Replication of Dapagliflozin and Cardiovascular Outcomes in Type 2 Diabetes (DECLARE–TIMI 58 Trial)

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

Dapagliflozin and Cardiovascular Outcomes in Type 2 Diabetes (DECLARE–TIMI 58)

1.2 Intended aim(s)

The primary objective will be evaluated in 2 steps. The first step will determine if dapagliflozin is noninferior to placebo for the incidence of MACE assessed with a noninferiority margin of 1.3. If noninferiority is statistically confirmed, the second step will be to determine if dapagliflozin reduces the incidence of the co-primary efficacy end points.

1.3 Primary endpoints for replication and RCT finding

- Major Adverse Cardiovascular Events, Including CV Death, Nonfatal Myocardial Infarction (MI), and Nonfatal Stroke
- Cardiovascular death (CVD) or hospitalization for heart failure (HHF)

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

A total of 1,390 subjects with MACE events will be required to have 85% power to demonstrate superiority of dapagliflozin to placebo if the true HR is 0.85. The trial was not formally powered for the second of the co-primary end points, CVD or HHF. However, we anticipate 87% power to detect an HR of 0.80 with a 1-sided α of .0231.

1.5 Trial estimate

- MACE- HR, 0.93 (0.84 to 1.03) comparing dapagliflozin to placebo (Wiviott et al.)
- Cardiovascular death or hospitalization for heart failure- HR, 0.83 (0.73 to 0.95) comparing dapagliflozin to placebo

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.

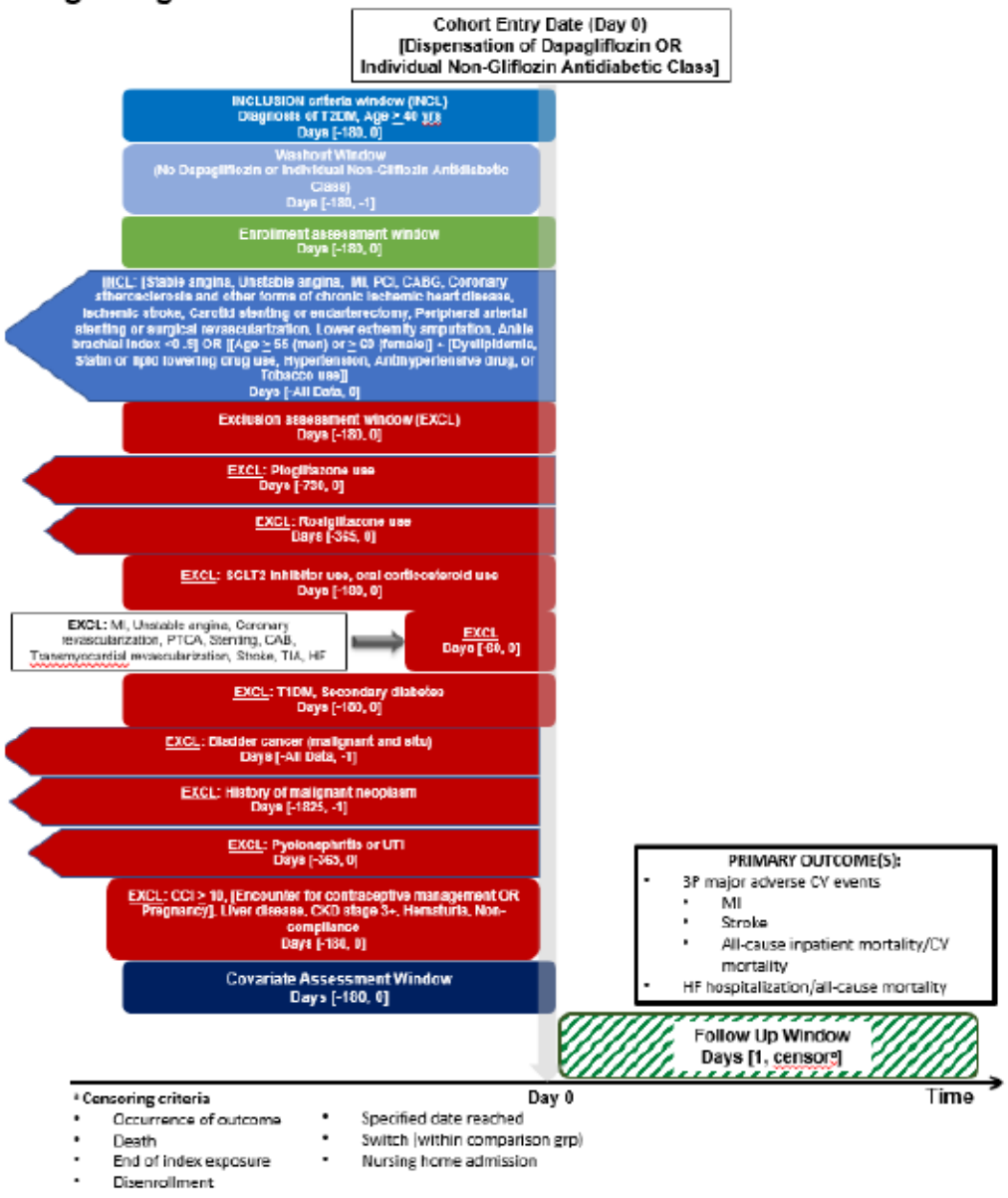
3. Data Source(s)

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 – DECLARE TRIAL REPLICATION



5. Cohort Identification

5.1 Cohort Summary

This study will involve a new user, parallel group, cohort study design comparing dapagliflozin to the DPP-4 inhibitor (DPP4i) antidiabetic class. DPP4is 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. 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 outcomes (a. 3P-MACE and b. composite of heart failure hospitalization/all-cause mortality), 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 dapagliflozin in the U.S. started on January 8, 2014.

- For Marketscan and Medicare: Jan 8, 2014-Dec 31, 2017 (end of data availability).
- For Optum: Jan 8, 2014-Mar 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 dapagliflozin 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

Patients who used exposure or a reference between January 8, 2014 to Dec 2017 (for Marketscan/Medicare)/March 2019 (for Optum)	-74,319,657	545,227	-191,316,290	673,745	-21,925,514	1,540,661
Patients who have continuous 6 months registration in the database	-76,221	469,006	-55,637	618,108	-415,687	1,124,974
Excluded due to prior use of referent	-351,484	117,522	-416,417	201,691	-784,720	340,254
Excluded due to prior use of exposure	-15,355	102,167	-58,415	143,276	-19,316	320,938
Excluded because patient qualified in >1 exposure category	-39	102,128	-166	143,110	-96	320,842
Excluded based on missing Age	-3	102,125	0	143,110	0	320,842
Excluded based on missing Gender	-9	102,116	0	143,110	0	320,842
Excluded based on Inclusion 1- Age >= 40	-2,873	99,243	-6,212	136,898	0	320,842
Excluded based on Inclusion 2- DM Type 2	-4,077	95,166	-6,581	130,317	-3,494	317,348
Excluded based on Inclusion 4- High Risk for CV event defined as having either established CV disease and/or multiple risk factors	-34,224	60,942	-30,651	99,666	-260	317,088
Excluded based on Exclusion 1a- Current or recent (within 24 months) treatment with pioglitazone	-2,241	58,701	-2,798	96,868	-11,793	305,295
Excluded based on Exclusion 1b- Current or recent (within 12 months) treatment with rosiglitazone	-3	58,698	-6	96,862	-13	305,282
Excluded based on Exclusion 1c- Previous treatment with any SGLT2 inhibitor (Empagliflozin, ertugliflozin, or canagliflozin) in prior 6 months	-1,292	57,406	-2,269	94,593	-4,526	300,756
Excluded based on Exclusion 1d- Any patient currently receiving chronic (>30 consecutive days) treatment with an oral steroid	-965	56,441	-1,000	93,593	-7,968	292,788
Excluded based on Exclusion 2- Acute cardiovascular event (in prior 60 days)	-660	55,781	-1,528	92,065	-9,725	283,063
Excluded based on Exclusion 4- DM Type 1 OR Secondary DM	-1,900	53,881	-2,091	89,974	-10,363	272,700
Excluded based on Exclusion 5 - History of Malignant Neoplasm (prior 5 years)	-2,587	51,294	-2,869	87,105	-19,117	253,583
Excluded based on Exclusion 6- History of Bladder cancer (malignant and situ) anytime prior	-2	51,292	-1	87,104	-21	253,562

Excluded based on Exclusion 7- Chronic cystitis and/or recurrent urinary tract infections (prior year)	-2,023	49,269	-1,761	85,343	-12,690	240,872
Excluded based on Exclusion 8- CCI (180 days)- >= 10	-235	49,034	-61	85,282	-665	240,207
Excluded based on Exclusion 9-Pregnancy	-1	49,033	-3	85,279	0	240,207
Excluded based on Exclusion 15- Liver disease	-187	48,846	-691	84,588	-2,261	237,946
Excluded based on Exclusion 16- CKD stage 3 and above	-1,479	47,367	-809	83,779	-6,680	231,266
Excluded based on Exclusion 17- Hematuria	-129	47,238	-173	83,606	-630	230,636
Excluded based on Exclusion 18- Non-compliance	-4	47,234	-103	83,503	-642	229,994
Final cohort		**47,234**		**83,503**		**229,994**

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

6. Variables

6.1 Exposure-related variables:

Study drug:

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

Comparator agents-

- Initiators of dapagliflozin will be compared to initiators of-
    - DPP4i

We will also run feasibility numbers for these antidiabetic classes separately to identify the most appropriate comparator. Because dapagliflozin and comparators are frequently used as second or third line treatments of T2DM, we expect it to be unlikely that dapagliflozin and comparators are initiated in patients with substantially different baseline risk for proposed outcomes.

6.2 Covariates:

- Age

- Sex
- Combined Comorbidity Index (CCI), measured over the 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**):

- **Co-primary outcome**: 3-point major adverse cardiovascular events (MACE), i.e., non-fatal myocardial infarction, non-fatal stroke, or CV mortality
- **Co-primary outcome**: Hospitalization for heart failure (HHF)/All-cause 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)
    - Hospital admission for heart failure
    - 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 outcome of interest (control outcome only serve to assess aspects of study validity but are not further interpreted):

1. Diabetic Ketoacidosis (we expect to see a positive association; Neal et al., 2017)

Control outcome definition

Outcome	Definition	Comments
Control Outcomes		
Diabetic Ketoacidosis	Inpatient ICD-9 diagnosis: 250.1x	Note- 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 dapagliflozin 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 (dapagliflozin 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 dapagliflozin 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

Aetion report name:

For Dapagliflozin vs. DPP4i

Optum- https://bwh-dope.aetion.com/projects/details/664/results/42809/result/0
Marketscan- https://bwh-dope.aetion.com/projects/details/665/results/42810/result/0
Medicare- https://bwh-dope.aetion.com/projects/details/666/results/42811/result/0

Date conducted: 10/15/2019

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 Dapagliflozin vs. DPP4i

Optum- https://bwh-dope.aetion.com/projects/details/664/results/42812/result/0
Marketscan- https://bwh-dope.aetion.com/projects/details/665/results/42813/result/0
Medicare- https://bwh-dope.aetion.com/projects/details/666/results/42814/result/0

Date conducted: 10/15/2019

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, FDA, and assigned members of advisory board.

Reviewed by PI:	Jessica Franklin	Date reviewed:	11/4/2019
Reviewed by FDA:	Ken Quinto	Date reviewed:	11/6/2019
Reasons for stopping analysis (if required):			

9. Balance Assessment after PS matching

Aetion report name:
Optum- https://bwh-dope.aetion.com/projects/details/664/results/45428/result/0
Marketscan- https://bwh-dope.aetion.com/projects/details/665/results/45429/result/0
Medicare- https://bwh-dope.aetion.com/projects/details/666/results/45430/result/0

Date conducted: 11/30/2019

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.

	Overall	Referent	Exposure
Dummy Outcome	0 (0.00%)	0 (0.00%)	0 (0.00%)
Death	116 (0.23%)	67 (0.27%)	49 (0.20%)
Start of an additional exposure	1,724 (3.46%)	411 (1.65%)	1,313 (5.27%)
End of index exposure	29,607 (59.46%)	14,752 (59.26%)	14,855 (59.67%)
Specified date reached	11,094 (22.28%)	5,670 (22.78%)	5,424 (21.79%)
End of patient enrollment	6,215 (12.48%)	3,125 (12.55%)	3,090 (12.41%)
Switch to other DPP4i (for censoring) + nursing home admission	1,034 (2.08%)	870 (3.49%)	164 (0.66%)

- Report follow-up time by treatment group.

	Median Follow-Up Time (Days) [IQR]		
Patient Group	**Optum**	**Marketscan**	**Medicare**
Overall Patient Population	119 [58-267]	139 [61-310]	118 [58-250]
Referent	119 [58-286]	120 [67-261]	120 [67-261]
Exposure	120 [58-251]	118 [58-240]	118 [58-240]

- Report overall risk of the primary outcome.

	Optum	Marketscan	Medicare
Risk per 1,000 patients (MACE)	14.24	8.74	21.83
Risk per 1,000 patients (composite of Heart failure hospitalization-any diagnosis position)/All-cause mortality	22.46	13.19	37.16

10. Final Power Assessment

Date conducted: 12/1/2019

- 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).

- Pooled
  - **For dapagliflozin vs. DPP4i (Primary outcome- MACE)**

Superiority Analysis		**Non-inferiority Analysis**	
Number of patients matched		Number of patients matched	
Reference	24,895	Reference	24,895
Exposed	24,895	Exposed	24,895
Risk per 1,000 patients	14.94	Risk per 1,000 patients	14.94
Desired HR from RCT	0.85	Assumed HR from RCT	1
Alpha (2-sided)	0.05	Alpha (2-sided)	0.05
		Non-inferiority margin	1.3
Number of events expected	743.8626	Number of events expected	743.8626
Power	0.601152916	Power	0.947155457

  - **For dapagliflozin vs. DPP4i (Co-primary outcome- Heart failure (any position)/all-cause mortality)**

Superiority Analysis		**Non-inferiority Analysis**	
Number of patients matched		Number of patients matched	
Reference	24,895	Reference	24,895
Exposed	24,895	Exposed	24,895
Risk per 1,000 patients	24.27	Risk per 1,000 patients	24.27
Desired HR from RCT	0.8	Assumed HR from RCT	1
Alpha (2-sided)	0.05	Alpha (2-sided)	0.05
		Non-inferiority margin	1.3
Number of events expected	1208.4033	Number of events expected	1208.4033
Power	0.972476483	Power	0.995341553

- Optum
  - **For dapagliflozin vs. DPP4i (Primary outcome- MACE)**

Superiority Analysis		**Non-inferiority Analysis**	
Number of patients matched		Number of patients matched	
Reference	3,316	Reference	3,316
Exposed	3,316	Exposed	3,316
Risk per 1,000 patients	14.24	Risk per 1,000 patients	14.24
Desired HR from RCT	0.85	Assumed HR from RCT	1
Alpha (2-sided)	0.05	Alpha (2-sided)	0.05
		Non-inferiority margin	1.3
Number of events expected	94.43968	Number of events expected	94.43968
Power	0.12392638	Power	0.246629377

- **For dapagliflozin vs. DPP4i (Co-primary outcome- Heart failure (any position)/all-cause mortality)**

Superiority Analysis		**Non-inferiority Analysis**	
Number of patients matched		Number of patients matched	
Reference	3,316	Reference	3,316
Exposed	3,316	Exposed	3,316
Risk per 1,000 patients	22.46	Risk per 1,000 patients	22.46
Desired HR from RCT	0.8	Assumed HR from RCT	1
Alpha (2-sided)	0.05	Alpha (2-sided)	0.05
		Non-inferiority margin	1.3
Number of events expected	148.95472	Number of events expected	148.95472
Power	0.275279358	Power	0.359825479

- Marketscan
  - **For dapagliflozin vs. DPP4i (Primary outcome- MACE)**

Superiority Analysis		**Non-inferiority Analysis**	
Number of patients matched		Number of patients matched	
Reference	12,415	Reference	12,415
Exposed	12,415	Exposed	12,415
Risk per 1,000 patients	8.74	Risk per 1,000 patients	8.74
Desired HR from RCT	0.85	Assumed HR from RCT	1
Alpha (2-sided)	0.05	Alpha (2-sided)	0.05
		Non-inferiority margin	1.3
Number of events expected	217.0142	Number of events expected	217.0142
Power	0.223558993	Power	0.489043518

- **For dapagliflozin vs. DPP4i (Co-primary outcome- Heart failure (any position)/all-cause mortality)**

Superiority Analysis		**Non-inferiority Analysis**	
Number of patients matched		Number of patients matched	
Reference	12,415	Reference	12,415
Exposed	12,415	Exposed	12,415
Risk per 1,000 patients	13.19	Risk per 1,000 patients	13.19
Desired HR from RCT	0.8	Assumed HR from RCT	1
Alpha (2-sided)	0.05	Alpha (2-sided)	0.05
		Non-inferiority margin	1.3
Number of events expected	327.5077	Number of events expected	327.5077
Power	0.52362617	Power	0.660585599

- Medicare
  - **For dapagliflozin vs. DPP4i (Primary outcome- MACE)**

Superiority Analysis		**Non-inferiority Analysis**	
Number of patients matched		Number of patients matched	
Reference	9,164	Reference	9,164
Exposed	9,164	Exposed	9,164
Risk per 1,000 patients	21.83	Risk per 1,000 patients	21.83
Desired HR from RCT	0.85	Assumed HR from RCT	1
Alpha (2-sided)	0.05	Alpha (2-sided)	0.05
		Non-inferiority margin	1.3
Number of events expected	400.10024	Number of events expected	400.10024
Power	0.369142646	Power	0.746657207

- **For dapagliflozin vs. DPP4i (Co-primary outcome- Heart failure (any position)/all-cause mortality)**

Superiority Analysis		**Non-inferiority Analysis**	
Number of patients matched		Number of patients matched	
Reference	9,164	Reference	9,164
Exposed	9,164	Exposed	9,164
Risk per 1,000 patients	37.16	Risk per 1,000 patients	37.16
Desired HR from RCT	0.8	Assumed HR from RCT	1
Alpha (2-sided)	0.05	Alpha (2-sided)	0.05
		Non-inferiority margin	1.3
Number of events expected	681.06848	Number of events expected	681.06848
Power	0.829390401	Power	0.928339341

- 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:	12/5/2019
Reviewed by FDA:	David Martin	Date reviewed:	12/20/2019
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

Date conducted:

- Register the study on clinicalTrials.gov and upload this document.

13. Comparative Analyses

Aetion report name:
Date conducted:

13.1 For **primary analysis:**

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

13.2 For secondary analyses:

- In the pre-matched cohort, 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 dapagliflozin 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:

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**

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;139: :2822-30.

Wiviott SD, Raz I, Bonaca MP, Mosenzon O, Kato ET, Cahn A, et al. Dapagliflozin and Cardiovascular Outcomes in Type 2 Diabetes. The New England Journal of Medicine. 2019;380(4):347-57.

Appendix A

#	DECLARE-TIMI 58 trial definitions	Implementation in routine care	References/Rationale	Color coding
	Trial details- Estimated Study Completion Date : July 18, 2018. Actual Enrollment : 17,276 participants		Please see the following Google Drive for further details or any missing information: [illegible]	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: [illegible]	Adequate mapping in claims
	dapagliflozin 10 mg/day vs. placebo	New use of dapagliflozin vs. individual non-gliflozin antidiabetic class (ie, a DPP-4i, a GLP-1 RA, and a sulfonylurea)		Intermediate mapping in claims
	Safety and co-primary efficacy			Poor mapping or cannot be measured in claims
	3P-MACE– CV death, non-fatal MI, non-fatal ischemic stroke	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 diagnosis: 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, Harrold 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, Mitchel 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
	Co-primary efficacy			
	– CV death, hospitalization due to heart failure	Measured 1 days after drug initiation in any diagnosis position and inpatient care setting: Heart failure requiring hospitalization- ICD-9 diagnosis: 428.x, 398.91, 402.01, 402.11, 402.91, 404.01, 404.11, 404.91, 404.03, 404.13, 404.93 CV death- Dependent on data source, see mortality sheet		
	INCLUSION CRITERIA			
1	1. Provision of informed consent prior to any study specific procedures (including run-in)	N/A		
2	2. Female or male aged ≥ 40 years	Age ≥40 years at drug initiation		
3	3. Diagnosed with T2DM • Diagnosis of T2DM can be based on the following: – Prior documentation of type 2 diabetes AND/OR – Treatment with anti-hyperglycemic medications and/or diet AND/OR – ADA criteria: plasma random glucose >200 mg/dl (11.1 mmol/L) or fasting >126 mg/dl (7.0 mmol/L) or 2-h plasma glucose >200 mg/dl (7.0 mmol/L) during an oral glucose tolerance test or HbA1C ≥6.5%	Measured 180 days prior to and including day of drug initiation in any diagnosis position and the inpatient or outpatient care setting Type 2 Diabetes ICD-9 diagnosis: 250.x0, 250.x2	Patorno, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gliflozin 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	
4	4. High Risk for CV event defined as having either established CV disease and/or multiple risk factors:	Measured anytime prior to and including day of drug initiation in any procedure position and inpatient care setting Stable angina: 413.x Unstable angina/ACS: 411.x		
	– Established CV Disease (See below for details)	-		
	4.1 Established Vascular Disease-	-		
	• Ischemic heart disease (any of the following):	-		
	– Documented Myocardial Infarction	Measured anytime prior to and including day of drug initiation in any diagnosis position and the inpatient or outpatient care setting Acute MI ICD-9 diagnosis: 410.xx, Old MI ICD-9 diagnosis: 412.xx	Patorno, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gliflozin 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	
	– Percutaneous Coronary Intervention	PTCA: Measured anytime prior to and including day of 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 anytime prior to and including day of 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 Stenting: Measured anytime prior to and including day of drug initiation in any procedure position and inpatient care setting- CPT-4: 92980, 92981, 92928 – 92929, 92933 - 92934 OR – Measured anytime prior to and including day of drug initiation in any procedure position and inpatient or outpatient care setting- ICD-9 procedure: 36.06, 36.07 Transmyocardial revascularization: Measured anytime prior to and including day of drug initiation in any procedure position and inpatient care setting- CPT-4: 33140, 33141 OR – Measured anytime prior to and including day of drug initiation in any procedure position and inpatient or outpatient care setting- ICD-9 procedure: 36.31-36.34	Patorno, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gliflozin 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	

Appendix A

	– Coronary Artery Bypass Grafting	CABG Measured anytime prior to and including day of drug initiation in any procedure position and inpatient care setting –CPT-4: 33510 – 33536, 33545, 33572 – OR – Measured anytime prior to and including day of drug initiation in any procedure position and inpatient or outpatient care setting – ICD-9 procedure: 36.1x, 36.2x	
	– Objective Findings of Coronary Stenosis (> 50%) in at least 2 coronary arteries	Measured anytime prior to and including day of drug initiation in any diagnosis position and inpatient or outpatient care setting – Coronary atherosclerosis and other forms of chronic ischemic heart disease ICD-9 diagnosis: 414.xx	Patorno, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gli flozin antidiabetic drugs: population based cohort study." BMJ 2018;360:k119 https://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
	+ Cerebrovascular disease (any of the following):	-	
	– Documented Ischemic Stroke	Measured anytime prior to and including day of drug initiation in any diagnosis position and inpatient or outpatient care setting – Ischemic stroke (and exclusion of cerebral hemorrhage) ICD-9 diagnosis: 433.xx, 434.xx, 436.xx	Patorno, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gli flozin antidiabetic drugs: population based cohort study." BMJ 2018;360:k119 https://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
	– Known transient ischemic attack, primary intracerebral hemorrhage or subarachnoid hemorrhage do not qualify.	N/A	
	– Carotid stenting or endarterectomy	Measured anytime prior to and including day of drug initiation in any procedure position and inpatient or outpatient care setting – Carotid stenting or endarterectomy ICD-9 procedure: 38.12, 00.61, 00.63 CPT-4: 35301	ICD-9 procedure code 00.62 is regarding intracranial vessel and was not included.
	+ Peripheral Arterial Disease (any of the following):	-	
	– peripheral arterial stenting or surgical revascularization	Measured anytime prior to and including day of drug initiation in any procedure position and the inpatient or outpatient care setting Peripheral arterial stenting or surgical revascularization ICD-9 procedure: 39.25, 39.50, 39.99	Patorno, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gli flozin antidiabetic drugs: population based cohort study." BMJ 2018;360:k119 https://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
	– lower extremity amputation as a result of peripheral arterial obstructive disease	Measured anytime prior to and including day of drug initiation in any diagnosis/procedure position and the inpatient or outpatient care setting Lower extremity amputation ICD-9 diagnosis: V49.7x ICD-9 procedure: 84.10-84.18 (Outpatient only) CPT-4: 27590, 27591, 27592, 27880, 27881, 27882, 27884, 27886, 27888, 27889, 28800, 28805, 28810, 28820, 28825	Patorno, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gli flozin antidiabetic drugs: population based cohort study." BMJ 2018;360:k119 https://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
	– Current symptoms of intermittent claudication AND ankle/brachial index (ABI) < 0.90 documented within last 12 months	Measured anytime prior to and including day of drug initiation in any diagnosis position and the inpatient or outpatient care setting Ankle brachial index (ABI) ICD-9 diagnosis: 440.21	
		-	
	OR	-	
		-	
	4b. No known cardiovascular disease AND at least two cardiovascular risk factors in addition to T2DM, defined as:	-	
	– Age ≥ 55 years in men and ≥ 60 in women	– Age ≥ 55 years in men and ≥ 60 in women at drug initiation	Note: This is the first risk factor.
	AND presence of at least 1 of the following additional risk factors (see below for details)		
	– Dyslipidemia (at least one of the following)	Measured anytime prior to and including day of drug initiation in any diagnosis position and the inpatient or outpatient care setting Hyperlipidemia ICD-9 diagnosis: 272.0x-272.4x	Patorno, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gli flozin antidiabetic drugs: population based cohort study." BMJ 2018;360:k119 https://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
	– Low-density lipoprotein cholesterol (LDL-C) >130 mg/dl (3.36 mmol/L) within last 12 months	-	
	– On lipid lowering therapy prescribed by a physician for dyslipidemia	Measured anytime prior to and including day of drug initiation as a dispensing of one of the following medications listed in the 'statins or lipid lowering RX' sheet.	
	– Hypertension (at least one of the following)	Measured anytime prior to and including day of drug initiation in any diagnosis position and the inpatient or outpatient care setting Hypertension ICD-9 diagnosis: 401.x – 405.x	Patorno, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gli flozin antidiabetic drugs: population based cohort study." BMJ 2018;360:k119 https://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
	– BP >140/90 mm/Hg at enrollment visit	N/A	
	– On anti-hypertensive therapy prescribed by a physician for blood pressure lowering	Measured anytime prior to and including day of drug initiation as a dispensing of one of the following medications listed in the 'antihypertensive RX' sheet.	
	– Tobacco use (5 cigarettes/day or more for at least 1 year at randomization)	Measured anytime prior to and including day of drug initiation in any diagnosis/procedure position and the care setting indicated below Smoking: [inpatient or outpatient) ICD-9 diagnosis: V15.82, 305.1x, 989.84 [outpatient) CPT-4/HCPCS procedure: 99406, 99407, G0436, G0437, G9016, S9453, S4995, G9276, G9458, 1034F, 4004F, 4001F – OR – Measure anytime prior to and including day of drug initiation as a dispensing of at least one nicotine or varenicline prescription: NICOTINE NICOTINE BITARTRATE NICOTINE POLACRILEX VARENICLINE TARTRATE	Patorno, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gli flozin antidiabetic drugs: population based cohort study." BMJ 2018;360:k119 https://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
5	5. WOCBP must take precautions to avoid pregnancy throughout the study and for 4 weeks after intake of the last dose. – WOCBP must have a negative urine pregnancy test. WOCBP include any female who has experienced menarche and who has not undergone successful surgical sterilization (hysterectomy, bilateral tubal ligation or bilateral oophorectomy) or is not postmenopausal. – WOCBP must be willing to use a medically accepted method of contraception that is considered reliable in the judgment of the investigator.	-	Exclusion for pregnancy applied below in #6.

Appendix A

	EXCLUSION CRITERIA		
	Patients should not meet any exclusion criteria at the time of randomization. If at the time of enrollment, it is known that the patient will not meet criteria after a successful run-in period he/she should not be entered into run in.	N/A	
1	1. Use of the following excluded medications:	-	
1a	• Current or recent (within 24 months) treatment with pioglitazone and/or use of pioglitazone for 2 years or more at any time	Measured 730 days prior to and including day of drug initiation as a dispensing of pioglitazone	
1b	• Current or recent (within 12 months) treatment with rosiglitazone	Measured 365 days prior to and including day of drug initiation as a dispensing of rosiglitazone	
1c	• Previous treatment with any SGLT2 inhibitor	Measured 180 days prior to and including day of drug initiation as a dispensing of rosiglitazone empagliflozin, ertugliflozin, or canagliflozin	
1d	• Any patient currently receiving chronic (>30 consecutive days) treatment with an oral steroid at a dose equivalent to oral prednisolone ≥10 mg (e.g., betamethasone ≥1.2 mg, dexamethasone ≥1.5 mg, hydrocortisone ≥40 mg) per day	Measured 180 days prior to and including day of drug initiation as a dispensing of an oral corticosteroid with days supply ≥60 days Oral corticosteroids: Cortisone, hydrocortisone, prednisone, prednisolone, methylprednisolone, triamcinolone, dexamethasone, betamethasone	Patorno, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gli flozin antidiabetic drugs: population based cohort study." BMJ 2018;360:k119 https://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 * Excluded based on generic name without consideration of dosage
2	2. Acute cardiovascular event (e.g., acute coronary syndrome (ACS), transient ischemic attack (TIA), stroke, any revascularization, decompensated HF, sustained tachycardia <8 weeks prior to randomization. Patients with acute cardiovascular events can be enrolled in the run-in period as long as randomization does not occur within 8 weeks of the event.	Measured 90 days prior to and including day of drug initiation in any diagnosis/procedure position and the care setting indicated below MI (Inpatient/Outpatient) ICD-9 diagnosis 410.xx Unstable angina (Inpatient/Outpatient) ICD-9 diagnosis 411.xx Coronary revascularization: PTCA (Inpatient) CPT-4: 92970, 92982, 92984, 92995, 92996, 92920 –92921, 92924 –92925, 92927, 92928, 92941, 92943, 92944 – OR – (Inpatient/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/Outpatient) ICD-9 procedure: 36.06, 36.07 CABG (Inpatient) CPT-4: 33510 – 33536, 33545, 33572 – OR – (Inpatient) ICD-9 procedure: 36.1x, 36.2x Transmyocardial revascularization: (Inpatient) CPT-4: 33140, 33141 – OR – (Inpatient/Outpatient) ICD-9 procedure: 36.31-36.34 Stroke (Inpatient) ICD-9 diagnosis 430.xx, 431.xx, 433.x1, 434.x1, 436.x TIA (Inpatient/Outpatient) ICD-9 diagnosis 435.x Heart failure (Inpatient) ICD-9 diagnosis 428.x, 398.91, 402.01, 402.11, 402.91, 404.01, 404.11, 404.91, 404.03, 404.13, 404.93	Patorno, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gli flozin antidiabetic drugs: population based cohort study." BMJ 2018;360:k119 https://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
3	3. Systolic BP >180 or diastolic BP >100 mmHg at randomization		
4	4. Diagnosis of Type 1 diabetes mellitus, Maturity onset diabetes of the young (MODY), or secondary diabetes mellitus	Measured 180 days prior to and including day of drug initiation in any diagnosis position and the inpatient or outpatient care setting Old type 1 ICD-9 diagnosis: 250.x1, 250.x3 Secondary diabetes ICD-9 procedure: 249.xx	Patorno, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gli flozin antidiabetic drugs: population based cohort study." BMJ 2018;360:k119 https://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
5	5. History of bladder cancer or history of radiation therapy to the lower abdomen or pelvis at any time	Measured from that start all available data prior to drug initiation in any diagnosis position and the inpatient or outpatient care setting Bladder cancer (malignant and situ) ICD-9 diagnosis: 233.7x	Patorno, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gli flozin antidiabetic drugs: population based cohort study." BMJ 2018;360:k119 https://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
6	6. History of any other malignancy within 5 years (with the exception of successfully treated non-melanoma skin cancers)	Measured 1825 days prior to drug initiation in any diagnosis position and the inpatient or outpatient care setting History of malignant neoplasm ICD-9 diagnosis: 140.xx-208.xx (except 173.xx, non-melanoma skin cancer)	
7	7. Chronic cystitis and/or recurrent urinary tract infections (3 or more in the last year)	Measured 365 days prior to and including the day of drug initiation in any diagnosis position and the inpatient or outpatient care setting Pyelonephritis or urinary tract infection (UTI) ICD-9 diagnosis: 590.x, 599.0	
8	8. Any conditions that, in the opinion of the investigator, may render the patient unable to complete the study including but not limited to cardiovascular (NYHA class IV CHF, recurrent ventricular arrhythmias) or non-cardiovascular disease (e.g., active malignancy with the exception of basal cell carcinoma, cirrhosis, chronic lung disease, severe autoimmune disease) and/or a likely fatal outcome within 5 years	Measured 180 days prior to and including the day of drug initiation - CCI >= 10	Gagne, Joshi 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.
9	9. Pregnant or breast-feeding patients	Measured 180 days prior to and including day of drug initiation in any diagnosis position and inpatient or outpatient care setting Pregnancy - see "Pregnancy" for ICD-9 diagnosis and procedure codes.	Iruretagoyena, Alexis A, et. al. "Study protocol for the dabigatran, apixaban, rivaroxaban, edoxaban, warfarin comparative effectiveness research study." J. Comp. Eff. Res. (2018) 7(1), 57-66. doi: 10.2217/cer-2017-0053.

Appendix A

10	10. Involvement in the planning and/or conduct of the study or other dapagliflozin studies (applies to AZ, BMS, Hadassah and Thrombolysis in Myocardial Infarction [TIMI] or representative staff and/or staff at the study site)	N/A	
11	11. Previous randomization in the present study		
12	12. Active participation in another clinical study with IP and/or investigational device		
13	13. Individuals at risk for poor protocol or medication compliance during run-in period (reasonable compliance defined as 80–120%, unless a reason for non-compliance is judged acceptable by the investigator). If for any reason, the investigator believes that the patient will not tolerate or be compliant with IP or study procedures, the patient should not be randomized and considered a run-in failure.	N/A	
	Patients will be excluded during run-in and should not be randomized if the following are observed from laboratory or observation during enrollment and run-in assessments:		
14	14. HbA1c ≥12% or HbA1c<6.5%	N/A	
15	15. AST or ALT >3x ULN or Total bilirubin >2.5 x ULN	Measured 180 days prior to and including day of 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: 50.1x, 42.91	Patorno, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gliflozin antidiabetic drugs: population based cohort study." BMJ 2018;360:k119 https://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	16. CrCl < 60 ml/min (based on the Cockroft-Gault equation)	Measured 180 days prior to and including day of drug initiation in any diagnosis position and inpatient or outpatient care setting CKD stage 3+ ICD-9 diagnosis: 585.3, 585.4, 585.5, 585.6	
17	17. Hematuria (confirmed by microscopy at Visit 1) with no explanation as judged by the investigator up to randomization. If bladder cancer is identified, patients are not eligible to participate.	Measured 180 days prior to and including day of drug initiation in any diagnosis position and inpatient or outpatient care setting Hematuria ICD-9 diagnosis: 599.7x	
18	18. Any reason the investigator believes the patient is not likely to be compliant with the study medication and protocol.	Measured 180 days prior to and including day of drug initiation in any diagnosis position and inpatient or outpatient care setting Non-compliance ICD-9 diagnosis: V15.81, V65.12	

Appendix A

Trial ID	sNDA21
Trial Name (with web links)	DECLARE–TIMI 58
Trial Name (with pdf links)	
NCT	NCT01730534
Trial category	Secondary indication
Run-in period Description	
Run-in period?	
Therapeutic Area	Endocrinology
Study batch	Diabetes medications
RCT Category	4a- Unintended S with label change
Brand Name	Farxiga
Generic Name	Dapagliflozin
Sponsor	
Year	2019
Measurable endpoint	• Cardiovascular death (CVD) or hospitalization for heart failure (HHF) • Major Adverse Cardiovascular Events, Including CV Death, Nonfatal Myocardial Infarction (MI), and Nonfatal Stroke
Exposure	Dapagliflozin
Comparator	Placebo
Population	Patients with type 2 diabetes who had or were at risk for atherosclerotic cardiovascular disease
Trial finding	HR, 0.83 (0.73 to 0.95) for Cardiovascular death or hospitalization for heart failure comparing dapagliflozin to placebo
Notes	
No. of Patients	17160
Non-inferiority margin	HR = 1.30
Assay Sens. Outcome	
Assay Sens. Endpoint (from trial)	
Power	A total of 1,390 subjects with MACE events will be required to have 85% power to demonstrate superiority of dapagliflozin to placebo if the true HR is 0.85. The trial was not formally powered for the second of the co-primary end points, CVD or HHF. However, we anticipate 87% power to detect an HR of 0.80 with a 1-sided α of .0231.
Blinding	Double-blinded
Statistical Method	
Approval indication	

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

Antidiabetic class	Specific agent	Notes
SGLT2-inhibitors	Canagliflozin	Approved 3/29/2013
	Dapagliflozin	
	Empagliflozin	
	Ertugliflozin	Approved Dec 21, 2017
2nd 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 *(search with NPH, don't want bf-pk)*	
	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	
1st generation sulfonylureas	Acetohexamide	
	Chlorpropamide	
	Tolazamide	
	Tolbutamide	

Appendix A

Statins and Other Lipid Lowering Medications
AMLODIPINE BESYLATE/ATORVASTATIN CALCIUM
ARGININE/NIACIN/YOHIMBE BARK/GINSENG/GNK/DAMIANA/SCHISANDRA
ATORVASTATIN CALCIUM
CERAMIDES 1,3,6-11/NIACINAMIDE
CERAMIDES 1,3,6-11/NIACINAMIDE/HYALURONIC ACID
CHOLESTYRAMINE
CHOLESTYRAMINE (WITH SUGAR)
CHOLESTYRAMINE/ASPARTAME
COLESEVELAM HCL
COLESTIPOL HCL
EZETIMIBE
EZETIMIBE/ATORVASTATIN CALCIUM
EZETIMIBE/SIMVASTATIN
FENOFIBRATE
FENOFIBRATE NANOCRYSTALLIZED
FENOFIBRATE,MICRONIZED
FLUVASTATIN SODIUM
FOLIC ACID/NIACINAMIDE/CUPRIC OXIDE/ZINC OXIDE
FOLIC ACID/NIACINAMIDE/ZINC
GEMFIBROZIL
INOSITOL NIACINATE
IRON PYROPHOSPHATE/CYANOCOBALAMIN/FA/NIACIN/PYRIDOXINE HCL
LECITHIN/SITOSTEROLS/NIACIN/BETAINE/CHITOSAN
LOVASTATIN
LYSINE HCL/NIACINAMIDE/THIAMINE
MELATONIN/TRYPTOPHAN/VALERIAN/CHAMOMILE/NIACIN/INOSITOL/B6
NIACIN
NIACIN (INOSITOL NIACINATE)
NIACIN/CAPSAICIN/YOHIMBE BARK/GINSENG/GNK BI EX/DAMIANA/OATS
NIACIN/LOVASTATIN
NIACIN/SIMVASTATIN
NIACINAMIDE

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NIACINAMIDE ASCORBATE
NIACINAMIDE/AZELAIC ACID/ZINC OXIDE/VIT B6/COPPER/FA
PECTIN/INOSITOL/BIOFLAVONOIDS/NIACIN/SOYBEAN
PITAVASTATIN CALCIUM
POLICOSANOL/INOSITOL NIACINATE/GARLIC
PRAVASTATIN SODIUM
ROSUVASTATIN CALCIUM
SIMVASTATIN
SITAGLIPTIN PHOSPHATE/SIMVASTATIN
THIAMINE HCL/RIBOFLAVIN/NIACINAMIDE/CYANOCOBALAMIN/PROTEASE
THIAMINE HCL/RIBOFLAVIN/NIACINAMIDE/DEXPANTHENOL/PYRIDOXINE
THIAMINE M.NIT/RIBOFLAVIN/NIACIN/CA PANTOTHENATE/B6/B12/C/FA
THIAMINE/RIBOFLAVIN/NIACIN/CA PANTOTHENATE/B6/B12/VIT C/FA
THIAMINE/RIBOFLAVIN/NIACIN/CA PANTOTHENATE/VIT B6/B12/IRON
THIAMINE/RIBOFLAVIN/NIACIN/PANT ACID/B6/IRON/METHION/CHOLINE
VITAMIN B COMPLEX/NIACINAMIDE/PANTOTHENIC ACID/HERBAL DRUGS

Appendix A

Antihypertensive Medications
ACEBUTOLOL HCL
ALISKIREN HEMIFUMARATE/AMLODIPINE BESYLATE
ALISKIREN HEMIFUMARATE/AMLODIPINE/HYDROCHLOROTHIAZIDE
AMLODIPINE BESYLATE
AMLODIPINE BESYLATE/ATORVASTATIN CALCIUM
AMLODIPINE BESYLATE/BENAZEPRIL HCL
AMLODIPINE BESYLATE/OLMESARTAN MEDOXOMIL
AMLODIPINE BESYLATE/VALSARTAN
AMLODIPINE BESYLATE/VALSARTAN/HYDROCHLOROTHIAZIDE
APRACLONIDINE HCL
ATENOLOL
ATENOLOL/CHLORTHALIDONE
AZILSARTAN MEDOXOMIL
AZILSARTAN MEDOXOMIL/CHLORTHALIDONE
BENAZEPRIL HCL
BENAZEPRIL HCL/HYDROCHLOROTHIAZIDE
BENDROFLUMETHIAZIDE
BEPRIDIL HCL
BETAXOLOL HCL
BISOPROLOL FUMARATE
BISOPROLOL FUMARATE/HYDROCHLOROTHIAZIDE
BRIMONIDINE TARTRATE/TIMOLOL MALEATE
BUMETANIDE
CANDESARTAN CILEXETIL
CANDESARTAN CILEXETIL/HYDROCHLOROTHIAZIDE
CAPTOPRIL
CAPTOPRIL/HYDROCHLOROTHIAZIDE
CARTEOLOL HCL
CARVEDILOL
CARVEDILOL PHOSPHATE
CHLOROTHIAZIDE
CHLORTHALIDONE

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CLEVIDIPINE BUTYRATE
CLONIDINE
CLONIDINE HCL
CLONIDINE HCL/CHLORTHALIDONE
CLONIDINE HCL/PF
DILTIAZEM HCL
DILTIAZEM HCL IN 0.9 % SODIUM CHLORIDE
DILTIAZEM HCL/DEXTROSE 5 % IN WATER
DILTIAZEM MALATE
DORZOLAMIDE HCL/TIMOLOL MALEATE
DORZOLAMIDE HCL/TIMOLOL MALEATE/PF
DOXAZOSIN MESYLATE
ENALAPRIL MALEATE
ENALAPRIL MALEATE/DILTIAZEM MALATE
ENALAPRIL MALEATE/FELODIPINE
ENALAPRIL MALEATE/HYDROCHLOROTHIAZIDE
ENALAPRILAT DIHYDRATE
EPLERENONE
EPROSARTAN MESYLATE
EPROSARTAN MESYLATE/HYDROCHLOROTHIAZIDE
ESMOLOL HCL
ETHACRYNIC ACID
FELODIPINE
FOSINOPRIL SODIUM
FOSINOPRIL SODIUM/HYDROCHLOROTHIAZIDE
FUROSEMIDE
GUANABENZ ACETATE
GUANADREL SULFATE
GUANETHIDINE SULFATE
GUANFACINE HCL
HYDRALAZINE HCL
HYDRALAZINE HCL/HYDROCHLOROTHIAZIDE
HYDRALAZINE HCL/RESERPINE/HYDROCHLOROTHIAZIDE

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HYDROCHLOROTHIAZIDE
HYDROFLUMETHIAZIDE
INDAPAMIDE
IRBESARTAN
IRBESARTAN/HYDROCHLOROTHIAZIDE
ISOSORBIDE DINITRATE
ISOSORBIDE DINITRATE/HYDRALAZINE HCL
ISOSORBIDE MONONITRATE
ISRADIPINE
LABETALOL HCL
LISINOPRIL
LISINOPRIL/DIETARY SUPPLEMENT,COMB.10
LISINOPRIL/HYDROCHLOROTHIAZIDE
LOSARTAN POTASSIUM
LOSARTAN POTASSIUM/HYDROCHLOROTHIAZIDE
METHYCLOTHIAZIDE
METHYLDOPA
METHYLDOPA/CHLOROTHIAZIDE
METHYLDOPA/HYDROCHLOROTHIAZIDE
METHYLDOPATE HCL
METOLAZONE
METOPROLOL SUCCINATE
METOPROLOL SUCCINATE/HYDROCHLOROTHIAZIDE
METOPROLOL TARTRATE
METOPROLOL TARTRATE/HYDROCHLOROTHIAZIDE
METYROSINE
MIBEFRADIL DI-HCL
MINOXIDIL
MOEXIPRIL HCL
MOEXIPRIL HCL/HYDROCHLOROTHIAZIDE
NEBIVOLOL HCL
NICARDIPINE HCL
NIFEDIPINE

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NIMODIPINE
NISOLDIPINE
NITROGLYCERIN
OLMESARTAN MEDOXOMIL
OLMESARTAN MEDOXOMIL/AMLODIPINE BESYLATE/HYDROCHLOROTHIAZIDE
OLMESARTAN MEDOXOMIL/HYDROCHLOROTHIAZIDE
PERINDOPRIL ARGININE/AMLODIPINE BESYLATE
PERINDOPRIL ERBUMINE
POLYTHIAZIDE
PRAZOSIN HCL
PRAZOSIN HCL/POLYTHIAZIDE
QUINAPRIL HCL
QUINAPRIL HCL/HYDROCHLOROTHIAZIDE
RAMIPRIL
RANOLAZINE
RESERPINE
RESERPINE/CHLOROTHIAZIDE
RESERPINE/HYDROCHLOROTHIAZIDE
RESERPINE/HYDROFLUMETHIAZIDE
RESERPINE/METHYCLOTHIAZIDE
RESERPINE/POLYTHIAZIDE
SOTALOL HCL
SPIRONOLACTONE
TELMISARTAN
TELMISARTAN/AMLODIPINE BESYLATE
TELMISARTAN/HYDROCHLOROTHIAZIDE
TERAZOSIN HCL
TIMOLOL
TIMOLOL MALEATE
TIMOLOL MALEATE/HYDROCHLOROTHIAZIDE
TIMOLOL MALEATE/PF
TORSEMIDE
TRANDOLAPRIL

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TRANDOLAPRIL/VERAPAMIL HCL
TRIAMTERENE
TRICHLORMETHIAZIDE
VALSARTAN
VALSARTAN/HYDROCHLOROTHIAZIDE
VERAPAMIL HCL

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

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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 B

Optum	MarketScan	Medicare
BEFORE PS MATCHING		
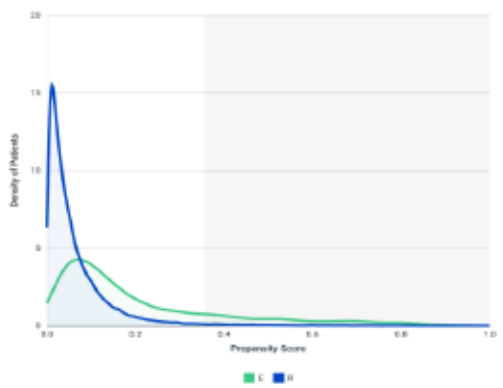	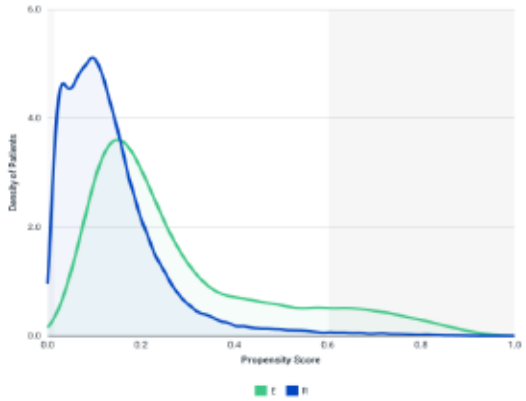	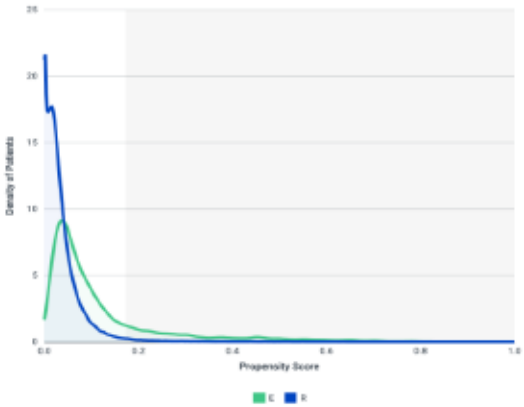
Figure 49: Pre-matching propensity score overlap	Figure 49: Pre-matching propensity score overlap	Figure 24: Pre-matching propensity score overlap
The c-statistics for the propensity score model, pre-matching was 0.802. The post-matching c-statistic was 0.555.	**The c-statistics for the propensity score model, pre-matching was 0.757. The post-matching c-statistic was 0.528.**	**The c-statistics for the propensity score model, pre-matching was 0.792. The post-matching c-statistic was 0.536.**
AFTER PS MATCHING		
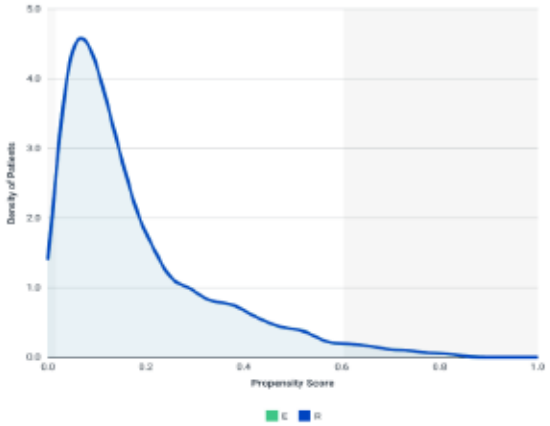	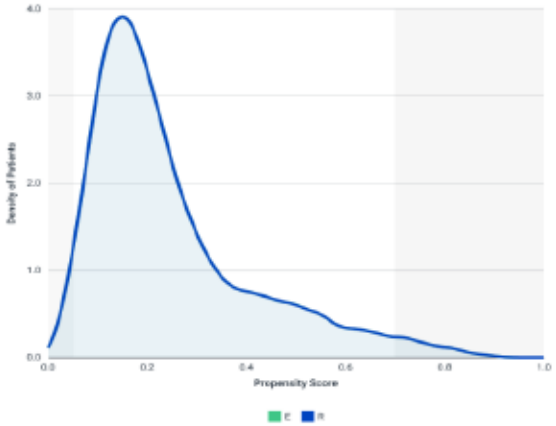	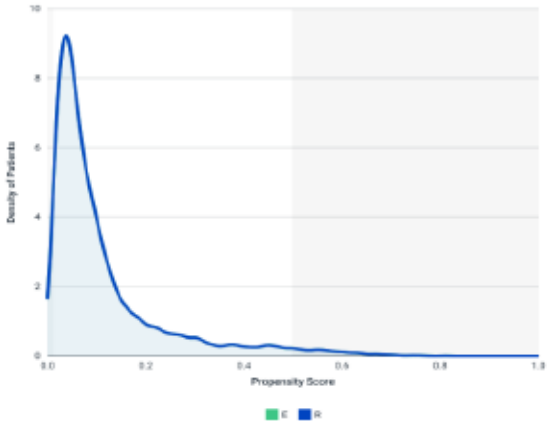
Figure 50: Post-matching propensity score overlap	Figure 50: Post-matching propensity score overlap	Figure 25: Post-matching propensity score overlap

Table 1

	Unmatched								
	Optum		MarketScan		Medicare		POOLED		
Variable	Reference- DPP4i v2	Exposure - Dapagliflozin v2	Reference- DPP4i v2	Exposure - Dapagliflozin v2	Reference- DPP4i v2	Exposure - Dapagliflozin v2	Reference- DPP4i v2	Exposure - Dapagliflozin v2	St. Diff.
Number of patients	43,710	3,481	70,087	13,292	220,061	9,217	333,858	25,990	
Age									
...mean (sd)	64.48 (9.80)	58.44 (6.69)	61.12 (8.57)	57.95 (5.83)	73.25 (6.69)	70.29 (4.93)	69.56 (7.58)	62.39 (5.66)	1.07
...median [IQR]	63.00 [57.00, 71.00]	58.00 [54.00, 62.00]	60.00 [56.00, 64.00]	58.00 [55.00, 61.00]	72.00 [68.00, 77.00]	9.00 [67.00, 73.00]	68.30 (7.58)	61.90 (5.66)	0.96
Age categories without zero category									
...18 - 34; n (%)	6,388 (14.6%)	907 (26.1%)	12,884 (18.4%)	3,220 (24.2%)	0 (0.0%)	0 (0.0%)	19,272 (5.8%)	4,127 (15.9%)	-0.33
...35 - 64; n (%)	17,548 (40.1%)	2,099 (60.3%)	41,083 (58.6%)	9,162 (68.9%)	2,206 (1.0%)	79 (0.9%)	60,837 (18.2%)	11,340 (43.6%)	-0.57
...65 - 74; n (%)	12,125 (27.7%)	390 (11.2%)	9,946 (14.2%)	754 (5.7%)	138,975 (63.2%)	7,545 (81.9%)	161,046 (48.2%)	8,689 (33.4%)	0.30
...>=75; n (%)	7,649 (17.5%)	85 (2.4%)	6,174 (8.8%)	156 (1.2%)	78,880 (35.8%)	1,593 (17.3%)	92,703 (27.8%)	1,834 (7.1%)	0.57
Gender without zero category- United									
...Males; n (%)	25,356 (58.0%)	2,199 (63.2%)	41,300 (58.9%)	8,073 (60.7%)	102,718 (46.7%)	4,790 (52.0%)	169,374 (50.7%)	15,062 (58.0%)	-0.15
...Females; n (%)	18,354 (42.0%)	1,282 (36.8%)	28,787 (41.1%)	5,219 (39.3%)	117,343 (53.3%)	4,427 (48.0%)	164,484 (49.3%)	10,928 (42.0%)	0.15
Race									
...White; n (%)	N/A	N/A	N/A	N/A	165,288 (75.1%)	7,433 (80.6%)	165,288 (75.1%)	7,433 (80.6%)	-0.13
...Black; n (%)	N/A	N/A	N/A	N/A	24,910 (11.3%)	760 (8.2%)	24,910 (11.3%)	760 (8.2%)	0.10
...Asian; n (%)	N/A	N/A	N/A	N/A	9,877 (4.5%)	303 (3.3%)	9,877 (4.5%)	303 (3.3%)	0.06
...Hispanic; n (%)	N/A	N/A	N/A	N/A	9,330 (4.2%)	298 (3.2%)	9,330 (4.2%)	298 (3.2%)	0.05
...North American Native; n (%)	N/A	N/A	N/A	N/A	1,273 (0.6%)	25 (0.3%)	1,273 (0.6%)	25 (0.3%)	0.04
...Other/Unknown; n (%)	N/A	N/A	N/A	N/A	9,383 (4.3%)	398 (4.3%)	9,383 (4.3%)	398 (4.3%)	0.00
Region without zero category- United v3 (lumping missing&other category with West)									
...Northeast; n (%)	5,438 (12.4%)	223 (6.4%)	14,081 (20.1%)	1,756 (13.2%)	43,499 (19.8%)	1,537 (16.7%)	63,018 (18.9%)	3,516 (13.5%)	0.15
...South; n (%)	21,918 (50.1%)	1,967 (56.5%)	16,006 (22.8%)	2,196 (16.5%)	93,209 (42.4%)	4,286 (46.5%)	131,133 (39.3%)	8,449 (32.5%)	0.14
...Midwest; n (%)	8,880 (20.3%)	846 (24.3%)	33,051 (47.2%)	8,242 (62.0%)	47,609 (21.6%)	1,828 (19.8%)	89,540 (26.8%)	10,916 (42.0%)	-0.32
...West; n (%)	7,474 (17.1%)	445 (12.8%)	6,248 (8.9%)	1,033 (7.8%)	35,744 (16.2%)	1,566 (17.0%)	49,466 (14.8%)	3,044 (11.7%)	0.09
...Unknown+missing; n (%)	N/A	N/A	701 (1.0%)	65 (0.5%)	N/A	N/A	701 (1.0%)	65 (0.5%)	0.06
CV Covariates									
Ischemic heart disease; n (%)	12,863 (29.4%)	666 (19.1%)	13,724 (19.6%)	2,236 (16.8%)	52,757 (24.0%)	2,042 (22.2%)	79,344 (23.8%)	4,944 (19.0%)	0.12
Acute MI; n (%)	594 (1.4%)	33 (0.9%)	437 (0.6%)	73 (0.5%)	1,148 (0.5%)	45 (0.5%)	2,179 (0.7%)	151 (0.6%)	0.01
ACS/unstable angina; n (%)	773 (1.8%)	39 (1.1%)	590 (0.8%)	104 (0.8%)	1,486 (0.7%)	52 (0.6%)	2,849 (0.9%)	195 (0.8%)	0.01
Old MI; n (%)	1,758 (4.0%)	80 (2.3%)	1,031 (1.5%)	149 (1.1%)	5,358 (2.4%)	190 (2.1%)	8,147 (2.4%)	419 (1.6%)	0.06
Stable angina; n (%)	2,754 (6.3%)	112 (3.2%)	1,780 (2.5%)	340 (2.6%)	6,214 (2.8%)	286 (3.1%)	10,748 (3.2%)	738 (2.8%)	0.02
Coronary atherosclerosis and other forms of chronic ischer	11,791 (27.0%)	621 (17.8%)	12,885 (18.4%)	2,047 (15.4%)	50,482 (22.9%)	1,958 (21.2%)	75,158 (22.5%)	4,626 (17.8%)	0.12
Other atherosclerosis with ICD10 v2 Copy; n (%)	368 (0.8%)	22 (0.6%)	488 (0.7%)	55 (0.4%)	2,671 (1.2%)	80 (0.9%)	3,527 (1.1%)	157 (0.6%)	0.05
Previous cardiac procedure (CABG or PTCA or Stent) v4; n (%	300 (0.7%)	23 (0.7%)	263 (0.4%)	42 (0.3%)	530 (0.2%)	17 (0.2%)	1,093 (0.3%)	82 (0.3%)	0.00
History of CABG or PTCA; n (%)	3,143 (7.2%)	147 (4.2%)	1,788 (2.6%)	284 (2.1%)	12,768 (5.8%)	493 (5.3%)	17,699 (5.3%)	924 (3.6%)	0.08
Any stroke; n (%)	3,268 (7.5%)	119 (3.4%)	3,412 (4.9%)	441 (3.3%)	15,616 (7.1%)	545 (5.9%)	22,296 (6.7%)	1,105 (4.3%)	0.11
Ischemic stroke (w and w/o mention of cerebral infarction)	3,222 (7.4%)	115 (3.3%)	3,384 (4.8%)	441 (3.3%)	15,455 (7.0%)	544 (5.9%)	22,061 (6.6%)	1,100 (4.2%)	0.11
Hemorrhagic stroke; n (%)	111 (0.3%)	4 (0.1%)	66 (0.1%)	3 (0.0%)	**	**	**	**	**
TIA; n (%)	577 (1.3%)	19 (0.5%)	420 (0.6%)	70 (0.5%)	1,800 (0.8%)	76 (0.8%)	2,797 (0.8%)	165 (0.6%)	0.02
Other cerebrovascular disease; n (%)	797 (1.8%)	22 (0.6%)	688 (1.0%)	82 (0.6%)	3,866 (1.8%)	113 (1.2%)	5,351 (1.6%)	217 (0.8%)	0.07
Late effects of cerebrovascular disease; n (%)	825 (1.9%)	14 (0.4%)	481 (0.7%)	52 (0.4%)	3,254 (1.5%)	79 (0.9%)	4,560 (1.4%)	145 (0.6%)	0.08
Cerebrovascular procedure; n (%)	73 (0.2%)	4 (0.1%)	53 (0.1%)	5 (0.0%)	**	**	**	**	**
Heart failure (CHF); n (%)	3,344 (7.7%)	147 (4.2%)	2,486 (3.5%)	300 (2.3%)	15,991 (7.3%)	511 (5.5%)	21,821 (6.5%)	958 (3.7%)	0.13
Peripheral Vascular Disease (PVD) or PVD Surgery v2; n (%)	3,644 (8.3%)	128 (3.7%)	2,871 (4.1%)	407 (3.1%)	19,371 (8.8%)	645 (7.0%)	25,886 (7.8%)	1,180 (4.5%)	0.14
Atrial fibrillation; n (%)	3,088 (7.1%)	121 (3.5%)	3,280 (4.7%)	384 (2.9%)	20,557 (9.3%)	684 (7.4%)	26,925 (8.1%)	1,189 (4.6%)	0.14
Other cardiac dysrhythmia; n (%)	4,016 (9.2%)	184 (5.3%)	4,007 (5.7%)	509 (3.8%)	22,999 (10.5%)	846 (9.2%)	31,022 (9.3%)	1,539 (5.9%)	0.13
Cardiac conduction disorders; n (%)	1,154 (2.6%)	55 (1.6%)	1,065 (1.5%)	152 (1.1%)	6,393 (3.0%)	234 (2.5%)	8,812 (2.6%)	441 (1.7%)	0.06
Other CVD; n (%)	4,947 (11.3%)	232 (6.7%)	5,164 (7.4%)	668 (5.0%)	26,017 (11.8%)	932 (10.1%)	36,128 (10.8%)	1,832 (7.0%)	0.13
Diabetes-related complications									
Diabetic retinopathy; n (%)	2,281 (5.2%)	152 (4.4%)	2,156 (3.1%)	410 (3.1%)	13,152 (6.0%)	623 (6.8%)	17,589 (5.3%)	1,185 (4.6%)	0.03
Diabetes with other ophthalmic manifestations; n (%)	270 (0.6%)	3 (0.1%)	1,356 (1.9%)	223 (1.7%)	5,038 (2.3%)	194 (2.1%)	6,664 (2.0%)	420 (1.6%)	0.03
Retinal detachment, vitreous hemorrhage, vitrectomy; n (%	140 (0.3%)	10 (0.3%)	179 (0.3%)	33 (0.2%)	703 (0.3%)	31 (0.3%)	1,022 (0.3%)	74 (0.3%)	0.00
Retinal laser coagulation therapy; n (%)	189 (0.4%)	8 (0.2%)	305 (0.4%)	58 (0.4%)	1,041 (0.5%)	60 (0.7%)	1,535 (0.5%)	126 (0.5%)	0.00
Occurrence of Diabetic Neuropathy v2 Copy; n (%)	7,714 (17.6%)	506 (14.5%)	7,231 (10.3%)	1,572 (11.8%)	37,142 (16.9%)	1,753 (19.0%)	52,087 (15.6%)	3,831 (14.7%)	0.03

Table 1

Occurrence of diabetic nephropathy V3 with ICD10 Copy; r	3,743 (8.6%)	180 (5.2%)	2,838 (4.0%)	525 (3.9%)	12,264 (5.6%)	503 (5.5%)	18,845 (5.6%)	1,208 (4.6%)	0.05
Hypoglycemia v2; n (%)	983 (2.2%)	76 (2.2%)	1,292 (1.8%)	215 (1.6%)	4,479 (2.0%)	116 (1.3%)	6,754 (2.0%)	407 (1.6%)	0.03
Hyperglycemia; n (%)	1,941 (4.4%)	109 (3.1%)	2,407 (3.4%)	462 (3.5%)	8,655 (3.9%)	346 (3.8%)	13,003 (3.9%)	917 (3.5%)	0.02
Disorders of fluid electrolyte and acid-base balance; n (%)	2,385 (5.5%)	99 (2.8%)	2,318 (3.3%)	351 (2.6%)	11,157 (5.1%)	289 (3.1%)	15,860 (4.8%)	739 (2.8%)	0.10
Diabetic ketoacidosis; n (%)	75 (0.2%)	7 (0.2%)	112 (0.2%)	12 (0.1%)	388 (0.2%)	10 (0.1%)	575 (0.2%)	29 (0.1%)	0.03
Hyperosmolar hyperglycemic nonketotic syndrome (HONK	218 (0.5%)	10 (0.3%)	287 (0.4%)	49 (0.4%)	906 (0.4%)	50 (0.5%)	1,411 (0.4%)	109 (0.4%)	0.00
Diabetes with peripheral circulatory disorders with ICD-10	3,048 (7.0%)	122 (3.5%)	2,146 (3.1%)	302 (2.3%)	13,823 (6.3%)	524 (5.7%)	19,017 (5.7%)	948 (3.6%)	0.10
Diabetic Foot; n (%)	998 (2.3%)	69 (2.0%)	1,020 (1.5%)	196 (1.5%)	4,442 (2.0%)	169 (1.8%)	6,460 (1.9%)	434 (1.7%)	0.02
Gangrene v2; n (%)	143 (0.3%)	6 (0.2%)	127 (0.2%)	19 (0.1%)	**	**	**	**	**
Lower extremity amputation; n (%)	413 (0.9%)	22 (0.6%)	223 (0.3%)	43 (0.3%)	922 (0.4%)	29 (0.3%)	1,558 (0.5%)	094 (0.4%)	0.01
Osteomyelitis; n (%)	326 (0.7%)	21 (0.6%)	270 (0.4%)	56 (0.4%)	862 (0.4%)	28 (0.3%)	1,458 (0.4%)	105 (0.4%)	0.00
Skin infections v2; n (%)	2,389 (5.5%)	200 (5.7%)	3,272 (4.7%)	654 (4.9%)	12,212 (5.5%)	521 (5.7%)	17,873 (5.4%)	1,375 (5.3%)	0.00
Erectile dysfunction; n (%)	1,344 (3.1%)	148 (4.3%)	1,904 (2.7%)	416 (3.1%)	4,876 (2.2%)	268 (2.9%)	8,124 (2.4%)	832 (3.2%)	-0.05
Diabetes with unspecified complication; n (%)	2,256 (5.2%)	139 (4.0%)	3,047 (4.3%)	724 (5.4%)	9,808 (4.5%)	520 (5.6%)	15,111 (4.5%)	1,383 (5.3%)	-0.04
Diabetes mellitus without mention of complications; n (%)	38,070 (87.1%)	3,082 (88.5%)	63,750 (91.0%)	11,623 (87.4%)	203,187 (92.3%)	8,184 (88.8%)	305,007 (91.4%)	22,889 (88.1%)	0.11
Hypertension: 1 inpatient or 2 outpatient claims within 36	35,414 (81.0%)	2,709 (77.8%)	50,237 (71.7%)	9,739 (73.3%)	191,800 (87.2%)	7,981 (86.6%)	277,451 (83.1%)	20,429 (78.6%)	0.11
Hyperlipidemia v2; n (%)	31,957 (73.1%)	2,632 (75.6%)	47,756 (68.1%)	9,565 (72.0%)	167,881 (76.3%)	7,097 (77.0%)	247,594 (74.2%)	19,294 (74.2%)	0.00
Edema; n (%)	2,298 (5.3%)	153 (4.4%)	2,224 (3.2%)	370 (2.8%)	14,695 (6.7%)	559 (6.1%)	19,217 (5.8%)	1,082 (4.2%)	0.07
Renal Dysfunction (non-diabetic) v2; n (%)	4,552 (10.4%)	148 (4.3%)	3,654 (5.2%)	420 (3.2%)	21,679 (9.9%)	525 (5.7%)	29,885 (9.0%)	1,093 (4.2%)	0.19
Occurrence of acute renal disease v2; n (%)	817 (1.9%)	15 (0.4%)	736 (1.1%)	53 (0.4%)	3,193 (1.5%)	51 (0.6%)	4,746 (1.4%)	119 (0.5%)	0.09
Occurrence of chronic renal insufficiency; n (%)	2,889 (6.6%)	96 (2.8%)	1,885 (2.7%)	225 (1.7%)	14,526 (6.6%)	330 (3.6%)	19,300 (5.8%)	651 (2.5%)	0.17
Chronic kidney disease v2; n (%)	2,594 (5.9%)	79 (2.3%)	1,599 (2.3%)	184 (1.4%)	12,582 (5.7%)	285 (3.1%)	16,775 (5.0%)	548 (2.1%)	0.16
CKD Stage 3-4; n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	#VALUE!	000 (0.0%)	#VALUE!
Occurrence of hypertensive nephropathy; n (%)	1,135 (2.6%)	41 (1.2%)	811 (1.2%)	103 (0.8%)	4,671 (2.1%)	137 (1.5%)	6,617 (2.0%)	281 (1.1%)	0.07
Occurrence of miscellaneous renal insufficiency v2; n (%)	1,450 (3.3%)	55 (1.6%)	1,386 (2.0%)	149 (1.1%)	8,794 (4.0%)	238 (2.6%)	11,630 (3.5%)	442 (1.7%)	0.11
Glaucoma or cataracts v2; n (%)	7,468 (17.1%)	424 (12.2%)	9,759 (13.9%)	1,525 (11.5%)	57,293 (26.0%)	2,348 (25.5%)	74,520 (22.3%)	4,297 (16.5%)	0.15
Cellulitis or abscess of toe; n (%)	574 (1.3%)	32 (0.9%)	616 (0.9%)	128 (1.0%)	2,388 (1.1%)	119 (1.3%)	3,578 (1.1%)	279 (1.1%)	0.00
Foot ulcer; n (%)	961 (2.2%)	64 (1.8%)	1,012 (1.4%)	196 (1.5%)	4,383 (2.0%)	164 (1.8%)	6,356 (1.9%)	424 (1.6%)	0.02
Bladder stones; n (%)	32 (0.1%)	0 (0.0%)	34 (0.0%)	6 (0.0%)	**	**	**	**	**
Kidney stones; n (%)	652 (1.5%)	49 (1.4%)	971 (1.4%)	164 (1.2%)	3,229 (1.5%)	135 (1.5%)	4,852 (1.5%)	348 (1.3%)	0.02
Urinary tract infections (UTIs); n (%)	310 (0.7%)	6 (0.2%)	322 (0.5%)	59 (0.4%)	1,604 (0.7%)	63 (0.7%)	2,236 (0.7%)	128 (0.5%)	0.03
Dipstick urinalysis; n (%)	13,140 (30.1%)	896 (25.7%)	19,643 (28.0%)	3,866 (29.1%)	66,715 (30.3%)	2,706 (29.4%)	99,498 (29.8%)	7,468 (28.7%)	0.02
Non-dipstick urinalysis; n (%)	17,924 (41.0%)	1,446 (41.5%)	24,807 (35.4%)	5,524 (41.6%)	88,718 (40.3%)	3,834 (41.6%)	131,449 (39.4%)	10,804 (41.6%)	-0.04
Urine function test; n (%)	597 (1.4%)	27 (0.8%)	986 (1.4%)	118 (0.9%)	4,593 (2.1%)	171 (1.9%)	6,176 (1.8%)	316 (1.2%)	0.05
Cytology; n (%)	149 (0.3%)	6 (0.2%)	185 (0.3%)	21 (0.2%)	627 (0.3%)	30 (0.3%)	#VALUE!	57 (0.2%)	#VALUE!
Cystoscopy; n (%)	148 (0.3%)	10 (0.3%)	281 (0.4%)	38 (0.3%)	883 (0.4%)	34 (0.4%)	1,312 (0.4%)	082 (0.3%)	0.02
Other Covariates									
Liver disease; n (%)	1,363 (3.1%)	75 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1,363 (0.4%)	075 (0.3%)	0.02
Osteoarthritis; n (%)	6,248 (14.3%)	369 (10.6%)	7,350 (10.8%)	1,251 (9.4%)	44,989 (20.4%)	1,818 (19.7%)	58,787 (17.6%)	3,438 (13.2%)	0.12
Other arthritis, arthropathies and musculoskeletal pain; n (	15,128 (34.6%)	1,076 (30.9%)	20,490 (29.2%)	3,770 (28.4%)	87,318 (39.7%)	3,527 (38.3%)	122,936 (36.8%)	8,373 (32.2%)	0.10
Dorsopathies; n (%)	9,446 (21.6%)	711 (20.4%)	12,419 (17.7%)	2,401 (18.1%)	52,738 (24.0%)	2,297 (24.9%)	74,603 (22.3%)	5,409 (20.8%)	0.04
Fractures; n (%)	1,033 (2.4%)	59 (1.7%)	1,335 (1.9%)	174 (1.3%)	6,400 (2.9%)	204 (2.2%)	8,768 (2.6%)	437 (1.7%)	0.06
Falls v2; n (%)	1,217 (2.8%)	42 (1.2%)	730 (1.0%)	65 (0.5%)	7,186 (3.3%)	202 (2.2%)	9,133 (2.7%)	309 (1.2%)	0.11
Osteoporosis; n (%)	1,611 (3.7%)	57 (1.6%)	1,263 (1.8%)	144 (1.1%)	15,314 (7.0%)	485 (5.3%)	18,388 (5.5%)	686 (2.6%)	0.15
Hyperthyroidism; n (%)	283 (0.6%)	20 (0.6%)	373 (0.5%)	73 (0.5%)	1,823 (0.8%)	71 (0.8%)	2,479 (0.7%)	164 (0.6%)	0.01
Hypothyroidism v2; n (%)	6,367 (14.6%)	492 (14.1%)	8,029 (11.5%)	1,618 (12.2%)	26,926 (12.2%)	966 (10.5%)	41,322 (12.4%)	3,076 (11.8%)	0.02
Other disorders of thyroid gland V2; n (%)	1,621 (3.7%)	146 (4.2%)	2,343 (3.3%)	512 (3.9%)	8,330 (3.9%)	426 (4.6%)	12,494 (3.7%)	1,084 (4.2%)	-0.03
Depression; n (%)	3,619 (8.3%)	251 (7.2%)	4,285 (6.1%)	852 (6.4%)	19,362 (8.8%)	702 (7.6%)	27,266 (8.2%)	1,805 (6.9%)	0.05
Anxiety; n (%)	3,526 (8.1%)	223 (6.4%)	3,861 (5.5%)	795 (6.0%)	16,485 (7.5%)	657 (7.1%)	23,872 (7.2%)	1,675 (6.4%)	0.03
Sleep_Disorder; n (%)	2,998 (6.9%)	348 (10.0%)	5,787 (8.3%)	1,097 (8.3%)	14,646 (6.7%)	530 (5.8%)	23,431 (7.0%)	1,975 (7.6%)	-0.02
Dementia; n (%)	1,413 (3.2%)	24 (0.7%)	1,007 (1.4%)	62 (0.5%)	11,942 (5.4%)	218 (2.4%)	14,362 (4.3%)	304 (1.2%)	0.19
Delirium; n (%)	381 (0.9%)	12 (0.3%)	317 (0.5%)	25 (0.2%)	2,125 (1.0%)	38 (0.4%)	2,823 (0.8%)	75 (0.3%)	0.07
Psychosis; n (%)	463 (1.1%)	12 (0.3%)	337 (0.5%)	37 (0.3%)	3,030 (1.4%)	62 (0.7%)	3,830 (1.1%)	111 (0.4%)	0.08
Obesity; n (%)	8,934 (20.4%)	909 (26.1%)	10,456 (14.9%)	2,628 (19.8%)	28,022 (12.7%)	1,534 (16.6%)	47,412 (14.2%)	5,071 (19.5%)	-0.14
Overweight; n (%)	2,478 (5.7%)	148 (4.3%)	1,974 (2.8%)	371 (2.8%)	8,173 (3.7%)	369 (4.0%)	12,625 (3.8%)	888 (3.4%)	0.02
Smoking; n (%)	5,327 (12.2%)	326 (9.4%)	4,014 (5.7%)	706 (5.3%)	23,022 (10.5%)	981 (10.6%)	32,363 (9.7%)	2,013 (7.7%)	0.07
Alcohol abuse or dependence; n (%)	393 (0.9%)	27 (0.8%)	340 (0.5%)	46 (0.3%)	1,034 (0.5%)	41 (0.4%)	1,767 (0.5%)	114 (0.4%)	0.01
Drug abuse or dependence; n (%)	631 (1.4%)	31 (0.9%)	415 (0.6%)	73 (0.5%)	1,673 (0.8%)	78 (0.8%)	2,719 (0.8%)	182 (0.7%)	0.01
COPD; n (%)	3,746 (8.6%)	138 (4.0%)	3,000 (4.3%)	386 (2.9%)	19,390 (8.9%)	752 (8.2%)	26,336 (7.9%)	1,276 (4.9%)	0.12

Table 1

Asthma; n (%)	2,352 (5.4%)	162 (4.7%)	2,922 (4.2%)	479 (3.6%)	11,824 (5.4%)	496 (5.4%)	17,098 (5.1%)	1,137 (4.4%)	0.03
Obstructive sleep apnea; n (%)	4,416 (10.1%)	410 (11.8%)	7,088 (10.1%)	1,623 (12.2%)	13,492 (6.1%)	847 (9.2%)	24,996 (7.5%)	2,880 (11.1%)	-0.12
Pneumonia; n (%)	860 (2.0%)	43 (1.2%)	998 (1.4%)	121 (0.9%)	4,495 (2.0%)	134 (1.5%)	6,353 (1.9%)	298 (1.1%)	0.07
Imaging; n (%)	66 (0.2%)	1 (0.0%)	24 (0.0%)	3 (0.0%)	**	**	**	**	**
Diabetes Medications									
DM Medications - AGIs; n (%)	187 (0.4%)	7 (0.2%)	203 (0.3%)	35 (0.3%)	1,130 (0.5%)	57 (0.6%)	1,520 (0.5%)	99 (0.4%)	0.01
DM Medications - Glitazones; n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	#VALUE!	000 (0.0%)	#VALUE!
DM Medications - GLP-1 RA; n (%)	1,549 (3.5%)	754 (21.7%)	2,487 (3.5%)	2,764 (20.8%)	4,959 (2.3%)	1,516 (16.4%)	8,995 (2.7%)	5,034 (19.4%)	-0.55
DM Medications - Insulin; n (%)	6,845 (15.7%)	933 (26.8%)	8,963 (12.8%)	3,433 (25.8%)	33,577 (15.3%)	2,551 (27.7%)	49,385 (14.8%)	6,917 (26.6%)	-0.29
DM Medications - Megitinides; n (%)	407 (0.9%)	21 (0.6%)	761 (1.1%)	117 (0.9%)	3,328 (1.5%)	154 (1.7%)	4,496 (1.3%)	292 (1.1%)	0.02
DM Medications - Metformin; n (%)	33,521 (76.7%)	2,635 (75.7%)	56,394 (80.7%)	10,496 (79.0%)	163,913 (74.5%)	6,881 (74.7%)	254,028 (76.1%)	20,012 (77.0%)	-0.02
Concomitant initiation or current use of 2nd Generation SI	13,270 (30.4%)	919 (26.4%)	20,051 (28.6%)	3,167 (23.8%)	77,226 (35.1%)	2,975 (32.3%)	110,547 (33.1%)	7,061 (27.2%)	0.13
Concomitant initiation or current use of AGIs; n (%)	131 (0.3%)	3 (0.1%)	138 (0.2%)	23 (0.2%)	829 (0.4%)	40 (0.4%)	1,098 (0.3%)	66 (0.3%)	0.00
Concomitant initiation or current use of Glitazones; n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	#VALUE!	000 (0.0%)	#VALUE!
Concomitant initiation or current use of GLP-1 RA; n (%)	901 (2.1%)	531 (15.3%)	1,451 (2.1%)	1,985 (14.9%)	2,539 (1.2%)	1,128 (12.2%)	4,891 (1.5%)	3,644 (14.0%)	-0.48
Concomitant initiation or current use of Insulin; n (%)	5,120 (11.7%)	687 (19.7%)	6,746 (9.6%)	2,633 (19.8%)	25,867 (11.8%)	2,042 (22.2%)	37,733 (11.3%)	5,362 (20.6%)	-0.26
Concomitant initiation or current use of Megitinides; n (%	299 (0.7%)	14 (0.4%)	568 (0.8%)	68 (0.5%)	2,421 (1.1%)	108 (1.2%)	3,288 (1.0%)	190 (0.7%)	0.03
Concomitant initiation or current use of Metformin; n (%)	29,232 (66.9%)	2,143 (61.6%)	50,259 (71.7%)	9,068 (68.2%)	142,769 (64.9%)	5,925 (64.3%)	222,260 (66.6%)	17,136 (65.9%)	0.01
Past use of 2nd Generation SUs Copy; n (%)	3,105 (7.1%)	280 (8.0%)	4,603 (6.6%)	855 (6.4%)	15,787 (7.2%)	632 (6.9%)	23,495 (7.0%)	1,767 (6.8%)	0.01
Past use of AGIs Copy; n (%)	56 (0.1%)	4 (0.1%)	65 (0.1%)	12 (0.1%)	301 (0.1%)	17 (0.2%)	422 (0.1%)	33 (0.1%)	0.00
Past use of Glitazones Copy; n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	#VALUE!	000 (0.0%)	#VALUE!
Past use of GLP-1 RA Copy; n (%)	705 (1.6%)	254 (7.3%)	1,101 (1.6%)	839 (6.3%)	2,421 (1.1%)	388 (4.2%)	4,227 (1.3%)	1,481 (5.7%)	-0.24
Past use of Insulin Copy; n (%)	1,725 (3.9%)	246 (7.1%)	2,218 (3.2%)	800 (6.0%)	7,713 (3.5%)	509 (5.5%)	11,636 (3.5%)	1,555 (6.0%)	-0.12
Past use of Megitinides Copy; n (%)	108 (0.2%)	7 (0.2%)	193 (0.3%)	49 (0.4%)	907 (0.4%)	46 (0.5%)	1,208 (0.4%)	102 (0.4%)	0.00
Past use of metformin (final) Copy; n (%)	4,289 (9.8%)	492 (14.1%)	6,335 (9.0%)	1,428 (10.7%)	21,144 (9.6%)	956 (10.4%)	31,768 (9.5%)	2,876 (11.1%)	-0.05
Other Medications									
Use of ACE inhibitors; n (%)	19,467 (44.5%)	1,538 (44.2%)	30,496 (43.5%)	5,845 (44.0%)	97,611 (44.4%)	3,934 (42.7%)	147,574 (44.2%)	11,317 (43.5%)	0.01
Use of ARBs; n (%)	12,584 (28.8%)	999 (28.7%)	20,278 (28.9%)	4,039 (30.4%)	69,754 (31.7%)	3,122 (33.9%)	102,616 (30.7%)	8,160 (31.4%)	-0.02
Use of Loop Diuretics - United; n (%)	5,037 (11.5%)	242 (7.0%)	5,607 (8.0%)	892 (6.7%)	31,180 (14.2%)	1,117 (12.1%)	41,824 (12.5%)	2,251 (8.7%)	0.12
Use of other diuretics- United; n (%)	1,343 (3.1%)	74 (2.1%)	1,784 (2.5%)	307 (2.3%)	6,652 (3.0%)	278 (3.0%)	9,779 (2.9%)	659 (2.5%)	0.02
Use of nitrates-United; n (%)	3,045 (7.0%)	137 (3.9%)	3,294 (4.7%)	474 (3.6%)	13,835 (6.3%)	474 (5.1%)	20,174 (6.0%)	1,085 (4.2%)	0.08
Use of other hypertension drugs; n (%)	2,609 (6.0%)	134 (3.8%)	3,205 (4.6%)	489 (3.7%)	15,257 (6.9%)	550 (6.0%)	21,071 (6.3%)	1,173 (4.5%)	0.08
Use of digoxin- United; n (%)	757 (1.7%)	33 (0.9%)	977 (1.4%)	91 (0.7%)	5,889 (2.7%)	198 (2.1%)	7,623 (2.3%)	322 (1.2%)	0.08
Use of Anti-arrhythmics; n (%)	613 (1.4%)	28 (0.8%)	807 (1.2%)	110 (0.8%)	3,689 (1.7%)	122 (1.3%)	5,109 (1.5%)	260 (1.0%)	0.05
Use of COPD/asthma meds- United; n (%)	6,650 (15.2%)	414 (11.9%)	10,129 (14.5%)	1,811 (13.6%)	36,341 (16.5%)	1,501 (16.3%)	53,120 (15.9%)	3,726 (14.3%)	0.04
Use of statins; n (%)	30,612 (70.0%)	2,331 (67.0%)	46,308 (66.1%)	8,857 (66.6%)	156,377 (71.1%)	6,648 (72.1%)	233,297 (69.9%)	17,836 (68.6%)	0.03
Use of other lipid-lowering drugs; n (%)	5,220 (11.9%)	475 (13.6%)	9,349 (13.3%)	1,910 (14.4%)	26,311 (12.0%)	1,189 (12.9%)	40,880 (12.2%)	3,574 (13.8%)	-0.05
Use of antiplatelet agents; n (%)	7,356 (16.8%)	404 (11.6%)	9,660 (13.8%)	1,637 (12.3%)	30,271 (13.8%)	1,179 (12.8%)	47,287 (14.2%)	3,220 (12.4%)	0.05
Use of oral anticoagulants (Dabigatran, Rivaroxaban, Apixa	2,845 (6.5%)	148 (4.3%)	3,431 (4.9%)	440 (3.3%)	18,185 (8.3%)	672 (7.3%)	24,461 (7.3%)	1,260 (4.8%)	0.11
Use of heparin and other low-molecular weight heparins; n	134 (0.3%)	5 (0.1%)	4 (0.0%)	1 (0.0%)	661 (0.3%)	19 (0.2%)	799 (0.2%)	025 (0.1%)	0.03
Use of NSAIDs; n (%)	7,110 (16.3%)	579 (16.6%)	11,464 (16.4%)	2,469 (18.6%)	36,034 (16.4%)	1,610 (17.5%)	54,608 (16.4%)	4,658 (17.9%)	-0.04
Use of oral corticosteroids; n (%)	5,386 (12.3%)	378 (10.9%)	8,380 (12.0%)	1,564 (11.8%)	28,350 (12.9%)	1,209 (13.1%)	42,116 (12.6%)	3,151 (12.1%)	0.02
Use of bisphosphonate (United); n (%)	762 (1.7%)	20 (0.6%)	631 (0.9%)	70 (0.5%)	6,860 (3.1%)	185 (2.0%)	8,253 (2.5%)	275 (1.1%)	0.11
Use of opioids- United; n (%)	9,929 (22.7%)	810 (23.3%)	14,956 (21.3%)	2,977 (22.4%)	46,726 (21.2%)	1,905 (20.7%)	71,611 (21.4%)	5,692 (21.9%)	-0.01
Use of antidepressants; n (%)	10,234 (23.4%)	757 (21.7%)	14,545 (20.8%)	3,235 (24.3%)	51,686 (23.5%)	2,284 (24.8%)	76,465 (22.9%)	6,276 (24.1%)	-0.03
Use of antipsychotics; n (%)	1,102 (2.5%)	53 (1.5%)	1,152 (1.6%)	211 (1.6%)	6,028 (2.7%)	188 (2.0%)	8,282 (2.5%)	452 (1.7%)	0.06
Use of anticonvulsants; n (%)	7,085 (16.2%)	484 (13.9%)	8,267 (11.8%)	1,618 (12.2%)	34,448 (15.7%)	1,475 (16.0%)	49,800 (14.9%)	3,577 (13.8%)	0.03
Use of lithium- United; n (%)	89 (0.2%)	2 (0.1%)	78 (0.1%)	17 (0.1%)	246 (0.1%)	12 (0.1%)	413 (0.1%)	031 (0.1%)	0.00
Use of Benzos- United; n (%)	4,586 (10.5%)	347 (10.0%)	6,362 (9.1%)	1,350 (10.2%)	22,806 (10.4%)	919 (10.0%)	33,754 (10.1%)	2,616 (10.1%)	0.00
Use of anxiolytics/hypnotics- United; n (%)	2,481 (5.7%)	222 (6.4%)	3,970 (5.7%)	858 (6.5%)	11,436 (5.2%)	516 (5.6%)	17,907 (5.4%)	1,596 (6.1%)	-0.03
Use of dementia meds- United; n (%)	832 (1.9%)	13 (0.4%)	726 (1.0%)	30 (0.2%)	8,955 (4.1%)	162 (1.8%)	10,513 (3.1%)	205 (0.8%)	0.17
Use of antiparkinsonian meds- United; n (%)	962 (2.2%)	49 (1.4%)	1,279 (1.8%)	235 (1.8%)	6,237 (2.8%)	267 (2.9%)	8,478 (2.5%)	551 (2.1%)	0.03
Any use of pramlintide; n (%)	2 (0.0%)	1 (0.0%)	6 (0.0%)	11 (0.1%)	**	**	**	**	**
Any use of 1st generation sulfonylureas; n (%)	0 (0.0%)	0 (0.0%)	6 (0.0%)	0 (0.0%)	20 (0.0%)	0 (0.0%)	026 (0.0%)	000 (0.0%)	0.00
Entresto (sacubitril/valsartan); n (%)	78 (0.2%)	3 (0.1%)	49 (0.1%)	1 (0.0%)	109 (0.0%)	12 (0.1%)	236 (0.1%)	016 (0.1%)	0.00
Initiation as monotherapy v4 Copy; n (%)	35,682 (81.6%)	3,155 (90.6%)	56,616 (80.8%)	11,790 (88.7%)	198,099 (90.0%)	9,217 (100.0%)	290,397 (87.0%)	24,162 (93.0%)	-0.20
Labs							113,797	16,773	
Lab values- HbA1c (%) v3; n (%)	18,338 (42.0%)	1,391 (40.0%)	4,710 (6.7%)	861 (6.5%)	N/A	N/A	23,048 (20.3%)	2,252 (13.4%)	0.19
Lab values- HbA1c (%) (within 3 months) v3; n (%)	14,895 (34.1%)	1,138 (32.7%)	3,877 (5.5%)	703 (5.3%)	N/A	N/A	18,772 (16.5%)	1,841 (11.0%)	0.16

Table 1

Lab values- HbA1c (%) (within 6 months) v3; n (%)	18,338 (42.0%)	1,391 (40.0%)	4,710 (6.7%)	861 (6.5%)	N/A	N/A	23,048 (20.3%)	2,252 (13.4%)	0.19
Lab values- BNP; n (%)	353 (0.8%)	8 (0.2%)	62 (0.1%)	4 (0.0%)	N/A	N/A	415 (0.4%)	012 (0.1%)	0.06
Lab values- BNP (within 3 months); n (%)	218 (0.5%)	7 (0.2%)	40 (0.1%)	4 (0.0%)	N/A	N/A	258 (0.2%)	011 (0.1%)	0.03
Lab values- BNP (within 6 months); n (%)	353 (0.8%)	8 (0.2%)	62 (0.1%)	4 (0.0%)	N/A	N/A	415 (0.4%)	012 (0.1%)	0.06
Lab values- BUN (mg/dl); n (%)	18,021 (41.2%)	1,412 (40.6%)	4,595 (6.6%)	804 (6.0%)	N/A	N/A	22,616 (19.9%)	2,216 (13.2%)	0.18
Lab values- BUN (mg/dl) (within 3 months); n (%)	14,331 (32.8%)	1,123 (32.3%)	3,628 (5.2%)	628 (4.7%)	N/A	N/A	17,959 (15.8%)	1,751 (10.4%)	0.16
Lab values- BUN (mg/dl) (within 6 months); n (%)	18,021 (41.2%)	1,412 (40.6%)	4,595 (6.6%)	804 (6.0%)	N/A	N/A	22,616 (19.9%)	2,216 (13.2%)	0.18
Lab values- Creatinine (mg/dl) v2; n (%)	18,551 (42.4%)	1,450 (41.7%)	4,918 (7.0%)	857 (6.4%)	N/A	N/A	23,469 (20.6%)	2,307 (13.8%)	0.18
Lab values- Creatinine (mg/dl) (within 3 months) v2; n (%)	14,772 (33.8%)	1,156 (33.2%)	3,902 (5.6%)	672 (5.1%)	N/A	N/A	18,674 (16.4%)	1,828 (10.9%)	0.16
Lab values- Creatinine (mg/dl) (within 6 months) v2; n (%)	18,551 (42.4%)	1,450 (41.7%)	4,918 (7.0%)	857 (6.4%)	N/A	N/A	23,469 (20.6%)	2,307 (13.8%)	0.18
Lab values- HDL level (mg/dl); n (%)	15,811 (36.2%)	1,242 (35.7%)	4,322 (6.2%)	822 (6.2%)	N/A	N/A	20,133 (17.7%)	2,064 (12.3%)	0.15
Lab values- HDL level (mg/dl) (within 3 months); n (%)	12,021 (27.5%)	941 (27.0%)	3,317 (4.7%)	615 (4.6%)	N/A	N/A	15,338 (13.5%)	1,556 (9.3%)	0.13
Lab values- HDL level (mg/dl) (within 6 months); n (%)	15,811 (36.2%)	1,242 (35.7%)	4,322 (6.2%)	822 (6.2%)	N/A	N/A	20,133 (17.7%)	2,064 (12.3%)	0.15
Lab values- LDL level (mg/dl) v2; n (%)	16,269 (37.2%)	1,262 (36.3%)	4,427 (6.3%)	797 (6.0%)	N/A	N/A	20,696 (18.2%)	2,059 (12.3%)	0.16
Lab values- LDL level (mg/dl) (within 3 months) v2; n (%)	12,390 (28.3%)	955 (27.4%)	3,400 (4.9%)	599 (4.5%)	N/A	N/A	15,790 (13.9%)	1,554 (9.3%)	0.14
Lab values- LDL level (mg/dl) (within 6 months) v2; n (%)	16,269 (37.2%)	1,262 (36.3%)	4,427 (6.3%)	797 (6.0%)	N/A	N/A	20,696 (18.2%)	2,059 (12.3%)	0.16
Lab values- NT-proBNP; n (%)	46 (0.1%)	3 (0.1%)	12 (0.0%)	1 (0.0%)	N/A	N/A	58 (0.1%)	6 (0.0%)	0.04
Lab values- NT-proBNP (within 3 months); n (%)	26 (0.1%)	3 (0.1%)	8 (0.0%)	0 (0.0%)	N/A	N/A	34 (0.0%)	3 (0.0%)	-
Lab values- NT-proBNP (within 6 months); n (%)	46 (0.1%)	3 (0.1%)	12 (0.0%)	1 (0.0%)	N/A	N/A	58 (0.1%)	6 (0.0%)	-
Lab values- Total cholesterol (mg/dl) v2; n (%)	16,044 (36.7%)	1,274 (36.6%)	4,327 (6.2%)	827 (6.2%)	N/A	N/A	20,371 (17.9%)	2,101 (12.5%)	0.15
Lab values- Total cholesterol (mg/dl) (within 3 months) v2;	12,207 (27.9%)	964 (27.7%)	3,321 (4.7%)	619 (4.7%)	N/A	N/A	15,528 (13.6%)	1,583 (9.4%)	0.13
Lab values- Total cholesterol (mg/dl) (within 6 months) v2;	16,044 (36.7%)	1,274 (36.6%)	4,327 (6.2%)	827 (6.2%)	N/A	N/A	20,371 (17.9%)	2,101 (12.5%)	0.15
Lab values- Triglyceride level (mg/dl); n (%)	15,910 (36.4%)	1,273 (36.6%)	4,281 (6.1%)	812 (6.1%)	N/A	N/A	20,191 (17.7%)	2,085 (12.4%)	0.15
Lab values- Triglyceride level (mg/dl) (within 3 months); n (%	12,111 (27.7%)	965 (27.7%)	3,287 (4.7%)	609 (4.6%)	N/A	N/A	15,398 (13.5%)	1,574 (9.4%)	0.13
Lab values- Triglyceride level (mg/dl) (within 6 months); n (%	15,910 (36.4%)	1,273 (36.6%)	4,281 (6.1%)	812 (6.1%)	N/A	N/A	20,191 (17.7%)	2,085 (12.4%)	0.15
Lab result number- HbA1c (%) mean (only 2 to 20 included	18,235	1,383	4,628	854	N/A	N/A	22,863	2,237	
...mean (sd)	8.35 (1.78)	8.60 (1.74)	8.43 (1.87)	8.50 (1.80)	N/A	N/A	8.37 (1.80)	8.56 (1.76)	-0.11
...median [IQR]	8.00 [7.10, 9.20]	8.20 [7.40, 9.50]	8.00 [7.10, 9.30]	8.00 [7.10, 9.55]	N/A	N/A	8.00 (1.80)	8.12 (1.76)	-0.07
...Missing; n (%)	25,475 (58.3%)	2,098 (60.3%)	65,459 (93.4%)	12,438 (93.6%)	N/A	N/A	90,934 (79.9%)	14,536 (86.7%)	-0.18
Lab result number- BNP mean v2	353	8	62	4	N/A	N/A	415	12	
...mean (sd)	154.08 (373.54)	62.94 (82.60)	526.58 (2,180.80)	25.75 (28.92)	N/A	N/A	209.73 (907.39)	50.54 (74.74)	0.25
...median [IQR]	65.40 [27.20, 164.00]	13.10 [1.23, 159.75]	71.00 [26.75, 193.75]	20.00 [1.50, 35.75]	N/A	N/A	#VALUE!	15.40 (74.74)	#VALUE!
...Missing; n (%)	43,357 (99.2%)	3,473 (99.8%)	70,025 (99.9%)	13,288 (100.0%)	N/A	N/A	113,382 (99.6%)	16,761 (99.9%)	-0.06
Lab result number- BUN (mg/dl) mean v2	18,021	1,412	4,595	804	N/A	N/A	22,616	2,216	
...mean (sd)	16.92 (6.36)	15.66 (4.60)	1,098.70 (12,576.94)	221.02 (3,818.55)	N/A	N/A	236.71 (3668.81)	90.17 (3504.95)	0.03
...median [IQR]	16.00 [13.00, 20.00]	15.00 [12.50, 18.00]	15.67 [13.00, 19.00]	15.00 [13.00, 18.00]	N/A	N/A	#VALUE!	#VALUE!	#VALUE!
...Missing; n (%)	25,689 (58.8%)	2,069 (59.4%)	65,492 (93.4%)	12,488 (94.0%)	N/A	N/A	91,181 (80.1%)	14,357 (86.8%)	-0.18
Lab result number- Creatinine (mg/dl) mean (only 0.1 to 15	18,407	1,444	4,354	725	N/A	N/A	22,761	2,169	
...mean (sd)	0.95 (0.27)	0.88 (0.19)	0.95 (0.25)	0.90 (0.20)	N/A	N/A	0.95 (0.27)	0.89 (0.19)	0.26
...median [IQR]	0.91 [0.77, 1.08]	0.88 [0.74, 1.00]	0.92 [0.78, 1.05]	0.90 [0.77, 1.00]	N/A	N/A	0.91 (0.27)	0.89 (0.19)	0.09
...Missing; n (%)	25,303 (57.9%)	2,037 (58.5%)	65,733 (93.8%)	12,567 (94.5%)	N/A	N/A	91,036 (80.0%)	14,604 (87.1%)	-0.19
Lab result number- HDL level (mg/dl) mean (only =<3000 in	15,811	1,242	4,292	822	N/A	N/A	20,103	2,064	
...mean (sd)	45.18 (13.27)	43.30 (12.25)	45.19 (45.80)	43.92 (12.86)	N/A	N/A	45.18 (24.21)	43.55 (12.50)	0.08
...median [IQR]	43.00 [36.00, 52.00]	41.50 [35.00, 50.25]	43.00 [36.00, 52.00]	42.00 [35.00, 51.00]	N/A	N/A	43.00 (24.21)	41.70 (12.50)	0.07
...Missing; n (%)	27,899 (63.8%)	2,239 (64.3%)	65,795 (93.9%)	12,470 (93.8%)	N/A	N/A	93,694 (82.3%)	14,709 (87.7%)	-0.15
Lab result number- LDL level (mg/dl) mean (only =<3000 in	15,877	1,250	3,990	713	N/A	N/A	19,867	1,963	
...mean (sd)	86.40 (40.73)	81.75 (39.30)	89.57 (42.63)	88.81 (43.09)	N/A	N/A	87.04 (41.12)	84.31 (40.73)	0.07
...median [IQR]	84.00 [62.00, 110.00]	83.00 [60.00, 105.00]	88.00 [64.00, 114.12]	87.00 [62.50, 112.50]	N/A	N/A	84.80 (41.12)	84.45 (40.73)	0.01
...Missing; n (%)	27,833 (63.7%)	2,231 (64.1%)	66,097 (94.3%)	12,579 (94.6%)	N/A	N/A	93,930 (82.5%)	14,810 (88.3%)	-0.16
Lab result number- Total cholesterol (mg/dl) mean (only =<	16,029	1,274	4,296	827	N/A	N/A	20,325	2,101	
...mean (sd)	173.66 (47.24)	172.86 (43.86)	176.94 (50.12)	176.61 (49.24)	N/A	N/A	174.35 (47.86)	174.34 (46.06)	0.00
...median [IQR]	167.00 [142.00, 198.50]	168.00 [143.00, 195.00]	172.45 [146.50, 204.00]	170.00 [143.00, 203.00]	N/A	N/A	168.15 (47.86)	168.79 (46.06)	-0.01
...Missing; n (%)	27,681 (63.3%)	2,207 (63.4%)	65,791 (93.9%)	12,465 (93.8%)	N/A	N/A	93,472 (82.1%)	14,672 (87.5%)	-0.15

Table 1

Lab result number- Triglyceride level (mg/dl) mean (only =<	15,908	1,273	4,249	812	N/A	N/A	20,157	2,085	
...mean (sd)	192.30 (164.03)	209.27 (181.46)	195.18 (180.30)	204.88 (191.63)	N/A	N/A	192.91 (167.59)	207.56 (185.53)	-0.08
...median [IQR]	154.00 [110.00, 222.00]	163.50 [118.00, 237.00]	154.00 [107.50, 225.00]	162.00 [110.00, 240.00]	N/A	N/A	154.00 [167.59]	162.92 [185.53]	-0.05
...Missing: n (%)	27,802 (63.6%)	2,208 (63.4%)	65,838 (93.9%)	12,480 (93.9%)	N/A	N/A	93,640 (82.3%)	14,688 (87.6%)	-0.15
Lab result number- Hemoglobin mean (only >0 included)	12,801	918	3,389	553	N/A	N/A	16,190	1,471	
...mean (sd)	13.76 (1.64)	14.24 (1.56)	919.77 (11,005.88)	13.93 (1.55)	N/A	N/A	203.41 (5035.16)	14.12 (1.56)	0.05
...median [IQR]	13.80 [12.70, 14.90]	14.38 [13.20, 15.30]	13.90 [12.80, 15.00]	14.00 [13.00, 15.00]	N/A	N/A	#VALUE!	14.24 (1.56)	#VALUE!
...Missing: n (%)	30,909 (70.7%)	2,563 (73.6%)	66,698 (95.2%)	12,739 (95.8%)	N/A	N/A	97,607 (85.8%)	15,302 (91.2%)	-0.17
Lab result number- Serum sodium mean (only > 90 and < 15	18,022	1,415	4,636	852	N/A	N/A	22,638	2,267	
...mean (sd)	139.31 (2.76)	139.24 (2.48)	138.90 (2.60)	138.79 (2.34)	N/A	N/A	139.23 (2.73)	139.07 (2.43)	0.06
...median [IQR]	139.50 [138.00, 141.00]	139.00 [138.00, 141.00]	139.00 [137.00, 141.00]	139.00 [137.00, 140.00]	N/A	N/A	139.40 (2.73)	139.00 (2.43)	0.15
...Missing: n (%)	25,688 (58.8%)	2,066 (59.4%)	65,451 (93.4%)	12,440 (93.6%)	N/A	N/A	91,139 (80.1%)	14,506 (86.5%)	-0.17
Lab result number- Albumin mean (only >0 and <=10 incluc	16,951	1,345	3,947	731	N/A	N/A	20,898	2,076	
...mean (sd)	4.29 (0.32)	4.34 (0.30)	4.18 (0.52)	4.20 (0.40)	N/A	N/A	4.27 (0.37)	4.29 (0.34)	-0.06
...median [IQR]	4.30 [4.10, 4.50]	4.35 [4.20, 4.55]	4.20 [4.00, 4.45]	4.20 [4.00, 4.45]	N/A	N/A	4.28 (0.37)	4.30 (0.34)	-0.06
...Missing: n (%)	26,759 (61.2%)	2,136 (61.4%)	66,140 (94.4%)	12,561 (94.5%)	N/A	N/A	92,899 (81.6%)	14,697 (87.6%)	-0.17
Lab result number- Glucose (fasting or random) mean (only	18,028	1,418	4,677	855	N/A	N/A	22,705	2,273	
...mean (sd)	178.82 (71.82)	176.07 (65.32)	179.62 (73.30)	179.02 (66.34)	N/A	N/A	178.98 (72.13)	177.18 (65.72)	0.03
...median [IQR]	161.50 [129.67, 210.00]	160.00 [130.50, 209.00]	162.00 [129.50, 212.00]	164.00 [134.00, 213.50]	N/A	N/A	161.60 (72.13)	161.50 (65.72)	0.00
...Missing: n (%)	25,682 (58.8%)	2,063 (59.3%)	65,410 (93.3%)	12,437 (93.6%)	N/A	N/A	91,092 (80.0%)	14,500 (86.4%)	-0.17
Lab result number- Potassium mean (only 1-7 included)	18,422	1,437	4,485	779	N/A	N/A	22,907	2,216	
...mean (sd)	4.46 (0.41)	4.42 (0.40)	4.34 (0.44)	4.29 (0.42)	N/A	N/A	4.44 (0.42)	4.37 (0.41)	0.17
...median [IQR]	4.45 [4.20, 4.70]	4.40 [4.20, 4.70]	4.30 [4.00, 4.60]	4.30 [4.00, 4.50]	N/A	N/A	4.42 (0.42)	4.36 (0.41)	0.14
...Missing: n (%)	25,288 (57.9%)	2,044 (58.7%)	65,602 (93.6%)	12,513 (94.1%)	N/A	N/A	90,890 (79.9%)	14,557 (86.8%)	-0.19
Comorbidity Scores									
CCI (180 days)- ICD9 and ICD10 v2									
...mean (sd)	2.24 (1.70)	1.70 (1.28)	1.58 (1.30)	1.52 (1.10)	2.28 (1.64)	2.10 (1.41)	2.13 (1.58)	1.75 (1.24)	0.27
...median [IQR]	2.00 [1.00, 3.00]	1.00 [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]	1.79 (1.58)	1.35 (1.24)	0.31
Frailty Score: Qualitative Version 365 days as Categories, v1									
...0; n (%)	23,256 (53.2%)	1,863 (53.5%)	35,399 (50.5%)	7,831 (58.9%)	93,519 (42.5%)	5,672 (61.5%)	152,174 (45.6%)	15,366 (59.1%)	-0.27
...1 to 2; n (%)	13,464 (30.8%)	1,221 (35.1%)	25,165 (35.9%)	4,308 (32.4%)	74,925 (34.0%)	2,385 (25.9%)	113,554 (34.0%)	7,914 (30.5%)	0.07
...3 or more; n (%)	6,990 (16.0%)	397 (11.4%)	9,523 (13.6%)	1,133 (8.7%)	51,617 (23.5%)	1,160 (12.6%)	68,130 (20.4%)	2,710 (10.4%)	0.28
Frailty Score: Empirical Version 365 days as Categories, v3									
...<0.12908; n (%)	11,607 (26.6%)	1,220 (35.0%)	22,110 (31.5%)	4,747 (35.7%)	35,188 (16.0%)	1,811 (19.6%)	68,905 (20.6%)	7,778 (29.9%)	-0.22
...0.12908 - 0.1631167; n (%)	13,502 (30.9%)	1,260 (36.2%)	23,555 (33.6%)	4,834 (36.4%)	64,537 (29.3%)	3,036 (32.9%)	101,594 (30.4%)	9,130 (35.1%)	-0.10
...>=0.1631167; n (%)	18,601 (42.6%)	1,001 (28.8%)	24,422 (34.8%)	3,711 (27.9%)	120,336 (54.7%)	4,370 (47.4%)	163,359 (48.9%)	9,082 (34.9%)	0.29
Non-Frailty; n (%)	24,902 (57.0%)	1,839 (52.8%)	36,675 (52.3%)	6,921 (52.1%)	10,548 (4.8%)	381 (4.1%)	72,125 (21.6%)	9,141 (35.2%)	-0.31
Frailty Score (mean): Qualitative Version 365 days, v1									
...mean (sd)	1.11 (1.71)	0.93 (1.37)	1.04 (1.47)	0.76 (1.19)	1.50 (1.91)	0.87 (1.45)	1.35 (1.80)	0.82 (1.31)	0.34
...median [IQR]	0.00 [0.00, 2.00]	0.00 [0.00, 1.00]	0.00 [0.00, 2.00]	0.00 [0.00, 1.00]	1.00 [0.00, 2.00]	0.00 [0.00, 1.00]	0.66 (1.80)	0.00 (1.31)	0.42
Frailty Score (mean): Empirical Version 365 days, v2									
...mean (sd)	0.17 (0.05)	0.15 (0.04)	0.15 (0.04)	0.14 (0.04)	0.18 (0.06)	0.17 (0.05)	0.17 (0.06)	0.15 (0.04)	0.39
...median [IQR]	0.15 [0.13, 0.19]	0.14 [0.12, 0.17]	0.14 [0.12, 0.17]	0.14 [0.12, 0.16]	0.17 [0.14, 0.21]	0.16 [0.13, 0.19]	0.16 (0.06)	0.15 (0.04)	0.20
Healthcare Utilization									
Any hospitalization; n (%)	3,020 (6.9%)	138 (4.0%)	3,300 (4.7%)	397 (3.0%)	12,377 (5.6%)	313 (3.4%)	18,697 (5.6%)	848 (3.3%)	0.11
Any hospitalization within prior 30 days; n (%)	1,005 (2.3%)	23 (0.7%)	896 (1.3%)	52 (0.4%)	3,315 (1.5%)	48 (0.5%)	5,216 (1.6%)	123 (0.5%)	0.11
Any hospitalization during prior 31-180 days; n (%)	2,160 (4.9%)	117 (3.4%)	2,481 (3.5%)	351 (2.6%)	9,436 (4.3%)	273 (3.0%)	14,097 (4.2%)	741 (2.9%)	0.07
Endocrinologist Visit; n (%)	4,365 (10.0%)	719 (20.7%)	6,290 (9.0%)	2,264 (17.0%)	23,625 (10.7%)	1,457 (15.8%)	34,280 (10.3%)	4,440 (17.1%)	-0.20
Endocrinologist Visit (30 days prior); n (%)	2,869 (6.6%)	548 (15.7%)	4,237 (6.0%)	1,753 (13.2%)	15,268 (6.9%)	970 (10.5%)	22,374 (6.7%)	3,271 (12.6%)	-0.20
Endocrinologist Visit (31 to 180 days prior); n (%)	2,851 (6.5%)	505 (14.5%)	4,089 (5.8%)	1,488 (11.2%)	16,666 (7.6%)	1,117 (12.1%)	23,606 (7.1%)	3,110 (12.0%)	-0.17
Internal medicine/family medicine visits; n (%)	33,818 (77.4%)	2,030 (58.3%)	61,531 (87.8%)	11,642 (87.6%)	178,740 (81.2%)	7,344 (79.7%)	274,089 (82.1%)	21,016 (80.9%)	0.03
Internal medicine/family medicine visits (30 days prior) v2;	25,331 (58.0%)	1,353 (38.9%)	46,643 (66.6%)	8,792 (66.1%)	129,466 (58.8%)	5,186 (56.3%)	201,440 (60.3%)	15,331 (59.0%)	0.03
Internal medicine/family medicine visits (31 to 180 days pr	28,677 (65.6%)	1,697 (48.8%)	49,865 (71.1%)	9,603 (72.2%)	152,425 (69.3%)	6,433 (69.8%)	230,967 (69.2%)	17,733 (68.2%)	0.02
Cardiologist visit; n (%)	13,109 (30.0%)	740 (21.3%)	14,339 (20.5%)	2,488 (18.7%)	62,166 (28.2%)	2,290 (24.8%)	89,614 (26.8%)	5,518 (21.2%)	0.13
Number of Cardiologist visits (30 days prior); n (%)	4,705 (10.8%)	251 (7.2%)	4,808 (6.9%)	735 (5.5%)	20,600 (9.4%)	690 (7.5%)	30,113 (9.0%)	1,676 (6.4%)	0.10

Table 1

Number of Cardiologist visits (31 to 180 days prior); n (%)	11,053 (25.3%)	622 (17.9%)	12,065 (17.2%)	2,109 (15.9%)	53,433 (24.3%)	1,998 (21.7%)	76,551 (22.9%)	4,729 (18.2%)	0.12
Electrocardiogram v2; n (%)	13,667 (31.3%)	812 (23.3%)	19,434 (27.7%)	3,190 (24.0%)	64,105 (29.1%)	2,449 (26.6%)	97,206 (29.1%)	6,451 (24.8%)	0.10
Use of glucose test strips; n (%)	1,583 (3.6%)	143 (4.1%)	2,505 (3.6%)	523 (3.9%)	6,748 (3.1%)	228 (2.5%)	10,836 (3.2%)	894 (3.4%)	-0.01
Dialysis; n (%)	3 (0.0%)	1 (0.0%)	3 (0.0%)	0 (0.0%)	25 (0.0%)	0 (0.0%)	031 (0.0%)	001 (0.0%)	#DIV/0!
Naive new user v8 Copy; n (%)	8,086 (18.5%)	369 (10.6%)	12,706 (18.1%)	1,626 (12.2%)	31,513 (14.3%)	879 (9.5%)	52,305 (15.7%)	2,874 (11.1%)	0.14
Nantidiabetic drugs at index date v3 Copy									
...mean (sd)	2.12 (0.75)	2.24 (0.89)	2.13 (0.72)	2.28 (0.86)	2.14 (0.76)	2.33 (0.86)	2.14 (0.75)	2.29 (0.86)	-0.19
...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 (0.75)	2.00 (0.86)	0.00
number of different/distinct medication prescriptions									
...mean (sd)	9.83 (4.85)	9.60 (4.67)	8.91 (4.34)	9.66 (4.53)	9.38 (4.19)	9.76 (4.29)	9.34 (4.31)	9.69 (4.47)	-0.08
...median [IQR]	9.00 [6.00, 12.00]	9.00 [6.00, 12.00]	8.00 [6.00, 11.00]	9.00 [6.00, 12.00]	9.00 [6.00, 12.00]	9.00 [7.00, 12.00]	8.79 (4.31)	9.00 (4.47)	-0.05
Number of Hospitalizations									
...mean (sd)	0.08 (0.33)	0.04 (0.22)	0.05 (0.25)	0.03 (0.19)	0.07 (0.30)	0.04 (0.23)	0.07 (0.29)	0.03 (0.21)	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 (0.29)	0.00 (0.21)	0.00
Number of hospital days									
...mean (sd)	0.45 (2.50)	0.19 (1.12)	0.28 (1.87)	0.15 (1.13)	0.40 (2.56)	0.21 (1.62)	0.38 (2.42)	0.18 (1.32)	0.10
...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 (2.42)	0.00 (1.32)	0.00
Number of Emergency Department (ED) visits v3									
...mean (sd)	0.35 (1.12)	0.20 (0.71)	0.10 (1.08)	0.06 (0.65)	0.36 (1.08)	0.28 (0.94)	0.30 (1.09)	0.16 (0.77)	0.15
...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 (0.77)	0.00
Number of Office visits									
...mean (sd)	4.60 (3.62)	4.33 (3.24)	4.23 (3.37)	4.32 (3.23)	4.74 (3.65)	4.96 (3.55)	4.61 (3.59)	4.55 (3.35)	0.02
...median [IQR]	4.00 [2.00, 6.00]	3.00 [2.00, 6.00]	3.00 [2.00, 5.00]	4.00 [2.00, 6.00]	4.00 [2.00, 6.00]	4.00 [2.00, 7.00]	3.79 (3.59)	3.87 (3.35)	-0.02
Number of Endocrinologist visits									
...mean (sd)	0.46 (2.19)	1.21 (3.74)	0.39 (2.06)	0.92 (3.24)	0.59 (2.92)	1.02 (4.01)	0.53 (2.67)	0.99 (3.60)	-0.15
...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 (2.67)	0.00 (3.60)	0.00
Number of internal medicine/family medicine visits									
...mean (sd)	8.04 (11.91)	4.73 (8.01)	6.69 (8.43)	6.65 (7.61)	7.09 (9.42)	7.18 (10.03)	7.13 (9.59)	6.58 (8.60)	0.06
...median [IQR]	4.00 [1.00, 10.00]	2.00 [0.00, 6.00]	4.00 [2.00, 9.00]	5.00 [2.00, 9.00]	4.00 [1.00, 9.00]	4.00 [1.00, 10.00]	4.00 (9.59)	4.24 (8.60)	-0.03
Number of Cardiologist visits									
...mean (sd)	1.44 (3.70)	0.97 (2.93)	0.84 (2.68)	0.70 (2.14)	1.37 (3.88)	1.14 (3.20)	1.27 (3.64)	0.89 (2.67)	0.12
...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, 0.00]	0.00 (3.64)	0.00 (2.67)	0.00
Number electrocardiograms received v2									
...mean (sd)	0.60 (1.39)	0.36 (0.93)	0.47 (1.10)	0.38 (0.89)	0.53 (1.14)	0.46 (1.03)	0.53 (1.17)	0.41 (0.95)	0.11
...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 (1.17)	0.00 (0.95)	0.00
Number of HbA1c tests ordered									
...mean (sd)	1.24 (0.88)	1.28 (0.85)	1.07 (0.85)	1.32 (0.81)	1.40 (0.82)	1.49 (0.81)	1.31 (0.83)	1.37 (0.82)	-0.07
...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]	1.00 [1.00, 2.00]	1.00 (0.83)	1.00 (0.82)	0.00
Number of glucose tests ordered									
...mean (sd)	0.52 (3.68)	0.38 (0.97)	0.36 (1.40)	0.41 (1.07)	0.39 (0.98)	0.42 (0.98)	0.40 (1.68)	0.41 (1.03)	-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 (1.68)	0.00 (1.03)	0.00
Number of lipid tests ordered									
...mean (sd)	0.99 (0.93)	1.06 (0.98)	0.90 (1.15)	1.11 (1.15)	1.01 (0.80)	1.07 (0.83)	0.98 (0.90)	1.09 (1.02)	-0.11
...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 (0.90)	1.00 (1.02)	0.00
Number of creatinine tests ordered									
...mean (sd)	0.04 (0.28)	0.04 (0.28)	0.04 (0.29)	0.03 (0.22)	0.06 (0.31)	0.06 (0.32)	0.05 (0.30)	0.04 (0.27)	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 (0.30)	0.00 (0.27)	0.00
Number of BUN tests ordered									
...mean (sd)	0.02 (0.21)	0.02 (0.18)	0.03 (0.23)	0.02 (0.16)	0.04 (0.24)	0.04 (0.24)	0.04 (0.23)	0.03 (0.19)	0.05
...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 (0.23)	0.00 (0.19)	0.00
Number of tests for microalbuminuria									
...mean (sd)	0.75 (1.12)	0.74 (1.11)	0.61 (1.00)	0.73 (1.09)	0.45 (0.66)	0.47 (0.68)	0.52 (0.81)	0.64 (0.97)	-0.13
...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 (0.81)	0.00 (0.97)	0.00
Total N distinct ICD9/ICD10 diagnoses at the 3rd digit level Copy									
...mean (sd)	5.95 (7.69)	3.93 (6.05)	2.58 (4.25)	2.81 (3.90)	5.37 (7.03)	6.54 (6.84)	4.86 (6.64)	4.28 (5.41)	0.10
...median [IQR]	4.00 [0.00, 9.00]	0.00 [0.00, 6.00]	0.00 [0.00, 4.00]	0.00 [0.00, 5.00]	4.00 [0.00, 8.00]	5.00 [0.00, 10.00]	3.16 (6.64)	1.77 (5.41)	0.23
Use of thiazide; n (%)	4,816 (11.0%)	361 (10.4%)	7,336 (10.5%)	1,284 (9.7%)	30,023 (13.6%)	1,165 (12.6%)	42,175 (12.6%)	2,810 (10.8%)	0.06
Use of beta blockers; n (%)	17,867 (40.9%)	1,105 (31.7%)	24,668 (35.2%)	4,337 (32.6%)	97,465 (44.3%)	3,864 (41.9%)	140,000 (41.9%)	9,306 (35.8%)	0.13
Use of calcium channel blockers; n (%)	11,695 (26.8%)	766 (22.0%)	17,484 (24.9%)	3,114 (23.4%)	70,925 (32.2%)	2,700 (29.3%)	100,104 (30.0%)	6,580 (25.3%)	0.11

Table 1

PS-matched									
	Optum		MarketScan		Medicare		POOLED		
Variable	Reference- DPP4i v2	Exposure - Dapagliflozin v2	Reference- DPP4i v2	Exposure - Dapagliflozin v2	Reference- DPP4i v2	Exposure - Dapagliflozin v2	Reference- DPP4i v2	Exposure - Dapagliflozin v2	St. Diff.
Number of patients	3316	3316	12415	12415	9164	9164	24,895	24,895	
Age									
...mean (sd)	58.44 (7.64)	58.61 (6.71)	57.91 (6.56)	58.10 (5.82)	70.32 (4.86)	70.31 (4.94)	62.55 (6.16)	62.66 (5.63)	-0.02
...median [IQR]	58.00 [54.00, 62.00]	58.00 [54.00, 62.00]	58.00 [54.00, 61.00]	58.00 [55.00, 61.00]	69.00 [67.00, 73.00]	69.00 [67.00, 73.00]	62.05 (6.16)	62.05 (5.63)	0.00
Age categories without zero category									
...18 - 34; n (%)	1,019 (30.7%)	840 (25.3%)	3,275 (26.4%)	2,905 (23.4%)	0 (0.0%)	0 (0.0%)	4,294 (17.2%)	3,745 (15.0%)	0.06
...35 - 64; n (%)	1,697 (51.2%)	2,003 (60.4%)	7,958 (64.1%)	8,622 (69.4%)	106 (1.2%)	78 (0.9%)	9,761 (39.2%)	10,703 (43.0%)	-0.08
...65 - 74; n (%)	475 (14.3%)	388 (11.7%)	942 (7.6%)	733 (5.9%)	7,436 (81.1%)	7,495 (81.8%)	8,853 (35.6%)	8,616 (34.6%)	0.02
...>=75; n (%)	125 (3.8%)	85 (2.6%)	240 (1.9%)	155 (1.2%)	1,622 (17.7%)	1,591 (17.4%)	1,987 (8.0%)	1,831 (7.4%)	0.02
Gender without zero category- United									
...Males; n (%)	2,032 (61.3%)	2,082 (62.8%)	7,531 (60.7%)	7,552 (60.8%)	4,783 (52.2%)	4,759 (51.9%)	14,346 (57.6%)	14,393 (57.8%)	0.00
...Females; n (%)	1,284 (38.7%)	1,234 (37.2%)	4,884 (39.3%)	4,863 (39.2%)	4,381 (47.8%)	4,405 (48.1%)	10,549 (42.4%)	10,502 (42.2%)	0.00
Race									
...White; n (%)	N/A	N/A	N/A	N/A	7,401 (80.8%)	7,387 (80.6%)	7,401 (80.8%)	7,387 (80.6%)	0.01
...Black; n (%)	N/A	N/A	N/A	N/A	799 (8.7%)	756 (8.2%)	799 (8.7%)	756 (8.2%)	0.02
...Asian; n (%)	N/A	N/A	N/A	N/A	280 (3.1%)	301 (3.3%)	280 (3.1%)	301 (3.3%)	-0.01
...Hispanic; n (%)	N/A	N/A	N/A	N/A	283 (3.1%)	298 (3.3%)	283 (3.1%)	298 (3.3%)	-0.01
...North American Native; n (%)	N/A	N/A	N/A	N/A	29 (0.3%)	25 (0.3%)	29 (0.3%)	25 (0.3%)	0.00
...Other/Unknown; n (%)	N/A	N/A	N/A	N/A	372 (4.1%)	397 (4.3%)	372 (4.1%)	397 (4.3%)	-0.01
Region without zero category- United v3 (lumping missing&other category with West)									
...Northeast; n (%)	214 (6.5%)	217 (6.5%)	1,671 (13.5%)	1,687 (13.6%)	1,564 (17.1%)	1,528 (16.7%)	3,449 (13.9%)	3,432 (13.8%)	0.00
...South; n (%)	1,859 (56.1%)	1,874 (56.5%)	2,045 (16.5%)	2,095 (16.9%)	4,342 (47.4%)	4,257 (46.5%)	8,246 (33.1%)	8,226 (33.0%)	0.00
...Midwest; n (%)	832 (25.1%)	795 (24.0%)	7,690 (61.9%)	7,595 (61.2%)	1,780 (19.4%)	1,822 (19.9%)	10,302 (41.4%)	10,212 (41.0%)	0.01
...West; n (%)	411 (12.4%)	430 (13.0%)	943 (7.6%)	974 (7.8%)	1,478 (16.1%)	1,557 (17.0%)	2,832 (11.4%)	2,961 (11.9%)	-0.02
...Unknown+missing; n (%)	N/A	N/A	66 (0.5%)	64 (0.5%)	N/A	N/A	66 (0.5%)	64 (0.5%)	0.00
CV Covariates									
Ischemic heart disease; n (%)	611 (18.4%)	644 (19.4%)	2,081 (16.8%)	2,091 (16.8%)	2,043 (22.3%)	2,032 (22.2%)	4,735 (19.0%)	4,767 (19.1%)	0.00
Acute MI; n (%)	31 (0.9%)	32 (1.0%)	68 (0.5%)	68 (0.5%)	45 (0.5%)	45 (0.5%)	144 (0.6%)	145 (0.6%)	0.00
ACS/unstable angina; n (%)	39 (1.2%)	37 (1.1%)	100 (0.8%)	96 (0.8%)	49 (0.5%)	52 (0.6%)	188 (0.8%)	185 (0.7%)	0.01
Old MI; n (%)	82 (2.5%)	79 (2.4%)	148 (1.2%)	140 (1.1%)	179 (2.0%)	190 (2.1%)	409 (1.6%)	409 (1.6%)	0.00
Stable angina; n (%)	99 (3.0%)	107 (3.2%)	296 (2.4%)	320 (2.6%)	292 (3.2%)	283 (3.1%)	687 (2.8%)	710 (2.9%)	-0.01
Coronary atherosclerosis and other forms of chronic ischemic heart disease; n (%)	564 (17.0%)	602 (18.2%)	1,946 (15.7%)	1,919 (15.5%)	1,945 (21.2%)	1,948 (21.3%)	4,455 (17.9%)	4,469 (18.0%)	0.00
Other atherosclerosis with ICD10 v2 Copy; n (%)	27 (0.8%)	21 (0.6%)	55 (0.4%)	53 (0.4%)	82 (0.9%)	80 (0.9%)	164 (0.7%)	154 (0.6%)	0.01
Previous cardiac procedure (CABG or PTCA or Stent) v4; n (%)	11 (0.3%)	21 (0.6%)	44 (0.4%)	39 (0.3%)	16 (0.2%)	17 (0.2%)	071 (0.3%)	077 (0.3%)	0.00
History of CABG or PTCA; n (%)	147 (4.4%)	145 (4.4%)	265 (2.1%)	270 (2.2%)	526 (5.7%)	491 (5.4%)	938 (3.8%)	906 (3.6%)	0.01
Any stroke; n (%)	105 (3.2%)	118 (3.6%)	408 (3.3%)	415 (3.3%)	525 (5.7%)	543 (5.9%)	1,038 (4.2%)	1,076 (4.3%)	0.00
Ischemic stroke (w and w/o mention of cerebral infarction); n (%)	105 (3.2%)	115 (3.5%)	407 (3.3%)	415 (3.3%)	519 (5.7%)	542 (5.9%)	1,031 (4.1%)	1,072 (4.3%)	-0.01
Hemorrhagic stroke; n (%)	1 (0.0%)	3 (0.1%)	7 (0.1%)	3 (0.0%)	**	**	**	**	**
TIA; n (%)	17 (0.5%)	19 (0.6%)	53 (0.4%)	66 (0.5%)	84 (0.9%)	75 (0.8%)	154 (0.6%)	160 (0.6%)	0.00
Other cerebrovascular disease; n (%)	26 (0.8%)	22 (0.7%)	75 (0.6%)	75 (0.6%)	101 (1.1%)	113 (1.2%)	202 (0.8%)	210 (0.8%)	0.00
Late effects of cerebrovascular disease; n (%)	12 (0.4%)	14 (0.4%)	50 (0.4%)	51 (0.4%)	63 (0.7%)	79 (0.9%)	125 (0.5%)	144 (0.6%)	-0.01
Cerebrovascular procedure; n (%)	3 (0.1%)	4 (0.1%)	4 (0.0%)	5 (0.0%)	**	**	**	**	**
Heart failure (CHF); n (%)	149 (4.5%)	142 (4.3%)	255 (2.1%)	275 (2.2%)	538 (5.9%)	510 (5.6%)	942 (3.8%)	927 (3.7%)	0.01
Peripheral Vascular Disease (PVD) or PVD Surgery v2; n (%)	122 (3.7%)	127 (3.8%)	376 (3.0%)	382 (3.1%)	632 (6.9%)	641 (7.0%)	1,130 (4.5%)	1,150 (4.6%)	0.00
Atrial fibrillation; n (%)	120 (3.6%)	117 (3.5%)	329 (2.7%)	363 (2.9%)	667 (7.3%)	682 (7.4%)	1,116 (4.5%)	1,162 (4.7%)	-0.01
Other cardiac dysrhythmia; n (%)	165 (5.0%)	175 (5.3%)	472 (3.8%)	483 (3.9%)	849 (9.3%)	842 (9.2%)	1,486 (6.0%)	1,500 (6.0%)	0.00
Cardiac conduction disorders; n (%)	53 (1.6%)	52 (1.6%)	131 (1.1%)	148 (1.2%)	244 (2.7%)	233 (2.5%)	428 (1.7%)	433 (1.7%)	0.00
Other CVD; n (%)	231 (7.0%)	223 (6.7%)	650 (5.2%)	629 (5.1%)	947 (10.3%)	927 (10.1%)	1,828 (7.3%)	1,779 (7.1%)	0.01
Diabetes-related complications									
Diabetic retinopathy; n (%)	124 (3.7%)	142 (4.3%)	367 (3.0%)	373 (3.0%)	590 (6.4%)	615 (6.7%)	1,081 (4.3%)	1,130 (4.5%)	-0.01
Diabetes with other ophthalmic manifestations; n (%)	2 (0.1%)	3 (0.1%)	173 (1.4%)	203 (1.6%)	196 (2.1%)	193 (2.1%)	371 (1.5%)	399 (1.6%)	-0.01
Retinal detachment, vitreous hemorrhage, vitrectomy; n (%)	5 (0.2%)	9 (0.3%)	36 (0.3%)	30 (0.2%)	46 (0.5%)	31 (0.3%)	087 (0.3%)	070 (0.3%)	0.00
Retinal laser coagulation therapy; n (%)	10 (0.3%)	6 (0.2%)	59 (0.5%)	55 (0.4%)	62 (0.7%)	60 (0.7%)	131 (0.5%)	121 (0.5%)	0.00
Occurrence of Diabetic Neuropathy v2 Copy; n (%)	477 (14.4%)	470 (14.2%)	1,395 (11.2%)	1,410 (11.4%)	1,699 (18.5%)	1,740 (19.0%)	3,571 (14.3%)	3,620 (14.5%)	-0.01

Table 1

Occurrence of diabetic nephropathy V3 with ICD10 Copy; n (%)	183 (5.5%)	172 (5.2%)	455 (3.7%)	479 (3.9%)	481 (5.2%)	495 (5.4%)	1,119 (4.5%)	1,146 (4.6%)	0.00
Hypoglycemia v2; n (%)	73 (2.2%)	71 (2.1%)	191 (1.5%)	200 (1.6%)	128 (1.4%)	116 (1.3%)	392 (1.6%)	387 (1.6%)	0.00
Hyperglycemia; n (%)	112 (3.4%)	107 (3.2%)	449 (3.6%)	437 (3.5%)	348 (3.8%)	345 (3.8%)	909 (3.7%)	889 (3.6%)	0.01
Disorders of fluid electrolyte and acid-base balance; n (%)	91 (2.7%)	94 (2.8%)	343 (2.8%)	332 (2.7%)	271 (3.0%)	288 (3.1%)	705 (2.8%)	714 (2.9%)	-0.01
Diabetic ketoacidosis; n (%)	10 (0.3%)	7 (0.2%)	13 (0.1%)	12 (0.1%)	**	**	**	**	**
Hyperosmolar hyperglycemic nonketotic syndrome (HONK); n (%)	9 (0.3%)	9 (0.3%)	47 (0.4%)	47 (0.4%)	43 (0.5%)	50 (0.5%)	099 (0.4%)	106 (0.4%)	0.00
Diabetes with peripheral circulatory disorders with ICD-10 v2 Copy; n (%)	112 (3.4%)	117 (3.5%)	289 (2.3%)	275 (2.2%)	548 (6.0%)	522 (5.7%)	949 (3.8%)	914 (3.7%)	0.01
Diabetic Foot; n (%)	65 (2.0%)	64 (1.9%)	181 (1.5%)	172 (1.4%)	178 (1.9%)	168 (1.8%)	424 (1.7%)	404 (1.6%)	0.01
Gangrene v2; n (%)	5 (0.2%)	5 (0.2%)	15 (0.1%)	18 (0.1%)	**	**	**	**	**
Lower extremity amputation; n (%)	21 (0.6%)	20 (0.6%)	48 (0.4%)	38 (0.3%)	35 (0.4%)	29 (0.3%)	104 (0.4%)	087 (0.3%)	0.02
Osteomyelitis; n (%)	21 (0.6%)	19 (0.6%)	46 (0.4%)	51 (0.4%)	34 (0.4%)	27 (0.3%)	101 (0.4%)	097 (0.4%)	0.00
Skin infections v2; n (%)	186 (5.6%)	189 (5.7%)	606 (4.9%)	603 (4.9%)	533 (5.8%)	518 (5.7%)	1,325 (5.3%)	1,310 (5.3%)	0.00
Erectile dysfunction; n (%)	147 (4.4%)	136 (4.1%)	385 (3.1%)	387 (3.1%)	295 (3.2%)	268 (2.9%)	827 (3.3%)	791 (3.2%)	0.01
Diabetes with unspecified complication; n (%)	131 (4.0%)	131 (4.0%)	638 (5.1%)	669 (5.4%)	509 (5.6%)	515 (5.6%)	1,278 (5.1%)	1,315 (5.3%)	-0.01
Diabetes mellitus without mention of complications; n (%)	2,897 (87.4%)	2,934 (88.5%)	10,922 (88.0%)	10,899 (87.8%)	8,127 (88.7%)	8,148 (88.9%)	21,946 (88.2%)	21,981 (88.3%)	0.00
Hypertension: 1 inpatient or 2 outpatient claims within 365 days; n (%)	2,554 (77.0%)	2,578 (77.7%)	9,099 (73.3%)	9,066 (73.0%)	7,910 (86.3%)	7,933 (86.6%)	19,563 (78.6%)	19,577 (78.6%)	0.00
Hyperlipidemia v2; n (%)	2,478 (74.7%)	2,491 (75.1%)	8,830 (71.1%)	8,863 (71.4%)	7,044 (76.9%)	7,056 (77.0%)	18,352 (73.7%)	18,410 (74.0%)	-0.01
Edema; n (%)	158 (4.8%)	146 (4.4%)	358 (2.9%)	343 (2.8%)	540 (5.9%)	557 (6.1%)	1,056 (4.2%)	1,046 (4.2%)	0.00
Renal Dysfunction (non-diabetic) v2; n (%)	136 (4.1%)	143 (4.3%)	373 (3.0%)	394 (3.2%)	534 (5.8%)	525 (5.7%)	1,043 (4.2%)	1,062 (4.3%)	0.00
Occurrence of acute renal disease v2; n (%)	16 (0.5%)	15 (0.5%)	49 (0.4%)	50 (0.4%)	43 (0.5%)	51 (0.6%)	108 (0.4%)	116 (0.5%)	-0.01
Occurrence of chronic renal insufficiency; n (%)	82 (2.5%)	91 (2.7%)	195 (1.6%)	212 (1.7%)	309 (3.4%)	330 (3.6%)	586 (2.4%)	633 (2.5%)	-0.01
Chronic kidney disease v2; n (%)	63 (1.9%)	76 (2.3%)	169 (1.4%)	173 (1.4%)	276 (3.0%)	285 (3.1%)	508 (2.0%)	534 (2.1%)	-0.01
CKD Stage 3-4; 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!
Occurrence of hypertensive nephropathy; n (%)	41 (1.2%)	39 (1.2%)	92 (0.7%)	93 (0.7%)	137 (1.5%)	134 (1.5%)	270 (1.1%)	266 (1.1%)	0.00
Occurrence of miscellaneous renal insufficiency v2; n (%)	50 (1.5%)	55 (1.7%)	126 (1.0%)	143 (1.2%)	255 (2.8%)	238 (2.6%)	431 (1.7%)	436 (1.8%)	-0.01
Glaucoma or cataracts v2; n (%)	410 (12.4%)	403 (12.2%)	1,445 (11.6%)	1,423 (11.5%)	2,357 (25.7%)	2,332 (25.4%)	4,212 (16.9%)	4,158 (16.7%)	0.01
Cellulitis or abscess of toe; n (%)	47 (1.4%)	32 (1.0%)	118 (1.0%)	119 (1.0%)	97 (1.1%)	117 (1.3%)	262 (1.1%)	268 (1.1%)	0.00
Foot ulcer; n (%)	61 (1.8%)	59 (1.8%)	175 (1.4%)	173 (1.4%)	169 (1.8%)	163 (1.8%)	405 (1.6%)	395 (1.6%)	0.00
Bladder stones; n (%)	3 (0.1%)	0 (0.0%)	4 (0.0%)	6 (0.0%)	**	**	**	**	**
Kidney stones; n (%)	40 (1.2%)	49 (1.5%)	141 (1.1%)	150 (1.2%)	152 (1.7%)	135 (1.5%)	333 (1.3%)	334 (1.3%)	0.00
Urinary tract infections (UTIs); n (%)	7 (0.2%)	6 (0.2%)	57 (0.5%)	56 (0.5%)	60 (0.7%)	63 (0.7%)	124 (0.5%)	125 (0.5%)	0.00
Dipstick urinalysis; n (%)	911 (27.5%)	853 (25.7%)	3,737 (30.1%)	3,629 (29.2%)	2,677 (29.2%)	2,690 (29.4%)	7,325 (29.4%)	7,172 (28.8%)	0.01
Non-dipstick urinalysis; n (%)	1,387 (41.8%)	1,371 (41.3%)	5,150 (41.5%)	5,074 (40.9%)	3,897 (42.5%)	3,816 (41.6%)	10,434 (41.9%)	10,261 (41.2%)	0.01
Urine function test; n (%)	22 (0.7%)	24 (0.7%)	124 (1.0%)	108 (0.9%)	196 (2.1%)	168 (1.8%)	342 (1.4%)	300 (1.2%)	0.02
Cytology; n (%)	8 (0.2%)	6 (0.2%)	23 (0.2%)	19 (0.2%)	23 (0.3%)	30 (0.3%)	054 (0.2%)	055 (0.2%)	0.00
Cystoscopy; n (%)	7 (0.2%)	8 (0.2%)	37 (0.3%)	36 (0.3%)	48 (0.5%)	34 (0.4%)	092 (0.4%)	078 (0.3%)	0.02
Other Covariates									
Liver disease; n (%)	68 (2.1%)	73 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	068 (0.3%)	073 (0.3%)	0.00
Osteoarthritis; n (%)	324 (9.8%)	358 (10.8%)	1,189 (9.6%)	1,184 (9.5%)	1,832 (20.0%)	1,811 (19.8%)	3,345 (13.4%)	3,353 (13.5%)	0.00
Other arthritis, arthropathies and musculoskeletal pain; n (%)	1,072 (32.3%)	1,027 (31.0%)	3,446 (27.8%)	3,493 (28.1%)	3,560 (38.8%)	3,511 (38.3%)	8,078 (32.4%)	8,031 (32.3%)	0.00
Dorsopathies; n (%)	678 (20.4%)	678 (20.4%)	2,251 (18.1%)	2,230 (18.0%)	2,285 (24.9%)	2,283 (24.9%)	5,214 (20.9%)	5,191 (20.9%)	0.00
Fractures; n (%)	46 (1.4%)	58 (1.7%)	176 (1.4%)	163 (1.3%)	200 (2.2%)	204 (2.2%)	422 (1.7%)	425 (1.7%)	0.00
Falls v2; n (%)	35 (1.1%)	41 (1.2%)	64 (0.5%)	62 (0.5%)	198 (2.2%)	202 (2.2%)	297 (1.2%)	305 (1.2%)	0.00
Osteoporosis; n (%)	54 (1.6%)	55 (1.7%)	136 (1.1%)	136 (1.1%)	480 (5.2%)	482 (5.3%)	670 (2.7%)	673 (2.7%)	0.00
Hyperthyroidism; n (%)	20 (0.6%)	20 (0.6%)	63 (0.5%)	68 (0.5%)	78 (0.9%)	71 (0.8%)	161 (0.6%)	159 (0.6%)	0.00
Hypothyroidism v2; n (%)	467 (14.1%)	462 (13.9%)	1,539 (12.4%)	1,494 (12.0%)	952 (10.4%)	955 (10.4%)	2,958 (11.9%)	2,911 (11.7%)	0.01
Other disorders of thyroid gland V2; n (%)	144 (4.3%)	134 (4.0%)	453 (3.6%)	463 (3.7%)	462 (5.0%)	415 (4.5%)	1,059 (4.3%)	1,012 (4.1%)	0.01
Depression; n (%)	252 (7.6%)	237 (7.1%)	792 (6.4%)	788 (6.3%)	734 (8.0%)	699 (7.6%)	1,778 (7.1%)	1,724 (6.9%)	0.01
Anxiety; n (%)	227 (6.8%)	220 (6.6%)	732 (5.9%)	724 (5.8%)	698 (7.6%)	652 (7.1%)	1,657 (6.7%)	1,596 (6.4%)	0.01
Sleep Disorder; n (%)	303 (9.1%)	328 (9.9%)	1,020 (8.2%)	1,001 (8.1%)	529 (5.8%)	530 (5.8%)	1,852 (7.4%)	1,859 (7.5%)	0.00
Dementia; n (%)	31 (0.9%)	24 (0.7%)	40 (0.3%)	57 (0.5%)	223 (2.4%)	216 (2.4%)	294 (1.2%)	297 (1.2%)	0.00
Delirium; n (%)	16 (0.5%)	12 (0.4%)	19 (0.2%)	24 (0.2%)	40 (0.4%)	38 (0.4%)	075 (0.3%)	074 (0.3%)	0.00
Psychosis; n (%)	19 (0.6%)	12 (0.4%)	32 (0.3%)	35 (0.3%)	67 (0.7%)	62 (0.7%)	118 (0.5%)	109 (0.4%)	0.01
Obesity; n (%)	841 (25.4%)	845 (25.5%)	2,353 (19.0%)	2,343 (18.9%)	1,566 (17.1%)	1,517 (16.6%)	4,760 (19.1%)	4,705 (18.9%)	0.01
Overweight; n (%)	144 (4.3%)	146 (4.4%)	354 (2.9%)	344 (2.8%)	371 (4.0%)	368 (4.0%)	869 (3.5%)	858 (3.4%)	0.01
Smoking; n (%)	285 (8.6%)	314 (9.5%)	649 (5.2%)	680 (5.5%)	981 (10.7%)	974 (10.6%)	1,915 (7.7%)	1,968 (7.9%)	-0.01
Alcohol abuse or dependence; n (%)	15 (0.5%)	26 (0.8%)	44 (0.4%)	44 (0.4%)	46 (0.5%)	41 (0.4%)	105 (0.4%)	111 (0.4%)	0.00
Drug abuse or dependence; n (%)	42 (1.3%)	31 (0.9%)	65 (0.5%)	71 (0.6%)	92 (1.0%)	78 (0.9%)	199 (0.8%)	180 (0.7%)	0.01
COPD; n (%)	119 (3.6%)	134 (4.0%)	363 (2.9%)	369 (3.0%)	744 (8.1%)	747 (8.2%)	1,226 (4.9%)	1,250 (5.0%)	0.00

Table 1

Asthma; n (%)	151 (4.6%)	158 (4.8%)	435 (3.5%)	441 (3.6%)	500 (5.5%)	493 (5.4%)	1,086 (4.4%)	1,092 (4.4%)	0.00
Obstructive sleep apnea; n (%)	375 (11.3%)	387 (11.7%)	1,490 (12.0%)	1,464 (11.8%)	820 (8.9%)	841 (9.2%)	2,685 (10.8%)	2,692 (10.8%)	0.00
Pneumonia; n (%)	53 (1.6%)	43 (1.3%)	108 (0.9%)	110 (0.9%)	130 (1.4%)	134 (1.5%)	291 (1.2%)	287 (1.2%)	0.00
Imaging; n (%)	2 (0.1%)	1 (0.0%)	5 (0.0%)	3 (0.0%)	**	**	**	**	**
Diabetes Medications									
DM Medications - AGIs; n (%)	10 (0.3%)	7 (0.2%)	31 (0.2%)	32 (0.3%)	77 (0.8%)	56 (0.6%)	118 (0.5%)	095 (0.4%)	0.01
DM Medications - Glitazones; 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!
DM Medications - GLP-1 RA; n (%)	598 (18.0%)	599 (18.1%)	1,777 (14.3%)	1,937 (15.6%)	1,480 (16.2%)	1,463 (16.0%)	3,855 (15.5%)	3,999 (16.1%)	-0.02
DM Medications - Insulin; n (%)	797 (24.0%)	830 (25.0%)	2,835 (22.8%)	2,944 (23.7%)	2,495 (27.2%)	2,509 (27.4%)	6,127 (24.6%)	6,283 (25.2%)	-0.01
DM Medications - Megitinides; n (%)	18 (0.5%)	20 (0.6%)	106 (0.9%)	113 (0.9%)	147 (1.6%)	153 (1.7%)	271 (1.1%)	286 (1.1%)	0.00
DM Medications - Metformin; n (%)	2,488 (75.0%)	2,517 (75.9%)	9,948 (80.1%)	9,865 (79.5%)	6,908 (75.4%)	6,854 (74.8%)	19,344 (77.7%)	19,236 (77.3%)	0.01
Concomitant initiation or current use of 2nd Generation SUs; n (%)	885 (26.7%)	882 (26.6%)	3,002 (24.2%)	3,012 (24.3%)	2,916 (31.8%)	2,966 (32.4%)	6,803 (27.3%)	6,860 (27.6%)	-0.01
Concomitant initiation or current use of AGIs; n (%)	6 (0.2%)	3 (0.1%)	20 (0.2%)	21 (0.2%)	49 (0.5%)	40 (0.4%)	075 (0.3%)	064 (0.3%)	0.00
Concomitant initiation or current use of Glitazones; 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!
Concomitant initiation or current use of GLP-1 RA; n (%)	395 (11.9%)	402 (12.1%)	1,158 (9.3%)	1,271 (10.2%)	1,033 (11.3%)	1,075 (11.7%)	2,586 (10.4%)	2,748 (11.0%)	-0.02
Concomitant initiation or current use of Insulin; n (%)	594 (17.9%)	609 (18.4%)	2,180 (17.6%)	2,233 (18.0%)	2,018 (22.0%)	2,002 (21.8%)	4,792 (19.2%)	4,844 (19.5%)	-0.01
Concomitant initiation or current use of Meglitinides; n (%)	15 (0.5%)	13 (0.4%)	87 (0.7%)	64 (0.5%)	100 (1.1%)	107 (1.2%)	202 (0.8%)	184 (0.7%)	0.01
Concomitant initiation or current use of Metformin; n (%)	2,021 (60.9%)	2,049 (61.8%)	8,574 (69.1%)	8,537 (68.8%)	5,896 (64.3%)	5,902 (64.4%)	16,491 (66.2%)	16,488 (66.2%)	0.00
Past use of 2nd Generation SUs Copy; n (%)	279 (8.4%)	267 (8.1%)	803 (6.5%)	810 (6.5%)	687 (7.5%)	631 (6.9%)	1,769 (7.1%)	1,708 (6.9%)	0.01
Past use of AGIs Copy; n (%)	4 (0.1%)	4 (0.1%)	11 (0.1%)	11 (0.1%)	28 (0.3%)	16 (0.2%)	043 (0.2%)	031 (0.1%)	0.03
Past use of Glitazones Copy; 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!
Past use of GLP-1 RA Copy; n (%)	230 (6.9%)	223 (6.7%)	675 (5.4%)	712 (5.7%)	447 (4.9%)	388 (4.2%)	1,352 (5.4%)	1,323 (5.3%)	0.00
Past use of Insulin Copy; n (%)	203 (6.1%)	221 (6.7%)	656 (5.3%)	711 (5.7%)	477 (5.2%)	507 (5.5%)	1,336 (5.4%)	1,439 (5.8%)	-0.02
Past use of Megitinides Copy; n (%)	3 (0.1%)	7 (0.2%)	19 (0.2%)	49 (0.4%)	47 (0.5%)	46 (0.5%)	069 (0.3%)	102 (0.4%)	-0.02
Past use of metformin (final) Copy; n (%)	467 (14.1%)	468 (14.1%)	1,374 (11.1%)	1,328 (10.7%)	1,012 (11.0%)	952 (10.4%)	2,853 (11.5%)	2,748 (11.0%)	0.02
Other Medications									
Use of ACE inhibitors; n (%)	1,452 (43.8%)	1,471 (44.4%)	5,393 (43.4%)	5,453 (43.9%)	3,888 (42.4%)	3,912 (42.7%)	10,733 (43.1%)	10,836 (43.5%)	-0.01
Use of ARBs; n (%)	922 (27.8%)	939 (28.3%)	3,785 (30.5%)	3,740 (30.1%)	3,074 (33.5%)	3,092 (33.7%)	7,781 (31.3%)	7,771 (31.2%)	0.00
Use of Loop Diuretics - United; n (%)	225 (6.8%)	237 (7.1%)	828 (6.7%)	829 (6.7%)	1,147 (12.5%)	1,113 (12.1%)	2,200 (8.8%)	2,179 (8.8%)	0.00
Use of other diuretics- United; n (%)	81 (2.4%)	72 (2.2%)	299 (2.4%)	281 (2.3%)	273 (3.0%)	277 (3.0%)	653 (2.6%)	630 (2.5%)	0.01
Use of nitrates-United; n (%)	135 (4.1%)	130 (3.9%)	441 (3.6%)	453 (3.6%)	454 (5.0%)	471 (5.1%)	1,030 (4.1%)	1,054 (4.2%)	-0.01
Use of other hypertension drugs; n (%)	126 (3.8%)	128 (3.9%)	445 (3.6%)	458 (3.7%)	530 (5.8%)	550 (6.0%)	1,101 (4.4%)	1,136 (4.6%)	-0.01
Use of digoxin- United; n (%)	23 (0.7%)	30 (0.9%)	84 (0.7%)	87 (0.7%)	189 (2.1%)	197 (2.1%)	296 (1.2%)	314 (1.3%)	-0.01
Use of Anti-arrhythmics; n (%)	24 (0.7%)	28 (0.8%)	102 (0.8%)	106 (0.9%)	132 (1.4%)	122 (1.3%)	258 (1.0%)	256 (1.0%)	0.00
Use of COPD/asthma meds- United; n (%)	415 (12.5%)	401 (12.1%)	1,700 (13.7%)	1,678 (13.5%)	1,468 (16.0%)	1,490 (16.3%)	3,583 (14.4%)	3,569 (14.3%)	0.00
Use of statins; n (%)	2,212 (66.7%)	2,214 (66.8%)	8,213 (66.2%)	8,228 (66.3%)	6,530 (71.3%)	6,605 (72.1%)	16,955 (68.1%)	17,047 (68.5%)	-0.01
Use of other lipid-lowering drugs; n (%)	402 (12.1%)	436 (13.1%)	1,714 (13.8%)	1,755 (14.1%)	1,196 (13.1%)	1,176 (12.8%)	3,312 (13.3%)	3,367 (13.5%)	-0.01
Use of antiplatelet agents; n (%)	395 (11.9%)	386 (11.6%)	1,527 (12.3%)	1,529 (12.3%)	1,184 (12.9%)	1,168 (12.7%)	3,106 (12.5%)	3,083 (12.4%)	0.00
Use of oral anticoagulants (Dabigatran, Rivaroxaban, Apixaban, Warfarin); n (%)	153 (4.6%)	143 (4.3%)	397 (3.2%)	415 (3.3%)	677 (7.4%)	668 (7.3%)	1,227 (4.9%)	1,226 (4.9%)	0.00
Use of heparin and other low-molecular weight heparins; n (%)	8 (0.2%)	5 (0.2%)	0 (0.0%)	1 (0.0%)	20 (0.2%)	19 (0.2%)	028 (0.1%)	025 (0.1%)	0.00
Use of NSAIDs; n (%)	540 (16.3%)	555 (16.7%)	2,347 (18.9%)	2,306 (18.6%)	1,677 (18.3%)	1,600 (17.5%)	4,564 (18.3%)	4,461 (17.9%)	0.01
Use of oral corticosteroids; n (%)	365 (11.0%)	359 (10.8%)	1,459 (11.8%)	1,469 (11.8%)	1,213 (13.2%)	1,205 (13.1%)	3,037 (12.2%)	3,033 (12.2%)	0.00
Use of bisphosphonate (United); n (%)	16 (0.5%)	20 (0.6%)	67 (0.5%)	66 (0.5%)	192 (2.1%)	185 (2.0%)	275 (1.1%)	271 (1.1%)	0.00
Use of opioids- United; n (%)	749 (22.6%)	782 (23.6%)	2,822 (22.7%)	2,776 (22.4%)	1,931 (21.1%)	1,891 (20.6%)	5,502 (22.1%)	5,449 (21.9%)	0.00
Use of antidepressants; n (%)	698 (21.0%)	732 (22.1%)	2,889 (23.3%)	2,958 (23.8%)	2,255 (24.6%)	2,267 (24.7%)	5,842 (23.5%)	5,957 (23.9%)	-0.01
Use of antipsychotics; n (%)	58 (1.7%)	51 (1.5%)	176 (1.4%)	198 (1.6%)	183 (2.0%)	187 (2.0%)	417 (1.7%)	436 (1.8%)	-0.01
Use of anticonvulsants; n (%)	478 (14.4%)	462 (13.9%)	1,471 (11.8%)	1,488 (12.0%)	1,448 (15.8%)	1,463 (16.0%)	3,397 (13.6%)	3,413 (13.7%)	0.00
Use of lithium- United; n (%)	6 (0.2%)	2 (0.1%)	17 (0.1%)	16 (0.1%)	**	**	**	**	**
Use of Benzos- United; n (%)	336 (10.1%)	327 (9.9%)	1,239 (10.0%)	1,241 (10.0%)	926 (10.1%)	914 (10.0%)	2,501 (10.0%)	2,482 (10.0%)	0.00
Use of anxiolytics/hypnotics- United; n (%)	201 (6.1%)	211 (6.4%)	791 (6.4%)	786 (6.3%)	530 (5.8%)	514 (5.6%)	1,522 (6.1%)	1,511 (6.1%)	0.00
Use of dementia meds- United; n (%)	13 (0.4%)	13 (0.4%)	20 (0.2%)	30 (0.2%)	159 (1.7%)	160 (1.7%)	192 (0.8%)	203 (0.8%)	0.00
Use of antiparkinsonian meds- United; n (%)	48 (1.4%)	48 (1.4%)	221 (1.8%)	220 (1.8%)	289 (3.2%)	265 (2.9%)	558 (2.2%)	533 (2.1%)	0.01
Any use of pramlintide; n (%)	0 (0.0%)	1 (0.0%)	3 (0.0%)	10 (0.1%)	**	**	**	**	**
Any use of 1st generation sulfonylureas; n (%)	0 (0.0%)	0 (0.0%)	1 (0.0%)	0 (0.0%)	**	**	**	**	**
Entresto (sacubitril/valsartan); n (%)	4 (0.1%)	3 (0.1%)	8 (0.1%)	1 (0.0%)	**	**	**	**	**
Initiation as monotherapy v4 Copy; n (%)	2,967 (89.5%)	2,990 (90.2%)	10,986 (88.5%)	10,913 (87.9%)	9,164 (100.0%)	9,164 (100.0%)	23,117 (92.9%)	23,067 (92.7%)	0.01
Labs							15,731	15,731	
Lab values- HbA1c (%) v3; n (%)	1,334 (40.2%)	1,332 (40.2%)	941 (7.6%)	798 (6.4%)	N/A	N/A	2,275 (14.5%)	2,130 (13.5%)	0.03
Lab values- HbA1c (%) (within 3 months) v3; n (%)	1,092 (32.9%)	1,085 (32.7%)	788 (6.3%)	646 (5.2%)	N/A	N/A	1,880 (12.0%)	1,731 (11.0%)	0.03

Table 1

Lab values- HbA1c (%) (within 6 months) v3; n (%)	1,334 (40.2%)	1,332 (40.2%)	941 (7.6%)	798 (6.4%)	N/A	N/A	2,275 (14.5%)	2,130 (13.5%)	0.03
Lab values- BNP; n (%)	14 (0.4%)	8 (0.2%)	5 (0.0%)	4 (0.0%)	N/A	N/A	019 (0.1%)	012 (0.1%)	0.00
Lab values- BNP (within 3 months); n (%)	8 (0.2%)	7 (0.2%)	3 (0.0%)	4 (0.0%)	N/A	N/A	011 (0.1%)	011 (0.1%)	0.00
Lab values- BNP (within 6 months); n (%)	14 (0.4%)	8 (0.2%)	5 (0.0%)	4 (0.0%)	N/A	N/A	019 (0.1%)	012 (0.1%)	0.00
Lab values- BUN (mg/dl); n (%)	1,336 (40.3%)	1,345 (40.6%)	889 (7.2%)	743 (6.0%)	N/A	N/A	2,225 (14.1%)	2,088 (13.3%)	0.02
Lab values- BUN (mg/dl) (within 3 months); n (%)	1,055 (31.8%)	1,066 (32.1%)	707 (5.7%)	575 (4.6%)	N/A	N/A	1,762 (11.2%)	1,641 (10.4%)	0.03
Lab values- BUN (mg/dl) (within 6 months); n (%)	1,336 (40.3%)	1,345 (40.6%)	889 (7.2%)	743 (6.0%)	N/A	N/A	2,225 (14.1%)	2,088 (13.3%)	0.02
Lab values- Creatinine (mg/dl) v2; n (%)	1,381 (41.6%)	1,381 (41.6%)	970 (7.8%)	792 (6.4%)	N/A	N/A	2,351 (14.9%)	2,173 (13.8%)	0.03
Lab values- Creatinine (mg/dl) (within 3 months) v2; n (%)	1,095 (33.0%)	1,098 (33.1%)	775 (6.2%)	616 (5.0%)	N/A	N/A	1,870 (11.9%)	1,714 (10.9%)	0.03
Lab values- Creatinine (mg/dl) (within 6 months) v2; n (%)	1,381 (41.6%)	1,381 (41.6%)	970 (7.8%)	792 (6.4%)	N/A	N/A	2,351 (14.9%)	2,173 (13.8%)	0.03
Lab values- HDL level (mg/dl); n (%)	1,219 (36.8%)	1,180 (35.6%)	869 (7.0%)	761 (6.1%)	N/A	N/A	2,088 (13.3%)	1,941 (12.3%)	0.03
Lab values- HDL level (mg/dl) (within 3 months); n (%)	925 (27.9%)	890 (26.8%)	664 (5.3%)	564 (4.5%)	N/A	N/A	1,589 (10.1%)	1,454 (9.2%)	0.03
Lab values- HDL level (mg/dl) (within 6 months); n (%)	1,219 (36.8%)	1,180 (35.6%)	869 (7.0%)	761 (6.1%)	N/A	N/A	2,088 (13.3%)	1,941 (12.3%)	0.03
Lab values- LDL level (mg/dl) v2; n (%)	1,241 (37.4%)	1,203 (36.3%)	879 (7.1%)	738 (5.9%)	N/A	N/A	2,120 (13.5%)	1,941 (12.3%)	0.04
Lab values- LDL level (mg/dl) (within 3 months) v2; n (%)	944 (28.5%)	907 (27.4%)	671 (5.4%)	550 (4.4%)	N/A	N/A	1,615 (10.3%)	1,457 (9.3%)	0.03
Lab values- LDL level (mg/dl) (within 6 months) v2; n (%)	1,241 (37.4%)	1,203 (36.3%)	879 (7.1%)	738 (5.9%)	N/A	N/A	2,120 (13.5%)	1,941 (12.3%)	0.04
Lab values- NT-proBNP; n (%)	3 (0.1%)	5 (0.2%)	1 (0.0%)	1 (0.0%)	N/A	N/A	04 (0.0%)	0 (0.0%)	-
Lab values- NT-proBNP (within 3 months); n (%)	1 (0.0%)	3 (0.1%)	1 (0.0%)	0 (0.0%)	N/A	N/A	02 (0.0%)	0 (0.0%)	-
Lab values- NT-proBNP (within 6 months); n (%)	3 (0.1%)	5 (0.2%)	1 (0.0%)	1 (0.0%)	N/A	N/A	04 (0.0%)	6 (0.0%)	-
Lab values- Total cholesterol (mg/dl) v2; n (%)	1,249 (37.7%)	1,212 (36.6%)	875 (7.0%)	766 (6.2%)	N/A	N/A	2,124 (13.5%)	1,978 (12.6%)	0.03
Lab values- Total cholesterol (mg/dl) (within 3 months) v2; n (%)	950 (28.6%)	913 (27.5%)	668 (5.4%)	568 (4.6%)	N/A	N/A	1,618 (10.3%)	1,481 (9.4%)	0.03
Lab values- Total cholesterol (mg/dl) (within 6 months) v2; n (%)	1,249 (37.7%)	1,212 (36.6%)	875 (7.0%)	766 (6.2%)	N/A	N/A	2,124 (13.5%)	1,978 (12.6%)	0.03
Lab values- Triglyceride level (mg/dl); n (%)	1,237 (37.3%)	1,211 (36.5%)	868 (7.0%)	752 (6.1%)	N/A	N/A	2,105 (13.4%)	1,963 (12.5%)	0.03
Lab values- Triglyceride level (mg/dl) (within 3 months); n (%)	941 (28.4%)	914 (27.6%)	662 (5.3%)	559 (4.5%)	N/A	N/A	1,603 (10.2%)	1,473 (9.4%)	0.03
Lab values- Triglyceride level (mg/dl) (within 6 months); n (%)	1,237 (37.3%)	1,211 (36.5%)	868 (7.0%)	752 (6.1%)	N/A	N/A	2,105 (13.4%)	1,963 (12.5%)	0.03
Lab result number- HbA1c (%) mean (only 2 to 20 included) v4	1,326	1,325	930	791	N/A	N/A	2,256	2,116	
...mean (sd)	8.62 (1.81)	8.59 (1.74)	8.57 (1.88)	8.51 (1.81)	N/A	N/A	8.60 (1.84)	8.56 (1.77)	0.02
...median [IQR]	8.25 [7.30, 9.60]	8.20 [7.40, 9.50]	8.10 [7.30, 9.60]	8.00 [7.20, 9.50]	N/A	N/A	8.19 (1.84)	8.13 (1.77)	0.03
...Missing; n (%)	1,990 (60.0%)	1,991 (60.0%)	11,485 (92.5%)	11,624 (93.6%)	N/A	N/A	13,475 (85.7%)	13,615 (86.5%)	-0.02
Lab result number- BNP mean v2	14	8	5	4	N/A	N/A	19	12	
...mean (sd)	116.35 (114.30)	62.94 (82.60)	234.87 (258.20)	25.75 (28.92)	N/A	N/A	147.54 (165.17)	50.54 (74.74)	0.76
...median [IQR]	56.45 [47.44, 207.60]	13.10 [1.23, 159.75]	147.00 [53.00, 460.67]	20.00 [1.50, 55.75]	N/A	N/A	#VALUE!	15.40 (74.74)	#VALUE!
...Missing; n (%)	3,302 (99.6%)	3,308 (99.8%)	12,410 (100.0%)	12,411 (100.0%)	N/A	N/A	15,712 (99.9%)	15,719 (99.9%)	0.00
Lab result number- BUN (mg/dl) mean v2	1,336	1,345	889	743	N/A	N/A	2,225	2,088	
...mean (sd)	13.77 (5.28)	13.66 (4.62)	1,028.37 (11,952.55)	237.83 (6,052.69)	N/A	N/A	420.35 (7556.05)	94.72 (3610.75)	0.05
...median [IQR]	13.00 [12.00, 18.00]	13.00 [12.50, 18.00]	13.33 [13.00, 18.50]	13.00 [12.67, 18.00]	N/A	N/A	#VALUE!	#VALUE!	#VALUE!
...Missing; n (%)	1,980 (59.7%)	1,971 (59.4%)	11,526 (92.8%)	11,672 (94.0%)	N/A	N/A	13,506 (85.9%)	13,643 (86.7%)	-0.02
Lab result number- Creatinine (mg/dl) mean (only 0.1 to 15 included) v3	1,365	1,375	833	671	N/A	N/A	2,198	2,046	
...mean (sd)	0.91 (0.24)	0.88 (0.19)	0.94 (0.25)	0.90 (0.19)	N/A	N/A	0.92 (0.24)	0.89 (0.19)	0.14
...median [IQR]	0.88 [0.76, 1.02]	0.88 [0.74, 1.00]	0.92 [0.77, 1.05]	0.89 [0.76, 1.00]	N/A	N/A	0.90 (0.24)	0.88 (0.19)	0.09
...Missing; n (%)	1,951 (58.8%)	1,941 (58.5%)	11,582 (93.3%)	11,744 (94.6%)	N/A	N/A	13,533 (86.0%)	13,685 (87.0%)	-0.03
Lab result number- HDL level (mg/dl) mean (only =<3000 included) v2	1,219	1,180	862	761	N/A	N/A	2,081	1,941	
...mean (sd)	44.13 (12.67)	43.43 (12.38)	44.38 (13.55)	44.06 (12.72)	N/A	N/A	44.23 (13.04)	43.68 (12.52)	0.04
...median [IQR]	42.00 [36.00, 51.00]	42.00 [35.00, 51.00]	42.58 [36.00, 52.12]	42.50 [36.00, 51.00]	N/A	N/A	42.24 (13.04)	42.20 (12.52)	0.00
...Missing; n (%)	2,097 (63.2%)	2,136 (64.4%)	11,553 (93.1%)	11,654 (93.9%)	N/A	N/A	13,650 (86.8%)	13,790 (87.7%)	-0.03
Lab result number- LDL level (mg/dl) mean (only =<3000 included) v2	1,214	1,193	783	638	N/A	N/A	1,997	1,831	
...mean (sd)	87.83 (43.08)	82.21 (39.52)	89.06 (43.42)	89.56 (43.82)	N/A	N/A	88.31 (43.22)	84.82 (41.11)	0.08
...median [IQR]	88.00 [62.88, 112.50]	83.00 [61.00, 105.75]	88.00 [64.00, 116.00]	88.00 [63.00, 114.00]	N/A	N/A	88.00 (43.22)	84.78 (41.11)	0.08
...Missing; n (%)	2,102 (63.4%)	2,123 (64.0%)	11,632 (93.7%)	11,757 (94.7%)	N/A	N/A	13,734 (87.3%)	13,880 (88.2%)	-0.03
Lab result number- Total cholesterol (mg/dl) mean (only =<3000 included) v2	1,249	1,212	868	766	N/A	N/A	2,117	1,978	
...mean (sd)	179.01 (47.89)	173.61 (44.15)	180.73 (52.25)	177.64 (49.97)	N/A	N/A	179.72 (49.74)	175.17 (46.50)	0.09
...median [IQR]	173.00 [149.00, 203.75]	169.00 [143.00, 196.00]	176.00 [150.00, 206.75]	170.00 [144.00, 204.00]	N/A	N/A	174.23 (49.74)	169.39 (46.50)	0.10
...Missing; n (%)	2,067 (62.3%)	2,104 (63.4%)	11,547 (93.0%)	11,649 (93.8%)	N/A	N/A	13,614 (86.5%)	13,753 (87.4%)	-0.03

Table 1

Lab result number- Triglyceride level (mg/dl) mean (only =<5000 included) v2	1,237	1,211	860	752	N/A	N/A	2,097	1,963	
...mean (sd)	212.55 (198.62)	210.19 (184.38)	214.38 (222.01)	204.46 (193.38)	N/A	N/A	213.30 (208.58)	207.99 (187.93)	0.03
...median [IQR]	162.00 [114.25, 239.00]	164.00 [118.00, 237.00]	159.00 [110.00, 239.00]	162.00 [110.21, 238.75]	N/A	N/A	160.77 (208.58)	163.23 (187.93)	-0.01
...Missing; n (%)	2,079 (62.7%)	2,105 (63.5%)	11,555 (93.1%)	11,663 (93.9%)	N/A	N/A	13,634 (86.7%)	13,768 (87.5%)	-0.02
Lab result number- Hemoglobin mean (only >0 included)	897	876	629	508	N/A	N/A	1,526	1,384	
...mean (sd)	14.17 (1.61)	14.23 (1.56)	1,097.16 (12,155.32)	13.93 (1.54)	N/A	N/A	460.57 (7805.42)	14.12 (1.55)	0.08
...median [IQR]	14.20 [13.10, 15.30]	14.30 [13.20, 15.26]	13.95 [12.80, 15.00]	14.00 [13.00, 15.00]	N/A	N/A	#VALUE!	14.19 (1.55)	#VALUE!
...Missing; n (%)	2,419 (72.9%)	2,440 (73.6%)	11,786 (94.9%)	11,907 (95.9%)	N/A	N/A	14,205 (90.3%)	14,347 (91.2%)	-0.03
Lab result number- Serum sodium mean (only >90 and <190 included)	1,350	1,348	929	787	N/A	N/A	2,279	2,135	
...mean (sd)	139.04 (2.65)	139.22 (2.47)	138.78 (2.67)	138.83 (2.36)	N/A	N/A	138.93 (2.66)	139.08 (2.43)	-0.06
...median [IQR]	139.00 [137.00, 141.00]	139.00 [138.00, 141.00]	139.00 [137.00, 140.50]	139.00 [137.00, 140.25]	N/A	N/A	139.00 (2.66)	139.00 (2.43)	0.00
...Missing; n (%)	1,966 (59.3%)	1,968 (59.3%)	11,486 (92.5%)	11,628 (93.7%)	N/A	N/A	13,452 (85.5%)	13,596 (86.4%)	-0.03
Lab result number- Albumin mean (only >0 and <=10 included)	1,299	1,279	786	678	N/A	N/A	2,085	1,957	
...mean (sd)	4.33 (0.30)	4.34 (0.30)	4.18 (0.44)	4.20 (0.40)	N/A	N/A	4.27 (0.36)	4.29 (0.34)	-0.06
...median [IQR]	4.30 [4.15, 4.50]	4.35 [4.20, 4.55]	4.20 [4.00, 4.40]	4.20 [4.00, 4.45]	N/A	N/A	4.26 (0.36)	4.30 (0.34)	-0.11
...Missing; n (%)	2,017 (60.8%)	2,037 (61.4%)	11,629 (93.7%)	11,737 (94.5%)	N/A	N/A	13,646 (86.7%)	13,774 (87.6%)	-0.03
Lab result number- Glucose (fasting or random) mean (only 10-1000 included)	1,348	1,350	938	790	N/A	N/A	2,286	2,140	
...mean (sd)	184.77 (72.64)	176.69 (65.63)	184.89 (75.51)	178.63 (66.52)	N/A	N/A	184.82 (73.85)	177.41 (65.98)	0.11
...median [IQR]	168.75 [131.00, 221.00]	160.58 [132.00, 209.00]	167.00 [134.00, 218.00]	164.00 [133.88, 212.00]	N/A	N/A	168.03 (73.85)	161.84 (65.98)	0.09
...Missing; n (%)	1,968 (59.3%)	1,966 (59.3%)	11,477 (92.4%)	11,625 (93.6%)	N/A	N/A	13,445 (85.5%)	13,591 (86.4%)	-0.03
Lab result number- Potassium mean (only 1-7 included)	1,368	1,369	886	720	N/A	N/A	2,254	2,089	
...mean (sd)	4.44 (0.39)	4.42 (0.39)	4.33 (0.43)	4.29 (0.42)	N/A	N/A	4.40 (0.41)	4.38 (0.40)	0.05
...median [IQR]	4.40 [4.20, 4.70]	4.40 [4.20, 4.65]	4.30 [4.00, 4.60]	4.30 [4.00, 4.50]	N/A	N/A	4.36 (0.41)	4.37 (0.40)	-0.02
...Missing; n (%)	1,948 (58.7%)	1,947 (58.7%)	11,529 (92.9%)	11,695 (94.2%)	N/A	N/A	13,477 (85.7%)	13,642 (86.7%)	-0.03
Comorbidity Scores									
CCI (180 days)- ICD9 and ICD10 v2									
...mean (sd)	1.69 (1.30)	1.71 (1.29)	1.49 (1.10)	1.51 (1.10)	2.11 (1.41)	2.10 (1.41)	1.74 (1.25)	1.75 (1.25)	-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, 3.00]	2.00 [1.00, 3.00]	1.37 (1.25)	1.37 (1.25)	0.00
Frailty Score: Qualitative Version 365 days as Categories, v1									
...0; n (%)	1,875 (56.5%)	1,788 (53.9%)	7,443 (60.0%)	7,280 (58.6%)	5,602 (61.1%)	5,623 (61.4%)	14,920 (59.9%)	14,691 (59.0%)	0.02
...1 to 2; n (%)	1,063 (32.1%)	1,151 (34.7%)	3,907 (31.5%)	4,036 (32.5%)	2,368 (25.8%)	2,382 (26.0%)	7,338 (29.5%)	7,569 (30.4%)	-0.02
...3 or more; n (%)	378 (11.4%)	377 (11.4%)	1,065 (8.6%)	1,099 (8.9%)	1,194 (13.0%)	1,159 (12.6%)	2,637 (10.6%)	2,635 (10.6%)	0.00
Frailty Score: Empirical Version 365 days as Categories, v3									
...<0.12908; n (%)	1,208 (36.4%)	1,152 (34.7%)	4,498 (36.2%)	4,477 (36.1%)	1,848 (20.2%)	1,794 (19.6%)	7,554 (30.3%)	7,423 (29.8%)	0.01
...0.12908 - 0.1631167; n (%)	1,121 (33.8%)	1,199 (36.2%)	4,449 (35.8%)	4,461 (35.9%)	2,986 (32.6%)	3,028 (33.0%)	8,556 (34.4%)	8,688 (34.9%)	-0.01
...>=0.1631167; n (%)	987 (29.8%)	963 (29.1%)	3,468 (27.9%)	3,477 (28.0%)	4,330 (47.3%)	4,342 (47.4%)	8,785 (35.3%)	8,784 (35.3%)	0.00
Non-Frailty; n (%)	1,787 (53.9%)	1,739 (52.4%)	6,483 (52.2%)	6,469 (52.1%)	514 (5.6%)	381 (4.2%)	8,784 (35.3%)	8,589 (34.5%)	0.02
Frailty Score (mean): Qualitative Version 365 days, v1									
...mean (sd)	0.88 (1.38)	0.92 (1.38)	0.74 (1.17)	0.77 (1.20)	0.88 (1.49)	0.87 (1.45)	0.81 (1.32)	0.83 (1.32)	-0.02
...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]	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	0.00 (1.32)	0.00 (1.32)	0.00
Frailty Score (mean): Empirical Version 365 days, v2									
...mean (sd)	0.15 (0.04)	0.15 (0.04)	0.14 (0.04)	0.14 (0.04)	0.17 (0.05)	0.17 (0.05)	0.15 (0.04)	0.15 (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]	0.16 [0.13, 0.19]	0.16 [0.14, 0.19]	0.15 (0.04)	0.15 (0.04)	0.00
Healthcare Utilization									
Any hospitalization; n (%)	120 (3.6%)	132 (4.0%)	362 (2.9%)	380 (3.1%)	322 (3.5%)	313 (3.4%)	804 (3.2%)	825 (3.3%)	-0.01
Any hospitalization within prior 30 days; n (%)	27 (0.8%)	23 (0.7%)	38 (0.3%)	52 (0.4%)	44 (0.5%)	48 (0.5%)	109 (0.4%)	123 (0.5%)	-0.01
Any hospitalization during prior 31-180 days; n (%)	95 (2.9%)	111 (3.3%)	325 (2.6%)	334 (2.7%)	281 (3.1%)	273 (3.0%)	701 (2.8%)	718 (2.9%)	-0.01
Endocrinologist Visit; n (%)	586 (17.7%)	605 (18.2%)	1,792 (14.4%)	1,866 (15.0%)	1,429 (15.6%)	1,435 (15.7%)	3,807 (15.3%)	3,906 (15.7%)	-0.01
Endocrinologist Visit (30 days prior); n (%)	433 (13.1%)	449 (13.5%)	1,363 (11.0%)	1,398 (11.3%)	943 (10.3%)	951 (10.4%)	2,739 (11.0%)	2,798 (11.2%)	-0.01
Endocrinologist Visit (31 to 180 days prior); n (%)	413 (12.5%)	416 (12.5%)	1,163 (9.4%)	1,207 (9.7%)	1,107 (12.1%)	1,100 (12.0%)	2,683 (10.8%)	2,723 (10.9%)	0.00
Internal medicine/family medicine visits; n (%)	1,971 (59.4%)	1,968 (59.3%)	10,936 (88.1%)	10,932 (88.1%)	7,411 (80.9%)	7,303 (79.7%)	20,318 (81.6%)	20,203 (81.2%)	0.01
Internal medicine/family medicine visits (30 days prior) v2; n (%)	1,303 (39.3%)	1,325 (40.0%)	8,395 (67.6%)	8,318 (67.0%)	5,254 (57.3%)	5,160 (56.3%)	14,952 (60.1%)	14,803 (59.5%)	0.01
Internal medicine/family medicine visits (31 to 180 days prior) v2; n (%)	1,618 (48.8%)	1,643 (49.5%)	8,990 (72.4%)	8,967 (72.2%)	6,447 (70.4%)	6,396 (69.8%)	17,055 (68.5%)	17,006 (68.3%)	0.00
Cardiologist visit; n (%)	722 (21.8%)	707 (21.3%)	2,377 (19.1%)	2,316 (18.7%)	2,283 (24.9%)	2,279 (24.9%)	5,382 (21.6%)	5,302 (21.3%)	0.01
Number of Cardiologist visits (30 days prior); n (%)	268 (8.1%)	243 (7.3%)	708 (5.7%)	698 (5.6%)	680 (7.4%)	687 (7.5%)	1,656 (6.7%)	1,628 (6.5%)	0.01

Table 1

Number of Cardiologist visits (31 to 180 days prior): n (%)	593 (17.9%)	591 (17.8%)	2,013 (16.2%)	1,958 (15.8%)	1,972 (21.5%)	1,989 (21.7%)	4,578 (18.4%)	4,538 (18.2%)	0.01
Electrocardiogram v2: n (%)	792 (23.9%)	780 (23.5%)	3,120 (25.1%)	3,010 (24.2%)	2,420 (26.4%)	2,441 (26.6%)	6,332 (25.4%)	6,231 (25.0%)	0.01
Use of glucose test strips; n (%)	134 (4.0%)	128 (3.9%)	476 (3.8%)	472 (3.8%)	214 (2.3%)	227 (2.5%)	824 (3.3%)	827 (3.3%)	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 Copy; n (%)	396 (11.9%)	368 (11.1%)	1,573 (12.7%)	1,609 (13.0%)	864 (9.4%)	877 (9.6%)	2,833 (11.4%)	2,854 (11.5%)	0.00
N antidiabetic drugs at index date v3 Copy									
...mean (sd)	2.19 (0.83)	2.20 (0.87)	2.21 (0.79)	2.22 (0.83)	2.31 (0.77)	2.32 (0.86)	2.24 (0.79)	2.25 (0.85)	-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 (0.79)	2.00 (0.85)	0.00
number of different/distinct medication prescriptions									
...mean (sd)	9.40 (4.76)	9.51 (4.66)	9.50 (4.58)	9.50 (4.46)	9.75 (4.27)	9.75 (4.29)	9.58 (4.49)	9.59 (4.43)	0.00
...median [IQR]	9.00 [6.00, 12.00]	9.00 [6.00, 12.00]	9.00 [6.00, 12.00]	9.00 [6.00, 12.00]	9.00 [7.00, 12.00]	9.00 [7.00, 12.00]	9.00 (4.49)	9.00 (4.43)	0.00
Number of Hospitalizations									
...mean (sd)	0.04 (0.21)	0.04 (0.22)	0.03 (0.19)	0.03 (0.20)	0.04 (0.23)	0.04 (0.23)	0.04 (0.21)	0.04 (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 hospital days									
...mean (sd)	0.18 (1.23)	0.19 (1.14)	0.16 (1.37)	0.15 (1.15)	0.23 (1.63)	0.21 (1.63)	0.19 (1.45)	0.18 (1.35)	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 (1.45)	0.00 (1.35)	0.00
Number of Emergency Department (ED) visits v3									
...mean (sd)	0.20 (0.68)	0.20 (0.73)	0.05 (0.57)	0.06 (0.67)	0.28 (0.87)	0.28 (0.94)	0.15 (0.71)	0.16 (0.79)	-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 (0.71)	0.00 (0.79)	0.00
Number of Office visits									
...mean (sd)	4.33 (3.62)	4.31 (3.24)	4.27 (3.24)	4.27 (3.21)	4.98 (3.66)	4.96 (3.55)	4.54 (3.45)	4.53 (3.34)	0.00
...median [IQR]	3.00 [2.00, 6.00]	3.00 [2.00, 6.00]	3.00 [2.00, 6.00]	3.00 [2.00, 6.00]	4.00 [2.00, 7.00]	4.00 [2.00, 7.00]	3.37 (3.45)	3.37 (3.34)	0.00
Number of Endocrinologist visits									
...mean (sd)	0.92 (3.08)	1.02 (3.47)	0.67 (2.55)	0.79 (3.02)	0.90 (3.58)	1.02 (4.01)	0.79 (3.04)	0.91 (3.47)	-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 (3.04)	0.00 (3.47)	0.00
Number of internal medicine/family medicine visits									
...mean (sd)	3.03 (9.27)	4.85 (8.11)	6.75 (7.93)	6.68 (7.61)	7.04 (9.32)	7.19 (10.03)	6.63 (8.65)	6.62 (8.64)	0.00
...median [IQR]	2.00 [0.00, 7.00]	2.00 [0.00, 7.00]	5.00 [2.00, 9.00]	5.00 [2.00, 9.00]	4.00 [1.00, 9.00]	4.00 [1.00, 10.00]	4.23 (8.65)	4.23 (8.64)	0.00
Number of Cardiologist visits									
...mean (sd)	0.96 (2.96)	0.97 (2.94)	0.75 (2.40)	0.71 (2.17)	1.13 (3.38)	1.14 (3.20)	0.92 (2.87)	0.90 (2.70)	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 (2.87)	0.00 (2.70)	0.00
Number electrocardiograms received v2									
...mean (sd)	0.37 (0.87)	0.37 (0.94)	0.40 (0.94)	0.38 (0.90)	0.45 (0.98)	0.46 (1.03)	0.41 (0.95)	0.41 (0.96)	0.00
...median [IQR]	0.00 [0.00, 0.00]	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 (0.95)	0.00 (0.96)	0.00
Number of HbA1c tests ordered									
...mean (sd)	1.27 (0.86)	1.27 (0.85)	1.31 (0.86)	1.30 (0.80)	1.48 (0.85)	1.48 (0.81)	1.37 (0.86)	1.36 (0.81)	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]	1.00 [1.00, 2.00]	1.00 [1.00, 2.00]	1.00 (0.86)	1.00 (0.81)	0.00
Number of glucose tests ordered									
...mean (sd)	0.37 (0.91)	0.37 (0.96)	0.41 (1.25)	0.40 (1.07)	0.41 (0.94)	0.42 (0.98)	0.40 (1.10)	0.40 (1.02)	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 (1.10)	0.00 (1.02)	0.00
Number of lipid tests ordered									
...mean (sd)	1.05 (0.95)	1.05 (0.96)	1.10 (1.39)	1.09 (1.12)	1.08 (0.83)	1.07 (0.83)	1.09 (1.16)	1.08 (1.00)	0.01
...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 (1.16)	1.00 (1.00)	0.00
Number of creatinine tests ordered									
...mean (sd)	0.04 (0.25)	0.04 (0.28)	0.03 (0.23)	0.03 (0.22)	0.06 (0.30)	0.06 (0.32)	0.04 (0.26)	0.04 (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 (0.26)	0.00 (0.27)	0.00
Number of BUN tests ordered									
...mean (sd)	0.02 (0.19)	0.02 (0.17)	0.02 (0.18)	0.02 (0.16)	0.04 (0.24)	0.04 (0.24)	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 tests for microalbuminuria									
...mean (sd)	0.73 (1.06)	0.74 (1.11)	0.73 (1.08)	0.71 (1.08)	0.47 (0.68)	0.47 (0.68)	0.63 (0.95)	0.63 (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 (0.95)	0.00 (0.96)	0.00
Total N distinct ICD9/ICD10 diagnoses at the 3rd digit level Copy									
...mean (sd)	4.05 (5.92)	4.03 (6.10)	2.84 (3.82)	2.79 (3.90)	6.52 (6.78)	6.53 (6.84)	4.36 (5.37)	4.33 (5.46)	0.01
...median [IQR]	0.00 [0.00, 7.00]	0.00 [0.00, 6.00]	1.00 [0.00, 5.00]	0.00 [0.00, 5.00]	5.00 [0.00, 10.00]	5.00 [0.00, 10.00]	2.34 (5.37)	1.84 (5.46)	0.09
Use of thiazide; n (%)	322 (9.7%)	334 (10.1%)	1,229 (9.9%)	1,212 (9.8%)	1,152 (12.6%)	1,156 (12.6%)	2,703 (10.9%)	2,702 (10.9%)	0.00
Use of beta blockers; n (%)	1,034 (31.2%)	1,051 (31.7%)	4,049 (32.6%)	4,037 (32.5%)	3,834 (41.8%)	3,838 (41.9%)	8,917 (35.8%)	8,926 (35.9%)	0.00
Use of calcium channel blockers; n (%)	706 (21.3%)	721 (21.7%)	2,893 (23.3%)	2,917 (23.5%)	2,728 (29.8%)	2,685 (29.3%)	6,327 (25.4%)	6,323 (25.4%)	0.00