89)	N/A	N/A	200.17 (4883.23)	398.32 (7543.23)	-0.03
...median [IQR]	16.00 [13.00, 19.50]	16.00 [13.00, 19.00]	15.83 [13.00, 19.00]	16.00 [13.00, 19.00]	N/A	N/A	#VALUE!	#VALUE!	#VALUE!
...Missing; n (%)	9,817 (58.6%)	9,627 (57.5%)	21,655 (93.1%)	21,918 (94.2%)	N/A	N/A	31,472 (78.7%)	31,545 (78.9%)	0.00
Lab result number- Creatinine (mg/dl) mean (only 0.1 to 15 included)	7,065	7,319	1,572	1,354	N/A	N/A	8,637	8,673	
...mean (sd)	0.95 (0.29)	0.92 (0.24)	0.95 (0.28)	0.92 (0.23)	N/A	N/A	0.95 (0.29)	0.92 (0.24)	0.11
...median [IQR]	0.90 [0.76, 1.07]	0.89 [0.76, 1.04]	0.91 [0.76, 1.06]	0.89 [0.76, 1.05]	N/A	N/A	0.90 (0.29)	0.89 (0.24)	0.04
...Missing; n (%)	9,675 (57.8%)	9,421 (56.3%)	21,693 (93.2%)	21,911 (94.2%)	N/A	N/A	31,368 (78.4%)	31,332 (78.3%)	0.00
Lab result number- HDL level (mg/dl) mean (only <=5000 included)	6,063	6,278	1,600	1,341	N/A	N/A	7,663	7,619	
...mean (sd)	44.91 (13.29)	45.34 (13.17)	44.01 (13.95)	46.54 (108.97)	N/A	N/A	44.72 (13.43)	45.55 (47.25)	-0.02
...median [IQR]	43.00 [36.00, 52.00]	43.50 [36.28, 52.00]	43.00 [36.00, 51.00]	43.00 [35.00, 50.75]	N/A	N/A	43.00 (13.43)	43.41 (47.25)	-0.01
...Missing; n (%)	10,677 (63.8%)	10,462 (62.5%)	21,665 (93.1%)	21,924 (94.2%)	N/A	N/A	32,342 (80.8%)	32,386 (81.0%)	-0.01
Lab result number- LDL level (mg/dl) mean (only <=5000 included)	6,127	6,357	1,464	1,218	N/A	N/A	7,591	7,575	
...mean (sd)	85.82 (40.64)	84.61 (39.33)	89.35 (41.61)	86.98 (40.52)	N/A	N/A	86.50 (40.83)	84.99 (39.53)	0.04
...median [IQR]	84.00 [62.00, 109.00]	82.00 [61.00, 113.50]	88.25 [65.00, 113.50]	85.88 [63.00, 112.00]	N/A	N/A	84.82 (40.83)	82.62 (39.53)	0.05
...Missing; n (%)	10,613 (63.4%)	10,383 (62.0%)	21,801 (93.7%)	22,047 (94.8%)	N/A	N/A	32,414 (81.0%)	32,430 (81.1%)	0.00
Lab result number- Total cholesterol (mg/dl) mean (only <=5000 included)	6,190	6,403	1,597	1,344	N/A	N/A	7,787	7,747	
...mean (sd)	174.42 (47.37)	172.68 (46.78)	175.05 (50.49)	172.22 (55.71)	N/A	N/A	174.55 (48.03)	172.60 (48.45)	0.04
...median [IQR]	169.00 [143.00, 199.00]	167.00 [142.00, 196.00]	171.00 [145.00, 202.00]	170.00 [144.50, 197.00]	N/A	N/A	169.41 (48.03)	167.52 (48.45)	0.04
...Missing; n (%)	10,550 (63.0%)	10,337 (61.8%)	21,668 (93.1%)	21,921 (94.2%)	N/A	N/A	32,218 (80.5%)	32,258 (80.6%)	0.00

Table 1

Lab result number- Triglyceride level (mg/dl) mean (only <=5000 included)	6,138	6,365	1,585	1,324	N/A	N/A	7,723	7,689	
...mean (sd)	199.03 (170.61)	197.06 (178.97)	193.72 (167.75)	195.36 (188.68)	N/A	N/A	197.94 (170.04)	196.77 (180.69)	0.01
...median [IQR]	159.00 [111.00, 231.00]	157.33 [112.00, 226.00]	155.00 [109.00, 223.75]	160.00 [112.00, 227.00]	N/A	N/A	158.18 (170.04)	157.79 (180.69)	0.00
...Missing; n (%)	10,602 (63.3%)	10,375 (62.0%)	21,680 (93.2%)	21,941 (94.3%)	N/A	N/A	32,282 (80.7%)	32,316 (80.8%)	0.00
Lab result number- Hemoglobin mean (only >0 included)	4,465	4,725	1,110	856	N/A	N/A	5,575	5,581	
...mean (sd)	13.82 (1.54)	14.06 (1.56)	10,214.28 (300,385.23)	14,006.95 (342,165.79)	N/A	N/A	2044.76 (134010.49)	2160.25 (133961.62)	0.00
...median [IQR]	13.83 [12.80, 14.80]	14.10 [13.00, 15.10]	13.80 [12.80, 14.70]	14.00 [12.00, 15.00]	N/A	N/A	#VALUE!	#VALUE!	#VALUE!
...Missing; n (%)	12,275 (73.3%)	12,015 (71.8%)	22,155 (95.2%)	22,409 (96.3%)	N/A	N/A	34,430 (86.1%)	34,424 (86.0%)	0.00
Lab result number- Serum sodium mean (only >90 and < 190 included)	6,917	7,194	1,610	1,327	N/A	N/A	8,527	8,521	
...mean (sd)	139.22 (2.73)	139.28 (2.62)	138.81 (2.80)	139.05 (2.41)	N/A	N/A	139.14 (2.74)	139.24 (2.59)	-0.04
...median [IQR]	139.00 [137.67, 141.00]	139.00 [138.00, 141.00]	139.00 [137.00, 140.50]	139.00 [138.00, 140.67]	N/A	N/A	139.00 (2.74)	139.00 (2.59)	0.00
...Missing; n (%)	9,823 (58.7%)	9,546 (57.0%)	21,655 (93.1%)	21,938 (94.3%)	N/A	N/A	31,478 (78.7%)	31,484 (78.7%)	0.00
Lab result number- Albumin mean (only >0 and <=10 included)	6,438	6,794	1,399	1,117	N/A	N/A	7,837	7,911	
...mean (sd)	4.29 (0.30)	4.30 (0.30)	4.19 (0.62)	4.16 (0.70)	N/A	N/A	4.27 (0.38)	4.28 (0.38)	-0.03
...median [IQR]	4.30 [4.10, 4.50]	4.30 [4.10, 4.50]	4.30 [4.00, 4.50]	4.30 [4.00, 4.50]	N/A	N/A	4.30 (0.38)	4.30 (0.38)	0.00
...Missing; n (%)	10,302 (61.5%)	9,946 (59.4%)	21,866 (94.0%)	22,148 (95.2%)	N/A	N/A	32,168 (80.4%)	32,094 (80.2%)	0.01
Lab result number- Glucose (fasting or random) mean (only 10-1000 included)	6,905	7,185	1,588	1,309	N/A	N/A	8,493	8,494	
...mean (sd)	182.23 (74.88)	178.16 (69.58)	182.28 (74.67)	176.56 (63.34)	N/A	N/A	182.24 (74.85)	177.91 (68.66)	0.06
...median [IQR]	164.00 [130.45, 217.00]	162.00 [130.00, 211.00]	164.25 [131.00, 214.75]	163.00 [132.00, 209.00]	N/A	N/A	164.05 (74.85)	162.15 (68.66)	0.03
...Missing; n (%)	9,835 (58.8%)	9,555 (57.1%)	21,677 (93.2%)	21,956 (94.4%)	N/A	N/A	31,512 (78.8%)	31,511 (78.8%)	0.00
Lab result number- Potassium mean (only 1-7 included)	7,074	7,329	1,561	1,293	N/A	N/A	8,635	8,622	
...mean (sd)	4.45 (0.40)	4.44 (0.40)	4.37 (0.43)	4.36 (0.41)	N/A	N/A	4.44 (0.41)	4.43 (0.40)	0.02
...median [IQR]	4.40 [4.20, 4.70]	4.40 [4.20, 4.70]	4.35 [4.05, 4.60]	4.35 [4.10, 4.60]	N/A	N/A	4.39 (0.41)	4.39 (0.40)	0.00
...Missing; n (%)	9,666 (57.7%)	9,411 (56.2%)	21,704 (93.3%)	21,972 (94.4%)	N/A	N/A	31,370 (78.4%)	31,383 (78.4%)	0.00
Comorbidity Scores									
CCI (180 days)- ICD9 and ICD10									
...mean (sd)	2.07 (1.27)	2.07 (1.28)	1.65 (0.99)	1.65 (0.98)	2.36 (1.50)	2.37 (1.51)	2.05 (1.29)	2.05 (1.30)	0.00
...median [IQR]	2.00 [1.00, 2.00]	2.00 [1.00, 2.00]	1.00 [1.00, 2.00]	1.00 [1.00, 2.00]	2.00 [1.00, 3.00]	2.00 [1.00, 3.00]	1.66 (1.29)	1.66 (1.30)	0.00
Frailty Score: Qualitative Version 365 days as Categories,									
...0; n (%)	10,978 (65.6%)	10,837 (64.7%)	12,728 (54.7%)	12,498 (53.7%)	13,174 (45.7%)	13,018 (45.1%)	36,880 (53.6%)	36,353 (52.8%)	0.02
...1 to 2; n (%)	4,527 (27.0%)	4,585 (27.4%)	8,508 (36.6%)	8,680 (37.3%)	10,071 (34.9%)	10,062 (34.9%)	23,106 (33.6%)	23,327 (33.9%)	-0.01
...3 or more; n (%)	1,235 (7.4%)	1,318 (7.9%)	2,029 (8.7%)	2,087 (9.0%)	5,600 (19.4%)	5,765 (20.0%)	8,864 (12.9%)	9,170 (13.3%)	-0.01
Frailty Score: Empirical Version 365 days as Categories,									
...< 0.12908; n (%)	5,736 (34.3%)	5,863 (35.0%)	7,903 (34.0%)	7,780 (33.4%)	4,472 (15.5%)	4,654 (16.1%)	18,111 (26.3%)	18,297 (26.6%)	-0.01
...0.12908 - 0.1631167; n (%)	6,275 (37.5%)	6,241 (37.3%)	9,182 (39.5%)	9,210 (39.6%)	9,121 (31.6%)	8,892 (30.8%)	24,578 (35.7%)	24,343 (35.4%)	0.01
...>= 0.1631167; n (%)	4,729 (28.2%)	4,636 (27.7%)	6,180 (26.6%)	6,275 (27.0%)	15,252 (52.9%)	15,299 (53.0%)	26,161 (38.0%)	26,210 (38.1%)	0.00
Non-Frailty; n (%)	9,549 (57.0%)	9,735 (58.2%)	12,416 (53.4%)	12,489 (53.7%)	1,626 (5.6%)	1,331 (4.6%)	23,591 (34.3%)	23,555 (34.2%)	0.00
Frailty Score (mean): Qualitative Version 365 days,									
...mean (sd)	0.64 (1.16)	0.67 (1.20)	0.81 (1.19)	0.83 (1.20)	1.29 (1.69)	1.31 (1.69)	0.97 (1.42)	0.99 (1.43)	-0.01
...median [IQR]	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	1.00 [0.00, 2.00]	1.00 [0.00, 2.00]	0.42 (1.42)	0.42 (1.43)	0.00
Frailty Score (mean): Empirical Version 365 days,									
...mean (sd)	0.15 (0.04)	0.15 (0.04)	0.14 (0.04)	0.14 (0.04)	0.18 (0.05)	0.18 (0.05)	0.16 (0.04)	0.16 (0.04)	0.00
...median [IQR]	0.14 [0.12, 0.17]	0.14 [0.12, 0.17]	0.14 [0.12, 0.16]	0.14 [0.12, 0.16]	0.17 [0.14, 0.20]	0.17 [0.14, 0.20]	0.15 (0.04)	0.15 (0.04)	0.00
Healthcare Utilization									
Any hospitalization; n (%)	422 (2.5%)	395 (2.4%)	472 (2.0%)	486 (2.1%)	1,130 (3.9%)	1,123 (3.9%)	2,024 (2.9%)	2,004 (2.9%)	0.00
Any hospitalization within prior 30 days; n (%)	73 (0.4%)	63 (0.4%)	66 (0.3%)	77 (0.3%)	166 (0.6%)	186 (0.6%)	305 (0.4%)	326 (0.5%)	-0.01
Any hospitalization during prior 31-180 days; n (%)	352 (2.1%)	333 (2.0%)	411 (1.8%)	413 (1.8%)	985 (3.4%)	959 (3.3%)	1,748 (2.5%)	1,705 (2.5%)	0.00
Endocrinologist Visit; n (%)	2,703 (16.1%)	2,677 (16.0%)	3,720 (16.0%)	3,721 (16.0%)	5,251 (18.2%)	5,303 (18.4%)	11,674 (17.0%)	11,701 (17.0%)	0.00
Endocrinologist Visit (30 days prior); n (%)	1,886 (11.3%)	1,922 (11.5%)	2,696 (11.6%)	2,851 (12.3%)	3,533 (12.2%)	3,750 (13.0%)	8,115 (11.8%)	8,523 (12.4%)	-0.02
Endocrinologist Visit (31 to 180 days prior); n (%)	1,914 (11.4%)	1,900 (11.4%)	2,567 (11.0%)	2,647 (11.4%)	3,948 (13.7%)	4,050 (14.0%)	8,429 (12.2%)	8,597 (12.5%)	-0.01
Internal medicine/family medicine visits; n (%)	12,196 (72.9%)	11,920 (71.2%)	20,638 (88.7%)	20,362 (87.5%)	24,256 (84.1%)	23,791 (82.5%)	57,090 (82.9%)	56,073 (81.4%)	0.04
Internal medicine/family medicine visits (30 days prior) ; n (%)	8,667 (51.8%)	8,658 (51.7%)	15,681 (67.4%)	15,619 (67.1%)	17,442 (60.5%)	17,316 (60.0%)	41,790 (60.7%)	41,593 (60.4%)	0.01
Internal medicine/family medicine visits (31 to 180 days prior) ; n (%)	10,237 (61.2%)	10,229 (61.1%)	17,149 (73.7%)	17,062 (73.3%)	21,118 (73.2%)	21,055 (73.0%)	48,504 (70.4%)	48,346 (70.2%)	0.00
Cardiologist visit; n (%)	3,197 (19.1%)	3,226 (19.3%)	3,866 (16.6%)	3,917 (16.8%)	8,193 (28.4%)	8,255 (28.6%)	15,256 (22.2%)	15,398 (22.4%)	0.00
Number of Cardiologist visits (30 days prior); n (%)	990 (5.9%)	1,022 (6.1%)	1,192 (5.1%)	1,175 (5.1%)	2,541 (8.8%)	2,563 (8.9%)	4,723 (6.9%)	4,760 (6.9%)	0.00

Table 1

Number of Cardiologist visits (31 to 180 days prior); n (%)	2,698 (16.1%)	2,721 (16.3%)	3,272 (14.1%)	3,308 (14.2%)	7,110 (24.6%)	7,144 (24.8%)	13,080 (19.0%)	13,173 (19.1%)	0.00
Electrocardiogram ; n (%)	3,814 (22.8%)	3,833 (22.9%)	5,351 (23.0%)	5,482 (23.6%)	8,209 (28.5%)	8,398 (29.1%)	17,374 (25.2%)	17,713 (25.7%)	-0.01
Use of glucose test strips; n (%)	578 (3.5%)	584 (3.5%)	926 (4.0%)	953 (4.1%)	932 (3.2%)	953 (3.3%)	2,436 (3.5%)	2,490 (3.6%)	-0.01
Dialysis; n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	000 (0.0%)	000 (0.0%)	#DIV/0!
Naive new user v8 Copy; n (%)	1,847 (11.0%)	1,869 (11.2%)	1,991 (8.6%)	2,032 (8.7%)	1,870 (6.5%)	1,975 (6.8%)	5,708 (8.3%)	5,876 (8.5%)	-0.01
N antidiabetic drugs at index date Copy									
...mean (sd)	2.26 (0.88)	2.26 (0.86)	2.32 (0.90)	2.32 (0.88)	2.33 (0.89)	2.35 (0.88)	2.31 (0.89)	2.32 (0.88)	-0.01
...median [IQR]	2.00 [2.00, 3.00]	2.00 [2.00, 3.00]	2.00 [2.00, 3.00]	2.00 [2.00, 3.00]	2.00 [2.00, 3.00]	2.00 [2.00, 3.00]	2.00 (0.89)	2.00 (0.88)	0.00
number of different/distinct medication prescriptions									
...mean (sd)	9.99 (4.51)	9.95 (4.43)	9.68 (4.21)	9.71 (4.16)	10.40 (4.33)	10.45 (4.40)	10.06 (4.33)	10.08 (4.33)	0.00
...median [IQR]	9.00 [7.00, 12.00]	9.00 [7.00, 12.00]	9.00 [7.00, 12.00]	9.00 [7.00, 12.00]	10.00 [7.00, 13.00]	10.00 [7.00, 13.00]	9.42 (4.33)	9.42 (4.33)	0.00
Number of Hospitalizations									
...mean (sd)	0.03 (0.24)	0.03 (0.17)	0.02 (0.15)	0.02 (0.16)	0.04 (0.23)	0.04 (0.23)	0.03 (0.21)	0.03 (0.19)	0.00
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 (0.21)	0.00 (0.19)	0.00
Number of hospital days									
...mean (sd)	0.12 (1.00)	0.12 (0.97)	0.09 (0.81)	0.10 (0.88)	0.22 (1.56)	0.23 (1.87)	0.15 (1.22)	0.16 (1.40)	-0.01
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 (1.22)	0.00 (1.40)	0.00
Number of Emergency Department (ED) visits									
...mean (sd)	0.21 (0.72)	0.21 (0.76)	0.04 (0.74)	0.04 (0.55)	0.31 (0.95)	0.31 (1.07)	0.19 (0.83)	0.19 (0.85)	0.00
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 (0.83)	0.00 (0.85)	0.00
Number of Office visits									
...mean (sd)	4.29 (3.42)	4.24 (3.06)	4.23 (3.30)	4.21 (3.07)	5.08 (3.83)	5.08 (3.60)	4.60 (3.56)	4.58 (3.30)	0.01
...median [IQR]	3.00 [2.00, 6.00]	3.00 [2.00, 6.00]	3.00 [2.00, 5.00]	3.00 [2.00, 5.00]	4.00 [2.00, 7.00]	4.00 [3.00, 7.00]	3.42 (3.56)	3.42 (3.30)	0.00
Number of Endocrinologist visits									
...mean (sd)	0.77 (2.73)	0.85 (3.12)	0.72 (2.61)	0.87 (3.27)	1.08 (4.08)	1.22 (4.66)	0.88 (3.33)	1.01 (3.88)	-0.04
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 (3.33)	0.00 (3.88)	0.00
Number of internal medicine/family medicine visits									
...mean (sd)	7.13 (11.56)	7.03 (10.98)	6.26 (7.11)	6.46 (7.42)	7.46 (10.23)	7.75 (9.99)	6.97 (9.67)	7.14 (9.47)	-0.02
...median [IQR]	4.00 [0.00, 9.00]	4.00 [0.00, 9.00]	4.00 [2.00, 8.00]	4.00 [2.00, 9.00]	4.00 [2.00, 10.00]	5.00 [2.00, 10.00]	4.00 (9.67)	4.42 (9.47)	-0.04
Number of Cardiologist visits									
...mean (sd)	0.78 (2.61)	0.76 (2.44)	0.61 (2.04)	0.63 (2.14)	1.33 (3.71)	1.35 (3.65)	0.95 (2.97)	0.96 (2.93)	0.00
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	0.00 (2.97)	0.00 (2.93)	0.00
Number electrocardiograms received									
...mean (sd)	0.36 (0.86)	0.36 (0.86)	0.35 (0.82)	0.35 (0.83)	0.50 (1.05)	0.50 (1.07)	0.42 (0.93)	0.42 (0.94)	0.00
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	0.00 (0.93)	0.00 (0.94)	0.00
Number of HbA1c tests ordered									
...mean (sd)	1.36 (0.89)	1.35 (0.87)	1.28 (0.88)	1.28 (0.85)	1.56 (0.90)	1.56 (0.82)	1.42 (0.89)	1.41 (0.84)	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]	2.00 [1.00, 2.00]	2.00 [1.00, 2.00]	1.42 (0.89)	1.42 (0.84)	0.00
Number of glucose tests ordered									
...mean (sd)	0.43 (1.87)	0.43 (1.71)	0.39 (1.63)	0.39 (1.03)	0.47 (1.34)	0.47 (1.11)	0.43 (1.58)	0.43 (1.26)	0.00
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 (1.58)	0.00 (1.26)	0.00
Number of lipid tests ordered									
...mean (sd)	1.06 (0.96)	1.06 (0.94)	1.06 (1.29)	1.06 (1.13)	1.13 (0.88)	1.13 (0.83)	1.09 (1.05)	1.09 (0.97)	0.00
...median [IQR]	1.00 [0.00, 2.00]	1.00 [0.00, 2.00]	1.00 [0.00, 1.00]	1.00 [0.00, 2.00]	1.00 [1.00, 2.00]	1.00 [1.00, 2.00]	1.00 (1.05)	1.00 (0.97)	0.00
Number of creatinine tests ordered									
...mean (sd)	0.03 (0.22)	0.03 (0.20)	0.03 (0.23)	0.04 (0.24)	0.07 (0.34)	0.07 (0.32)	0.05 (0.28)	0.05 (0.27)	0.00
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 (0.28)	0.00 (0.27)	0.00
Number of BUN tests ordered									
...mean (sd)	0.02 (0.16)	0.02 (0.16)	0.02 (0.18)	0.02 (0.18)	0.04 (0.28)	0.04 (0.26)	0.03 (0.22)	0.03 (0.21)	0.00
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 (0.22)	0.00 (0.21)	0.00
Number of tests for microalbuminuria									
...mean (sd)	0.84 (1.19)	0.85 (1.18)	0.74 (1.11)	0.74 (1.10)	0.53 (0.73)	0.54 (0.73)	0.68 (0.99)	0.68 (0.99)	0.00
...median [IQR]	0.00 [0.00, 2.00]	0.00 [0.00, 2.00]	0.00 [0.00, 2.00]	0.00 [0.00, 2.00]	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	0.00 (0.99)	0.00 (0.99)	0.00
Total N distinct ICD9/ICD10 diagnoses at the 3rd digit level Copy									
...mean (sd)	5.56 (5.86)	5.43 (6.00)	2.09 (3.20)	2.05 (3.27)	5.91 (6.84)	5.82 (6.92)	4.53 (5.60)	4.45 (5.69)	0.01
...median [IQR]	5.00 [0.00, 8.00]	5.00 [0.00, 8.00]	0.00 [0.00, 4.00]	0.00 [0.00, 4.00]	4.00 [0.00, 9.00]	4.00 [0.00, 9.00]	2.89 (5.60)	2.89 (5.69)	0.00
Use of thiazide; n (%)	2,040 (12.2%)	2,060 (12.3%)	2,782 (12.0%)	2,737 (11.8%)	4,125 (14.3%)	4,100 (14.2%)	8,947 (13.0%)	8,897 (12.9%)	0.00
Use of beta blockers; n (%)	6,033 (36.0%)	6,038 (36.1%)	8,159 (35.1%)	8,198 (35.2%)	13,867 (48.1%)	13,913 (48.2%)	28,059 (40.8%)	28,149 (40.9%)	0.00
Use of calcium channel blockers; n (%)	4,836 (28.9%)	4,820 (28.8%)	6,641 (28.5%)	6,697 (28.8%)	9,762 (33.8%)	9,796 (34.0%)	21,239 (30.8%)	21,313 (31.0%)	0.00