

Dabigatran versus Warfarin in Patients with Atrial Fibrillation (RELY trial)

DUPLICATE-RELY

May 26, 2021

NCT04593043

1. RCT Details

1.1 Title

Dabigatran versus Warfarin in Patients with Atrial Fibrillation ([RELY](#) trial)

1.2 Intended aim(s)

To compare the risk of stroke or systemic embolism in atrial fibrillation (AF) patients with dabigatran versus warfarin use.

1.3 Primary endpoint for replication

The primary outcome of the study was stroke and systemic embolism.

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

Assuming a 2-year recruitment period and at least 1 year of follow-up and a primary event rate of 1.6% per year, it was determined that at least 15,000 patients would be needed to achieve a minimum of 450 events. The study would have approximately 84% power to conclude noninferiority of dabigatran over warfarin at alpha of 0.025 (1-sided) level.

1.4 Secondary endpoint for replication (assay sensitivity) and RCT finding

Major bleeding; RR = 0.93 (95% CI 0.81-1.07)

1.5 Trial estimate

RR = 0.66 (95% CI 0.53-0.82) comparing 150mg dabigatran vs warfarin (Connolly et al., 2009)

2. Person responsible for implementation of replication in Aetion

Hemin Lee, MD, MPH and Ajinkya Pawar, PhD implemented the study design in the Aetion Evidence Platform. They are 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)

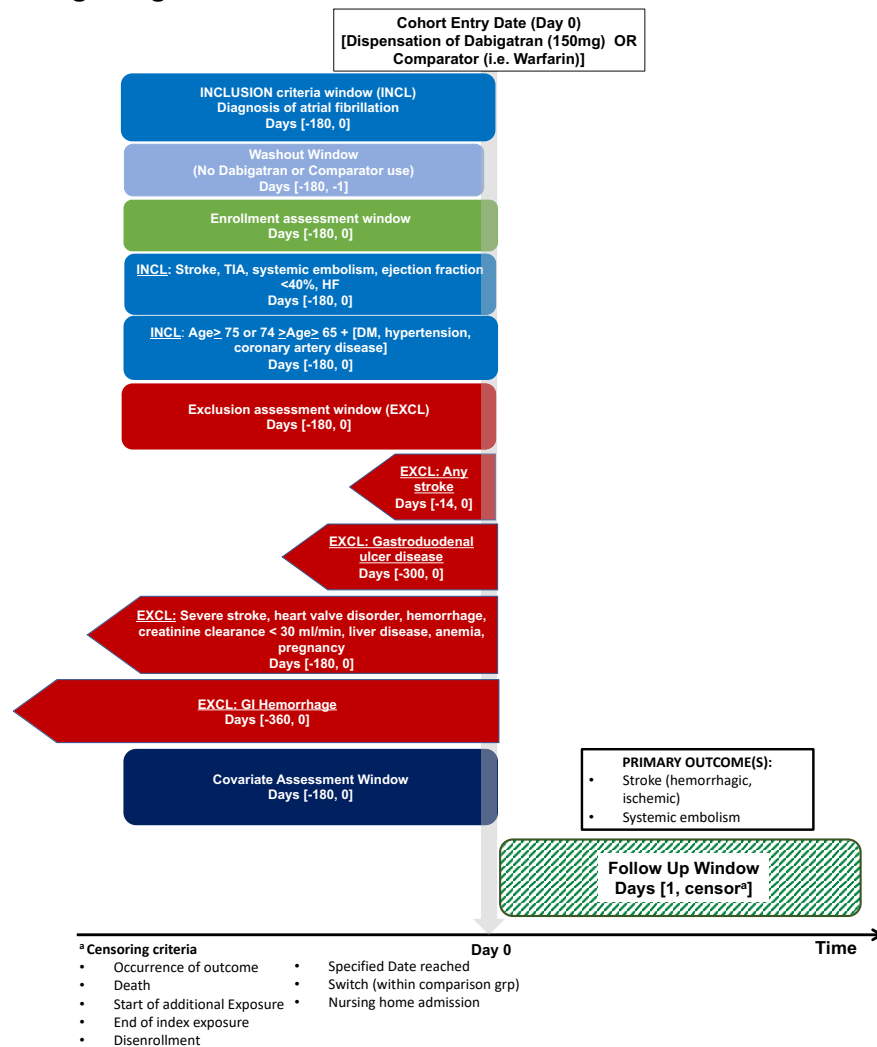
United/Optum, MarketScan, Medicare

4. Study Design Diagram

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

Figure 1.

Design Diagram – RE-LY TRIAL REPLICATION



5. Cohort Identification

5.1 Cohort Summary

This study will involve a new user, parallel group, propensity score-matched, retrospective cohort study design comparing dabigatran (150mg) to warfarin users. The patients will be required to have continuous enrollment during a baseline period of 180 days before initiation of dabigatran or warfarin (index date). We will restrict the analyses to patients with a diagnosis of AF with risk factors for stroke or systemic embolism in the 12 months prior to drug initiation.

5.2 Important steps for cohort formation

New users (defined as no use in 180 days prior to index date) of an exposure and a comparator drug will be identified.

5.2.1 Eligible cohort entry dates

Market availability of dabigatran in the U.S. for non-valvular atrial fibrillation started on October 19, 2010

- For Medicare: October 19, 2010 – December 31, 2017 (end of available data)
- For Marketscan: October 19, 2010 – December 31, 2018 (end of available data)
- For Optum: October 19, 2010 – December 31, 2019 (end of available data)

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 dabigatran 150mg vs. warfarin

	Optum		Truven		Medicare	
	Less Excluded Patients	Remaining Patients	Less Excluded Patients	Remaining Patients	Less Excluded Patients	Remaining Patients
All patients		77,673,639		200,203,908		6,886,908
Did not meet cohort entry criteria	76,847,731 ⁻	825,908	199,014,982 ⁻	1,188,926	-2,335,930	4,550,978

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

Excluded due to insufficient enrollment	-80,642	745,266	-107,905	1,081,021	-1,565,261	2,985,717
Excluded due to prior use of referent	-564,968	180,298	-751,832	329,189	-2,241,426	744,291
Excluded due to prior use of exposure	-44,640	135,658	-71,891	257,298	-196,688	547,603
Excluded because patient qualified in >1 exposure category	-5	135,653	-9	257,289	-24	547,579
Excluded based on Dabigatran (dose other than 150mg)	-306	135,347	-534	256,755	-2,557	545,022
Excluded based on Age	0	135,347	0	256,755	-162	544,860
Excluded based on Gender	0	135,347	0	256,755	0	544,860
Excluded based on Inclusion 1a or 1b or 1 c - Atrial fibrillation	-71,189	64,158	-135,349	121,406	-220,602	324,258
Excluded based on Inclusion 2a-2e History of Stroke, TIA, Systemic embolism / EF<40% / NYHA 2 or higher / Age >75 / Age 65+RF	-11,313	52,845	-17,737	103,669	-24,940	299,318
Excluded based on Inclusion 3 - Age >= 18	-1	52,844	-1	103,668	0	299,318
Excluded based on Exclusion 1 - History of heart valve disorders	-17,688	35,156	-5,687	97,981	-94,948	204,370
Excluded based on Exclusion 2a - Severe/disabling stroke	-576	34,580	-1,111	96,870	-3,090	201,280
Excluded based on Exclusion 2b - Any stroke	-960	33,620	-1,391	95,479	-3,948	197,332
Excluded based on Exclusion 3a - Major Surgery	-1,091	32,529	-2,526	92,953	-6,491	190,841
Excluded based on Exclusion 3c - Intracranial hemorrhage - Inpatient	-51	32,478	-331	92,622	-595	190,246
Excluded based on Exclusion 3d - Gastrointestinal hemorrhage	-4,848	27,630	-1,601	91,021	-5,353	184,893
Excluded based on Exclusion 3e - Symptomatic or endoscopically documented gastroduodenal ulcer disease	-121	27,509	-714	90,307	-3,148	181,745
Excluded based on Exclusion 3f - Hemorrhagic disorder or bleeding diathesis	-257	27,252	-756	89,551	-1,787	179,958
Excluded based on Exclusion 3i - Uncontrolled hypertension	-51	27,201	-400	89,151	-804	179,154

Excluded based on Exclusion 7 - Severe renal impairment	-1,301	25,900	-4,674	84,477	-12,016	167,138
Excluded based on Exclusion 8 & 9 - Active infective endocarditis and liver disease	-36	25,864	-255	84,222	-616	166,522
Excluded based on Exclusion 10 & 11 - Pregnancy & Anemia and Thrombocytopenia	-191	25,673	-1,229	82,993	-2,798	163,724
Excluded based on Exclusion 14 - Alcohol abuse or dependence	-28	25,645	-103	82,890	-138	163,586
Excluded based on Exclusion 14 - Drug abuse or dependence	-22	25,623	-47	82,843	-111	163,475
Excluded based on Exclusion 14 - CCI (180 days)	-7	25,616	-47	82,796	-1,939	161,536
Final cohort		25,616		82,796		161,536

* Medicare database includes all patients using a novel oral anticoagulant and a subset of patients using warfarin during 2011-2017.

6. Variables

6.1 Exposure-related variables:

Study drug:

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

Comparator agents-

- Initiators of dabigatran (150mg) will be compared to initiators of-
 - Warfarin

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**).

6.3 Outcome variables and study follow-up:

6.3.1 Outcome variables

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

- **Primary Outcome:** Stroke (hemorrhagic, ischemic) and systemic embolism
- **Secondary outcomes:** Individual components
 - Hospital admission for stroke (principal diagnosis position)
 - Hospital admission for systemic embolism (principal diagnosis position)

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

1. Major bleeding

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 apixaban 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 (dabigatran and comparator) plus a defined grace period (i.e., 10 days after the end of the last prescription's days' supply in main analyses).
- The date of augmentation or switching from exposure to comparator or vice versa or augmentation/switching to any other NOAC (e.g. switching from dabigatran or warfarin to apixaban 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
- Dispensing of a fibrinolytic agent

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

7. Initial Feasibility Analysis

Action report name:

For dabigatran vs. warfarin

Optum- <https://bwh-dope.action.com/projects/details/707/results/59579/result/0>

Marketscan- <https://bwh-dope.action.com/projects/details/708/results/59601/result/0>

Medicare- <https://bwh-dope.action.com/projects/details/709/results/59602/result/0>

Date conducted: 10/5/20 (Medicare 10/6/20)

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 study population
- Report median follow-up time by treatment group
- Report reasons for censoring in the overall study population

8. Initial Power Assessment

Action report name:

For dabigatran vs. warfarin

Optum- <https://bwh-dope.action.com/projects/details/707/results/53772/result/0>

Marketscan- <https://bwh-dope.action.com/projects/details/708/results/53771/result/0>

Medicare- <https://bwh-dope.action.com/projects/details/709/results/53770/result/0>

Date conducted: 05/11/2020

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

- Stop analyses until feasibility and power are reviewed by primary investigators and FDA. Reviewers evaluate the results of the analyses described above in Sections 7 and 8, including numbers of patients, patient characteristics, follow-up time, and reasons for censoring by treatment group, as well as overall rates of outcomes and study power. These parameters are re-evaluated and reported in the subsequent sections, after incorporating feedback and refining the protocol.
- 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:	6/3/20
Reviewed by FDA:	Ken Quinto	Date reviewed:	6/30/20
Reasons for stopping analysis (if required):			

9. Balance Assessment

Action report links:

Optum: <https://bwh-dope.action.com/projects/details/707/results/59580/result/0>

Marketscan: <https://bwh-dope.action.com/projects/details/708/results/59603/result/0>

Medicare: <https://bwh-dope.action.com/projects/details/709/results/59604/result/0>

Date conducted: 10/5/20 (Medicare 10/6/20)

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	657 (0.84%)	369 (0.94%)	288 (0.74%)
Start of an additional exposure	2,760 (3.53%)	1,189 (3.04%)	1,571 (4.02%)
End of index exposure	62,039 (79.39%)	31,190 (79.83%)	30,849 (78.96%)
Specified date reached (Dec 17/Dec 18/Dec 19)	2,483 (3.18%)	1,281 (3.28%)	1,202 (3.08%)
End of patient enrollment	4,128 (5.28%)	1,938 (4.96%)	2,190 (5.61%)
Switch to other NOACs (for censoring) + nursing home admission	6,073 (7.77%)	3,103 (7.94%)	2,970 (7.60%)

- Report follow-up time by treatment group.

Median Follow-Up Time (Days) [IQR]			
Patient Group	Optum	Truven	Medicare
Overall Patient Population	98 [38-191]	98 [38-193]	98 [38-202]

Referent	98 [43-192]	98 [43-178]	98 [42-196]
Exposure	98 [38-190]	98 [38-220]	98 [38-211]

- Report overall risk of the primary outcome.

	Optum	Marketscan	Medicare	Pooled
Risk per 1,000 patients	4.57	5.20	6.04	5.64

10. Final Power Assessment

Date conducted:

- Re-calculate power in the appropriate excel table, using the revised number of matched patients from the PS-match in Section 9. All other parameters in the table should be the same as in Section 8. If the study is to be implemented in more than one database, copy and paste excel sheet to report power for each database separately and for the pooled analysis that uses data from all databases together. Power calculations are based on the formulas from Chow et al. (2008).
 - For dabigatran 150mg vs. warfarin
 - Pooled

Superiority Analysis		Non-inferiority Analysis	
Number of patients matched	78,140	Number of patients matched	78,140
Reference	39,070	Reference	39,070
Exposed	39,070	Exposed	39,070
Risk per 1,000 patients	5.64	Risk per 1,000 patients	5.64
Desired HR from RCT	0.66	Assumed HR from RCT	1
Alpha (2-sided)	0.05	Alpha (2-sided)	0.05
		Non-inferiority margin	1.46
Number of events expected	440.7096	Number of events expected	440.7096
Power	0.991836251	Power	0.977906369

○ Optum

Superiority Analysis		Non-inferiority Analysis	
Number of patients matched	5,580	Number of patients matched	5,580
Reference	2,790	Reference	2,790
Exposed	2,790	Exposed	2,790
Risk per 1,000 patients	4.57	Risk per 1,000 patients	4.57
Desired HR from RCT	0.66	Assumed HR from RCT	1
Alpha (2-sided)	0.05	Alpha (2-sided)	0.05
		Non-inferiority margin	1.46
Number of events expected	25.5006	Number of events expected	25.5006
Power	0.182503488	Power	0.157581463

○ MarketScan

Superiority Analysis		Non-inferiority Analysis	
Number of patients matched	27,920	Number of patients matched	27,920
Reference	13,960	Reference	13,960
Exposed	13,960	Exposed	13,960
Risk per 1,000 patients	5.20	Risk per 1,000 patients	5.20
Desired HR from RCT	0.66	Assumed HR from RCT	1
Alpha (2-sided)	0.05	Alpha (2-sided)	0.05
		Non-inferiority margin	1.46
Number of events expected	145.184	Number of events expected	145.184
Power	0.70656205	Power	0.625504572

○ Medicare

Superiority Analysis		Non-inferiority Analysis	
Number of patients matched	44,640	Number of patients matched	44,640
Reference	22,320	Reference	22,320
Exposed	22,320	Exposed	22,320
Risk per 1,000 patients	6.04	Risk per 1,000 patients	6.04
Desired HR from RCT	0.66	Assumed HR from RCT	1
Alpha (2-sided)	0.05	Alpha (2-sided)	0.05
		Non-inferiority margin	1.46
Number of events expected	269.6256	Number of events expected	269.6256
Power	0.926676361	Power	0.874319968

- Stop analyses until balance and final power assessment are reviewed by primary investigators, FDA, and assigned members of advisory board.

Reviewed by PI:	Jessica Franklin	Date reviewed:	9/8/20
Reviewed by FDA:	Ken Quinto	Date reviewed:	9/29/20
Reasons for stopping analysis (if required):			

11. Study Confidence and Concerns

Deadline for voting on study confidence and listing concerns:

Date votes and concerns are summarized:

- 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.
- After the deadline for voting has passed, provide the distribution of responses and summarize all concerns here.

12. Register study protocol on clinicalTrials.gov

Date conducted:

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

13. Comparative Analyses

Action report name:

Date conducted:

13.1 For primary analysis:

13.2 For sensitivity analyses:

14. Requested Results

14.1 Table 1: Baseline characteristics before and after adjustment

Variable	Before adjustment			After adjustment		
	Referent	Exposure	Std. diff.	Referent	Exposure	Std. diff.
Number of patients			-			-
Age categories						
...						

14.2 Table 2: Follow-up time

Patient Group	Median Follow-Up Time (Days) [IQR]
Overall Patient Population	
Referent	
Exposure	

14.3 Table 3: Censoring events

	Overall	Referent	Exposure
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Outcome			
Death			
Start of an additional exposure			
End of index exposure			
Specified date reached			
End of patient data			
End of patient enrollment			
...			

14.4 Table 4: Results from primary analyses;

Analysis	No. exposed events	No. referent events	Exposed rate	Referent rate	HR (95% CI)
Crude					
Analysis 1					
Analysis 2					
...					

HR, Hazard Ratio; CI, Confidence Interval.

14.5 Table 5: Results from secondary analyses;

15. References

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

Connolly SJ, Ezekowitz MD, Yusuf S, et al. Dabigatran versus warfarin in patients with atrial fibrillation. *N Engl J Med*. 2009; 361:1139-51.

Appendix A

#	RE-LY trial definitions	Implementation in routine care	References/Rationale	Color coding
	Trial details- Primary approval; Unintended S with label change		Please see the following Google Drive for further details or any missing information: https://drive.google.com/open?id=1WD618wrywTJEaXrftTcuK-VCcn6b-jv	Criteria
	EXPOSURE vs. COMPARISON		ICD-10 codes are not listed in this document because of excel cell size limitations and excessive number of ICD-10 codes. Full ICD-10 code lists will be available in the above Google Drive Folder (link above). ICD-9 to ICD-10 code conversions were completed using a SAS macro that implements forward/ backward mapping based on the CMS ICD-9 to ICD-10 mapping: https://www.nber.org/data/icd9-icd10-cm-and-pcs-crosswalk-general-equivalence-mapping.html	Adequate mapping in claims
	Fixed doses of dabigatran (110 mg or 150 mg twice daily) vs. adjusted-dose warfarin	Dabigatran (110mg or 150mg twice daily) vs adjusted-dose warfarin		Intermediate mapping in claims
	PRIMARY OUTCOME			Poor mapping or cannot be measured in claims
	The primary outcome is a composite of stroke (including hemorrhagic) and systemic embolism event	<p>Measured 1 day after drug initiation in diagnosis position and care setting specified below.</p> <p>For stroke: Primary diagnosis position in inpatient care setting 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</p> <p>Systemic embolism (Arterial embolism and thrombosis): Primary diagnosis position in inpatient care setting ICD-9: 444.xx ICD-10: I74.x</p>	<p>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, Mitchell E, Gideon PS, Varas-Lorenzo C, Castellsague J, Griffin MR. Validation of ICD-9 codes with a high positive predictive value for incident strokes resulting in hospitalization using Medicaid health data. Pharmacoepidemiology and drug safety 2008;17:20-6.]</p>	Can't be measured in claims but not important for the analysis
	INCLUSION CRITERIA			
	1 AF documented as follows: (1a or 1b or 1c)			
	1a • There is ECG documented AF on the day of screening or randomization	<p>Measured 4 weeks prior to and including day of drug initiation in any diagnosis position and any care setting</p> <p>Atrial fibrillation ICD-9 diagnosis: 427.31 ICD-10 diagnosis: I48.0x, I48.1x, I48.2x, I48.9x</p>		
	1b • The patient has had a symptomatic episode of paroxysmal or persistent AF documented by 12-lead ECG within 6 m before randomization	<p>Measured 12 months prior to and including day of drug initiation in any diagnosis position and inpatient or outpatient care setting</p> <p>Atrial fibrillation ICD-9 diagnosis: 427.31 ICD-10 diagnosis: I48.0x, I48.1x, I48.2x, I48.9x</p>		
	1c • There is documentation of symptomatic or asymptomatic paroxysmal or persistent AF on 2 separate occasions, at least 1 day apart, one of which is within 6 m before randomization. In this case, AF may be documented by 12 lead ECG, rhythm strip, pacemaker/ICD electrogram, or Holter ECG. The duration of AF should be at least 30 s. Electrograms (not marker channels or mode switch episodes) from pacemakers and defibrillators can be used to document only 1 episode of paroxysmal or persistent AF	<p>>2 Diagnoses separated by 1 day to 30 days, measured 12 months prior to and including day of drug initiation in any diagnosis position and inpatient or outpatient care setting</p> <p>Atrial fibrillation ICD-9 diagnosis: 427.31 ICD-10 diagnosis: I48.0x, I48.1x, I48.2x, I48.9x</p>		
	2 In addition to documented AF, patients must have one of the following: (2a or 2b or 2c or 2d or 2e)			
	2a • History of previous stroke, TIA, or systemic embolism	<p>Measured any time prior to and including day of drug initiation in any diagnosis position and inpatient care setting</p> <p>Any stroke ICD-9 diagnosis: 430.xx, 431.xx, 433.xx, 434.xx, 436.xx</p> <p>Systemic embolism ICD-9 diagnosis: 444.xx (arterial embolism) ICD-10 diagnosis: I74.x arterial embolism and thrombosis</p> <p>TIA ICD-9 diagnosis: 435.xx (Transient cerebral ischemia)</p>		
	2b • Ejection fraction <40% documented by echocardiogram, radionuclide or contrast angiogram in the last 6 m	<p>Measured 180 days prior to and including day of drug initiation in any diagnosis position and inpatient care setting</p> <p>Heart failure, systolic ICD-9 diagnosis: 428.2x, 428.4x ICD-10 diagnosis: I50.2x, I50.4x</p>		
	2c • Symptomatic heart failure, New York Heart Association class 2 or higher in the last 6 m	<p>Measured 180 days prior to and including day of drug initiation in any diagnosis position and inpatient care setting</p> <p>Congestive heart failure 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 ICD-10 diagnosis: I50.1, I50.2x, I50.3x, I50.4x, I50.8x, I50.9, I09.81, I11.0, I13.0, I13.2</p>		
	2d • Age ≥75 y	<p>Measured on the day of drug initiation</p> <p>Age ≥75</p>		

Appendix A

2e	• Age ≥65 y and one of the following:	Measured on the day of drug initiation Age ≥65 +	
	– Diabetes mellitus on treatment	Measured any time prior to and including day of drug initiation in any diagnosis position and inpatient or outpatient care setting Diabetes mellitus ICD-9 diagnosis: 250.x1, 250.x3, 250.x0, 250.x2 ICD-10 diagnosis: E10.x, E11.x AND At least one of the following drug prescriptions from 0 to 30 days after diagnosis*: Bolus Insulin: Insulin human regular, Insulin Aspart, Insulin Glulisine, Insulin Lispro, Insulin Aspart/Insulin Aspart Protamine, Insulin Lispro/Insulin Lispro Protamine, insulin.pork purified Basal Insulin: Insulin human isophane (NPH), Insulin human regular/ Insulin human isophane (NPH), Insulin Detemir, Insulin Glargine, Insulin Degludec, Insulin zinc human rec, Insulin zinc extend human rec, Insulin nph human recom/insulin regular human rec, Insulin zinc human rec, Insulin nph human recom/insulin regular human rec Metformin DDP4 inhibitors : Alogliptin, Linagliptin, Saxagliptin, Sitagliptin Sulfonylureas Acetohexamide, Chlorpropamide, tolazamide, tolbutamide, Glipizide, Glyburide, Glimepiride Meglitinide derivatives Repaglinide, Nateglinide Alpha-glucosidase inhibitors Acarbose, Miglitol Thiazolidinediones (TZDs) Rosiglitazone, Pioglitazone Glucagonlike peptide–1 (GLP-1) agonists Exenatide, Liraglutide, Lixisenatide, Albiglutide, Dulaglutide, semaglutide SGLT2 inhibitors Canagliflozin, Dapagliflozin, Empagliflozin, Ertugliflozin Pramlintide Pramlintide	
	– Documented coronary artery disease (any of: prior myocardial infarction, positive stress test, positive nuclear perfusion study, prior CABG surgery or PCI, angiogram showing ≥75% stenosis in a major coronary artery)	Measured any time prior to and including day of drug initiation in diagnosis position and care setting specified below: Acute MI (inpatient, any position): ICD-9 diagnosis: 410.xx Old MI (inpatient, any position): ICD-9 diagnosis: 412.xx Angina pectoris (inpatient, any position): ICD-9 diagnosis: 413.x Unstable angina (inpatient, any position): ICD-9 diagnosis: 411.x ICD-10 diagnosis: I24.1x, I20.0x, I25.1x, I25.7x, I24.0x, I24.8x, I24.9x -OR- CABG (inpatient, any position): CPT-4: 33510 – 33536, 33545, 33572 ICD-9 procedure: 36.1x, 36.2x -OR- -OR- Coronary revascularization (PTCA, stenting) (inpatient, any position): CPT-4: 92973, 92982, 92984, 92995, 92996, 92920 – 92921, 92924 – 92925, 92937, 92938, 92941, 92943, 92944 ICD-9 procedure: 00.66, 36.01, 36.02, 36.03, 36.05, 36.09 ICD-10 procedure: Coronary bypass in Coronary Revascularization sheet -OR- Stenting: Stenting in Coronary Revascularization sheet -OR- Transmyocardial revascularization: CPT-4: 33140, 33141 OR - Inpatient ICD-9 procedure: 36.31-36.34 ICD-10: 021K0Z5, 021K4Z5, 021L0Z5, 021L4Z5, 02QA3ZZ, 02QA4ZZ, 02QB3ZZ, 02QB4ZZ, 02QC3ZZ, 02QC4ZZ	
	– Hypertension requiring medical treatment	Measured any time prior to and including day of drug initiation** in any diagnosis position and inpatient or outpatient care setting Hypertension ICD-9 diagnosis: 401.x – 405.x AND At least one drug prescriptions from 0 to 14 days after diagnosis*: ACE inhibitor Benazepril, captopril, enalapril, fosinopril, lisinopril, moexipril, perindopril, quinapril, ramipril, trandolapril ARB Azilsartan, candesartan, eprosartan, irbesartan, losartan, olmesartan, telmisartan, valsartan Beta blocker Acebutolol, atenolol, betaxolol, bisoprolol, carteolol, carvedilol, esmolol, labetalol, metoprolol tartrate, metoprolol succinate, propranolol, penbutolol, pindolol, nadolol, nebivolol, sotalol, timolol Calcium channel blocker Diltiazem, mibefradil, verapamil, amlodipine, clevidipine, bepridil, felodipine, isradipine, nicardipine, nifedipine, nimodipine, nisoldipine Other hypertension drugs Doxazosin, eplerenone, prazosin, terazosin, clonidine, guanabenz, guanadrel, guanethidine, guanfacine, hydralazine, methyl dopa, metyrosine, reserpine, minoxidil, aliskiren, apraclonidine	
3	Age >18 y at entry	Measured on the day of drug initiation Age >18	
4	Written, informed consent	N/A	
EXCLUSION CRITERIA			

Appendix A

1	History of heart valve disorders (ie, prosthetic valve or hemodynamically relevant valve disease)	<p>Measured anytime prior to and including day of drug initiation in any diagnosis position and inpatient care setting</p> <p>394.x (diseases of mitral valve), 395.x (diseases of aortic valve), 396.x (diseases of mitral and aortic valve)</p> <p>397.x (diseases of other endocardial structures), 398.9x (other and unspecified rheumatic heart diseases)</p> <p>V42.2 (heart valve replaced by transplant), V43.3 (heart valve replaced by a mechanical device/prosthesis)</p> <p>-OR-</p> <p>ICD-9 procedure code 35.1x (open heart valvuloplasty without replacement), 35.2x (replacement of heart valve)</p> <p>-OR- one of the following CPT codes:</p> <p>33660-33665 (atrioventricular valve repair)</p> <p>33400-33403 (aortic valve valvuloplasty)</p> <p>33405 (Replacement, aortic valve, with cardiopulmonary bypass; with prosthetic valve other than homograft or stentless valve)</p> <p>33420-33430 (mitral valve repair/valvuloplasty/replacement)</p> <p>33460 (valvectomy, tricuspid valve, with cardiopulmonary bypass)</p> <p>33463-33468 (tricuspid valve repair/valvuloplasty/replacement)</p> <p>33475 (replacement, pulmonary valve)</p> <p>33496 (prosthetic valve dysfunction repair)</p> <p>0257T (implantation of catheter-delivered prosthetic aortic heart valve; open thoracic approach)</p> <p>0258T (transthoracic cardiac exposure for catheter-delivered aortic valve replacement;without cardiopulmonary bypass)</p> <p>0259T (transthoracic cardiac exposure for catheter-delivered aortic valve replacement;with cardiopulmonary bypass)</p> <p>0262T (implantation of catheter-delivered prosthetic pulmonary valve, endovascular approach)</p>	
2	Severe, disabling stroke within the previous 6 months or Any stroke within the previous 14 days	<p>1) <u>Disabling stroke effects</u></p> <p>Measured 180 days prior to and including day of drug initiation in any diagnosis position and inpatient or outpatient care setting</p> <p>ICD-9 diagnosis: 438.xx (Late effects of cerebrovascular disease)</p> <p>ICD-10 diagnosis: I69 (Sequelae of cerebrovascular disease (hemiplegia etc))</p> <p>ICD10 diagnosis: Z73.6 (Limitation of activities due to disability)</p> <p>-OR-</p> <p>2) <u>Any stroke</u></p> <p>Measured 14 days prior to and including day of drug initiation in primary diagnosis position and inpatient care setting</p> <p>ICD-9 diagnosis: 430.xx, 431.xx, 433.xx, 434.xx, 436.xx</p>	
3	Conditions associated with an increased risk of bleeding:		
3a	Major surgery in the previous month	<p>Measured 30 days prior to and including day of drug initiation in any procedure position and inpatient or outpatient care setting-</p> <p>ICD-9 procedure codes:</p> <p>Major surgery selected from codes range 34.x- 84.x</p> <p>30-34 Operations On The Respiratory System</p> <p>35-39 Operations On The Cardiovascular System</p> <p>40-41 Operations On The Hemic And Lymphatic System</p> <p>42-54 Operations On The Digestive System</p> <p>55-59 Operations On The Urinary System</p> <p>60-64 Operations On The Male Genital Organs</p> <p>65-71 Operations On The Female Genital Organs</p> <p>72-75 Obstetrical Procedures</p> <p>76-84 Operations On The Musculoskeletal System</p>	
3b	Planned surgery or intervention in the next 3 m	N/A	
3c	History of intracranial, intraocular, spinal, retroperitoneal or atraumatic intra-articular bleeding	<p>Measured anytime prior to and including day of drug initiation in any diagnosis position and inpatient care setting</p> <p><u>Intracranial hemorrhage:</u></p> <p>ICD-9: 430.x, 431.x, 432.x</p> <p><u>Intraocular hemorrhage:</u></p> <p>379.23 vitreous hemorrhage,</p> <p>H43.1x</p> <p>362.81 retinal hemorrhage</p> <p>H35.6x</p>	

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3d	Gastrointestinal hemorrhage within the past year	<p>Measured 365 days prior to and including day of drug initiation in any diagnosis position and inpatient or outpatient care setting:</p> <p>ICD-9 diagnosis: 578.x Gastrointestinal hemorrhage</p> <p>ICD-10 diagnosis: K92.2 : Gastrointestinal hemorrhage, unspecified acute hemorrhagic gastritis (K29.01) peptic ulcer with hemorrhage (K25.x - excluding K25.9 - K26.x - excluding K26.9 - K27.x-K28.x) gastritis and duodenitis with hemorrhage (K29.x) diverticular disease with hemorrhage (K57.x) angiodysplasia of stomach with hemorrhage (K31.811)</p> <p>CPT/HCPCS: 0W3P8ZZ - (ICD10) Control Bleeding in Gastrointestinal Tract, Via Natural or Artificial Opening Endoscopic 43255 - (HCPCS) Esophagogastroduodenoscopy, flexible, transoral; with control of bleeding, any method / Upper gastrointestinal endoscopy including esophagus, stomach, and either the duodenum and/or jejunum as appropriate; with control of bleeding, any method 44.43 - (ICD9) ENDOSCOPIC CONTROL OF GASTRIC OR DUODENAL BLEEDING</p>	
3e	Symptomatic or endoscopically documented gastroduodenal ulcer disease in the previous 30 days	<p>Measured 30 days prior to and including day of drug initiation in any diagnosis position and inpatient or outpatient care setting:</p> <p>ICD-9 diagnosis: Disease of esophagus: 530.1x-530.4x, 530.8x, 530.9x Gastric ulcer: 531.x Duodenal ulcer: 532.x Peptic ulcer: 533.x Acute gastritis: 535.0x Other specified gastritis: 535.4x Unspecified gastritis and gastroduodenitis: 535.5x Duodenitis: 535.6x</p> <p>ICD-10 diagnosis: Peptic ulcer, site unspecified K27.x K25.9 - Gastric ulcer, unspecified as acute or chronic, without hemorrhage or perforation K26.9 Duodenal ulcer, unspecified as acute or chronic, without hemorrhage or perforation</p>	
3f	Hemorrhagic disorder or bleeding diathesis	<p>Measured 180 days prior to and including day of drug initiation in any diagnosis position and inpatient or outpatient care setting</p> <p>Bleeding diathesis: ICD-9 diagnosis: 286.x Coagulation defects 287.x Purpura and other hemorrhagic conditions</p> <p>ICD-10 diagnosis: D65.x Disseminated intravascular coagulation [defibrination syndrome] D66.x Hereditary factor VIII deficiency D67.x Hereditary factor IX deficiency D68.x Other coagulation defects D69.x Purpura and other hemorrhagic conditions</p>	
3g	Need for anticoagulant treatment of disorders other than Atrial fibrillation	N/A	
3h	Fibrinolytic agents within 48 h of study entry	<p>We will censor the patients upon initiating these drugs after cohort entry:</p> <p>Fibrinolytic agent: Alteplase, reteplase, tenecteplase, streptokinase, urkinase</p>	
3i	Uncontrolled hypertension (systolic blood pressure >180 mm Hg and/ or diastolic blood pressure >100 mm Hg)	<p>Measured 180 days prior to and including day of drug initiation in any diagnosis position and inpatient or outpatient care setting</p> <p>Malignant hypertension: ICD-9 diagnosis: 401.0x (no ICD-10) Hypertensive urgency/ Hypertensive crisis: ICD-10 diagnosis: I16.x (no ICD-9)</p>	
3j	Recent malignancy or radiation therapy (≤6 m) and not expected to survive 3 y	N/A	
4	Contraindication to warfarin treatment	N/A	
5	Reversible causes of atrial fibrillation (eg, cardiac surgery, pulmonary embolism, untreated hyperthyroidism).	N/A	
6	Plan to perform a pulmonary vein ablation or surgery for cure of the AF	N/A	
7	Severe renal impairment (estimated creatinine clearance ≤30 mL/min)	<p>Measured 180 days prior to and including day of drug initiation in any diagnosis position and inpatient or outpatient care setting</p> <p>CKD stage 4/5/ESRD ICD-9 diagnosis: 585.4x, 585.5x, 585.6x ICD-10 diagnosis: N18.4x, N18.5x, N18.6x</p> <p>Dialysis/ Renal transplant Codes are in the sheet "Dialysis and Renal Transplant"</p>	

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8	Active infective endocarditis	<p>Measured 180 days prior to and including day of drug initiation in any diagnosis position and inpatient or outpatient care setting</p> <p>Infective endocarditis ICD-9 diagnosis: 421.x ICD-10 diagnosis: I33.x</p>	
9	Active liver disease, including but not limited to:	<p>Measured 180 days prior to and including day of drug initiation in any diagnosis position and inpatient or outpatient care setting</p> <p>Acute Liver Disease: ICD-9 diagnosis: 070.xx, 570.xx- 573.xx, 576.8x, 782.4x, 789.5x ICD-10 diagnosis: B15.x, B16.x, B17.x, K76.x, R17.x, R18.x, K72.00, K76.2 ICD-9 procedure codes: 39.1x, 42.91</p>	
9a	• Persistent ALT, AST, Alk Phos > 2x ULN	N/A	
9b	• Known active hepatitis C (positive HCV RNA)	N/A	
9c	• Active hepatitis B (HBs antigen +, anti HBc IgM+)	N/A	
9d	• Active hepatitis A	N/A	
10	Women who are pregnant or of childbearing potential who refuse to use a medically acceptable form of contraception throughout the study	<p>Measured 180 days prior to and including day of drug initiation in any diagnosis position and inpatient or outpatient care setting</p> <p>Codes are in the sheet "Pregnancy"</p>	
11	Anemia (hemoglobin level < 100g/L) or thrombocytopenia (platelet count <100 x 109/L)	<p>Measured 180 days prior to and including day of drug initiation in any diagnosis position and inpatient or outpatient care setting</p> <p>Anemia (non-deficiency/neoplastic/chemotherapy/hemorrhagic associated) ICD-9 diagnosis: 282.x, 283.x, 284.x, 285.x ICD-10 diagnosis: D55 - D62, D63.0</p> <p>Thrombocytopenia: ICD-9 diagnosis: 287.3x, 287.4x, 287.5x ICD-10 diagnosis: D69.3x, D69.4x, D69.5x, D69.6x</p>	
12	Patients who have developed transaminase elevations upon exposure to ximelagatran.	N/A	
13	Patients who have received an investigational drug in the past 30 d	N/A	
14	Patients considered unreliable by the investigator or have a life expectancy less than the expected duration of the trial because of concomitant disease, or has any condition which in the opinion of the investigator, would not allow safe participation in the study (eg, drug addiction, alcohol abuse)	<p>Measured 180 days prior to and including day of drug initiation in any diagnosis position and inpatient or outpatient care setting</p> <p>CCI >=10 (life expectancy less than the expected duration of the trial)</p> <p>-OR- Alcohol abuse or dependence ICD-9 diagnosis: 291.xx, 303.xx, 305.0x, 571.0x, 571.1x, 571.2x, 571.3x, 357.5x, 425.5x, E860.0x (CMS has not released mapping for new ICD10 for this code), V11.3x ICD-10 diagnosis: F10.x, K70.x, G62.1, I42.6, 099.31x</p> <p>Drug abuse or dependence 292.xx, 304.xx, 305.2x-305.9x, 648.3x 965.0x, 967.xx, 969.4x-969.6x, 969.72-969.79, 970.81 ICD-10 diagnosis: F11.x, F12.x, F13.x, F14.x, F15.x, F16.x, F18.x, F19.x, G62.0, 099.32x</p>	
15	Any known hypersensitivity to galactose if the warfarin used contains galactose.	N/A	

Appendix A

<u>Trial ID</u>	pNDA22
<u>Trial Name (with web links)</u>	RE-LY
<u>NCT</u>	NCT00262600
<u>Therapeutic Area</u>	Cardiology/Vascular Diseases
<u>Brand Name</u>	Pradaxa
<u>Generic Name</u>	dabigatran etexilate mesylate
<u>Sponsor</u>	Boehringer Ingelheim
<u>Year</u>	2010
<u>pNDA Indication</u>	For the risk reduction of stroke and embolism due to atrial fibrillation
<u>Measurable endpoint</u>	primary composite endpoint of stroke and systemic embolism
<u>Trial finding</u>	Rates of the primary outcome were 1.69% per year in the warfarin group, as compared with 1.53% per year in the group that received 110 mg of dabigatran (relative risk with dabigatran, 0.91; 95% confidence interval [CI], 0.74 to 1.11; P<0.001 for noninferiority) and 1.11% per year in the group that received 150 mg of dabigatran (relative risk, 0.66; 95% CI, 0.53 to 0.82; P<0.001 for superiority).
<u>Blinding</u>	fixed doses of dabigatran — 110 mg or 150 mg twice daily —each administered in a blinded manner, and adjusted-dose warfarin in an unblinded fashion
<u>No. of Patients</u>	18,113
<u>Comparator</u>	Active

Pregnancy

Diagnosis 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+A2:J81
 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

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- 72.31 HIGH FORCEPS OPERATION WITH EPISIOTOMY
- 72.39 OTHER HIGH FORCEPS OPERATION
- 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

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

Appendix A

Dialysis codes

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

Codes include:

- ICD9 prox codes:

39.95, Hemodialysis

54.98, Peritoneal dialysis

- ICD9 dx codes:

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

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

V56.0x, encounter for dialysis NOS

V56.8x, encounter for peritoneal dialysis

V45.1x, renal dialysis status

- CPT4 codes:

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

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

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

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

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

90935, Hemodialysis procedure with single physician evaluation

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

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

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

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

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

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

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90993, Dialysis training, patient, including helper where applicable, any mode, completed course

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

90999, Unlisted dialysis procedure, inpatient or outpatient

99512, Home visit for hemodialysis

- HCPCS codes:

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

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

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

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

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

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

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

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

OR

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

Codes include:

- ICD9 dx codes:

V42.0x, Kidney transplant status

996.81 Complications of transplanted kidney

- ICD9 prox codes:

55.6x, Transplant of kidney (Exclude 55.61)

- CPT4 codes:

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

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

Documented Coronary Artery Disease

ICD10: Coronary Bypass -

02.10083, 02.1008x, 02.1009x, 02.100Ax, 02.100Jx, 02.100Kx, 02.100Zx, 02.10483, 02.10488, 02.10489, 02.1048x, 02.1049x, 02.1049x, 02.104Ax, 02.104Jx, 02.104Kx, 02.104Zx, 02.1108x, 02.1109x, 02.110Ax, 02.110Jx, 02.110Kx, 02.110Zx, 02.1148x, 02.1149x, 02.114Ax, 02.114Jx, 02.114Kx, 02.114Zx, 02.1208x, 02.1209x, 02.120Ax, 02.120Jx, 02.120Kx, 02.120Zx, 02.1248x, 02.1249x, 02.124Ax, 02.124Jx, 02.124Kx, 02.124Zx, 02.1308x, 02.1309x, 02.130Ax, 02.130Jx, 02.130Kx, 02.130Zx, 02.1348x, 02.1349x, 02.134Ax, 02.134x, 02.134Kx, 02.134Zx, 02.1K0Zx, 02.1K4Zx, 02.1L08X, 02.1L09x, 02.1L0Ax, 02.1L0Jx, 02.1L0Kx, 02.1I0Zx, 02.1L0Zx, 02.1L48X, 02.1L49x, 02.1L4xx, 02.7004x, 02.7006x, 02.7007x, 02.700Dx, 02.700Ex, 02.700Fx, 02.700Gx, 02.700Tx, 02.700Zx, 02.703xx, 02.704xx, 02.7104x, 02.7105x, 02.7106x, 02.7107x, 02.710Dx, 02.710Ex, 02.710Fx, 02.710Gx, 02.710Tx, 02.710Zx, 02.7134x, 02.7135x, 02.7136x, 02.7137x, 02.713Dx, 02.713Ex, 02.713Fx, 02.713Gx, 02.713Tx, 02.713Zx, 02.7144x, 02.7145x, 02.7146x, 02.7147x, 02.714Dx, 02.714Ex, 02.714Fx, 02.714Gx, 02.714Tx, 02.714Zx, 02.7204x, 02.72056, 02.72066, 02.7206Z, 02.72076, 02.7207Z, 02.720Dx, 02.720Ex, 02.720Fx, 02.720Tx, 02.720Zx, 02.7234x, 02.7235x, 02.7236x, 02.7237x, 02.7237x, 02.723Dx, 02.723Ex, 02.723Fx, 02.723Gx, 02.723Tx, 02.723Tx, 02.723Zx, 02.723Zx, 02.7244x, 02.7245x, 02.7246x, 02.7247x, 02.724Dx, 02.724Ex, 02.724Fx, 02.724Gx, 02.724Tx, 02.7304x, 02.7304x, 02.7305x, 02.7306x, 02.7307x, 02.730Dx, 02.730Ex, 02.730Fx, 02.730Gx, 02.730Tx, 02.730Zx, 02.7334x, 02.7335x, 02.7336x, 02.7337x, 02.733Dx, 02.733Ex, 02.733Fx, 02.733Gx, 02.733Tx, 02.733Zx, 02.7344x, 02.7345x, 02.7346x, 02.7347x, 02.734Dx, 02.734Ex, 02.734Fx, 02.734Gx, 02.734Tx, 02.734Zx, 02.C00Zx, 02.C03Zx, 02.C04Zx, 02.C10Zx, 02.C13Zx, 02.C14Zx, 02.C20Zx, 02.C23Zx, 02.C24Zx, 02.C30Zx, 02.C33Zx, 02.C34Zx

Stenting:

Inpatient CPT-4:

92980, 92981, 92928-92929, 92933-92934

OR-

Inpatient ICD-9 Procedure:

36.06

36.07

Inpatient ICD-10 Procedure:

02.7004x, 02.7005x, 02.7006x, 02.7007x, 02.700Dx, 02.700Ex, 02.700Fx, 02.700Gx, 02.700Tx, 02.700Zx, 02.7034x, 02.7035x, 02.7036x, 02.7037x, 02.703Dx, 02.703Ex, 02.703Fx, 02.703Gx, 02.703Tx, 02.703Zx, 02.7044x, 02.7045x, 02.7046x, 02.7047x, 02.704Dx, 02.704Ex, 02.704Fx, 02.704Gx, 02.704Tx, 02.704Zx, 02.7104x, 02.7105x, 02.7106x, 02.7107x, 02.710Dx, 02.710Ex, 02.710Fx, 02.710Gx, 02.710Tx, 02.710Zx,

Appendix A

02.71346, 02.7134Z, 02.71356, 02.7135Z, 02.71366, 02.7136Z, 02.71376, 02.7137Z, 02.713D6, 02.713DZ, 02.713E6, 02.713EZ, 02.713F6, 02.713FZ, 02.713G6, 02.713GZ, 02.713T6, 02.713TZ, 02.713Z6, 02.713ZZ, 02.71446, 02.7144Z, 02.71456, 02.7145Z, 02.71466, 02.7146Z, 02.71476, 02.7147Z, 02.714D6, 02.714DZ, 02.714E6, 02.714EZ, 02.714F6, 02.714FZ, 02.714G6, 02.714GZ, 02.714T6, 02.714TZ, 02.714ZZ, 02.72046, 02.7204Z, 02.72056, 02.7205Z, 02.72066, 02.7206Z, 02.72076, 02.7207Z, 02.720D6, 02.720DZ, 02.720E6, 02.720EZ, 02.720F6, 02.720FZ, 02.720G6, 02.720GZ, 02.720T6, 02.720TZ, 02.720Z6, 02.720ZZ, 02.72346, 02.7234Z, 02.72356, 02.7235Z, 02.72366, 02.7236Z, 02.72376, 02.7237Z, 02.723D6, 02.723DZ, 02.723E6, 02.723EZ, 02.723F6, 02.723FZ, 02.723G6, 02.723GZ, 02.723T6, 02.723TZ, 02.723Z6, 02.723ZZ, 02.72446, 02.7244Z, 02.72456, 02.7245Z, 02.72466, 02.7246Z, 02.72476, 02.7247Z, 02.724D6, 02.724DZ, 02.724E6, 02.724EZ, 02.724F6, 02.724FZ, 02.724G6, 02.724T6, 02.724TZ, 02.724Z6, 02.724ZZ, 02.73046, 02.7304Z, 02.73056, 02.7305Z, 02.73066, 02.7306Z, 02.73076, 02.7307Z, 02.730D6, 02.730DZ, 02.730E6, 02.730EZ, 02.730F6, 02.730FZ, 02.730G6, 02.730GZ, 02.730T6, 02.730TZ, 02.730TZ, 02.730Z6, 02.730ZZ, 02.73346, 02.7334Z, 02.73356, 02.7335Z, 02.73366, 02.7336Z, 02.73376, 02.73376, 02.7337Z, 02.733D6, 02.733DZ, 02.733E6, 02.733EZ, 02.733F6, 02.733FZ, 02.733G6, 02.733GZ, 02.733T6, 02.733TZ, 02.733Z6, 02.733ZZ, 02.733ZZ, 02.73446, 02.7344Z, 02.73456, 02.7345Z, 02.73466, 02.73476, 02.7347Z, 02.34D6, 02.734DZ, 02.734E6, 02.734EZ, 02.734F6, 02.734FZ, 02.734G6, 02.734GZ, 02.734T6, 02.734TZ, 02.734Z6, 02.734ZZ, 02.C00Z6, 02.C03Z6, 02.C03ZZ, 02.C04Z6, 02.C10Z6, 02.C13Z6, 02.C13ZZ, 02.C14Z6, 02.C20Z6, 02.C23Z6, 02.C23ZZ, 02.C24Z6, 02.C30Z6, 02.C33ZZ, 02.C34Z6

Appendix B

Optum

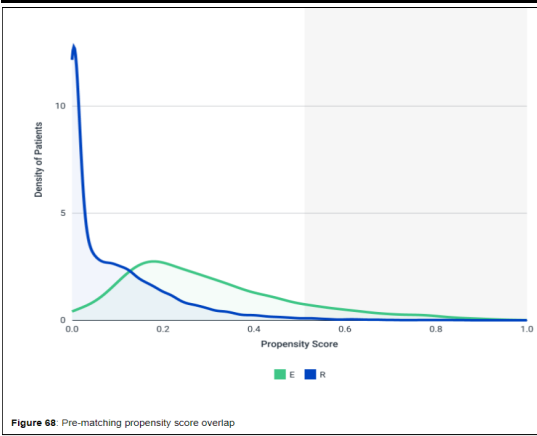


Figure 68: Pre-matching propensity score overlap

The c-statistics for the propensity score model, pre-matching was 0.857. The post-matching c-statistic was 0.556.

MarketScan

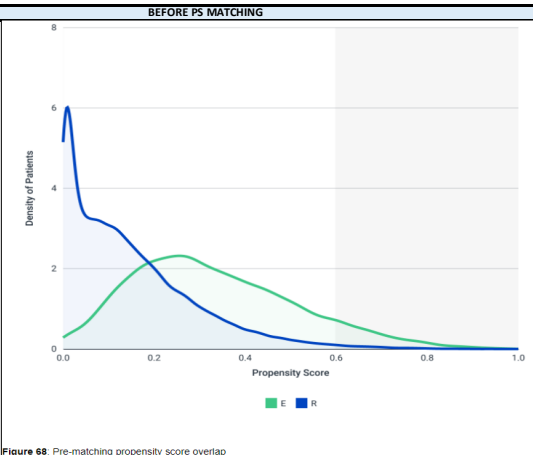


Figure 69: Pre-matching propensity score overlap

The c-statistics for the propensity score model, pre-matching was 0.806. The post-matching c-statistic was 0.539.

Medicare

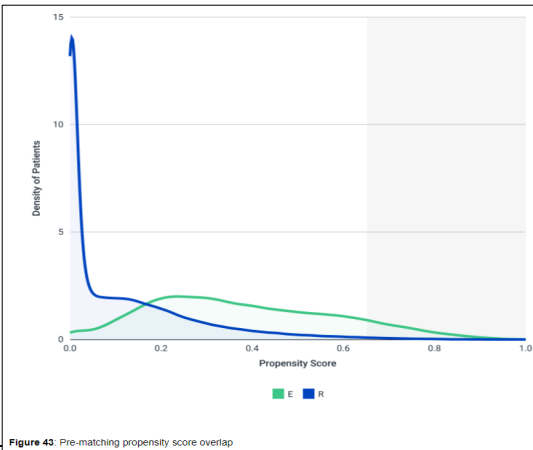


Figure 43: Pre-matching propensity score overlap

The c-statistics for the propensity score model, pre-matching was 0.868. The post-matching c-statistic was 0.53.

AFTER PS MATCHING

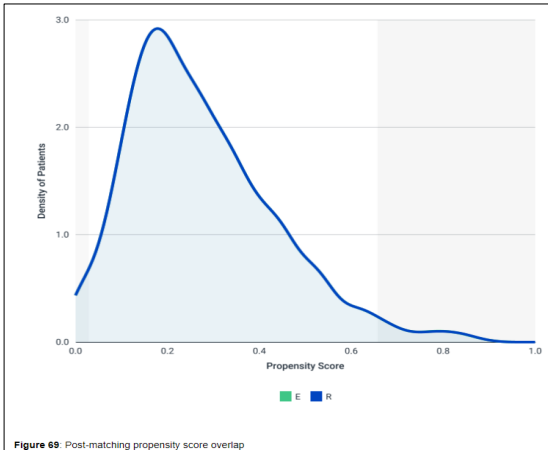


Figure 69: Post-matching propensity score overlap

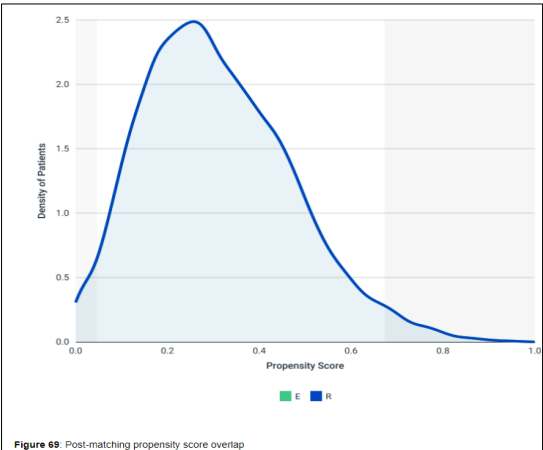


Figure 69: Post-matching propensity score overlap

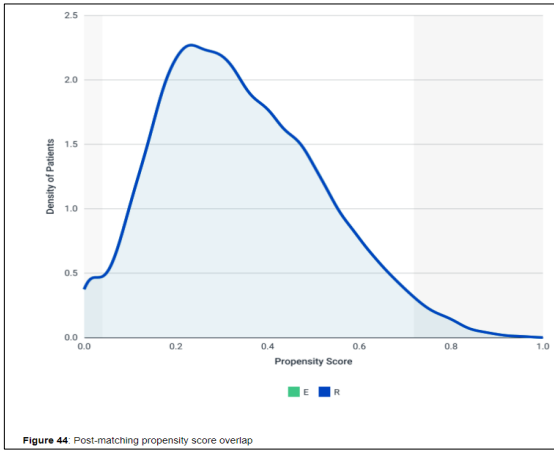


Figure 44: Post-matching propensity score overlap

Appendix B

Unmatched												
	Optum			MarketScan			Medicare			POOLED		
Variable	WARFARIN	Dabigatran 150mg	St. Diff.	Reference - warfarin	Exposure - Dabigatran 150mg	St. Diff.	Reference - warfarin	Exposure - Dabigatran 150mg	St. Diff.	Reference - warfarin	Exposure - Dabigatran 150mg	St. Diff.
Number of patients	22,665	2,936		67,790	14,929		136,087	25,230		226,542	43,095	
Age												
...mean (sd)	77.97 (6.21)	74.91 (7.65)	0.44	78.02 (9.20)	74.13 (9.67)	0.41	79.43 (7.37)	76.93 (6.88)	0.35	78.86 (7.86)	75.82 (8.01)	0.38
...median [IQR]	79.00 [76.00, 82.00]	77.00 [70.00, 80.00]	0.29	79.00 [74.00, 84.00]	76.00 [68.00, 81.00]	0.32	79.00 [75.00, 84.00]	77.00 [73.00, 81.00]	0.28	79.00 (7.86)	76.65 (8.01)	0.30
Age categories without zero category												
...18 - 54; n (%)	128 (0.6%)	54 (1.8%)	-0.11	1,319 (1.9%)	586 (3.9%)	-0.12	586 (0.4%)	123 (0.5%)	-0.01	2,033 (0.9%)	763 (1.8%)	-0.08
...55 - 64; n (%)	573 (2.5%)	198 (6.7%)	-0.20	4,878 (7.2%)	1,917 (12.8%)	-0.19	1,594 (1.2%)	351 (1.4%)	-0.02	7,045 (3.1%)	2,466 (5.7%)	-0.13
...65 - 74; n (%)	3,335 (14.7%)	705 (24.0%)	-0.24	11,624 (17.1%)	3,645 (24.4%)	-0.18	26,002 (19.1%)	7,382 (29.3%)	-0.24	40,961 (18.1%)	11,732 (27.2%)	-0.22
...≥ 75; n (%)	18,629 (82.2%)	1,979 (67.4%)	0.35	49,969 (73.7%)	8,781 (58.8%)	0.32	107,905 (79.3%)	17,374 (68.9%)	0.24	176,503 (77.9%)	28,134 (65.3%)	0.28
Gender without zero category- United												
...Males; n (%)	12,791 (56.4%)	1,776 (60.5%)	-0.08	36,708 (54.1%)	8,819 (59.1%)	-0.10	72,765 (53.5%)	14,393 (57.0%)	-0.07	122,264 (54.0%)	24,988 (58.0%)	-0.08
...Females; n (%)	9,874 (43.6%)	1,160 (39.5%)	0.08	31,082 (45.9%)	6,110 (40.9%)	0.10	63,322 (46.5%)	10,837 (43.0%)	0.07	104,278 (46.0%)	18,107 (42.0%)	0.08
Race												
...White; n (%)							127,987 (94.0%)	23,447 (92.9%)		127,987 (94.0%)	23,447 (92.9%)	0.00
...Black; n (%)							3,795 (2.8%)	714 (2.8%)		3,795 (2.8%)	714 (2.8%)	0.00
...Asian; n (%)							1,217 (0.9%)	344 (1.4%)		1,217 (0.9%)	344 (1.4%)	0.00
...Hispanic; n (%)							1,169 (0.9%)	245 (1.0%)		1,169 (0.9%)	245 (1.0%)	0.00
...North American Native; n (%)							428 (0.3%)	70 (0.3%)		428 (0.3%)	70 (0.3%)	0.00
...Other/Unknown; n (%)							1,491 (1.1%)	410 (1.6%)		1,491 (1.1%)	410 (1.6%)	0.00
Region without zero category- United v3 (lumping missing&other category with West)												
...Northeast; n (%)	2,860 (12.6%)	428 (14.6%)	-0.06	15,592 (23.0%)	3,464 (23.2%)	0.00	27,525 (20.2%)	4,871 (19.3%)	0.02	45,977 (20.3%)	8,763 (20.3%)	0.00
...South; n (%)	5,965 (26.3%)	1,026 (34.9%)	-0.19	21,981 (32.4%)	3,920 (26.3%)	0.13	44,598 (32.8%)	10,023 (39.7%)	-0.14	72,544 (32.0%)	14,969 (34.7%)	-0.06
...Midwest; n (%)	4,585 (20.2%)	473 (16.1%)	0.11	18,724 (27.6%)	5,249 (35.2%)	-0.16	38,803 (28.5%)	5,759 (22.8%)	0.13	62,112 (27.4%)	11,481 (26.6%)	0.02
...West; n (%)	9,255 (40.8%)	1,009 (34.4%)	0.13	11,263 (16.6%)	2,233 (15.0%)	0.04	25,161 (18.5%)	4,577 (18.1%)	0.01	45,679 (20.2%)	7,819 (18.1%)	0.05
...Unknown+missing; n (%)	N/A	N/A	#VALUE!	230 (0.3%)	63 (0.4%)	-0.02	N/A	N/A	#VALUE!	230 (0.3%)	63 (0.4%)	-0.02
CV Covariates												
Ischemic heart disease; n (%)	5,796 (25.6%)	854 (29.1%)	-0.08	22,356 (33.0%)	5,213 (34.9%)	-0.04	37,673 (27.7%)	8,145 (32.3%)	-0.10	65,825 (29.1%)	14,212 (33.0%)	-0.08
Acute MI; n (%)	192 (0.8%)	19 (0.6%)	0.02	1,721 (2.5%)	411 (2.8%)	-0.02	1,928 (1.4%)	380 (1.5%)	-0.01	3,795 (1.7%)	810 (1.9%)	-0.02
ACS/unstable angina; n (%)	196 (0.9%)	30 (1.0%)	-0.01	1,436 (2.1%)	412 (2.8%)	-0.05	1,896 (1.4%)	456 (1.8%)	-0.03	3,528 (1.6%)	898 (2.1%)	-0.04
Old MI; n (%)	654 (2.9%)	72 (2.5%)	0.02	2,040 (3.0%)	506 (3.4%)	-0.02	4,824 (3.5%)	1,089 (4.3%)	-0.04	7,518 (3.3%)	1,667 (3.9%)	-0.03
Stable angina; n (%)	557 (2.5%)	99 (3.4%)	-0.05	2,157 (3.2%)	612 (4.1%)	-0.05	3,376 (2.5%)	966 (3.8%)	-0.07	6,090 (2.7%)	1,677 (3.9%)	-0.07
Coronary atherosclerosis and other forms of chronic ischemic heart disease; n (%)	5,348 (23.6%)	808 (27.5%)	-0.09	20,511 (30.3%)	4,710 (31.5%)	-0.03	34,808 (25.6%)	7,439 (29.5%)	-0.09	60,667 (26.8%)	12,957 (30.1%)	-0.07
Other atherosclerosis with ICD10 v2 Copy; n (%)	291 (1.3%)	50 (1.7%)	-0.03	1,283 (1.9%)	237 (1.6%)	0.02	1,625 (1.2%)	346 (1.4%)	-0.02	3,199 (1.4%)	633 (1.5%)	-0.01
Previous cardiac procedure (CABG or PTCA or Stent) v4; n (%)	19 (0.1%)	7 (0.2%)	-0.03	712 (1.1%)	161 (1.1%)	0.00	893 (0.7%)	154 (0.6%)	0.01	1,624 (0.7%)	322 (0.7%)	0.00
History of CABG or PTCA; n (%)	1,022 (4.5%)	146 (5.0%)	-0.02	2,582 (3.8%)	672 (4.5%)	-0.04	8,074 (5.9%)	2,028 (8.0%)	-0.08	11,678 (5.2%)	2,846 (6.6%)	-0.06
Any stroke; n (%)	1,585 (7.0%)	271 (9.2%)	-0.08	5,866 (8.7%)	1,426 (9.6%)	-0.03	8,312 (6.1%)	1,840 (7.3%)	-0.05	15,763 (7.0%)	3,537 (8.2%)	-0.05
Ischemic stroke (w and w/o mention of cerebral infarction); n (%)	1,579 (7.0%)	270 (9.2%)	-0.08	5,843 (8.6%)	1,421 (9.5%)	-0.03	8,268 (6.1%)	1,832 (7.3%)	-0.05	15,690 (6.9%)	3,523 (8.2%)	-0.05
Hemorrhagic stroke; n (%)	12 (0.1%)	3 (0.1%)	0.00	41 (0.1%)	8 (0.1%)	0.00	56 (0.0%)	9 (0.0%)	#DIV/0!	109 (0.0%)	20 (0.0%)	#DIV/0!
TIA; n (%)	627 (2.8%)	151 (5.1%)	-0.12	2,260 (3.3%)	759 (5.1%)	-0.09	3,166 (2.3%)	811 (3.2%)	-0.06	6,053 (2.7%)	1,721 (4.0%)	-0.07
Other cerebrovascular disease; n (%)	386 (1.7%)	54 (1.8%)	-0.01	1,417 (2.1%)	315 (2.1%)	0.00	2,122 (1.6%)	433 (1.7%)	-0.01	3,925 (1.7%)	802 (1.9%)	-0.02
Late effects of cerebrovascular disease; n (%)	110 (0.5%)	10 (0.3%)	0.03	77 (0.1%)	19 (0.1%)	0.00	511 (0.4%)	69 (0.3%)	0.02	698 (0.3%)	98 (0.2%)	0.02
Cerebrovascular procedure; n (%)	2 (0.0%)	0 (0.0%)	#DIV/0!	73 (0.1%)	25 (0.2%)	-0.03	91 (0.1%)	21 (0.1%)	0.00	166 (0.1%)	46 (0.1%)	0.00
Heart failure (CHF); n (%)	3,108 (13.7%)	335 (11.4%)	0.07	15,297 (22.6%)	3,232 (21.6%)	0.02	17,205 (12.6%)	2,846 (11.3%)	0.04	35,610 (15.7%)	6,413 (14.9%)	0.02
Peripheral Vascular Disease (PVD) or PVD Surgery v2; n (%)	1,790 (7.9%)	210 (7.2%)	0.03	5,549 (8.2%)	974 (6.5%)	0.07	8,046 (5.9%)	1,363 (5.4%)	0.02	15,385 (6.8%)	2,547 (5.9%)	0.04
Atrial fibrillation; n (%)	21,440 (94.6%)	2,786 (94.9%)	-0.01	61,508 (90.7%)	14,189 (95.0%)	-0.17	121,089 (89.0%)	21,872 (86.7%)	0.07	204,037 (90.1%)	38,847 (90.1%)	0.00
Other cardiac dysrhythmia; n (%)	10,235 (45.2%)	1,233 (42.0%)	0.06	18,823 (27.8%)	4,688 (31.4%)	-0.08	47,883 (35.2%)	8,912 (35.3%)	0.00	76,941 (34.0%)	14,833 (34.4%)	-0.01
Cardiac conduction disorders; n (%)	1,169 (5.2%)	183 (6.2%)	-0.04	3,958 (5.8%)	953 (6.4%)	-0.03	6,776 (5.0%)	1,425 (5.6%)	-0.03	11,903 (5.3%)	2561 (5.9%)	-0.03
Other CVD; n (%)	2,744 (12.1%)	358 (12.2%)	0.00	18,692 (27.6%)	4,297 (28.8%)	-0.03	14,045 (10.3%)	2,647 (10.5%)	-0.01	35,481 (15.7%)	7,302 (16.9%)	-0.03
Diabetes-related complications												
Diabetic retinopathy; n (%)	311 (1.4%)	41 (1.4%)	0.00	852 (1.3%)	196 (1.3%)	0.00	1,343 (1.0%)	229 (0.9%)	0.01	2,506 (1.1%)	466 (1.1%)	0.00
Diabetes with other ophthalmic manifestations; n (%)	24 (0.1%)	2 (0.1%)	0.00	710 (1.0%)	130 (0.9%)	0.01	866 (0.6%)	162 (0.6%)	0.00	1,600 (0.7%)	294 (0.7%)	0.00
Retinal detachment, vitreous hemorrhage, vitrectomy; n (%)	41 (0.2%)	7 (0.2%)	0.00	157 (0.2%)	35 (0.2%)	0.00	214 (0.2%)	40 (0.2%)	0.00	412 (0.2%)	82 (0.2%)	0.00
Retinal laser coagulation therapy; n (%)	23 (0.1%)	2 (0.1%)	0.00	127 (0.2%)	34 (0.2%)	0.00	199 (0.1%)	35 (0.1%)	0.00	349 (0.2%)	71 (0.2%)	0.00
Occurrence of Diabetic Neuropathy v2 Copy; n (%)	1,095 (4.8%)	116 (4.0%)	0.04	2,494 (3.7%)	485 (3.2%)	0.03	3,720 (2.7%)	626 (2.5%)	0.01	7309 (3.2%)	1227 (2.8%)	0.02
Occurrence of diabetic nephropathy v3 with ICD10 Copy; n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!	#VALUE!	000 (0.0%)	#VALUE!
Hypoglycemia v2; n (%)	148 (0.7%)	19 (0.6%)	0.01	780 (1.2%)	138 (0.9%)	0.03	1,333 (1.0%)	221 (0.9%)	0.01	2,261 (1.0%)	378 (0.9%)	0.01
Hyperglycemia; n (%)	775 (3.4%)	114 (3.9%)	-0.04	1,082 (1.6%)	303 (2.0%)	-0.03	5,641 (4.1%)	1,169 (4.6%)	-0.02	7,498 (3.3%)	1586 (3.7%)	-0.02
Disorders of fluid electrolyte and acid-base balance; n (%)	797 (3.5%)	111 (3.8%)	-0.02	4,181 (6.2%)	939 (6.3%)	0.00	5,781 (4.2%)	1,199 (4.8%)	-0.03	10759 (4.7%)	2249 (5.2%)	-0.02
Diabetic ketoacidosis; n (%)	12 (0.1%)	2 (0.1%)	0.00	65 (0.1%)	9 (0.1%)	0.00	107 (0.1%)	23 (0.1%)	0.00	184 (0.1%)	34 (0.1%)	0.00
Hyperosmolar hyperglycemic nonketotic syndrome (HONK); n (%)	17 (0.1%)	1 (0.0%)	0.04	49 (0.1%)	7 (0.0%)	0.04	91 (0.1%)	24 (0.1%)	0.00	157 (0.1%)	32 (0.1%)	0.00
Diabetes with peripheral circulatory disorders with ICD-10 v2 Copy; n (%)	554 (2.4%)	48 (1.6%)	0.06	1,275 (1.9%)	239 (1.6%)	0.02	2,694 (2.0%)	433 (1.7%)	0.02	4523 (2.0%)	720 (1.7%)	0.02
Diabetic Foot; n (%)	413 (1.8%)	39 (1.3%)	0.04	1,743 (2.6%)	268 (1.8%)	0.05	3,207 (2.4%)	457 (1.8%)	0.04	5363 (2.4%)	764 (1.8%)	0.04
Gangrene v2; n (%)	19 (0.1%)	1 (0.0%)	0.04	103 (0.2%)	16 (0.1%)	0.03	108 (0.1%)	12 (0.0%)	0.04	230 (0.1%)	29 (0.1%)	0.00
Lower extremity amputation; n (%)	55 (0.2%)	8 (0.3%)	-0.02	131 (0.2%)	29 (0.2%)	0.00	277 (0.2%)	39 (0.2%)	0.00	463 (0.2%)	076 (0.2%)	0.00
Osteomyelitis; n (%)	40 (0.2%)	4 (0.1%)	0.03	274 (0.4%)	50 (0.3%)	0.02	404 (0.3%)	52 (0.2%)	0.02	718 (0.3%)	106 (0.2%)	0.02

Appendix B

Skin infections v2; n (%)	1,050 (4.6%)	137 (4.7%)	0.00	4,516 (6.7%)	784 (5.3%)	0.06	7,183 (5.3%)	1,151 (4.6%)	0.03	12749 (5.6%)	2072 (4.8%)	0.04
Erectile dysfunction; n (%)	343 (1.5%)	69 (2.4%)	-0.07	726 (1.1%)	237 (1.6%)	-0.04	904 (0.7%)	232 (0.9%)	-0.02	1973 (0.9%)	538 (1.2%)	-0.03
Diabetes with unspecified complication; n (%)	187 (0.8%)	20 (0.7%)	0.01	519 (0.7%)	101 (0.7%)	0.01	764 (0.6%)	139 (0.6%)	0.00	1470 (0.6%)	260 (0.6%)	0.00
Diabetes mellitus without mention of complications; n (%)	5,754 (25.4%)	833 (28.4%)	-0.07	16,310 (24.1%)	3,721 (24.9%)	-0.02	34,888 (25.6%)	6,813 (27.0%)	-0.03	56,952 (25.1%)	11,367 (26.4%)	-0.03
Hypertension: 1 inpatient or 2 outpatient claims within 365 days; n (%)	16,322 (72.0%)	2,239 (76.3%)	-0.10	42,997 (63.4%)	9,870 (66.1%)	-0.06	108,842 (80.0%)	21,120 (83.7%)	-0.10	168,161 (74.2%)	33,229 (77.1%)	-0.07
Hyperlipidemia v2; n (%)	11,780 (52.0%)	1,804 (61.4%)	-0.19	25,573 (37.7%)	6,296 (42.2%)	-0.09	59,674 (43.8%)	12,723 (50.4%)	-0.13	97,027 (42.8%)	20,823 (48.3%)	-0.11
Edema; n (%)	1,814 (8.0%)	243 (8.3%)	-0.01	5,614 (8.3%)	1,040 (7.0%)	0.05	8,853 (6.5%)	1,425 (5.6%)	0.04	16281 (7.2%)	2708 (6.3%)	0.04
Renal dysfunction (non-diabetic) v2; n (%)	7 (0.0%)	1 (0.0%)	#DIV/0!	50 (0.1%)	6 (0.0%)	0.04	33 (0.0%)		#VALUE!	#VALUE!	#VALUE!	#VALUE!
Occurrence of acute renal disease v2; n (%)	2 (0.0%)	1 (0.0%)	#DIV/0!	46 (0.1%)	6 (0.0%)	0.04	23 (0.0%)		**	#VALUE!	71 (0.0%)	#VALUE!
Occurrence of chronic renal insufficiency; n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!		**	0 (0.0%)	#VALUE!	000 (0.0%)	#VALUE!
Chronic kidney disease v2; n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!	#VALUE!	000 (0.0%)	#VALUE!
CKD Stage 3-4; n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!	#VALUE!	000 (0.0%)	#VALUE!
Occurrence of hypertensive nephropathy; n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!	#VALUE!	000 (0.0%)	#VALUE!
Occurrence of miscellaneous renal insufficiency v2; n (%)	1 (0.0%)	0 (0.0%)	#DIV/0!	4 (0.0%)	0 (0.0%)	#DIV/0!		**	0 (0.0%)	#VALUE!	000 (0.0%)	#VALUE!
Glaucoma or cataracts v2; n (%)	5,118 (22.6%)	675 (23.0%)	-0.01	15,190 (22.4%)	3,243 (21.7%)	0.02	1,139 (0.8%)	160 (0.6%)	0.02	21,447 (9.5%)	4,078 (9.5%)	0.00
Cellulitis or abscess of toe; n (%)	191 (0.8%)	17 (0.6%)	0.02	500 (0.7%)	93 (0.6%)	0.01	2,821 (2.1%)	399 (1.6%)	0.04	3512 (1.6%)	509 (1.2%)	0.03
Foot ulcer; n (%)	422 (1.9%)	40 (1.4%)	0.04	1,801 (2.7%)	271 (1.8%)	0.06	128 (0.1%)	27 (0.1%)	0.00	2351 (1.0%)	338 (0.8%)	0.02
Bladder stones; n (%)	26 (0.1%)	5 (0.2%)	-0.03	78 (0.1%)	28 (0.2%)	-0.03	1,422 (1.0%)	293 (1.2%)	-0.02	1526 (0.7%)	326 (0.8%)	-0.01
Kidney stones; n (%)	171 (0.8%)	33 (1.1%)	-0.03	813 (1.2%)	228 (1.5%)	-0.03	12,492 (9.2%)	2,078 (8.2%)	0.04	13476 (5.9%)	2339 (5.4%)	0.02
Urinary tract infections (UTIs); n (%)	1,630 (7.2%)	185 (6.3%)	0.04	5,324 (7.9%)	927 (6.2%)	0.07	40,989 (30.1%)	8,320 (33.0%)	-0.06	47,943 (21.2%)	9,432 (21.9%)	-0.02
Dipstick urinalysis; n (%)	5,873 (25.9%)	901 (30.7%)	-0.11	13,373 (19.7%)	3,156 (21.1%)	-0.03	14,042 (10.3%)	2,978 (11.8%)	-0.05	33,288 (14.7%)	7,035 (16.3%)	-0.04
Non-dipstick urinalysis; n (%)	2,541 (11.2%)	355 (12.1%)	-0.03	3,103 (4.6%)	801 (5.4%)	-0.04	5,152 (3.8%)	1,026 (4.1%)	-0.02	10,796 (4.8%)	2,182 (5.1%)	-0.01
Urine function test; n (%)	687 (3.0%)	102 (3.5%)	-0.03	2,778 (4.1%)	638 (4.3%)	-0.01	2,169 (1.6%)	447 (1.8%)	-0.02	5634 (2.5%)	1187 (2.8%)	-0.02
Cytology; n (%)	250 (1.1%)	38 (1.3%)	-0.02	1,664 (2.5%)	358 (2.4%)	0.01	2,833 (2.1%)	519 (2.1%)	0.00	4747 (2.1%)	915 (2.1%)	0.00
Cystoscopy; n (%)	380 (1.7%)	48 (1.6%)	0.01	1,732 (2.6%)	378 (2.5%)	0.01	#REF!	#REF!	#REF!	#REF!	#REF!	#REF!
Other Covariates												
Liver disease; n (%)	84 (0.4%)	14 (0.5%)	-0.01	343 (0.5%)	98 (0.7%)	-0.03	443 (0.3%)	100 (0.4%)	-0.02	870 (0.4%)	212 (0.5%)	-0.01
Osteoarthritis; n (%)	3,538 (15.6%)	497 (16.9%)	-0.04	10,558 (15.6%)	2,139 (14.3%)	0.04	21,641 (15.9%)	3,936 (15.6%)	0.01	35737 (15.8%)	6572 (15.3%)	0.01
Other arthritis, arthropathies and musculoskeletal pain; n (%)	7,087 (31.3%)	897 (30.6%)	0.02	23,692 (34.9%)	4,746 (31.8%)	0.07	41,341 (30.4%)	7,342 (29.1%)	0.03	72120 (31.8%)	12985 (30.1%)	0.04
Dorsopathies; n (%)	3,877 (17.1%)	535 (18.2%)	-0.03	12,398 (18.3%)	2,723 (18.2%)	0.00	22,378 (16.4%)	4,307 (17.1%)	-0.02	38653 (17.1%)	7565 (17.6%)	-0.01
Fractures; n (%)	627 (2.8%)	65 (2.2%)	0.04	3,305 (4.9%)	496 (3.3%)	0.08	5,148 (3.8%)	760 (3.0%)	0.04	9080 (4.0%)	1321 (3.1%)	0.05
Falls v2; n (%)	688 (3.0%)	67 (2.3%)	0.04	1,133 (1.7%)	149 (1.0%)	0.06	2,111 (1.6%)	262 (1.0%)	0.05	3932 (1.7%)	478 (1.1%)	0.05
Osteoporosis; n (%)	1,758 (7.8%)	188 (6.4%)	0.05	5,295 (7.8%)	1,008 (6.8%)	0.04	10,526 (7.7%)	1,911 (7.6%)	0.00	17579 (7.8%)	3107 (7.2%)	0.02
Hyperthyroidism; n (%)	163 (0.7%)	23 (0.8%)	-0.01	494 (0.7%)	104 (0.7%)	0.00	1,000 (0.7%)	248 (1.0%)	-0.03	1657 (0.7%)	375 (0.9%)	-0.02
Hypothyroidism v2; n (%)	3,397 (15.0%)	425 (14.5%)	0.01	7,128 (10.5%)	1,551 (10.4%)	0.00	15,444 (11.3%)	3,025 (12.0%)	-0.02	25969 (11.5%)	5001 (11.6%)	0.00
Other disorders of thyroid gland v2; n (%)	505 (2.2%)	74 (2.5%)	-0.02	1,546 (2.3%)	387 (2.6%)	-0.02	2,907 (2.1%)	676 (2.7%)	-0.04	4958 (2.2%)	1137 (2.6%)	-0.03
Depression; n (%)	1,103 (4.9%)	144 (4.9%)	0.00	3,463 (5.1%)	728 (4.9%)	0.01	6,172 (4.5%)	1,217 (4.8%)	-0.01	10738 (4.7%)	2089 (4.8%)	0.00
Anxiety; n (%)	973 (4.3%)	154 (5.2%)	-0.04	2,440 (3.6%)	592 (4.0%)	-0.02	5,217 (3.8%)	1,082 (4.3%)	-0.03	8630 (3.8%)	1828 (4.2%)	-0.02
Sleep_Disorder; n (%)	1,509 (6.7%)	291 (9.9%)	-0.12	6,461 (9.5%)	1,761 (11.8%)	-0.07	7,241 (5.3%)	1,661 (6.6%)	-0.05	15211 (6.7%)	3713 (8.6%)	-0.07
Dementia; n (%)	1,070 (4.7%)	113 (3.8%)	0.04	3,564 (5.3%)	483 (3.2%)	0.10	6,660 (4.9%)	919 (3.6%)	0.06	11294 (5.0%)	1515 (3.5%)	0.07
Delirium; n (%)	85 (0.4%)	16 (0.5%)	-0.01	960 (1.4%)	124 (0.8%)	0.06	1,006 (0.7%)	154 (0.6%)	0.01	2051 (0.9%)	294 (0.7%)	0.02
Psychosis; n (%)	119 (0.5%)	13 (0.4%)	0.01	772 (1.1%)	104 (0.7%)	0.04	944 (0.7%)	177 (0.7%)	0.00	1835 (0.8%)	294 (0.7%)	0.01
Obesity; n (%)	1,627 (7.2%)	283 (9.6%)	-0.09	3,572 (5.3%)	1,075 (7.2%)	-0.08	9,935 (7.3%)	2,313 (9.2%)	-0.07	15134 (6.7%)	3671 (8.5%)	-0.07
Overweight; n (%)	619 (2.7%)	83 (2.8%)	-0.01	498 (0.7%)	96 (0.6%)	0.01	2,324 (1.7%)	441 (1.7%)	0.00	3441 (1.5%)	620 (1.4%)	0.01
Smoking; n (%)	1,391 (6.1%)	228 (7.8%)	-0.07	2,660 (3.9%)	831 (5.6%)	-0.08	14,879 (10.9%)	3,432 (13.6%)	-0.08	18930 (8.4%)	4491 (10.4%)	-0.07
Alcohol abuse or dependence; n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!
Drug abuse or dependence; n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!
COPD; n (%)	2,521 (11.1%)	302 (10.3%)	0.03	9,289 (13.7%)	1,896 (12.7%)	0.03	12,605 (9.3%)	2,316 (9.2%)	0.00	24415 (10.8%)	4514 (10.5%)	0.01
Asthma; n (%)	928 (4.1%)	134 (4.6%)	-0.02	3,235 (4.8%)	799 (5.4%)	-0.03	4,679 (3.4%)	1,016 (4.0%)	-0.03	8842 (3.9%)	1949 (4.5%)	-0.03
Obstructive sleep apnea; n (%)	1,465 (6.5%)	273 (9.3%)	-0.10	5,202 (7.7%)	1,465 (9.8%)	-0.07	5,922 (4.4%)	1,420 (5.6%)	-0.06	12589 (5.6%)	3158 (7.3%)	-0.07
Pneumonia; n (%)	479 (2.1%)	46 (1.6%)	0.04	4,419 (6.5%)	880 (5.9%)	0.02	4,846 (3.6%)	865 (3.4%)	0.01	9744 (4.3%)	1791 (4.2%)	0.00
Imaging; n (%)	3 (0.0%)	1 (0.0%)	#DIV/0!	115 (0.2%)	18 (0.1%)	0.03	2,821 (2.1%)	399 (1.6%)	0.04	2939 (1.3%)	418 (1.0%)	0.03
Other Medications												
Use of ACE inhibitors; n (%)	7,637 (33.7%)	997 (34.0%)	-0.01	23,436 (34.6%)	5,249 (35.2%)	-0.01	47,332 (34.8%)	8,768 (34.8%)	0.00	78405 (34.6%)	15014 (34.8%)	0.00
Use of ARBs; n (%)	4,045 (17.8%)	571 (19.4%)	-0.04	14,719 (21.7%)	3,547 (23.8%)	-0.05	26,443 (19.4%)	5,734 (22.7%)	-0.08	45207 (20.0%)	9852 (22.9%)	-0.07
Use of Loop Diuretics - United; n (%)	4,781 (21.1%)	482 (16.4%)	0.12	21,128 (31.2%)	3,432 (23.0%)	0.19	34,289 (25.2%)	4,812 (19.1%)	0.15	60198 (26.6%)	8726 (20.2%)	0.15
Use of other diuretics- United; n (%)	859 (3.8%)	91 (3.1%)	0.04	4,266 (6.3%)	730 (4.9%)	0.06	6,138 (4.5%)	860 (3.4%)	0.06	11263 (5.0%)	1681 (3.9%)	0.05
Use of nitrates-United; n (%)	1,267 (5.6%)	146 (5.0%)	0.03	6,398 (9.4%)	1,249 (8.4%)	0.04	10,986 (8.1%)	1,964 (7.8%)	0.01	18651 (8.2%)	3359 (7.8%)	0.01
Use of other hypertension drugs; n (%)	1,739 (7.7%)	228 (7.8%)	0.00	5,200 (7.7%)	1,037 (6.9%)	0.03	9,777 (7.2%)	1,817 (7.2%)	0.00	16716 (7.4%)	3082 (7.2%)	0.01
Use of digoxin- United; n (%)	3,142 (13.9%)	318 (10.8%)	0.09	13,308 (19.6%)	2,168 (14.5%)	0.14	20,843 (15.3%)	2,997 (11.9%)	0.10	37293 (16.5%)	5483 (12.7%)	0.11
Use of Anti-arrhythmics; n (%)	2,154 (9.5%)	459 (15.6%)	-0.18	9,822 (14.5%)	3,029 (20.3%)	-0.15	15,578 (11.4%)	4,366 (17.3%)	-0.17	27554 (12.2%)	7554 (18.2%)	-0.17
Use of COPD/asthma meds- United; n (%)	3,022 (13.3%)	435 (14.8%)	-0.04	12,353 (18.2%)	2,900 (19.4%)	-0.03	20,518 (15.1%)	4,170 (16.5%)	-0.04	35893 (15.8%)	7805 (17.4%)	-0.04
Use of statins; n (%)	12,189 (53.8%)	1,579 (53.8%)	0.00	37,940 (56.0%)	8,310 (55.7%)	0.01	74,659 (54.9%)	14,235 (56.4%)	-0.03	124788 (55.1%)	24124 (56.0%)	-0.02
Use of other lipid-lowering drugs; n (%)	1,345 (5.9%)	221 (7.5%)	-0.06	6,440 (9.5%)	1,567 (10.5%)	-0.03	9,683 (7.1%)	2,038 (8.1%)	-0.04	17468 (7.7%)	3826 (8.9%)	-0.04
Use of antiplatelet agents; n (%)	1,466 (6.5%)	282 (9.6%)	-0.11	8,223 (12.1%)	2,505 (16.8%)	-0.13	12,346 (9.1%)	3,435 (13.6%)	-0.14	22035 (9.7%)	6222 (14.4%)	-0.14
Use of heparin and other low-molecular weight heparins; n (%)	501 (2.2%)	11 (0.4%)	0.16	29 (0.0%)	2 (0.0%)	#DIV/0!	5,084 (3.7%)	125 (0.5%)	0.22	5614 (2.5%)	138 (0.3%)	0.19
Use of NSAIDs; n (%)	1,606 (7.1%)	290 (9.9%)	-0.10	5,269 (7.8%)	1,572 (10.5%)	-0.09	11,395 (8.4%)	3,015 (12.0%)	-0.12	18270 (8.1%)	4877 (11.3%)	-0.11
Use of oral corticosteroids; n (%)	3,335 (14.7%)	475 (16.2%)	-0.04	12,514 (18.5%)	2,819 (18.9%)	-0.01	23,765 (17.5%)	4,688 (18.6%)	-0.03	39614 (17.5%)	7982 (18.5%)	-0.03
Use of bisphosphonate (United); n (%)	961 (4.2%)	109 (3.7%)	0.03	3,457 (5.1%)	681 (4.6%)	0.02	5,374 (3.9%)	1,024 (4.1%)	-0.01	9792 (4.3%)	1814 (4.2%)	0.00
Use of opioids- United; n (%)	4,335 (19.1%)	569 (19.4%)	-0.01	16,765 (24.7%)	3,550 (23.8%)	0.02	30,560 (22.5%)	5,619 (22.3%)	0.00	51660 (22.8%)	9738 (22.6%)	0.00
Use of antidepressants; n (%)	3,538 (15.6%)	473 (16.1%)	-0.01	12,223 (18.0%)	2,578 (17.3%)	0.02	24,350 (17.9%)	4,457 (17.7%)	0.01	40111 (17.7%)	7508 (17.4%)	0.01
Use of antipsychotics; n (%)	225 (1.0%)	25 (0.9%)	0.01	1,128 (1.7%)	168 (1.1%)	0.05	2,318 (1.7%)	392 (1.6%)	0.01	3671 (1.6%)	585 (1.4%)	0.02
Use of anticonvulsants; n (%)	2,045 (9.0%)	248 (8.4%)	0.02	6,508 (9.6%)	1,262 (8.5%)	0.04	13,821 (10.2%)	2,344 (9.3%)	0.03	22374 (9.9%)	3854 (8.9%)	0.03
Use of lithium- United; n (%)	16 (0.1%)	3 (0.1%)	0.00	46 (0.1%)	14 (0.1%)	0.00	57 (0.0%)	23 (0.1%)	-0.04	119 (0.1%)	40 (0.1%)	0.00
Use of Benzos- United; n (%)	1,463 (6.5%)	205 (7.0%)	-0.02	8,662 (12.8%)	1,940 (13.0%)	-0.01	10,944 (8.0%)	1,679 (6.7%)	0.05	21069 (9.3%)	3824 (8.9%)	0.01

Appendix B

Use of anxiolytics/hypnotics- United; n (%)	937 (4.1%)	184 (6.3%)	-0.10	4,377 (6.5%)	1,073 (7.2%)	-0.03	7,226 (5.3%)	1,699 (6.7%)	-0.06	12540 (5.5%)	2956 (6.9%)	-0.06
Use of dementia meds- United; n (%)	840 (3.7%)	98 (3.3%)	0.02	3,200 (4.7%)	474 (3.2%)	0.08	6,279 (4.6%)	927 (3.7%)	0.05	10319 (4.6%)	1499 (3.5%)	0.06
Use of antiparkinsonian meds- United; n (%)	492 (2.2%)	43 (1.5%)	0.05	1,880 (2.8%)	371 (2.5%)	0.02	3,833 (2.8%)	682 (2.7%)	0.01	6205 (2.7%)	1096 (2.5%)	0.01
Any use of pramlintide; n (%)	2 (0.0%)	0 (0.0%)	#DIV/0!	19 (0.0%)	8 (0.1%)	-0.04	11 (0.0%)	**	#VALUE!	32 (0.0%)	#VALUE!	#VALUE!
Any use of 1st generation sulfonylureas; n (%)	1 (0.0%)	0 (0.0%)	#DIV/0!	19 (0.0%)	5 (0.0%)	#DIV/0!	**	**	#VALUE!	#VALUE!	#VALUE!	0.00
Entresto (sacubitril/valsartan); n (%)	21 (0.1%)	3 (0.1%)	0.00	18 (0.0%)	2 (0.0%)	#DIV/0!	30 (0.0%)	**	#VALUE!	69 (0.0%)	#VALUE!	0.00
Labs												
Lab values- HbA1c (%) v3; n (%)	2,340 (10.3%)	328 (11.2%)	-0.03	682 (1.0%)	109 (0.7%)	0.03	N/A	N/A	#VALUE!	3,022 (3.3%)	437 (2.4%)	0.05
Lab values- HbA1c (%) (within 3 months) v3; n (%)	1,502 (6.6%)	212 (7.2%)	-0.02	480 (0.7%)	69 (0.5%)	0.03	N/A	N/A	#VALUE!	1,982 (2.2%)	281 (1.6%)	0.04
Lab values- HbA1c (%) (within 6 months) v3; n (%)	2,340 (10.3%)	328 (11.2%)	-0.03	682 (1.0%)	109 (0.7%)	0.03	N/A	N/A	#VALUE!	3,022 (3.3%)	437 (2.4%)	0.05
Lab values- BNP; n (%)	227 (1.0%)	28 (1.0%)	0.00	45 (0.1%)	17 (0.1%)	0.00	N/A	N/A	#VALUE!	272 (0.3%)	045 (0.3%)	0.00
Lab values- BNP (within 3 months); n (%)	165 (0.7%)	24 (0.8%)	-0.01	36 (0.1%)	14 (0.1%)	0.00	N/A	N/A	#VALUE!	201 (0.2%)	038 (0.2%)	0.00
Lab values- BNP (within 6 months); n (%)	227 (1.0%)	28 (1.0%)	0.00	45 (0.1%)	17 (0.1%)	0.00	N/A	N/A	#VALUE!	272 (0.3%)	045 (0.3%)	0.00
Lab values- BUN (mg/dl); n (%)	4,553 (20.1%)	704 (24.0%)	-0.09	559 (0.8%)	166 (1.1%)	-0.03	N/A	N/A	#VALUE!	5,112 (5.7%)	870 (4.9%)	0.04
Lab values- BUN (mg/dl) (within 3 months); n (%)	3,091 (13.6%)	479 (16.3%)	-0.08	387 (0.6%)	117 (0.8%)	-0.02	N/A	N/A	#VALUE!	3,478 (3.8%)	596 (3.3%)	0.03
Lab values- BUN (mg/dl) (within 6 months); n (%)	4,553 (20.1%)	704 (24.0%)	-0.09	559 (0.8%)	166 (1.1%)	-0.03	N/A	N/A	#VALUE!	5,112 (5.7%)	870 (4.9%)	0.04
Lab values- Creatinine (mg/dl) v2; n (%)	4,643 (20.5%)	718 (24.5%)	-0.10	577 (0.9%)	182 (1.2%)	-0.03	N/A	N/A	#VALUE!	5,220 (5.8%)	900 (5.0%)	0.04
Lab values- Creatinine (mg/dl) (within 3 months) v2; n (%)	3,146 (13.9%)	489 (16.7%)	-0.08	402 (0.6%)	125 (0.8%)	-0.02	N/A	N/A	#VALUE!	3,548 (3.9%)	614 (3.4%)	0.03
Lab values- Creatinine (mg/dl) (within 6 months) v2; n (%)	4,643 (20.5%)	718 (24.5%)	-0.10	577 (0.9%)	182 (1.2%)	-0.03	N/A	N/A	#VALUE!	5,220 (5.8%)	900 (5.0%)	0.04
Lab values- HDL level (mg/dl); n (%)	3,264 (14.4%)	532 (18.1%)	-0.10	539 (0.8%)	125 (0.8%)	0.00	N/A	N/A	#VALUE!	3,803 (4.2%)	657 (3.7%)	0.03
Lab values- HDL level (mg/dl) (within 3 months); n (%)	2,041 (9.0%)	340 (11.6%)	-0.09	367 (0.5%)	77 (0.5%)	0.00	N/A	N/A	#VALUE!	2,408 (2.7%)	417 (2.3%)	0.03
Lab values- HDL level (mg/dl) (within 6 months); n (%)	3,264 (14.4%)	532 (18.1%)	-0.10	539 (0.8%)	125 (0.8%)	0.00	N/A	N/A	#VALUE!	3,803 (4.2%)	657 (3.7%)	0.03
Lab values- LDL level (mg/dl) v2; n (%)	3,488 (15.4%)	561 (19.1%)	-0.10	689 (1.0%)	134 (0.9%)	0.01	N/A	N/A	#VALUE!	4,177 (4.6%)	695 (3.9%)	0.03
Lab values- LDL level (mg/dl) (within 3 months) v2; n (%)	2,174 (9.6%)	359 (12.2%)	-0.08	460 (0.7%)	83 (0.6%)	0.01	N/A	N/A	#VALUE!	2,634 (2.9%)	442 (2.5%)	0.02
Lab values- LDL level (mg/dl) (within 6 months) v2; n (%)	3,488 (15.4%)	561 (19.1%)	-0.10	689 (1.0%)	134 (0.9%)	0.01	N/A	N/A	#VALUE!	4,177 (4.6%)	695 (3.9%)	0.03
Lab values- NT-proBNP; n (%)	20 (0.1%)	2 (0.1%)	0.00	3 (0.0%)	0 (0.0%)	#DIV/0!	N/A	N/A	#VALUE!	23 (0.0%)	2 (0.0%)	#DIV/0!
Lab values- NT-proBNP (within 3 months); n (%)	16 (0.1%)	1 (0.0%)	0.04	2 (0.0%)	0 (0.0%)	#DIV/0!	N/A	N/A	#VALUE!	18 (0.0%)	1 (0.0%)	-
Lab values- NT-proBNP (within 6 months); n (%)	20 (0.1%)	2 (0.1%)	0.00	3 (0.0%)	0 (0.0%)	#DIV/0!	N/A	N/A	#VALUE!	23 (0.0%)	2 (0.0%)	-
Lab values- Total cholesterol (mg/dl) v2; n (%)	3,311 (14.6%)	542 (18.5%)	-0.11	560 (0.8%)	136 (0.9%)	-0.01	N/A	N/A	#VALUE!	3,871 (4.3%)	678 (3.8%)	0.03
Lab values- Total cholesterol (mg/dl) (within 3 months) v2; n (%)	2,069 (9.1%)	346 (11.8%)	-0.09	377 (0.6%)	82 (0.5%)	0.01	N/A	N/A	#VALUE!	2,446 (2.7%)	428 (2.4%)	0.02
Lab values- Total cholesterol (mg/dl) (within 6 months) v2; n (%)	3,311 (14.6%)	542 (18.5%)	-0.11	560 (0.8%)	136 (0.9%)	-0.01	N/A	N/A	#VALUE!	3,871 (4.3%)	678 (3.8%)	0.03
Lab values- Triglyceride level (mg/dl); n (%)	3,262 (14.4%)	537 (18.3%)	-0.11	535 (0.8%)	126 (0.8%)	0.00	N/A	N/A	#VALUE!	3,797 (4.2%)	663 (3.7%)	0.03
Lab values- Triglyceride level (mg/dl) (within 3 months); n (%)	2,035 (9.0%)	343 (11.7%)	-0.09	358 (0.5%)	77 (0.5%)	0.00	N/A	N/A	#VALUE!	2,393 (2.6%)	420 (2.4%)	0.01
Lab values- Triglyceride level (mg/dl) (within 6 months); n (%)	3,262 (14.4%)	537 (18.3%)	-0.11	535 (0.8%)	126 (0.8%)	0.00	N/A	N/A	#VALUE!	3,797 (4.2%)	663 (3.7%)	0.03
Lab result number- HbA1c (%) mean (only 2 to 20 included) v4	2,323	326		534	101		N/A	N/A		2,857	427	
...mean (sd)	6.47 (1.11)	6.53 (1.34)	-0.05	6.97 (1.28)	6.79 (1.17)	0.15	N/A	N/A	#VALUE!	6.56 (1.14)	6.59 (1.30)	-0.02
...median [IQR]	6.25 [5.80, 6.90]	6.30 [5.80, 6.91]	-0.04	6.60 [6.15, 7.50]	6.50 [5.95, 7.35]	-0.08	N/A	N/A	#VALUE!	6.32 (1.14)	6.35 (1.30)	-0.02
...Missing; n (%)	20,342 (89.8%)	2,610 (88.9%)	0.03	67,256 (99.2%)	14,828 (99.3%)	0.01	N/A	N/A	#VALUE!	87,598 (96.8%)	17,438 (97.6%)	-0.05
Lab result number- BNP mean v2	227	28		45	17		N/A	N/A		272	45	
...mean (sd)	261.46 (277.83)	214.33 (164.51)	0.21	247.18 (218.19)	180.30 (209.53)	0.31	N/A	N/A	#VALUE!	259.10 (269.51)	201.47 (184.72)	0.25
...median [IQR]	198.60 [99.39, 339.40]	170.15 [69.72, 343.75]	0.12	174.00 [78.80, 330.50]	121.00 [59.00, 245.00]	0.25	N/A	N/A	#VALUE!	194.53 (269.51)	151.58 (184.72)	0.19
...Missing; n (%)	22,438 (99.0%)	2,908 (99.0%)	0.00	67,745 (99.9%)	14,912 (99.9%)	0.00	N/A	N/A	#VALUE!	90,183 (99.7%)	17,820 (99.7%)	0.00
Lab result number- BUN (mg/dl) mean v2	4,553	704		559	166		N/A	N/A		5,112	870	
...mean (sd)	18.85 (6.58)	17.70 (5.20)	0.19	19.96 (8.62)	18.29 (6.07)	0.22	N/A	N/A	#VALUE!	18.97 (6.83)	17.81 (5.38)	0.19
...median [IQR]	18.00 [15.00, 22.00]	17.00 [14.00, 21.00]	0.17	18.50 [15.00, 23.00]	18.00 [14.88, 22.00]	0.07	N/A	N/A	#VALUE!	18.05 (6.83)	17.19 (5.38)	0.14
...Missing; n (%)	18,112 (79.9%)	2,232 (76.0%)	0.09	67,231 (99.2%)	14,763 (98.9%)	0.03	N/A	N/A	#VALUE!	85,343 (94.3%)	16,995 (95.1%)	-0.04
Lab result number- Creatinine (mg/dl) mean (only 0.1 to 15 included) v3	4,611	714		571	178		N/A	N/A		5,182	892	
...mean (sd)	1.01 (0.25)	0.98 (0.21)	0.13	1.05 (0.30)	0.98 (0.24)	0.26	N/A	N/A	#VALUE!	1.01 (0.26)	0.98 (0.22)	0.12
...median [IQR]	0.98 [0.84, 1.14]	0.96 [0.83, 1.10]	0.09	1.00 [0.85, 1.18]	0.96 [0.80, 1.13]	0.15	N/A	N/A	#VALUE!	0.98 (0.26)	0.96 (0.22)	0.08
...Missing; n (%)	18,054 (79.7%)	2,222 (75.7%)	0.10	67,219 (99.2%)	14,751 (98.8%)	0.04	N/A	N/A	#VALUE!	85,273 (94.3%)	16,973 (95.0%)	-0.03
Lab result number- HDL level (mg/dl) mean (only <=5000 included) v2	3,264	532		539	125		N/A	N/A		3,803	657	
...mean (sd)	51.06 (16.33)	52.25 (17.04)	-0.07	45.82 (14.49)	48.92 (17.38)	-0.19	N/A	N/A	#VALUE!	50.32 (16.08)	51.62 (17.12)	-0.08
...median [IQR]	48.00 [40.00, 60.00]	49.00 [41.00, 61.00]	-0.06	44.00 [37.00, 53.00]	48.00 [36.75, 60.00]	-0.25	N/A	N/A	#VALUE!	47.43 (16.08)	48.81 (17.12)	-0.08
...Missing; n (%)	19,401 (85.6%)	2,404 (81.9%)	0.10	67,251 (99.2%)	14,804 (99.2%)	0.00	N/A	N/A	#VALUE!	86,652 (95.8%)	17,208 (96.3%)	-0.03
Lab result number- LDL level (mg/dl) mean (only <=5000 included) v2	3,405	545		552	128		N/A	N/A		3,957	673	
...mean (sd)	86.00 [31.67]	87.70 [33.74]	-0.05	84.18 (33.47)	82.01 (35.36)	0.06	N/A	N/A	#VALUE!	85.75 (31.93)	86.62 (34.08)	-0.03
...median [IQR]	82.00 [65.00, 104.00]	82.00 [66.00, 109.00]	0.00	81.00 [62.25, 101.00]	81.00 [59.00, 102.75]	0.00	N/A	N/A	#VALUE!	81.86 (31.93)	81.81 (34.08)	0.00
...Missing; n (%)	19,260 (85.0%)	2,391 (81.4%)	0.10	67,238 (99.2%)	14,801 (99.1%)	0.01	N/A	N/A	#VALUE!	86,498 (95.6%)	17,192 (96.2%)	-0.03
Lab result number- Total cholesterol (mg/dl) mean (only <=5000 included) v2	3,310	542		560	136		N/A	N/A		3,870	678	
...mean (sd)	163.13 (39.87)	165.20 (40.26)	-0.05	157.07 (40.57)	160.25 (40.19)	-0.08	N/A	N/A	#VALUE!	162.25 (39.98)	164.21 (40.28)	-0.05
...median [IQR]	159.00 [137.00, 186.00]	159.50 [138.00, 192.00]	-0.01	155.00 [132.00, 177.00]	160.50 [137.25, 183.38]	-0.14	N/A	N/A	#VALUE!	158.42 (39.98)	159.70 (40.28)	-0.03
...Missing; n (%)	19,355 (85.4%)	2,394 (81.5%)	0.11	67,230 (99.2%)	14,793 (99.1%)	0.01	N/A	N/A	#VALUE!	86,585 (95.7%)	17,187 (96.2%)	-0.03
Lab result number- Triglyceride level (mg/dl) mean (only <=5000 included) v2	3,262	537		535	126		N/A	N/A		3,797	663	
...mean (sd)	129.05 (78.48)	121.50 (66.86)	0.10	139.12 (74.65)	141.59 (94.40)	-0.03	N/A	N/A	#VALUE!	130.47 (77.96)	125.32 (72.93)	0.07
...median [IQR]	111.00 [82.00, 156.00]	107.00 [77.50, 145.00]	0.05	122.00 [88.00, 175.00]	125.50 [89.38, 157.38]	-0.04	N/A	N/A	#VALUE!	112.55 (77.96)	110.52 (72.93)	0.03

Appendix B

...Missing; n (%)	19,403 (85.6%)	2,399 (81.7%)	0.11	67,255 (99.2%)	14,803 (99.2%)	0.00	N/A	N/A	#VALUE!	86,658 (95.8%)	17,202 (96.3%)	-0.03
Lab result number- Hemoglobin mean (only>0 included)	3,295	521		359	114		N/A	N/A		3,654	635	
...mean (sd)	13.87 (1.59)	14.08 (1.40)	-0.14	13.42 (1.59)	13.63 (2.34)	-0.10	N/A	N/A	#VALUE!	13.83 (1.59)	14.00 (1.61)	-0.11
...median [IQR]	13.90 [12.90, 14.90]	14.00 [13.20, 15.00]	-0.07	13.50 [12.40, 14.40]	13.95 [12.94, 15.00]	-0.22	N/A	N/A	#VALUE!	13.86 (1.59)	13.99 (1.61)	-0.08
...Missing; n (%)	19,370 (85.5%)	2,415 (82.3%)	0.09	67,431 (99.5%)	14,815 (99.2%)	0.04	N/A	N/A	#VALUE!	86,801 (96.0%)	17,230 (96.4%)	-0.02
Lab result number- Serum sodium mean (only > 90 and <190 included)	4,380	685		456	142		N/A	N/A		4,836	827	
...mean (sd)	140.12 (2.88)	140.14 (3.00)	-0.01	139.70 (2.75)	139.32 (2.94)	0.13	N/A	N/A	#VALUE!	140.08 (2.87)	140.00 (2.99)	0.03
...median [IQR]	140.00 [139.00, 142.00]	140.00 [139.00, 142.00]	0.00	140.00 [138.00, 141.00]	139.33 [138.00, 141.00]	0.24	N/A	N/A	#VALUE!	140.00 (2.87)	139.88 (2.99)	0.04
...Missing; n (%)	18,285 (80.7%)	2,251 (76.7%)	0.10	67,334 (99.3%)	14,787 (99.0%)	0.03	N/A	N/A	#VALUE!	85,619 (94.7%)	17,038 (95.4%)	-0.03
Lab result number- Albumin mean (only>0 and <=10 included)	3,911	632		366	120		N/A	N/A		4,277	752	
...mean (sd)	4.14 (0.32)	4.19 (0.31)	-0.16	4.05 (0.49)	4.06 (0.47)	-0.02	N/A	N/A	#VALUE!	4.13 (0.34)	4.17 (0.34)	-0.12
...median [IQR]	4.15 [3.95, 4.35]	4.20 [4.00, 4.40]	-0.16	4.10 [3.85, 4.30]	4.10 [3.90, 4.30]	0.00	N/A	N/A	#VALUE!	4.15 (0.34)	4.18 (0.34)	-0.09
...Missing; n (%)	18,754 (82.7%)	2,304 (78.5%)	0.11	67,424 (99.5%)	14,809 (99.2%)	0.04	N/A	N/A	#VALUE!	86,178 (95.3%)	17,113 (95.8%)	-0.02
Lab result number- Glucose (fasting or random) mean (only 10-1000 included)	4,320	676		439	130		N/A	N/A		4,759	806	
...mean (sd)	109.88 (33.22)	111.68 (39.94)	-0.05	130.34 (49.02)	127.55 (43.03)	0.06	N/A	N/A	#VALUE!	111.77 (34.98)	114.24 (40.48)	-0.07
...median [IQR]	101.00 [91.00, 118.00]	100.17 [91.00, 116.88]	0.02	116.50 [98.00, 148.00]	114.50 [101.81, 138.31]	0.04	N/A	N/A	#VALUE!	102.43 (34.98)	102.48 (40.48)	0.00
...Missing; n (%)	18,345 (80.9%)	2,260 (77.0%)	0.10	67,351 (99.4%)	14,799 (99.1%)	0.03	N/A	N/A	#VALUE!	85,696 (94.7%)	17,059 (95.5%)	-0.04
Lab result number- Potassium mean (only 1-7 included)	4,610	711		552	164		N/A	N/A		5,162	875	
...mean (sd)	4.35 (0.44)	4.38 (0.44)	-0.07	4.33 (0.43)	4.37 (0.38)	-0.10	N/A	N/A	#VALUE!	4.35 (0.44)	4.38 (0.43)	-0.07
...median [IQR]	4.30 [4.10, 4.60]	4.40 [4.10, 4.60]	-0.23	4.30 [4.10, 4.60]	4.40 [4.15, 4.60]	-0.25	N/A	N/A	#VALUE!	4.30 (0.44)	4.40 (0.43)	-0.23
...Missing; n (%)	18,055 (79.7%)	2,225 (75.8%)	0.09	67,238 (99.2%)	14,765 (98.9%)	0.03	N/A	N/A	#VALUE!	85,293 (94.3%)	16,990 (95.1%)	-0.04
Comorbidity Scores												
CCI (180 days)- ICD9 and ICD10 v2												
...mean (sd)	2.62 (1.44)	2.62 (1.34)	0.00	2.78 (1.68)	2.79 (1.56)	-0.01	1.42 (1.41)	1.32 (1.38)	0.07	1.95 (1.50)	1.92 (1.44)	0.02
...median [IQR]	2.00 [2.00, 3.00]	2.00 [2.00, 3.00]	0.00	2.00 [2.00, 4.00]	2.00 [2.00, 2.00]	0.00	1.00 [0.00, 2.00]	1.00 [0.00, 2.00]	0.00	1.40 (1.50)	1.41 (1.44)	-0.01
Non-Frailty; n (%)	12,577 (55.5%)	1,612 (54.9%)	0.01	33,237 (49.0%)	7,284 (48.8%)	0.00	3,400 (2.5%)	524 (2.1%)	0.03	49,214 (21.7%)	9,420 (21.9%)	0.00
Frailty Score (mean): Empirical Version 365 days, v2												
...mean (sd)	0.17 (0.04)	0.17 (0.04)	0.00	0.18 (0.05)	0.17 (0.05)	0.20	12.15 (9.76)	10.54 (9.32)	0.17	7.37 (7.56)	6.24 (7.13)	0.15
...median [IQR]	0.16 [0.14, 0.19]	0.16 [0.14, 0.19]	0.00	0.17 [0.15, 0.21]	0.16 [0.14, 0.19]	0.20	10.13 [5.57, 16.45]	8.75 [4.29, 14.71]	0.14	6.15 (7.56)	5.19 (7.13)	0.13
Healthcare Utilization												
Any hospitalization; n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	17,074 (25.2%)	4,804 (32.2%)	-0.16	19,589 (14.4%)	4,815 (19.1%)	-0.13	36,663 (16.2%)	9,619 (22.3%)	-0.16
Any hospitalization within prior 30 days; n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	9,626 (14.2%)	3,296 (22.1%)	-0.21	11,829 (8.7%)	2,910 (11.5%)	-0.09	21455 (9.5%)	6206 (14.4%)	-0.15
Any hospitalization during prior 31-180 days; n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	8,232 (12.1%)	1,717 (11.5%)	0.02	8,606 (6.3%)	2,082 (8.3%)	-0.08	16838 (7.4%)	3799 (8.8%)	-0.05
Endocrinologist Visit; n (%)	436 (1.9%)	84 (2.9%)	-0.07	1,932 (2.8%)	501 (3.4%)	-0.03	4,050 (3.0%)	874 (3.5%)	-0.03	6418 (2.8%)	1459 (3.4%)	-0.03
Endocrinologist Visit (30 days prior); n (%)	139 (0.6%)	21 (0.7%)	-0.01	633 (0.9%)	176 (1.2%)	-0.03	1,150 (0.8%)	276 (1.1%)	-0.03	1922 (0.8%)	473 (1.1%)	-0.03
Endocrinologist Visit (31 to 180 days prior); n (%)	381 (1.7%)	72 (2.5%)	-0.06	1,650 (2.4%)	413 (2.8%)	-0.03	3,536 (2.6%)	755 (3.0%)	-0.02	5567 (2.5%)	1240 (2.9%)	-0.02
Internal medicine/family medicine visits; n (%)	19,784 (87.3%)	2,435 (82.9%)	0.12	52,971 (78.1%)	11,827 (79.2%)	-0.03	108,913 (80.0%)	20,381 (80.8%)	-0.02	181668 (80.2%)	34643 (80.4%)	-0.01
Internal medicine/family medicine visits (30 days prior) v2; n (%)	13,564 (59.8%)	1,529 (52.1%)	0.16	33,572 (49.5%)	7,777 (52.1%)	-0.05	68,566 (50.4%)	12,510 (49.6%)	0.02	115702 (51.1%)	21816 (50.6%)	0.01
Internal medicine/family medicine visits (31 to 180 days prior) v2; n (%)	17,797 (78.5%)	2,119 (72.2%)	0.15	48,286 (71.2%)	10,294 (69.0%)	0.05	95,817 (70.4%)	17,389 (68.9%)	0.03	161900 (71.5%)	29802 (69.2%)	0.05
Cardiologist visit; n (%)	11,235 (49.6%)	1,976 (67.3%)	-0.37	1,976 (67.3%)	9,003 (60.3%)	-0.18	85,057 (62.5%)	19,330 (76.6%)	-0.31	131296 (58.0%)	30309 (70.3%)	-0.26
Number of Cardiologist visits (30 days prior); n (%)	6,801 (30.0%)	1,379 (47.0%)	-0.35	20,128 (29.7%)	6,908 (46.3%)	-0.35	53,448 (39.3%)	14,249 (56.5%)	-0.35	80377 (35.5%)	22536 (52.3%)	-0.34
Number of Cardiologist visits (31 to 180 days prior); n (%)	8,195 (36.2%)	1,255 (42.7%)	-0.13	27,617 (40.7%)	5,842 (39.1%)	0.03	61,773 (45.4%)	12,141 (48.1%)	-0.05	97585 (43.1%)	19238 (44.6%)	-0.03
Electrocardiogram v2; n (%)	11,225 (49.5%)	2,064 (70.3%)	-0.43	39,015 (57.6%)	11,173 (74.8%)	-0.37	77,673 (57.1%)	19,434 (77.0%)	-0.43	127913 (56.5%)	32671 (75.8%)	-0.42
Use of glucose test strips; n (%)	176 (0.8%)	33 (1.1%)	-0.03	475 (0.7%)	113 (0.8%)	-0.01	1,262 (0.9%)	261 (1.0%)	-0.01	1913 (0.8%)	407 (0.9%)	-0.01
Dialysis; n (%)	4 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!	**	0 (0.0%)	#VALUE!	#VALUE!	0 (0.0%)	#VALUE!
number of different/distinct medication prescriptions												
...mean (sd)	7.72 (3.82)	8.13 (4.07)	-0.10	9.26 (4.52)	9.27 (4.58)	0.00	8.30 (3.85)	8.59 (4.06)	-0.07	8.53 (4.06)	8.79 (4.25)	0.00
...median [IQR]	7.00 [5.00, 10.00]	8.00 [5.00, 10.00]	-0.25	9.00 [6.00, 12.00]	9.00 [6.00, 12.00]	0.00	8.00 [6.00, 10.00]	8.00 [6.00, 11.00]	0.00	5.79 (4.76)	6.43 (4.80)	0.00
Number of Hospitalizations												
...mean (sd)	0.00 (0.00)	0.00 (0.00)	#DIV/0!	0.28 (0.51)	0.35 (0.55)	-0.13	0.16 (0.43)	0.21 (0.47)	-0.11	0.18 (0.43)	0.24 (0.48)	0.00
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	#DIV/0!	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	0.00	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 (0.52)	0.00 (0.55)	0.00
Number of hospital days												
...mean (sd)	0.00 (0.11)	0.00 (0.00)	0.00	1.61 (4.76)	1.50 (3.28)	0.03	0.80 (2.85)	0.85 (2.46)	-0.02	0.96 (3.41)	1.02 (2.70)	0.00
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 [0.00, 1.00]	0.00 [0.00, 2.00]	0.00	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 (4.30)	0.00 (3.14)	0.00
Number of Emergency Department (ED) visits v3												
...mean (sd)	0.33 (0.88)	0.42 (1.03)	-0.09	0.38 (1.65)	0.45 (1.73)	-0.04	0.57 (1.27)	0.63 (1.27)	-0.05	0.49 (1.36)	0.55 (1.43)	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, 1.00]	0.00	0.00 (1.64)	0.00 (1.66)	0.00
Number of Office visits												
...mean (sd)	5.17 (4.16)	5.24 (3.67)	-0.02	6.39 (5.10)	5.79 (4.33)	0.13	11.99 (11.24)	11.79 (10.20)	0.02	9.63 (9.24)	9.27 (8.27)	0.00
...median [IQR]	4.00 [2.00, 7.00]	4.00 [3.00, 7.00]	0.00	5.00 [3.00, 9.00]	5.00 [3.00, 8.00]	0.00	9.00 [4.00, 16.00]	9.00 [5.00, 16.00]	0.00	4.59 (9.66)	5.12 (8.53)	0.00
Number of Endocrinologist visits												
...mean (sd)	0.07 (0.76)	0.11 (1.08)	-0.04	0.11 (0.99)	0.11 (0.87)	0.00	0.13 (1.28)	0.17 (1.51)	-0.03	0.12 (1.16)	0.15 (1.29)	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, 0.00]	0.00	0.00 (1.28)	0.00 (1.36)	0.00
Number of internal medicine/family medicine visits												
...mean (sd)	10.57 (13.09)	8.08 (12.69)	0.19	7.44 (10.97)	6.42 (9.19)	0.10	7.40 (9.26)	6.44 (7.85)	0.11	7.73 (10.23)	6.54 (8.74)	0.00
...median [IQR]	6.00 [2.00, 15.00]	4.00 [1.00, 10.00]	0.16	4.00 [1.00, 10.00]	4.00 [1.00, 8.00]	0.00	4.00 [1.00, 10.00]	4.00 [1.00, 9.00]	0.00	2.99 (11.87)	3.04 (9.82)	0.00
Number of Cardiologist visits												
...mean (sd)	2.53 (4.49)	3.44 (4.50)	-0.20	3.04 (5.45)	3.42 (5.10)	-0.07	3.93 (6.21)	4.80 (5.92)	-0.14	3.52 (5.84)	4.23 (5.56)	0.00
...median [IQR]	0.00 [0.00, 3.00]	2.00 [0.00, 5.00]	-0.44	1.00 [0.00, 4.00]	2.00 [0.00, 5.00]	-0.19	2.00 [0.00, 5.00]	3.00 [1.00, 7.00]	-0.16	0.90 (6.56)	1.87 (6.09)	0.00
Number electrocardiograms received v2												
...mean (sd)	0.96 (1.50)	1.61 (1.87)	-0.38	1.26 (1.82)	1.79 (1.99)	-0.28	1.24 (1.68)	1.89 (1.96)	-0.36	1.22 (1.71)	1.84 (1.96)	0.00

Appendix B

...median [IQR]	0.00 [0.00, 1.00]	1.00 [0.00, 2.00]	-0.59	1.00 [0.00, 2.00]	1.00 [0.00, 2.00]	0.00	1.00 [0.00, 2.00]	1.00 [1.00, 3.00]	0.00	0.60 (1.98)	0.76 (2.19)	0.00
Number of HbA1c tests ordered												
...mean (sd)	0.36 (0.67)	0.39 (0.70)	-0.04	0.14 (0.45)	0.16 (0.48)	-0.04	0.37 (0.69)	0.41 (0.72)	-0.06	0.30 (0.63)	0.32 (0.65)	0.00
...median [IQR]	0.00 [0.00, 1.00]	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, 1.00]	0.00 [0.00, 1.00]	0.00	0.00 (0.67)	0.00 (0.69)	0.00
Number of glucose tests ordered												
...mean (sd)	0.11 (0.90)	0.16 (0.94)	-0.05	0.10 (0.54)	0.11 (0.58)	-0.02	0.11 (0.52)	0.13 (0.49)	-0.04	0.11 (0.58)	0.13 (0.56)	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, 0.00]	0.00	0.00 (0.65)	0.00 (0.63)	0.00
Number of lipid tests ordered												
...mean (sd)	0.59 (0.80)	0.69 (0.85)	-0.12	0.22 (0.62)	0.26 (0.68)	-0.06	0.59 (0.71)	0.70 (0.75)	-0.15	0.48 (0.69)	0.55 (0.73)	0.00
...median [IQR]	0.00 [0.00, 1.00]	1.00 [0.00, 1.00]	-1.21	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 [0.00, 1.00]	1.00 [0.00, 1.00]	-1.37	0.00 (0.77)	0.41 (0.81)	-0.01
Number of creatinine tests ordered												
...mean (sd)	0.06 (0.32)	0.07 (0.32)	-0.03	0.07 (0.41)	0.05 (0.27)	0.06	0.09 (0.38)	0.09 (0.37)	0.00	0.08 (0.38)	0.07 (0.34)	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, 0.00]	0.00	0.00 (0.44)	0.00 (0.36)	0.00
Number of BUN tests ordered												
...mean (sd)	0.03 (0.24)	0.05 (0.25)	-0.08	0.04 (0.31)	0.03 (0.23)	0.04	0.05 (0.29)	0.06 (0.28)	-0.04	0.05 (0.29)	0.05 (0.26)	0.00
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 (0.34)	0.00 (0.28)	0.00
Number of tests for microalbuminuria												
...mean (sd)	0.18 (0.61)	0.19 (0.64)	-0.02	0.06 (0.36)	0.08 (0.39)	-0.05	0.10 (0.37)	0.12 (0.39)	-0.05	0.10 (0.40)	0.11 (0.41)	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, 0.00]	0.00	0.00 (0.44)	0.00 (0.45)	0.00
Total N distinct ICD9/CD10 diagnoses at the 3rd digit level Copy												
...mean (sd)	3.20 (4.99)	3.00 (5.09)	0.04	2.23 (5.06)	2.21 (4.86)	0.00	3.88 (6.40)	3.93 (6.39)	-0.01	3.32 (5.90)	3.27 (5.82)	0.00
...median [IQR]	0.00 [0.00, 5.00]	0.00 [0.00, 5.00]	0.00	0.00 [0.00, 2.00]	0.00 [0.00, 2.00]	0.00	0.00 [0.00, 6.00]	0.00 [0.00, 6.00]	0.00	0.00 (6.52)	0.00 (6.28)	0.00
For PS												
Hemorrhagic stroke+Other cerebrovascular disease+Cerebrovascular procedure (for PS); n (%)	392 (1.7%)	56 (1.9%)	-0.02	1,508 (2.2%)	344 (2.3%)	-0.01	2,242 (1.6%)	461 (1.8%)	-0.02	4142 (1.8%)	861 (2.0%)	-0.01
Occurrence of creatinine tests ordered (for PS); n (%)	1,003 (4.4%)	167 (5.7%)	-0.06	3,079 (4.5%)	535 (3.6%)	0.05	9,217 (6.8%)	1,813 (7.2%)	-0.02	13299 (5.9%)	2515 (5.8%)	0.00
Occurrence of BUN tests ordered (for PS); n (%)	611 (2.7%)	112 (3.8%)	-0.06	1,812 (2.7%)	365 (2.4%)	0.02	5,615 (4.1%)	1,169 (4.6%)	-0.02	8038 (3.5%)	1646 (3.8%)	-0.02
Occurrence of chronic renal insufficiency w/o CKD (for PS) v2; n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!
Chronic kidney disease Stage 1-2 (for PS); n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!	0	0	#VALUE!	#VALUE!	#VALUE!	#VALUE!
Chronic kidney disease Stage 3-6 (for PS); n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!
Bladder stones+Kidney stones (for PS); n (%)	187 (0.8%)	36 (1.2%)	-0.04	861 (1.3%)	245 (1.6%)	-0.03	1,494 (1.1%)	311 (1.2%)	-0.01	2542 (1.1%)	592 (1.4%)	-0.03
Diabetes with peripheral circulatory disorders+Gangrene+Osteomyelitis(for PS) v3 with ICD10 Copy; n (%)	601 (2.7%)	51 (1.7%)	0.07	1,554 (2.3%)	285 (1.9%)	0.03	3,124 (2.3%)	485 (1.9%)	0.03	5279 (2.3%)	821 (1.9%)	0.03
Alcohol abuse or dependence+Drug abuse or dependence (for PS); n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!
Diabetes with other ophthalmic manifestations+Retinal detachment, vitreous hemorrhage, vitrectomy+Retinal laser coagulation therapy (for PS); n (%)	86 (0.4%)	11 (0.4%)	0.00	937 (1.4%)	183 (1.2%)	0.02	1,247 (0.9%)	226 (0.9%)	0.00	2270 (1.0%)	420 (1.0%)	0.00
Other atherosclerosis+Cardiac conduction disorders+Other CVD (for PS) v2 Copy; n (%)	3,880 (17.1%)	540 (18.4%)	-0.03	21,635 (31.9%)	4,994 (33.5%)	-0.03	20,779 (15.3%)	4,065 (16.1%)	-0.02	46294 (20.4%)	9599 (22.3%)	-0.05
Previous cardiac procedure (CABG or PTCA or Stent) + History of CABG or PTCA (for PS) v3; n (%)	1,033 (4.6%)	148 (5.0%)	-0.02	3,026 (4.5%)	771 (5.2%)	-0.03	8,489 (6.2%)	2,092 (8.3%)	-0.08	12548 (5.5%)	3011 (7.0%)	-0.06
Hyperthyroidism + Hypothyroidism + Other disorders of thyroid gland (for PS); n (%)	3,831 (16.9%)	479 (16.3%)	0.02	8,436 (12.4%)	1,861 (12.5%)	0.00	17,662 (13.0%)	3,549 (14.1%)	-0.03	29929 (13.2%)	5889 (13.7%)	-0.01
Delirium + Psychosis (for PS); n (%)	198 (0.9%)	29 (1.0%)	-0.01	1,554 (2.3%)	211 (1.4%)	0.07	1,839 (1.4%)	311 (1.2%)	0.02	3591 (1.6%)	551 (1.3%)	0.03
Any use of Meglitinides (for PS); n (%)	38 (0.2%)	3 (0.1%)	0.03	324 (0.5%)	74 (0.5%)	0.00	377 (0.3%)	74 (0.3%)	0.00	739 (0.3%)	151 (0.4%)	-0.02
Any use of AGIs (for PS); n (%)	17 (0.1%)	4 (0.1%)	0.00	69 (0.1%)	28 (0.2%)	-0.03	109 (0.1%)	30 (0.1%)	0.00	195 (0.1%)	62 (0.1%)	0.00
CKD stage 3-6 + dialysis (for PS); n (%)	4 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!	**	0 (0.0%)	#VALUE!	#VALUE!	0 (0.0%)	#VALUE!
Use of thiazide- United; n (%)	2,786 (12.3%)	342 (11.6%)	0.02	7,453 (11.0%)	1,623 (10.9%)	0.00	16,971 (12.5%)	3,212 (12.7%)	-0.01	27210 (12.0%)	5177 (12.0%)	0.00
Use of beta blockers; n (%)	13,713 (60.5%)	1,820 (62.0%)	-0.03	44,683 (65.9%)	10,110 (67.7%)	-0.04	87,512 (64.3%)	16,625 (65.9%)	-0.03	145908 (64.4%)	28555 (66.3%)	-0.04
Use of calcium channel blockers; n (%)	7,737 (34.1%)	1,075 (36.6%)	-0.05	24,743 (36.5%)	5,699 (38.2%)	-0.04	48,655 (35.8%)	9,878 (39.2%)	-0.07	81135 (35.8%)	16652 (38.6%)	-0.06
All antidiabetic medications except Insulin; n (%)	4,109 (18.1%)	615 (20.9%)	-0.07	12,310 (18.2%)	2,931 (19.6%)	-0.04	25,209 (18.5%)	5,082 (20.1%)	-0.04	41628 (18.4%)	8628 (20.0%)	-0.04
DM Medications - Insulin Copy; n (%)	864 (3.8%)	128 (4.4%)	-0.03	3,888 (5.7%)	795 (5.3%)	0.02	5,129 (3.8%)	926 (3.7%)	0.01	9881 (4.4%)	1849 (4.3%)	0.00
Use of Low Intensity Statins; n (%)	8,138 (35.9%)	964 (32.8%)	0.07	23,820 (35.1%)	4,901 (32.8%)	0.05	48,921 (35.9%)	8,854 (35.1%)	0.02	80879 (35.7%)	14719 (34.2%)	0.03
Use of High Intensity Statins; n (%)	4,085 (18.0%)	619 (21.1%)	-0.08	13,552 (20.0%)	3,233 (21.7%)	-0.04	26,098 (19.2%)	5,459 (21.6%)	-0.06	43735 (19.3%)	9311 (21.6%)	-0.06
Malignant hypertension; n (%)	693 (3.1%)	107 (3.6%)	-0.03	27,053 (39.9%)	6,491 (43.5%)	-0.07	16,757 (12.3%)	4,133 (16.4%)	-0.12	44503 (19.6%)	10731 (24.9%)	-0.13
Cardiovascular stress test; n (%)	58 (0.3%)	13 (0.4%)	-0.02	449 (0.7%)	69 (0.5%)	0.03	579 (0.4%)	107 (0.4%)	0.00	1086 (0.5%)	189 (0.4%)	0.01
Echocardiogram; n (%)	3,464 (15.3%)	835 (28.4%)	-0.32	23,390 (34.5%)	7,438 (49.8%)	-0.31	29,798 (21.9%)	9,331 (37.0%)	-0.34	56652 (25.0%)	17604 (40.8%)	-0.34
Number of BNP tests												
...mean (sd)	0.08 (0.35)	0.09 (0.36)	-0.03	0.07 (0.40)	0.08 (0.35)	-0.03	0.11 (0.41)	0.13 (0.42)	-0.05	0.10 (0.40)	0.11 (0.39)	-0.03
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 (0.46)	0.00 (0.43)	0.00
Number of Cardiac biomarkers tests (troponin, CK-MBs, Myoglobin, CPK)												
...mean (sd)	0.22 (0.91)	0.37 (1.23)	-0.14	0.21 (0.98)	0.32 (1.30)	-0.10	0.19 (0.49)	0.25 (0.56)	-0.11	0.20 (0.72)	0.28 (0.93)	0.00
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 (0.90)	0.00 (1.13)	0.00
Number of Ambulatory Blood pressure monitoring tests												
...mean (sd)	0.00 (0.03)	0.00 (0.03)	0.00	0.00 (0.04)	0.00 (0.04)	0.00	0.00 (0.02)	0.00 (0.04)	0.00	0.00 (0.03)	0.00 (0.04)	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, 0.00]	0.00	0.00 (0.04)	0.00 (0.04)	0.00
N of days on antihypertensive medications during baseline							0	0				
...mean (sd)	130.02 (68.95)	129.85 (66.94)	0.00	135.76 (65.79)	131.96 (67.63)	0.06	138.23 (64.13)	137.11 (64.13)	0.02	136.67 (65.13)	134.83 (65.56)	0.00
...median [IQR]	171.00 [89.00, 181.00]	168.00 [91.00, 181.00]	0.04	174.00 [110.00, 181.00]	171.00 [94.00, 181.00]	0.04	174.00 [122.00, 181.00]	173.00 [116.00, 181.00]	0.02	121.24 (74.47)	130.61 (73.42)	0.00
N of days in database anytime prior							0	0				
...mean (sd)	1,750.74 (1,238.00)	1,753.82 (1,191.57)	0.00	2,172.37 (1,246.30)	2,083.21 (1,203.95)	0.07	833.53 (537.51)	873.46 (457.48)	-0.08	1325.93 (889.77)	1352.52 (849.34)	0.00

Appendix B

...median [IQR]	1,541.00 [660.00, 2,568.00]	1,604.00 [712.50, 2,511.00]	-0.05	2,222.00 [1,052.00, 3,178.25]	2,094.00 [997.50, 3,086.00]	0.10	388.00 [448.00, 1,064.00]	814.00 [530.00, 1,095.00]	-0.25	1024.96 (1122.48)	1116.67 (1033.38)	0.00
Mean Copay per prescription cost (charges in U.S. \$) (180-1 day prior)						0		0				
...mean (sd)	30.18 (42.11)	31.24 (39.86)	-0.03	20.81 (20.98)	22.85 (23.53)	-0.09	119.85 (114.12)	114.07 (117.32)	0.05	81.24 (90.18)	76.83 (91.42)	0.00
...median [IQR]	18.00 [8.44, 36.45]	20.77 [9.54, 39.82]	-0.07	16.05 [8.20, 27.50]	17.50 [8.75, 30.19]	-0.07	95.08 [66.22, 140.00]	90.00 [62.61, 132.00]	0.04	35.06 (90.91)	38.66 (92.15)	0.00
...Missing; n (%)	897 (4.0%)	62 (2.1%)	0.11	1,967 (2.9%)	447 (3.0%)	-0.01	3,658 (2.7%)	516 (2.0%)	0.05	6522 (2.9%)	1025 (2.4%)	0.03
Colonoscopy; n (%)	527 (2.3%)	97 (3.3%)	-0.06	1,843 (2.7%)	500 (3.3%)	-0.04	3,176 (2.3%)	762 (3.0%)	-0.04	5546 (2.4%)	1359 (3.2%)	-0.05
Fecal occult blood (FOB) test; n (%)	738 (3.3%)	119 (4.1%)	-0.04	1,273 (1.9%)	340 (2.3%)	-0.03	2,831 (2.1%)	742 (2.9%)	-0.05	4842 (2.1%)	1201 (2.8%)	-0.05
Flu vaccine; n (%)	4,911 (21.7%)	569 (19.4%)	0.06	8,030 (11.8%)	1,549 (10.4%)	0.04	45,927 (33.7%)	8,362 (33.1%)	0.01	58868 (26.0%)	10480 (24.3%)	0.04
Mammogram; n (%)	1,643 (7.2%)	230 (7.8%)	-0.02	3,465 (5.1%)	794 (5.3%)	-0.01	9,038 (6.6%)	1,984 (7.9%)	-0.05	14146 (6.2%)	3008 (7.0%)	-0.03
Pap smear; n (%)	238 (1.1%)	45 (1.5%)	-0.04	876 (1.3%)	243 (1.6%)	-0.03	1,723 (1.3%)	566 (2.2%)	-0.07	2837 (1.3%)	854 (2.0%)	-0.05
Pneumonia vaccine; n (%)	2,371 (10.5%)	268 (9.1%)	0.05	2,176 (3.2%)	469 (3.1%)	0.01	16,663 (12.2%)	2,980 (11.8%)	0.01	21210 (9.4%)	3717 (8.6%)	0.03
PSA test or Prostate exam for DRE; n (%)	3,062 (13.5%)	511 (17.4%)	-0.11	3,858 (5.7%)	1,151 (7.7%)	-0.08	18,750 (13.8%)	4,597 (18.2%)	-0.12	25670 (11.3%)	6259 (14.5%)	-0.10
Bone mineral density; n (%)	705 (3.1%)	107 (3.6%)	-0.03	1,213 (1.8%)	266 (1.8%)	0.00	3,836 (2.8%)	858 (3.4%)	-0.03	5754 (2.5%)	1231 (2.9%)	-0.02
Use of Sympathomimetic agents; n (%)	45 (0.2%)	11 (0.4%)	-0.04	231 (0.3%)	91 (0.6%)	-0.04	267 (0.2%)	61 (0.2%)	0.00	543 (0.2%)	163 (0.4%)	-0.04
Use of CNS stimulants; n (%)	24 (0.1%)	3 (0.1%)	0.00	250 (0.4%)	84 (0.6%)	-0.03	183 (0.1%)	33 (0.1%)	0.00	457 (0.2%)	120 (0.3%)	-0.02
Use of estrogens, progestins, androgens; n (%)	465 (2.1%)	88 (3.0%)	-0.06	2,275 (3.4%)	696 (4.7%)	-0.07	3,175 (2.3%)	880 (3.5%)	-0.07	5915 (2.6%)	1664 (3.9%)	-0.07
Use of Angiogenesis inhibitors; n (%)	4 (0.0%)	1 (0.0%)	#DIV/0!	28 (0.0%)	5 (0.0%)	#DIV/0!	29 (0.0%)	12 (0.0%)	#DIV/0!	61 (0.0%)	18 (0.0%)	#DIV/0!
Use of Oral Immunosuppressants; n (%)	6 (0.0%)	1 (0.0%)	0.00	69 (0.1%)	8 (0.1%)	0.00	19 (0.0%)	**	#VALUE!	94 (0.0%)	#VALUE!	#VALUE!
Use of fondaparinux or Bivalirudin; n (%)	3 (0.0%)	1 (0.0%)	#DIV/0!	61 (0.1%)	11 (0.1%)	0.00	61 (0.0%)	**	#VALUE!	125 (0.1%)	#VALUE!	#VALUE!
Use of other direct thrombin inhibitors (lepirudin, desirudin, argatroban); n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!
Use of Ticagrelor ON CED; n (%)	2 (0.0%)	2 (0.1%)	-0.04	43 (0.1%)	12 (0.1%)	0.00	26 (0.0%)	**	#VALUE!	71 (0.0%)	#VALUE!	#VALUE!
Use of Ticagrelor; n (%)	6 (0.0%)	3 (0.1%)	-0.04	62 (0.1%)	19 (0.1%)	0.00	165 (0.1%)	37 (0.1%)	0.00	233 (0.1%)	59 (0.1%)	0.00
Number of D-dimer tests												
...mean (sd)	0.01 (0.12)	0.02 (0.15)	-0.07	0.01 (0.12)	0.02 (0.16)	-0.07	0.02 (0.16)	0.03 (0.18)	-0.06	0.02 (0.15)	0.03 (0.17)	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, 0.00]	0.00	0.00 (0.16)	0.00 (0.19)	0.00
Numbe of CRP, high-sensitivity CRP tests												
...mean (sd)	0.04 (0.31)	0.06 (0.32)	-0.06	0.03 (0.23)	0.03 (0.20)	0.00	0.06 (0.35)	0.07 (0.36)	-0.03	0.05 (0.31)	0.06 (0.31)	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, 0.00]	0.00	0.00 (0.34)	0.00 (0.33)	0.00
Number of PT or aPTT tests												
...mean (sd)	3.36 (4.06)	0.45 (1.50)	0.95	1.97 (3.43)	0.38 (1.42)	0.61	3.73 (4.31)	0.40 (1.30)	1.05	3.17 (4.04)	0.40 (1.36)	0.01
...median [IQR]	2.00 [0.00, 6.00]	0.00 [0.00, 0.00]	0.65	0.00 [0.00, 3.00]	0.00 [0.00, 0.00]	0.00	2.00 [0.00, 6.00]	0.00 [0.00, 0.00]	0.63	0.80 (4.46)	0.00 (1.52)	0.00
Number of Bleeding time tests												
...mean (sd)	0.00 (0.01)	0.00 (0.00)	0.00	0.00 (0.01)	0.00 (0.01)	0.00	0.00 (0.02)	0.00 (0.02)	0.00	0.00 (0.02)	0.00 (0.02)	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, 0.00]	0.00	0.00 (0.02)	0.00 (0.02)	0.00
HAS-BLED Score (ICD-9 and ICD-10), 180 days												
...mean (sd)	3.18 (0.65)	3.23 (0.68)	-0.08	3.23 (0.70)	3.24 (0.75)	-0.01	3.23 (0.61)	3.29 (0.62)	-0.10	3.22 (0.64)	3.27 (0.67)	0.00
...median [IQR]	3.00 [3.00, 3.00]	3.00 [3.00, 4.00]	0.00	3.00 [3.00, 4.00]	3.00 [3.00, 4.00]	0.00	3.00 [3.00, 4.00]	3.00 [3.00, 4.00]	0.00	2.10 (0.75)	2.28 (0.77)	0.00
N of Generic name drugs												
...mean (sd)	15.76 (13.47)	14.43 (12.65)	0.10	13.67 (9.58)	12.24 (9.51)	0.15	15.17 (11.23)	14.50 (11.57)	0.06	14.78 (11.02)	13.71 (10.98)	0.00
...median [IQR]	12.00 [7.00, 20.00]	11.00 [6.00, 19.00]	0.08	12.00 [7.00, 18.00]	10.00 [6.00, 19.00]	0.21	13.00 [8.00, 19.00]	12.00 [7.00, 19.00]	0.09	8.68 (12.21)	8.37 (11.93)	0.00
N of Brand name drugs												
...mean (sd)	2.94 (4.50)	4.77 (5.14)	-0.38	4.27 (4.65)	5.81 (5.28)	-0.31	3.12 (4.33)	5.05 (5.37)	-0.40	3.45 (4.45)	5.29 (5.32)	0.00
...median [IQR]	1.00 [0.00, 4.00]	3.00 [1.00, 6.00]	-0.41	3.00 [1.00, 6.00]	4.00 [2.00, 8.00]	-0.20	2.00 [0.00, 5.00]	3.00 [1.00, 7.00]	-0.21	1.60 (5.13)	2.63 (5.92)	0.00
Use of clopidogrel ; n (%)	1,016 (4.5%)	190 (6.5%)	-0.09	5,477 (8.1%)	1,823 (12.2%)	-0.14	8,774 (6.4%)	2,571 (10.2%)	-0.14	15267 (6.7%)	4584 (10.6%)	-0.14
Systemic embolism; n (%)	117 (0.5%)	12 (0.4%)	0.01	588 (0.9%)	58 (0.4%)	0.06	713 (0.5%)	87 (0.3%)	0.03	1418 (0.6%)	157 (0.4%)	0.03
DVT; n (%)	887 (3.9%)	33 (1.1%)	0.18	3,510 (5.2%)	214 (1.4%)	0.21	6,763 (5.0%)	280 (1.1%)	0.23	11160 (4.9%)	527 (1.2%)	0.22
PE; n (%)	406 (1.8%)	4 (0.1%)	0.18	2,009 (3.0%)	91 (0.6%)	0.18	3,175 (2.3%)	74 (0.3%)	0.18	5590 (2.5%)	169 (0.4%)	0.18
Diabetes: 1 inpatient or 2 outpatient claims within 183 days ; n (%)	5,727 (25.3%)	791 (26.9%)	-0.04	16,089 (23.7%)	3,565 (23.9%)	0.00	33,792 (24.8%)	6,369 (25.2%)	-0.01	55608 (24.5%)	10725 (24.9%)	-0.01
Intracranial or retroperitoneal hemorrhage: 1 inpatient or 2 outpatient claims within 183 days; n (%)	27 (0.1%)	1 (0.0%)	0.04	89 (0.1%)	8 (0.1%)	0.00	90 (0.1%)	18 (0.1%)	0.00	206 (0.1%)	27 (0.1%)	0.00
Peptic Ulcer Disease; n (%)	1,599 (7.1%)	222 (7.6%)	-0.02	3,997 (5.9%)	908 (6.1%)	-0.01	8,879 (6.5%)	1,855 (7.4%)	-0.04	14475 (6.4%)	2985 (6.9%)	-0.02
Upper GI bleed; n (%)	2 (0.0%)	0 (0.0%)	#DIV/0!	17 (0.0%)	4 (0.0%)	#DIV/0!	18 (0.0%)	**	#VALUE!	37 (0.0%)	#VALUE!	#VALUE!
Lower/ unspecified GI bleed; n (%)	127 (0.6%)	25 (0.9%)	-0.03	491 (0.7%)	102 (0.7%)	0.00	705 (0.5%)	154 (0.6%)	-0.01	1323 (0.6%)	281 (0.7%)	-0.01
Urogenital bleed; n (%)	686 (3.0%)	91 (3.1%)	-0.01	2,289 (3.4%)	451 (3.0%)	0.02	4,121 (3.0%)	727 (2.9%)	0.01	7096 (3.1%)	1269 (2.9%)	0.01
Other bleeds; n (%)	297 (1.3%)	28 (1.0%)	0.03	1,189 (1.8%)	163 (1.1%)	0.06	1,919 (1.4%)	259 (1.0%)	0.04	3405 (1.5%)	450 (1.0%)	0.05
Prior cancer; n (%)	2,605 (11.5%)	307 (10.5%)	0.03	6,550 (9.7%)	1,366 (9.1%)	0.02	13,998 (10.3%)	2,691 (10.7%)	-0.01	23153 (10.2%)	4364 (10.1%)	0.00
Aspirin; n (%)	58 (0.3%)	13 (0.4%)	-0.02	593 (0.9%)	180 (1.2%)	-0.03	348 (0.3%)	118 (0.5%)	-0.03	999 (0.4%)	311 (0.7%)	-0.04
Aspirin/dipyridamole; n (%)	36 (0.2%)	11 (0.4%)	-0.04	243 (0.4%)	83 (0.6%)	-0.03	295 (0.2%)	103 (0.4%)	-0.04	574 (0.3%)	197 (0.5%)	-0.03
Other antiplatelet agents; n (%)	108 (0.5%)	13 (0.4%)	0.01	407 (0.6%)	83 (0.6%)	0.00	604 (0.4%)	148 (0.6%)	-0.03	1119 (0.5%)	244 (0.6%)	-0.01
PGP inhibitors; n (%)	8,231 (36.3%)	1,160 (39.5%)	-0.07	30,813 (45.5%)	7,267 (48.7%)	-0.06	54,573 (40.1%)	11,181 (44.3%)	-0.09	93617 (41.3%)	19608 (45.5%)	-0.08
Other gastroprotective agents; n (%)	89 (0.4%)	17 (0.6%)	-0.03	525 (0.8%)	142 (1.0%)	-0.02	866 (0.6%)	178 (0.7%)	-0.01	1480 (0.7%)	337 (0.8%)	-0.01
Number of lipid tests ordered												
...mean (sd)	0.59 (0.80)	0.69 (0.85)	-0.12	0.22 (0.62)	0.26 (0.68)	-0.06	0.62 (0.78)	0.74 (0.83)	-0.15	0.50 (0.74)	0.57 (0.78)	0.00
...median [IQR]	0.00 [0.00, 1.00]	1.00 [0.00, 1.00]	-1.21	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 [0.00, 1.00]	1.00 [0.00, 1.00]	-1.24	0.00 (0.81)	0.41 (0.85)	0.00
Proton pump inhibitor; n (%)	3,648 (16.1%)	468 (15.9%)	0.01	13,322 (19.7%)	2,930 (19.6%)	0.00	25,610 (18.8%)	4,816 (19.1%)	-0.01	42580 (18.8%)	8214 (19.1%)	-0.01
H2 receptor antagonist; n (%)	704 (3.1%)	99 (3.4%)	-0.02	2,254 (3.3%)	422 (2.8%)	0.03	5,175 (3.8%)	1,006 (4.0%)	-0.01	8133 (3.6%)	1527 (3.5%)	0.01
Vitamin K therapy; n (%)	18 (0.1%)	0 (0.0%)	0.04	180 (0.3%)	8 (0.1%)	0.04	101 (0.1%)	**	#VALUE!	299 (0.1%)	#VALUE!	#VALUE!
Number of neurologist visits												
...mean (sd)	0.15 (0.97)	0.17 (1.00)	-0.02	0.18 (1.18)	0.21 (1.01)	-0.03	0.20 (1.29)	0.24 (1.22)	-0.03	0.19 (1.23)	0.22 (1.14)	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, 0.00]	0.00	0.00 (1.39)	0.00 (1.24)	0.00
Number of INR (prothrombin) tests ordered												
...mean (sd)	3.26 (3.99)	0.35 (1.30)	0.98	1.88 (3.34)	0.29 (1.24)	0.63	3.71 (4.27)	0.37 (1.27)	1.06	3.12 (3.99)	0.34 (1.26)	0.01
...median [IQR]	1.00 [0.00, 6.00]	0.00 [0.00, 0.00]	0.34	0.00 [0.00, 2.00]	0.00 [0.00, 0.00]	0.00	2.00 [0.00, 6.00]	0.00 [0.00, 0.00]	0.63	0.70 (4.39)	0.00 (1.40)	0.00
Treating prescriber - Cardiologist; n (%)	6,838 (30.2%)	1,387 (47.2%)	-0.35	23,716 (35.0%)	8,267 (55.4%)	-0.42	53,448 (39.3%)	14,249 (56.5%)	-0.35	84002 (37.1%)	23903 (55.5%)	-0.38
Treating prescriber - Primary Care Physician; n (%)	14,075 (62.1%)	1,646 (56.1%)	0.12	18,447 (27.2%)	4,421 (29.6%)	-0.05	32,984 (24.2%)	5,914 (23.4%)	0.02	65506 (28.9%)	11981 (27.8%)	0.02

Appendix B

Treating prescriber - Other; n (%)	16,132 (71.2%)	2,151 (73.3%)	-0.05	50,911 (75.1%)	11,444 (76.7%)	-0.04	103,947 (76.4%)	19,204 (76.1%)	0.01	170990 (75.5%)	32799 (76.1%)	-0.01
Alpha blockers; n (%)	3,017 (13.3%)	415 (14.1%)	-0.02	9,114 (13.4%)	1,933 (12.9%)	0.01	18,132 (13.3%)	3,523 (14.0%)	-0.02	30263 (13.4%)	5871 (13.6%)	-0.01
CHADS2 score, 180 days, V												
...mean (sd)	1.86 (1.00)	1.87 (1.01)	-0.01	1.97 (1.09)	1.90 (1.08)	0.06	3.02 (1.28)	2.92 (1.27)	0.08	2.59 (1.20)	2.50 (1.19)	0.00
...median [IQR]	2.00 [1.00, 2.00]	2.00 [1.00, 2.00]	0.00	2.00 [1.00, 3.00]	2.00 [1.00, 2.50]	0.00	3.00 [2.00, 4.00]	3.00 [2.00, 4.00]	0.00	1.70 (1.34)	1.87 (1.30)	0.00
Use of Prasugrel; n (%)	14 (0.1%)	7 (0.2%)	-0.03	138 (0.2%)	72 (0.5%)	-0.05	11 (0.0%)	**	#VALUE!	163 (0.1%)	#VALUE!	#VALUE!
Use of Loop Diuretics+other diuretics+other hypertension drugs; n (%)	6,341 (28.0%)	695 (23.7%)	0.10	25,337 (37.4%)	4,384 (29.4%)	0.17	43,001 (31.6%)	6,494 (25.7%)	0.13	74679 (33.0%)	11573 (26.9%)	0.13
Commercial vs Medicare Advantage- Business Type Code - CORRECT ONE - OPTUM												
...Commercial; n (%)	2,194 (9.7%)	653 (22.2%)	-0.35	61,780 (91.1%)	12,464 (83.5%)	0.23	-	-	#VALUE!	63,974 (70.7%)	13,117 (73.4%)	-0.06
...Medicare Advantage; n (%)	20,471 (90.3%)	2283 (77.8%)	0.35	6,010 (8.9%)	2,465 (16.5%)	-0.23	-	-	#VALUE!	26,481 (29.3%)	4,748 (26.6%)	0.06
Commercial vs Medicare Advantage- Business Type Code												
...COM = COMMERCIAL; n (%)	2,194 (9.7%)	653 (22.2%)	-0.35	-	-	-	-	-	#VALUE!	2,194 (9.7%)	653 (22.2%)	-0.35
...MCR = MEDICARE; n (%)	20,471 (90.3%)	2,283 (77.8%)	0.35	-	-	-	-	-	#VALUE!	20,471 (90.3%)	2,283 (77.8%)	0.35
...MCD = MEDICAID; n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	-	-	-	-	-	#VALUE!	0 (0.0%)	0 (0.0%)	#DIV/0!
...NONE = NO BUSINESS LINE CODE (added in 2015); n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	-	-	-	-	-	#VALUE!	0 (0.0%)	0 (0.0%)	#DIV/0!
...UNK = UNKNOWN (added in 2015); n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	-	-	-	-	-	#VALUE!	0 (0.0%)	0 (0.0%)	#DIV/0!
Commercial vs Medicare Advantage- Data Type												
...1 - Fee For Service; n (%)	-	-		5,285 (7.8%)	2,211 (14.8%)	-0.22	-	-		5,285 (7.8%)	2,211 (14.8%)	-0.22
...2 - Encounter; n (%)	-	-		725 (1.1%)	254 (1.7%)	-0.05	-	-		725 (1.1%)	254 (1.7%)	-0.05
...3 - Medicare; n (%)	-	-		54,723 (80.7%)	11,573 (77.5%)	0.08	-	-		54,723 (80.7%)	11,573 (77.5%)	0.08
...4 - Medicare Encounter; n (%)	-	-		7,057 (10.4%)	891 (6.0%)	0.16	-	-		7,057 (10.4%)	891 (6.0%)	0.16
Metropolitan Statistical Area - Urban (any MSA) vs Rural (non-MSA)												
...Urban; n (%)	-	-		53,890 (79.5%)	11,905 (79.7%)	0.00	-	-		53,890 (79.5%)	11,905 (79.7%)	0.00
...Rural; n (%)	-	-		649 (1.0%)	117 (0.8%)	0.02	-	-		649 (1.0%)	117 (0.8%)	0.02
...Unknown/Missing; n (%)	-	-		13,251 (19.5%)	2,907 (19.5%)	0.00	-	-		13,251 (19.5%)	2,907 (19.5%)	0.00

Due to CMS cell suppression policy, all values less than 11 are denoted with **

Appendix B

PS-matched												
	Optum			MarketScan			Medicare			POOLED		
Variable	WARFARIN	Dabigatran 150mg	St. Diff.	Reference - warfarin	Exposure - Dabigatran 150mg	St. Diff.	Reference - warfarin	Exposure - Dabigatran 150mg	St. Diff.	Reference - warfarin	Exposure - Dabigatran 150mg	St. Diff.
Number of patients	2,790	2,790		13,960	13,960		22,320	22,320		39,070	39,070	
Age												
...mean (sd)	75.41 (7.35)	75.41 (7.13)	0.00	74.41 (10.11)	74.76 (9.22)	-0.04	77.04 (7.31)	77.18 (6.88)	-0.02	75.98 (8.42)	76.19 (7.81)	-0.03
...median [IQR]	77.00 [71.00, 81.00]	77.00 [71.00, 81.00]	0.00	76.00 [69.00, 81.00]	76.00 [69.00, 81.00]	0.00	77.00 [73.00, 82.00]	77.00 [73.00, 82.00]	0.00	76.64 (8.42)	76.64 (7.81)	0.00
Age categories without zero category												
...18 - 54; n (%)	50 (1.8%)	32 (1.1%)	0.06	628 (4.5%)	428 (3.1%)	0.07	209 (0.9%)	92 (0.4%)	0.06	887 (2.3%)	552 (1.4%)	0.07
...55 - 64; n (%)	145 (5.2%)	153 (5.5%)	-0.01	1,527 (10.9%)	1,634 (11.7%)	-0.03	414 (1.9%)	310 (1.4%)	0.04	2,086 (5.3%)	2,097 (5.4%)	0.00
...65 - 74; n (%)	661 (23.7%)	665 (23.8%)	0.00	3,394 (24.3%)	3,359 (24.1%)	0.00	6,138 (27.5%)	6,223 (27.9%)	-0.01	10,193 (26.1%)	10,247 (26.2%)	0.00
...≥ 75; n (%)	1,934 (69.3%)	1,940 (69.5%)	0.00	8,411 (60.3%)	8,539 (61.2%)	-0.02	15,559 (69.7%)	15,695 (70.3%)	-0.01	25,904 (66.3%)	26,174 (67.0%)	-0.01
Gender without zero category-United												
...Males; n (%)	1,675 (60.0%)	1,675 (60.0%)	0.00	8,106 (58.1%)	8,134 (58.3%)	0.00	12,689 (56.9%)	12,580 (56.4%)	0.01	22,470 (57.5%)	22,389 (57.3%)	0.00
...Females; n (%)	1,115 (40.0%)	1,115 (40.0%)	0.00	5,854 (41.9%)	5,826 (41.7%)	0.00	9,631 (43.1%)	9,740 (43.6%)	-0.01	16,600 (42.5%)	16,681 (42.7%)	0.00
Race												
...White; n (%)							20,699 (92.7%)	20,744 (92.9%)		20,699 (92.7%)	20,744 (92.9%)	0.00
...Black; n (%)							663 (3.0%)	656 (2.9%)		663 (3.0%)	656 (2.9%)	0.00
...Asian; n (%)							289 (1.3%)	290 (1.3%)		289 (1.3%)	290 (1.3%)	0.00
...Hispanic; n (%)							242 (1.1%)	219 (1.0%)		242 (1.1%)	219 (1.0%)	0.00
...North American Native; n (%)							73 (0.3%)	67 (0.3%)		73 (0.3%)	67 (0.3%)	0.00
...Other/Unknown; n (%)							354 (1.6%)	344 (1.5%)		354 (1.6%)	344 (1.5%)	0.00
Region without zero category-United v3 (lumping missing/Other category with West)												
...Northeast; n (%)	407 (14.6%)	401 (14.4%)	0.01	3,208 (23.0%)	3,249 (23.3%)	-0.01	4,283 (19.2%)	4,272 (19.1%)	0.00	7,898 (20.2%)	7,922 (20.3%)	0.00
...South; n (%)	945 (33.9%)	945 (33.9%)	0.00	3,797 (27.2%)	3,765 (27.0%)	0.00	8,706 (39.0%)	8,595 (38.5%)	0.01	13,448 (34.4%)	13,305 (34.1%)	0.01
...Midwest; n (%)	453 (16.2%)	456 (16.3%)	0.00	4,767 (34.1%)	4,766 (34.1%)	0.00	5,278 (23.6%)	5,344 (23.9%)	-0.01	10,498 (26.9%)	10,566 (27.0%)	0.00
...West; n (%)	985 (35.3%)	988 (35.4%)	0.00	2,126 (15.2%)	2,119 (15.2%)	0.00	4,053 (18.2%)	4,109 (18.4%)	-0.01	7,164 (18.3%)	7,216 (18.5%)	-0.01
...Unknown+missing; n (%)	N/A	N/A	#VALUE!	62 (0.4%)	61 (0.4%)	0.00	N/A	N/A	#VALUE!	62 (0.4%)	61 (0.4%)	0.00
CV Covariates												
Ischemic heart disease; n (%)	815 (29.2%)	800 (28.7%)	0.01	4,873 (34.9%)	4,841 (34.7%)	0.00	7,025 (31.5%)	6,988 (31.3%)	0.00	12,713 (32.5%)	12,629 (32.3%)	0.00
Acute MI; n (%)	18 (0.6%)	19 (0.7%)	-0.01	394 (2.8%)	378 (2.7%)	0.01	320 (1.4%)	337 (1.5%)	-0.01	732 (1.9%)	734 (1.9%)	0.00
ACS/unstable angina; n (%)	28 (1.0%)	28 (1.0%)	0.00	386 (2.8%)	384 (2.8%)	0.00	405 (1.8%)	400 (1.8%)	0.00	819 (2.1%)	812 (2.1%)	0.00
Old MI; n (%)	76 (2.7%)	69 (2.5%)	0.01	486 (3.5%)	464 (3.3%)	0.01	992 (4.4%)	952 (4.3%)	0.00	1554 (4.0%)	1485 (3.8%)	0.01
Stable angina; n (%)	100 (3.6%)	94 (3.4%)	0.01	556 (4.0%)	549 (3.9%)	0.01	864 (3.9%)	822 (3.7%)	0.01	1,520 (3.9%)	1,465 (3.7%)	0.01
Coronary atherosclerosis and other forms of chronic Ischemic heart disease; n (%)	759 (27.2%)	754 (27.0%)	0.00	4,442 (31.8%)	4,376 (31.3%)	0.01	6,399 (28.7%)	6,373 (28.6%)	0.00	11,600 (29.7%)	11,503 (29.4%)	0.01
Other atherosclerosis with ICD10 v2 Copy; n (%)	49 (1.8%)	44 (1.6%)	0.02	241 (1.7%)	223 (1.6%)	0.01	296 (1.3%)	296 (1.3%)	0.00	563 (1.5%)	563 (1.4%)	0.01
Previous cardiac procedure (CABG or PTCA or Stent) v4; n (%)	3 (0.1%)	7 (0.3%)	-0.04	221 (1.6%)	142 (1.0%)	0.05	222 (1.0%)	125 (0.6%)	0.04	446 (1.1%)	274 (0.7%)	0.04
History of CABG or PTCA; n (%)	152 (5.4%)	139 (5.0%)	0.02	585 (4.2%)	611 (4.4%)	-0.01	1,677 (7.5%)	1,720 (7.7%)	-0.01	2,414 (6.2%)	2,470 (6.3%)	0.00
Any stroke; n (%)	244 (8.7%)	243 (8.7%)	0.00	1,310 (9.4%)	1,263 (9.0%)	0.01	1,529 (6.9%)	1,560 (7.0%)	0.00	3,083 (7.9%)	3,066 (7.8%)	0.00
Ischemic stroke (w and w/o mention of cerebral infarction); n (%)	243 (8.7%)	243 (8.7%)	0.00	1,307 (9.4%)	1,258 (9.0%)	0.01	1,521 (6.8%)	1,552 (7.0%)	-0.01	3,071 (7.9%)	3,053 (7.8%)	0.00
Hemorrhagic stroke; n (%)	3 (0.1%)	2 (0.1%)	0.00	6 (0.0%)	8 (0.1%)	-0.04	**	**	#VALUE!	#VALUE!	#VALUE!	#VALUE!
TIA; n (%)	132 (4.7%)	137 (4.9%)	-0.01	655 (4.7%)	636 (4.6%)	0.00	690 (3.1%)	663 (3.0%)	0.01	1477 (3.8%)	1436 (3.7%)	0.01
Other cerebrovascular disease; n (%)	43 (1.5%)	51 (1.8%)	-0.02	274 (2.0%)	290 (2.1%)	-0.01	390 (1.7%)	375 (1.7%)	0.00	707 (1.8%)	716 (1.8%)	0.00
Late effects of cerebrovascular disease; n (%)	11 (0.4%)	9 (0.3%)	0.02	17 (0.1%)	19 (0.1%)	0.00	66 (0.3%)	68 (0.3%)	0.00	94 (0.2%)	96 (0.2%)	0.00
Cerebrovascular procedure; n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	21 (0.2%)	21 (0.2%)	0.00	19 (0.1%)	16 (0.1%)	0.00	040 (0.1%)	37 (0.1%)	0.00
Heart failure (CHF); n (%)	325 (11.6%)	326 (11.7%)	0.00	3,066 (22.0%)	3,013 (21.6%)	0.01	2,500 (11.2%)	2,580 (11.6%)	-0.01	5,891 (15.1%)	5,919 (15.1%)	0.00
Peripheral Vascular Disease (PVD) or PVD Surgery v2; n (%)	209 (7.5%)	203 (7.3%)	0.01	898 (6.4%)	922 (6.6%)	-0.01	1,212 (5.4%)	1,199 (5.4%)	0.00	2,319 (5.9%)	2,324 (5.9%)	0.00
Atrial fibrillation; n (%)	2,634 (94.4%)	2,641 (94.7%)	-0.01	13,289 (95.2%)	13,224 (94.7%)	0.02	19,244 (86.2%)	19,278 (86.4%)	-0.01	35,167 (90.0%)	35,143 (89.9%)	0.00
Other cardiac dysrhythmia; n (%)	1,200 (43.0%)	1,187 (42.5%)	0.01	4,384 (31.4%)	4,311 (30.9%)	0.01	8,194 (36.7%)	8,120 (36.4%)	0.01	13,778 (35.3%)	13,618 (34.9%)	0.01
Cardiac conduction disorders; n (%)	145 (5.2%)	174 (6.2%)	-0.04	894 (6.4%)	888 (6.4%)	0.00	1,301 (5.8%)	1,265 (5.7%)	0.00	2340 (6.0%)	2327 (6.0%)	0.00
Other CVD; n (%)	363 (13.0%)	333 (11.9%)	0.03	4,082 (29.2%)	4,009 (28.7%)	0.01	2,342 (10.5%)	2,297 (10.3%)	0.01	6,787 (17.4%)	6,639 (17.0%)	0.01
Diabetes-related complications												
Diabetic retinopathy; n (%)	38 (1.4%)	40 (1.4%)	0.00	187 (1.3%)	176 (1.3%)	0.00	222 (1.0%)	201 (0.9%)	0.01	#VALUE!	417 (1.1%)	#VALUE!
Diabetes with other ophthalmic manifestations; n (%)	1 (0.0%)	2 (0.1%)	-0.04	154 (1.1%)	121 (0.9%)	0.02	154 (0.7%)	137 (0.6%)	0.01	309 (0.8%)	260 (0.7%)	0.01
Retinal detachment, vitreous hemorrhage, vitrectomy; n (%)	9 (0.3%)	7 (0.3%)	0.00	36 (0.3%)	31 (0.2%)	0.02	31 (0.1%)	33 (0.1%)	0.00	076 (0.2%)	71 (0.2%)	0.00
Retinal laser coagulation therapy; n (%)	1 (0.0%)	2 (0.1%)	-0.04	26 (0.2%)	31 (0.2%)	0.00	43 (0.2%)	31 (0.1%)	0.03	70 (0.2%)	64 (0.2%)	0.00
Occurrence of Diabetic Neuropathy v2 Copy; n (%)	103 (3.7%)	110 (3.9%)	-0.01	436 (3.1%)	455 (3.3%)	-0.01	570 (2.6%)	569 (2.5%)	0.01	1109 (2.8%)	1134 (2.9%)	-0.01
Occurrence of diabetic nephropathy V3 with ICD10 Copy; n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!
Hypoglycemia v2; n (%)	15 (0.5%)	18 (0.6%)	-0.01	151 (1.1%)	128 (0.9%)	0.02	244 (1.1%)	190 (0.9%)	0.02	410 (1.0%)	336 (0.9%)	0.01
Hyperglycemia; n (%)	117 (4.2%)	105 (3.8%)	0.02	255 (1.8%)	282 (2.0%)	-0.01	1,028 (4.6%)	1,049 (4.7%)	0.00	1400 (3.6%)	1436 (3.7%)	-0.01
Disorders of fluid electrolyte and acid-base balance; n (%)	105 (3.8%)	107 (3.8%)	0.00	872 (6.2%)	880 (6.3%)	0.00	1,011 (4.5%)	1,061 (4.8%)	-0.01	1988 (5.1%)	2048 (5.2%)	0.00
Diabetic ketoacidosis; n (%)	2 (0.1%)	2 (0.1%)	0.00	19 (0.1%)	8 (0.1%)	0.00	24 (0.1%)	16 (0.1%)	0.00	45 (0.1%)	26 (0.1%)	0.00
Hyperosmolar hyperglycemic nonketotic syndrome (HONK); n (%)	2 (0.1%)	1 (0.0%)	0.04	12 (0.1%)	5 (0.0%)	0.04	17 (0.1%)	21 (0.1%)	0.00	31 (0.1%)	27 (0.1%)	0.00
Diabetes with peripheral circulatory disorders with ICD-10 v2 Copy; n (%)	68 (2.4%)	46 (1.6%)	0.06	242 (1.7%)	225 (1.6%)	0.01	361 (1.6%)	384 (1.7%)	-0.01	671 (1.7%)	655 (1.7%)	0.00
Diabetic Foot; n (%)	46 (1.6%)	38 (1.4%)	0.02	243 (1.7%)	261 (1.9%)	-0.02	358 (1.6%)	423 (1.9%)	-0.02	647 (1.7%)	722 (1.8%)	-0.01
Gangrene v2; n (%)	3 (0.1%)	1 (0.0%)	0.04	13 (0.1%)	15 (0.1%)	0.00	14 (0.1%)	11 (0.0%)	0.04	030 (0.1%)	27 (0.1%)	0.00
Lower extremity amputation; n (%)	2 (0.1%)	8 (0.3%)	-0.04	15 (0.1%)	27 (0.2%)	-0.03	33 (0.1%)	38 (0.2%)	-0.03	050 (0.1%)	073 (0.2%)	-0.03
Osteomyelitis; n (%)	5 (0.2%)	4 (0.1%)	0.03	40 (0.3%)	48 (0.3%)	0.00	43 (0.2%)	47 (0.2%)	0.00	88 (0.2%)	99 (0.3%)	-0.02
Skin infections v2; n (%)	119 (4.3%)	131 (4.7%)	-0.02	711 (5.1%)	748 (5.4%)	-0.02	967 (4.3%)	1,042 (4.7%)	-0.02	1797 (4.6%)	1921 (4.9%)	-0.01
Erectile dysfunction; n (%)	58 (2.1%)	63 (2.3%)	-0.01	215 (1.5%)	215 (1.5%)	0.00	223 (1.0%)	192 (0.9%)	0.01	496 (1.3%)	470 (1.2%)	0.01

Appendix B

Diabetes with unspecified complication; n (%)	19 (0.7%)	19 (0.7%)	0.00	115 (0.8%)	92 (0.7%)	0.01	150 (0.7%)	125 (0.6%)	0.01	284 (0.7%)	236 (0.6%)	0.01
Diabetes mellitus without mention of complications; n (%)	803 (28.8%)	788 (28.2%)	0.01	3,509 (25.1%)	3,454 (24.7%)	0.01	6,004 (26.9%)	5,993 (26.9%)	0.00	10,316 (26.4%)	10,235 (26.2%)	0.00
Hypertension: 1 inpatient or 2 outpatient claims within 365 days; n (%)	2,143 (76.8%)	2,129 (76.3%)	0.01	9,249 (66.3%)	9,189 (65.8%)	0.01	18,608 (83.4%)	18,599 (83.3%)	0.00	30,000 (76.8%)	29,917 (76.6%)	0.00
Hyperlipidemia v2; n (%)	1,705 (61.1%)	1,697 (60.8%)	0.01	5,935 (42.5%)	5,767 (41.3%)	0.02	11,060 (49.6%)	10,934 (49.0%)	0.01	18,700 (47.9%)	18,398 (47.1%)	0.02
Edema; n (%)	233 (8.4%)	230 (8.2%)	0.01	1,038 (7.4%)	981 (7.0%)	0.02	1,262 (5.7%)	1,296 (5.8%)	0.00	2533 (6.5%)	2507 (6.4%)	0.00
Renal Dysfunction (non-diabetic) v2; n (%)	1 (0.0%)	1 (0.0%)	#DIV/0!	6 (0.0%)	6 (0.0%)	#DIV/0!	**	**	#VALUE!	#VALUE!	#VALUE!	#VALUE!
Occurrence of acute renal disease v2; n (%)	0 (0.0%)	1 (0.0%)	#DIV/0!	6 (0.0%)	6 (0.0%)	#DIV/0!	**	**	#VALUE!	#VALUE!	#VALUE!	#VALUE!
Occurrence of chronic renal insufficiency; n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!
Chronic kidney disease v2; n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!
CKD Stage 3-4; n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!
Occurrence of hypertensive nephropathy; n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!
Occurrence of miscellaneous renal insufficiency v2; n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!
Glaucoma or cataracts v2; n (%)	605 (21.7%)	645 (23.1%)	-0.03	3,101 (22.2%)	3,062 (21.9%)	0.01	4,898 (21.9%)	5,044 (22.6%)	-0.02	8,604 (22.0%)	8,751 (22.4%)	-0.01
Cellulitis or abscess of toe; n (%)	15 (0.5%)	16 (0.6%)	-0.01	68 (0.5%)	89 (0.6%)	-0.01	143 (0.6%)	150 (0.7%)	-0.01	226 (0.6%)	255 (0.7%)	-0.01
Foot ulcer; n (%)	48 (1.7%)	39 (1.4%)	0.02	248 (1.8%)	264 (1.9%)	-0.01	310 (1.4%)	369 (1.7%)	-0.02	606 (1.6%)	672 (1.7%)	-0.01
Bladder stones; n (%)	8 (0.3%)	5 (0.2%)	0.02	15 (0.1%)	26 (0.2%)	-0.03	28 (0.1%)	23 (0.1%)	0.00	51 (0.1%)	54 (0.1%)	0.00
Kidney stones; n (%)	29 (1.0%)	32 (1.1%)	-0.01	181 (1.3%)	213 (1.5%)	-0.02	270 (1.2%)	257 (1.2%)	0.00	480 (1.2%)	502 (1.3%)	-0.01
Urine tract infections (UTIs); n (%)	194 (7.0%)	181 (6.6%)	0.02	860 (6.2%)	893 (6.4%)	-0.01	1,803 (8.1%)	1,851 (8.3%)	-0.01	2,857 (7.3%)	2,925 (7.5%)	-0.01
Dipstick urinalysis; n (%)	817 (29.3%)	853 (30.6%)	-0.03	2,796 (20.0%)	2,903 (20.8%)	-0.02	7,125 (31.9%)	7,263 (32.5%)	-0.01	10,738 (27.5%)	11,019 (28.2%)	-0.02
Non-dipstick urinalysis; n (%)	355 (12.7%)	332 (11.9%)	0.02	689 (4.9%)	710 (5.1%)	-0.01	2,558 (11.5%)	2,600 (11.6%)	0.00	3,602 (9.2%)	3,642 (9.3%)	0.00
Urine function test; n (%)	106 (3.8%)	93 (3.3%)	0.03	623 (4.5%)	599 (4.3%)	0.01	888 (4.0%)	889 (4.0%)	0.00	1617 (4.1%)	1581 (4.0%)	0.01
Cytology; n (%)	40 (1.4%)	37 (1.3%)	0.01	357 (2.6%)	338 (2.4%)	0.01	365 (1.6%)	391 (1.8%)	-0.02	762 (2.0%)	766 (2.0%)	0.00
Cystoscopy; n (%)	50 (1.8%)	45 (1.6%)	0.02	342 (2.4%)	361 (2.6%)	-0.01	493 (2.2%)	456 (2.0%)	0.01	885 (2.3%)	862 (2.2%)	0.01
Other Covariates												
Liver disease; n (%)	12 (0.4%)	13 (0.5%)	-0.01	85 (0.6%)	84 (0.6%)	0.00	93 (0.4%)	90 (0.4%)	0.00	190 (0.5%)	187 (0.5%)	0.00
Osteoarthritis; n (%)	488 (17.5%)	471 (16.9%)	0.02	2,145 (15.4%)	2,035 (14.6%)	0.02	3,559 (15.9%)	3,519 (15.8%)	0.00	6192 (15.8%)	6025 (15.4%)	0.01
Other arthritis, arthropathies and musculoskeletal pain; n (%)	865 (31.0%)	849 (30.4%)	0.01	4,550 (32.6%)	4,451 (31.9%)	0.01	6,586 (29.5%)	6,545 (29.3%)	0.00	12001 (30.7%)	11845 (30.3%)	0.01
Dorsopathies; n (%)	503 (18.0%)	500 (17.9%)	0.00	2,553 (18.3%)	2,541 (18.2%)	0.00	3,859 (17.3%)	3,772 (16.9%)	0.01	6915 (17.7%)	6813 (17.4%)	0.01
Fractures; n (%)	56 (2.0%)	62 (2.2%)	-0.01	474 (3.4%)	477 (3.4%)	0.00	701 (3.1%)	699 (3.1%)	0.00	1231 (3.2%)	1238 (3.2%)	0.00
Falls v2; n (%)	74 (2.7%)	67 (2.4%)	0.02	124 (0.9%)	135 (1.0%)	-0.01	260 (1.2%)	252 (1.1%)	0.01	458 (1.2%)	454 (1.2%)	0.00
Osteoporosis; n (%)	159 (5.7%)	177 (6.3%)	-0.03	973 (7.0%)	963 (6.9%)	0.00	1,668 (7.5%)	1,687 (7.6%)	0.00	2800 (7.2%)	2827 (7.2%)	0.00
Hyperthyroidism; n (%)	23 (0.8%)	23 (0.8%)	0.00	122 (0.9%)	92 (0.7%)	0.02	187 (0.8%)	207 (0.9%)	-0.01	332 (0.8%)	322 (0.8%)	0.00
Hypothyroidism v2; n (%)	381 (13.7%)	405 (14.5%)	-0.02	1,399 (10.0%)	1,455 (10.4%)	-0.01	2,639 (11.8%)	2,604 (11.7%)	0.00	4419 (11.3%)	4464 (11.4%)	0.00
Other disorders of thyroid gland V2; n (%)	56 (2.0%)	68 (2.4%)	-0.03	344 (2.5%)	361 (2.6%)	-0.01	593 (2.7%)	567 (2.5%)	0.01	993 (2.5%)	996 (2.5%)	0.00
Depression; n (%)	132 (4.7%)	135 (4.8%)	0.00	675 (4.8%)	663 (4.7%)	0.00	1,132 (5.1%)	1,065 (4.8%)	0.01	1939 (5.0%)	1863 (4.8%)	0.01
Anxiety; n (%)	144 (5.2%)	141 (5.1%)	0.00	545 (3.9%)	540 (3.9%)	0.00	1,013 (4.5%)	973 (4.4%)	0.00	1702 (4.4%)	1654 (4.2%)	0.01
Sleep_Disorder; n (%)	267 (9.6%)	255 (9.1%)	0.02	1,617 (11.6%)	1,579 (11.3%)	0.01	1,438 (6.4%)	1,405 (6.3%)	0.00	3322 (8.5%)	3239 (8.3%)	0.01
Dementia; n (%)	117 (4.2%)	106 (3.8%)	0.02	466 (3.3%)	469 (3.4%)	-0.01	822 (3.7%)	843 (3.8%)	-0.01	1405 (3.6%)	1418 (3.6%)	0.00
Delirium; n (%)	21 (0.8%)	15 (0.5%)	0.04	110 (0.8%)	121 (0.9%)	-0.01	135 (0.6%)	133 (0.6%)	0.00	266 (0.7%)	269 (0.7%)	0.00
Psychosis; n (%)	9 (0.3%)	12 (0.4%)	-0.02	100 (0.7%)	102 (0.7%)	0.00	168 (0.8%)	150 (0.7%)	0.01	277 (0.7%)	264 (0.7%)	0.00
Obesity; n (%)	273 (9.8%)	266 (9.5%)	0.01	1,009 (7.2%)	980 (7.0%)	0.01	2,080 (9.3%)	2,050 (9.2%)	0.00	3362 (8.6%)	3296 (8.4%)	0.01
Overweight; n (%)	79 (2.8%)	79 (2.8%)	0.00	102 (0.7%)	92 (0.7%)	0.00	424 (1.9%)	405 (1.8%)	0.01	605 (1.5%)	576 (1.5%)	0.00
Smoking; n (%)	230 (8.2%)	213 (7.6%)	0.02	743 (5.3%)	741 (5.3%)	0.00	3,157 (14.1%)	3,046 (13.6%)	0.01	4130 (10.6%)	4000 (10.2%)	0.01
Alcohol abuse or dependence; n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!
Drug abuse or dependence; n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!
COPD; n (%)	295 (10.6%)	294 (10.5%)	0.00	1,844 (13.2%)	1,797 (12.9%)	0.01	2,146 (9.3%)	2,079 (9.3%)	0.01	4285 (11.0%)	4170 (10.7%)	0.01
Asthma; n (%)	127 (4.6%)	130 (4.7%)	0.00	754 (5.4%)	749 (5.4%)	0.00	917 (4.1%)	881 (3.9%)	0.01	1798 (4.6%)	1760 (4.5%)	0.00
Obstructive sleep apnea; n (%)	270 (9.7%)	242 (8.7%)	0.03	1,345 (9.6%)	1,319 (9.4%)	0.01	1,262 (5.7%)	1,225 (5.5%)	0.01	2877 (7.4%)	2786 (7.1%)	0.01
Pneumonia; n (%)	33 (1.2%)	45 (1.6%)	-0.03	833 (6.0%)	848 (6.1%)	0.00	772 (3.5%)	783 (3.5%)	0.00	1638 (4.2%)	1676 (4.3%)	0.00
Imaging; n (%)	0 (0.0%)	1 (0.0%)	#DIV/0!	25 (0.2%)	17 (0.1%)	0.03	26 (0.1%)	30 (0.1%)	0.00	51 (0.1%)	48 (0.1%)	0.00
Other Medications												
Use of ACE inhibitors; n (%)	961 (34.4%)	951 (34.1%)	0.01	4,940 (35.4%)	4,936 (35.4%)	0.00	7,744 (34.7%)	7,830 (35.1%)	-0.01	13645 (34.9%)	13717 (35.1%)	0.00
Use of ARBs; n (%)	543 (19.5%)	542 (19.4%)	0.00	3,304 (23.7%)	3,285 (23.5%)	0.00	4,971 (22.3%)	4,922 (22.1%)	0.00	8818 (22.6%)	8749 (22.4%)	0.00
Use of Loop Diuretics - United; n (%)	467 (16.7%)	464 (16.6%)	0.00	3,441 (24.6%)	3,280 (23.5%)	0.03	4,396 (19.7%)	4,390 (19.7%)	0.00	8304 (21.3%)	8134 (20.8%)	0.01
Use of other diuretics- United; n (%)	80 (2.9%)	84 (3.0%)	-0.01	716 (5.1%)	693 (5.0%)	0.00	727 (3.3%)	771 (3.5%)	-0.01	1523 (3.9%)	1548 (4.0%)	-0.01
Use of nitrates-United; n (%)	170 (6.1%)	137 (4.9%)	0.05	1,278 (9.2%)	1,156 (8.3%)	0.03	1,979 (8.9%)	1,698 (7.6%)	0.05	3427 (8.8%)	2991 (7.7%)	0.04
Use of other hypertension drugs; n (%)	225 (8.1%)	220 (7.9%)	0.01	904 (6.5%)	997 (7.1%)	-0.02	1,616 (7.2%)	1,612 (7.2%)	0.00	2745 (7.0%)	2829 (7.2%)	-0.01
Use of digoxin - United; n (%)	319 (11.4%)	302 (10.8%)	0.02	2,692 (19.3%)	2,018 (14.5%)	0.13	2,933 (13.1%)	2,579 (11.6%)	0.05	5944 (15.2%)	4899 (12.5%)	0.08
Use of Anti-arrhythmics; n (%)	395 (14.2%)	406 (14.6%)	-0.01	2,766 (19.8%)	2,652 (19.0%)	0.02	3,619 (16.2%)	3,526 (15.8%)	0.01	6780 (17.4%)	6584 (16.9%)	0.01
Use of COPD/asthma meds- United; n (%)	436 (15.6%)	410 (14.7%)	0.03	2,621 (18.8%)	2,717 (19.5%)	-0.02	3,827 (17.1%)	3,626 (16.2%)	0.02	6884 (17.6%)	6753 (17.3%)	0.01
Use of statins; n (%)	1,516 (54.3%)	1,505 (53.9%)	0.01	7,744 (55.5%)	7,735 (55.4%)	0.00	12,406 (55.6%)	12,391 (55.5%)	0.00	21666 (55.5%)	21631 (55.4%)	0.00
Use of other lipid-lowering drugs; n (%)	228 (8.2%)	203 (7.3%)	0.03	1,425 (10.2%)	1,428 (10.2%)	0.00	1,695 (7.6%)	1,671 (7.5%)	0.00	3348 (8.6%)	3302 (8.5%)	0.00
Use of antiplatelet agents; n (%)	261 (9.4%)	258 (9.2%)	0.01	2,273 (16.3%)	2,255 (16.2%)	0.00	2,842 (12.7%)	2,828 (12.7%)	0.00	5376 (13.8%)	5341 (13.7%)	0.00
Use of heparin and other low-molecular weight heparins; n (%)	10 (0.4%)	11 (0.4%)	0.00	1 (0.0%)	2 (0.0%)	#DIV/0!	113 (0.5%)	125 (0.6%)	-0.01	124 (0.3%)	138 (0.4%)	-0.02
Use of NSAIDs; n (%)	284 (10.2%)	269 (9.6%)	0.02	1,482 (10.6%)	1,438 (10.3%)	0.01	2,600 (11.6%)	2,593 (11.6%)	0.00	4366 (11.2%)	4300 (11.0%)	0.01
Use of oral corticosteroids; n (%)	443 (15.9%)	443 (15.9%)	0.00	2,669 (19.1%)	2,624 (18.8%)	0.01	4,130 (18.5%)	4,126 (18.5%)	0.00	7242 (18.5%)	7193 (18.4%)	0.00
Use of bisphosphonate (United); n (%)	85 (3.0%)	102 (3.7%)	-0.04	671 (4.8%)	644 (4.6%)	0.01	894 (4.0%)	892 (4.0%)	0.00	1650 (4.2%)	1638 (4.2%)	0.00
Use of opioids - United; n (%)	534 (19.1%)	536 (19.2%)	0.00	3,392 (24.3%)	3,321 (23.8%)	0.01	5,044 (22.6%)	4,995 (22.4%)	0.00	8970 (23.0%)	8852 (22.7%)	0.01
Use of antidepressants; n (%)	452 (16.2%)	448 (16.1%)	0.00	2,414 (17.3%)	2,392 (17.1%)	0.01	4,003 (17.9%)	3,947 (17.7%)	0.01	6867 (17.6%)	6787 (17.4%)	0.01
Use of antipsychotics; n (%)	23 (0.8%)	23 (0.8%)	0.00	158 (1.1%)	158 (1.1%)	0.00	337 (1.5%)	349 (1.6%)	-0.01	518 (1.3%)	530 (1.4%)	-0.01
Use of anticonvulsants; n (%)	262 (9.4%)	232 (8.3%)	0.04	1,177 (8.4%)	1,202 (8.6%)	-0.01	2,161 (9.7%)	2,125 (9.5%)	0.01	3600 (9.2%)	3559 (9.1%)	0.00
Use of lithium- United; n (%)	3 (0.1%)	3 (0.1%)	0.00	12 (0.1%)	13 (0.1%)	0.00	11 (0.0%)	19 (0.1%)	-0.04	26 (0.1%)	35 (0.1%)	0.00
Use of Benzos- United; n (%)	177 (6.3%)	186 (6.7%)	-0.02	1,811 (13.0%)	1,800 (12.9%)	0.00	1,595 (7.1%)	1,599 (7.2%)	0.00	3583 (9.2%)	3585 (9.2%)	0.00
Use of anxiolytics/hypnotics- United; n (%)	167 (6.0%)	165 (5.9%)	0.00	1,000 (7.2%)	984 (7.0%)	0.01	1,478 (6.6%)	1,447 (6.5%)	0.00	2645 (6.8%)	2596 (6.6%)	0.01
Use of dementia meds- United; n (%)	103 (3.7%)	94 (3.4%)	0.02	447 (3.2%)	458 (3.3%)	-0.01	856 (3.8%)	821 (3.7%)	0.01	1406 (3.6%)	1373 (3.5%)	0.01
Use of anti parkinsonian meds- United; n (%)	41 (1.5%)	42 (1.5%)	0.00	345 (2.5%)	349 (2.5%)	0.00	623 (2.8%)	604 (2.7%)	0.01	1009 (2.6%)	995 (2.5%)	0.01
Any use of pramlintide; n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	3 (0.0%)	7 (0.1%)	-0.04	**	**	#VALUE!	#VALUE!	#VALUE!	#VALUE!

Appendix B

Any use of 1st generation sulfonylureas; n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	6 (0.0%)	5 (0.0%)	#DIV/0!	**	**	#VALUE!	#VALUE!	#VALUE!	0.00
Entresto (sacubitril/valsartan); n (%)	6 (0.2%)	3 (0.1%)	0.03	7 (0.1%)	1 (0.0%)	0.04	**	**	#VALUE!	#VALUE!	#VALUE!	0.00
Labs										16,750	16,750	
Lab values- HbA1c (%) v3; n (%)	319 (11.4%)	309 (11.1%)	0.01	113 (0.8%)	94 (0.7%)	0.01	N/A	N/A	#VALUE!	432 (2.6%)	403 (2.4%)	0.01
Lab values- HbA1c (%) (within 3 months) v3; n (%)	205 (7.3%)	202 (7.2%)	0.00	87 (0.6%)	61 (0.4%)	0.03	N/A	N/A	#VALUE!	292 (1.7%)	263 (1.6%)	0.01
Lab values- HbA1c (%) (within 6 months) v3; n (%)	319 (11.4%)	309 (11.1%)	0.01	113 (0.8%)	94 (0.7%)	0.01	N/A	N/A	#VALUE!	432 (2.6%)	403 (2.4%)	0.01
Lab values- BNP; n (%)	27 (1.0%)	28 (1.0%)	0.00	10 (0.1%)	17 (0.1%)	0.00	N/A	N/A	#VALUE!	37 (0.2%)	45 (0.3%)	-0.02
Lab values- BNP (within 3 months); n (%)	23 (0.8%)	24 (0.9%)	-0.01	8 (0.1%)	14 (0.1%)	0.00	N/A	N/A	#VALUE!	31 (0.2%)	38 (0.2%)	0.00
Lab values- BNP (within 6 months); n (%)	27 (1.0%)	28 (1.0%)	0.00	10 (0.1%)	17 (0.1%)	0.00	N/A	N/A	#VALUE!	37 (0.2%)	45 (0.3%)	-0.02
Lab values- BUN (mg/dl); n (%)	604 (21.6%)	673 (24.1%)	-0.06	111 (0.8%)	144 (1.0%)	-0.02	N/A	N/A	#VALUE!	715 (4.3%)	817 (4.9%)	-0.03
Lab values- BUN (mg/dl) (within 3 months); n (%)	421 (15.1%)	456 (16.3%)	-0.03	83 (0.6%)	105 (0.8%)	-0.02	N/A	N/A	#VALUE!	504 (3.0%)	561 (3.3%)	-0.02
Lab values- BUN (mg/dl) (within 6 months); n (%)	604 (21.6%)	673 (24.1%)	-0.06	111 (0.8%)	144 (1.0%)	-0.02	N/A	N/A	#VALUE!	715 (4.3%)	817 (4.9%)	-0.03
Lab values- Creatinine (mg/dl) v2; n (%)	614 (22.0%)	686 (24.6%)	-0.06	111 (0.8%)	159 (1.1%)	-0.03	N/A	N/A	#VALUE!	725 (4.3%)	845 (5.0%)	-0.03
Lab values- Creatinine (mg/dl) (within 3 months) v2; n (%)	427 (15.3%)	465 (16.7%)	-0.04	82 (0.6%)	112 (0.8%)	-0.02	N/A	N/A	#VALUE!	509 (3.0%)	577 (3.4%)	-0.02
Lab values- Creatinine (mg/dl) (within 6 months) v2; n (%)	614 (22.0%)	686 (24.6%)	-0.06	111 (0.8%)	159 (1.1%)	-0.03	N/A	N/A	#VALUE!	725 (4.3%)	845 (5.0%)	-0.03
Lab values- HDL level (mg/dl); n (%)	464 (16.6%)	500 (17.9%)	-0.03	94 (0.7%)	106 (0.8%)	-0.01	N/A	N/A	#VALUE!	558 (3.3%)	606 (3.6%)	-0.02
Lab values- HDL level (mg/dl) (within 3 months); n (%)	291 (10.4%)	320 (11.5%)	-0.04	70 (0.5%)	68 (0.5%)	0.00	N/A	N/A	#VALUE!	361 (2.2%)	388 (2.3%)	-0.01
Lab values- HDL level (mg/dl) (within 6 months); n (%)	464 (16.6%)	500 (17.9%)	-0.03	94 (0.7%)	106 (0.8%)	-0.01	N/A	N/A	#VALUE!	558 (3.3%)	606 (3.6%)	-0.02
Lab values- LDL level (mg/dl) v2; n (%)	487 (17.5%)	527 (18.9%)	-0.04	117 (0.8%)	115 (0.8%)	0.00	N/A	N/A	#VALUE!	604 (3.6%)	642 (3.8%)	-0.01
Lab values- LDL level (mg/dl) (within 3 months) v2; n (%)	305 (10.9%)	338 (12.1%)	-0.04	88 (0.6%)	74 (0.5%)	0.01	N/A	N/A	#VALUE!	393 (2.3%)	412 (2.5%)	-0.01
Lab values- LDL level (mg/dl) (within 6 months) v2; n (%)	487 (17.5%)	527 (18.9%)	-0.04	117 (0.8%)	115 (0.8%)	0.00	N/A	N/A	#VALUE!	604 (3.6%)	642 (3.8%)	-0.01
Lab values- NT-proBNP; n (%)	4 (0.1%)	1 (0.0%)	0.04	0 (0.0%)	0 (0.0%)	#DIV/0!	N/A	N/A	#VALUE!	04 (0.0%)	1 (0.0%)	#DIV/0!
Lab values- NT-proBNP (within 3 months); n (%)	3 (0.1%)	0 (0.0%)	0.04	0 (0.0%)	0 (0.0%)	#DIV/0!	N/A	N/A	#VALUE!	03 (0.0%)	0 (0.0%)	-
Lab values- NT-proBNP (within 6 months); n (%)	4 (0.1%)	1 (0.0%)	0.04	0 (0.0%)	0 (0.0%)	#DIV/0!	N/A	N/A	#VALUE!	04 (0.0%)	1 (0.0%)	-
Lab values- Total cholesterol (mg/dl) v2; n (%)	467 (16.7%)	508 (18.2%)	-0.04	95 (0.7%)	117 (0.8%)	-0.01	N/A	N/A	#VALUE!	562 (3.4%)	625 (3.7%)	-0.02
Lab values- Total cholesterol (mg/dl) (within 3 months) v2; n (%)	294 (10.5%)	325 (11.6%)	-0.04	70 (0.5%)	73 (0.5%)	0.00	N/A	N/A	#VALUE!	364 (2.2%)	398 (2.4%)	-0.01
Lab values- Total cholesterol (mg/dl) (within 6 months) v2; n (%)	467 (16.7%)	508 (18.2%)	-0.04	95 (0.7%)	117 (0.8%)	-0.01	N/A	N/A	#VALUE!	562 (3.4%)	625 (3.7%)	-0.02
Lab values- Triglyceride level (mg/dl); n (%)	464 (16.6%)	503 (18.0%)	-0.04	94 (0.7%)	107 (0.8%)	-0.01	N/A	N/A	#VALUE!	558 (3.3%)	610 (3.6%)	-0.02
Lab values- Triglyceride level (mg/dl) (within 3 months); n (%)	291 (10.4%)	322 (11.5%)	-0.04	71 (0.5%)	68 (0.5%)	0.00	N/A	N/A	#VALUE!	362 (2.2%)	390 (2.3%)	-0.01
Lab values- Triglyceride level (mg/dl) (within 6 months); n (%)	464 (16.6%)	503 (18.0%)	-0.04	94 (0.7%)	107 (0.8%)	-0.01	N/A	N/A	#VALUE!	558 (3.3%)	610 (3.6%)	-0.02
Lab result number- HbA1c (%) mean (only 2 to 20 included) v4	315	307		100	87		N/A	N/A		415	394	
...mean (sd)	6.57 (1.13)	6.54 (1.37)	0.02	7.01 (1.41)	6.75 (1.08)	0.21	N/A	N/A	#VALUE!	6.68 (1.20)	6.59 (1.31)	0.07
...median [IQR]	6.20 [5.80, 7.00]	6.30 [5.80, 7.00]	-0.08	6.60 [6.10, 7.77]	6.50 [6.00, 7.25]	0.08	N/A	N/A	#VALUE!	6.30 (1.20)	6.34 (1.31)	-0.03
...Missing; n (%)	2,475 (88.7%)	2,483 (89.0%)	-0.01	13,860 (99.3%)	13,873 (99.4%)	-0.01	N/A	N/A	#VALUE!	16,335 (97.5%)	16,356 (97.6%)	-0.01
Lab result number- BNP mean v2	27	28		10	17		N/A	N/A		37	45	
...mean (sd)	358.65 (541.48)	214.33 (164.51)	0.36	217.51 (147.78)	180.30 (209.53)	0.21	N/A	N/A	#VALUE!	320.50 (479.58)	201.47 (184.72)	0.33
...median [IQR]	216.30 [103.00, 361.00]	170.15 [69.72, 343.75]	0.12	233.50 [71.50, 328.00]	121.00 [59.00, 245.00]	0.62	N/A	N/A	#VALUE!	220.95 (479.58)	151.58 (184.72)	0.19
...Missing; n (%)	2,763 (99.0%)	2,762 (99.0%)	0.00	13,950 (99.9%)	13,943 (99.9%)	0.00	N/A	N/A	#VALUE!	16,713 (99.8%)	16,705 (99.7%)	0.02
Lab result number- BUN (mg/dl) mean v2	604	673		111	144		N/A	N/A		715	817	
...mean (sd)	17.89 (5.80)	17.74 (5.21)	0.03	17.65 (5.69)	18.46 (5.89)	-0.14	N/A	N/A	#VALUE!	17.85 (5.79)	17.87 (5.34)	0.00
...median [IQR]	17.50 [14.00, 21.00]	17.00 [14.00, 21.00]	0.09	17.00 [14.00, 21.00]	18.00 [15.00, 22.00]	-0.17	N/A	N/A	#VALUE!	17.42 (5.79)	17.18 (5.34)	0.04
...Missing; n (%)	2,186 (78.4%)	2,117 (75.9%)	0.06	13,849 (99.2%)	13,816 (99.0%)	0.02	N/A	N/A	#VALUE!	16,035 (95.7%)	15,933 (95.1%)	0.03
Lab result number- Creatinine (mg/dl) mean (only 0.1 to 15 included) v3	607	682		110	157		N/A	N/A		717	839	
...mean (sd)	0.98 (0.25)	0.98 (0.21)	0.00	0.98 (0.22)	0.98 (0.24)	0.00	N/A	N/A	#VALUE!	0.98 (0.25)	0.98 (0.22)	0.00
...median [IQR]	0.95 [0.82, 1.10]	0.96 [0.83, 1.10]	-0.04	0.96 [0.81, 1.10]	0.94 [0.80, 1.10]	0.09	N/A	N/A	#VALUE!	0.95 (0.25)	0.96 (0.22)	-0.04
...Missing; n (%)	2,183 (78.2%)	2,108 (75.6%)	0.06	13,850 (99.2%)	13,803 (98.9%)	0.03	N/A	N/A	#VALUE!	16,033 (95.7%)	15,911 (95.0%)	0.03
Lab result number- HDL level (mg/dl) mean (only <=5000 included) v2	464	500		94	106		N/A	N/A		558	606	
...mean (sd)	51.27 (15.97)	52.85 (17.18)	-0.10	45.87 (15.62)	48.01 (17.14)	-0.13	N/A	N/A	#VALUE!	50.36 (15.93)	52.00 (17.19)	-0.10
...median [IQR]	48.25 [40.00, 60.00]	50.00 [41.00, 62.00]	-0.11	45.50 [34.00, 54.12]	47.50 [35.75, 59.25]	-0.12	N/A	N/A	#VALUE!	47.79 (15.93)	49.56 (17.19)	-0.11
...Missing; n (%)	2,326 (83.4%)	2,290 (82.1%)	0.03	13,866 (99.3%)	13,854 (99.2%)	0.01	N/A	N/A	#VALUE!	16,192 (96.7%)	16,144 (96.4%)	0.02
Lab result number- LDL level (mg/dl) mean (only <=5000 included) v2	472	512		95	110		N/A	N/A		567	622	
...mean (sd)	89.15 (32.99)	87.59 (33.46)	0.05	82.89 (29.91)	79.99 (36.33)	0.09	N/A	N/A	#VALUE!	88.10 (32.53)	86.25 (34.01)	0.06
...median [IQR]	84.83 [68.50, 108.00]	82.00 [66.00, 109.00]	0.09	80.00 [64.50, 101.00]	79.25 [57.38, 101.25]	0.02	N/A	N/A	#VALUE!	84.02 (32.53)	81.51 (34.01)	0.08
...Missing; n (%)	2,318 (83.1%)	2,278 (81.6%)	0.04	13,865 (99.3%)	13,850 (99.2%)	0.01	N/A	N/A	#VALUE!	16,183 (96.6%)	16,128 (96.3%)	0.02
Lab result number- Total cholesterol (mg/dl) mean (only <=5000 included) v2	467	508		95	117		N/A	N/A		562	625	
...mean (sd)	166.51 (40.78)	165.12 (40.18)	0.03	154.47 (33.16)	157.68 (41.05)	-0.09	N/A	N/A	#VALUE!	164.47 (39.64)	163.73 (40.38)	0.02
...median [IQR]	162.00 [139.00, 192.00]	159.00 [138.00, 192.00]	0.07	154.00 [132.50, 175.00]	159.00 [136.00, 181.75]	-0.13	N/A	N/A	#VALUE!	160.65 (39.64)	159.00 (40.38)	0.04
...Missing; n (%)	2,323 (83.3%)	2,282 (81.8%)	0.04	13,865 (99.3%)	13,843 (99.2%)	0.01	N/A	N/A	#VALUE!	16,188 (96.6%)	16,125 (96.3%)	0.02
Lab result number- Triglyceride level (mg/dl) mean (only <=5000 included) v2	464	503		94	107		N/A	N/A		558	610	
...mean (sd)	129.01 (76.77)	119.47 (64.42)	0.13	130.38 (67.84)	144.37 (97.89)	-0.17	N/A	N/A	#VALUE!	129.24 (75.42)	123.84 (71.45)	0.07
...median [IQR]	112.00 [81.00, 151.38]	105.00 [77.00, 144.00]	0.10	114.50 [81.38, 175.00]	126.00 [91.00, 155.00]	-0.14	N/A	N/A	#VALUE!	112.42 (75.42)	108.68 (71.45)	0.05
...Missing; n (%)	2,326 (83.4%)	2,287 (82.0%)	0.04	13,866 (99.3%)	13,853 (99.2%)	0.01	N/A	N/A	#VALUE!	16,192 (96.7%)	16,140 (96.4%)	0.02
Lab result number- Hemoglobin mean (only >0 included)	447	494		69	99		N/A	N/A		516	593	
...mean (sd)	13.95 (1.46)	14.06 (1.41)	-0.08	13.65 (1.51)	13.64 (2.06)	0.01	N/A	N/A	#VALUE!	13.91 (1.47)	13.99 (1.54)	-0.05
...median [IQR]	14.00 [13.00, 14.90]	14.00 [13.10, 14.65]	0.00	13.88 [12.70, 14.65]	13.80 [12.90, 14.80]	0.04	N/A	N/A	#VALUE!	13.98 (1.47)	13.97 (1.54)	0.01
...Missing; n (%)	2,343 (84.0%)	2,296 (82.3%)	0.05	13,891 (99.5%)	13,861 (99.3%)	0.03	N/A	N/A	#VALUE!	16,234 (96.9%)	16,157 (96.5%)	0.02

Appendix B

result number- Serum sodium mean (only >90 and <190 included)	579	654	92	122		N/A	N/A	671	776			
...mean (sd)	140.03 (2.74)	140.11 (3.01)	-0.03	139.22 (2.71)	139.28 (2.99)	-0.02	N/A	N/A	#VALUE!	139.92 (2.74)	139.98 (3.01)	-0.02
...median [IQR]	140.00 [138.50, 142.00]	140.00 [139.00, 142.00]	0.00	139.80 [138.00, 141.00]	139.83 [137.50, 141.00]	-0.01	N/A	N/A	#VALUE!	139.97 (2.74)	139.97 (3.01)	0.00
...Missing; n (%)	2,211 (79.2%)	2,136 (76.6%)	0.06	13,868 (99.3%)	13,838 (99.1%)	0.02	N/A	N/A	#VALUE!	16,079 (96.0%)	15,974 (95.4%)	0.03
Lab result number- Albumin mean (only >0 and <=10 included)	530	601	72	102		N/A	N/A	602	703			
...mean (sd)	4.17 (0.31)	4.19 (0.31)	-0.06	4.10 (0.58)	4.03 (0.49)	0.13	N/A	N/A	#VALUE!	4.16 (0.35)	4.17 (0.34)	-0.03
...median [IQR]	4.20 [4.00, 4.40]	4.20 [4.00, 4.40]	0.00	4.20 [3.90, 4.40]	4.10 [3.89, 4.30]	0.19	N/A	N/A	#VALUE!	4.20 (0.35)	4.19 (0.34)	0.03
...Missing; n (%)	2,260 (81.0%)	2,189 (78.5%)	0.06	13,888 (99.5%)	13,858 (99.3%)	0.03	N/A	N/A	#VALUE!	16,148 (96.4%)	16,047 (95.8%)	0.03
Lab result number- Glucose (fasting or random) mean (only 10-1000 included)	576	645	91	111		N/A	N/A	667	756			
...mean (sd)	110.45 (33.39)	111.79 (39.37)	-0.04	139.94 (58.19)	128.83 (44.07)	0.22	N/A	N/A	#VALUE!	114.47 (37.74)	114.29 (40.12)	0.00
...median [IQR]	101.00 [91.00, 118.88]	100.50 [91.00, 117.00]	0.01	122.00 [96.75, 162.50]	117.00 [102.00, 140.00]	0.10	N/A	N/A	#VALUE!	103.87 (37.74)	102.92 (40.12)	0.02
...Missing; n (%)	2,214 (79.4%)	2,145 (76.9%)	0.06	13,869 (99.3%)	13,849 (99.2%)	0.01	N/A	N/A	#VALUE!	16,083 (96.0%)	15,994 (95.5%)	0.02
Lab result number- Potassium mean (only 1-7 included)	603	679	108	143		N/A	N/A	711	822			
...mean (sd)	4.35 (0.43)	4.38 (0.44)	-0.07	4.35 (0.37)	4.34 (0.38)	0.03	N/A	N/A	#VALUE!	4.35 (0.42)	4.37 (0.43)	-0.05
...median [IQR]	4.30 [4.10, 4.60]	4.40 [4.10, 4.65]	-0.23	4.30 [4.10, 4.60]	4.36 [4.10, 4.60]	-0.16	N/A	N/A	#VALUE!	4.30 (0.42)	4.39 (0.43)	-0.21
...Missing; n (%)	2,187 (78.4%)	2,111 (75.7%)	0.06	13,852 (99.2%)	13,817 (99.0%)	0.02	N/A	N/A	#VALUE!	16,039 (95.8%)	15,928 (95.1%)	0.03
Comorbidity Scores												
CCI (180 days)-ICD9 and ICD10 v2												
...mean (sd)	2.63 (1.40)	2.62 (1.35)	0.01	2.81 (1.57)	2.78 (1.56)	0.02	1.33 (1.37)	1.33 (1.39)	0.00	1.95 (1.45)	1.94 (1.45)	0.01
...median [IQR]	2.00 [2.00, 3.00]	2.00 [2.00, 3.00]	0.00	2.00 [2.00, 4.00]	2.00 [2.00, 4.00]	0.00	1.00 [0.00, 2.00]	1.00 [0.00, 2.00]	0.00	1.43 (1.45)	1.43 (1.45)	0.00
Non-Frailty; n (%)	1,525 (54.7%)	1,532 (54.9%)	0.00	6,845 (49.0%)	6,801 (48.7%)	0.01	669 (3.0%)	465 (2.1%)	0.06	9,039 (23.1%)	8,798 (22.5%)	0.01
Frailty Score (mean): Empirical Version 365 days, v2												
...mean (sd)	0.17 (0.04)	0.17 (0.04)	0.00	0.17 (0.05)	0.17 (0.05)	0.00	10.70 (9.15)	10.66 (9.45)	0.00	6.19 (6.92)	6.16 (7.14)	0.00
...median [IQR]	0.16 [0.14, 0.19]	0.16 [0.14, 0.19]	0.00	0.17 [0.14, 0.20]	0.17 [0.14, 0.20]	0.00	8.94 [4.50, 14.92]	8.82 [4.32, 14.85]	0.01	5.18 (6.92)	5.11 (7.14)	0.01
Healthcare Utilization												
Any hospitalization; n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	4,495 (32.2%)	4,381 (31.4%)	0.02	4,193 (18.8%)	4,147 (18.6%)	0.01	8,688 (22.2%)	8,528 (21.8%)	0.01
Any hospitalization within prior 30 days; n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	3,998 (22.2%)	3,908 (21.5%)	0.02	2,640 (11.8%)	2,607 (11.7%)	0.00	5738 (14.7%)	5605 (14.3%)	0.01
Any hospitalization during prior 31-180 days; n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	1,606 (11.5%)	1,567 (11.2%)	0.01	1,741 (7.8%)	1,691 (7.6%)	0.01	3347 (8.6%)	3258 (8.3%)	0.01
Endocrinologist Visit; n (%)	67 (2.4%)	77 (2.8%)	-0.03	474 (3.4%)	451 (3.2%)	0.01	783 (3.5%)	731 (3.3%)	0.01	1324 (3.4%)	1259 (3.2%)	0.01
Endocrinologist Visit (30 days prior); n (%)	24 (0.9%)	19 (0.7%)	0.02	165 (1.2%)	156 (1.1%)	0.01	233 (1.0%)	222 (1.0%)	0.00	422 (1.1%)	397 (1.0%)	0.01
Endocrinologist Visit (31 to 180 days prior); n (%)	56 (2.0%)	66 (2.4%)	-0.03	395 (2.8%)	374 (2.7%)	0.01	669 (3.0%)	636 (2.8%)	0.01	1120 (2.9%)	1076 (2.8%)	0.01
Internal medicine/family medicine visits; n (%)	2,317 (83.0%)	2,336 (83.7%)	-0.02	11,221 (80.4%)	11,040 (79.1%)	0.03	17,647 (79.1%)	17,982 (80.6%)	-0.04	31185 (79.8%)	31358 (80.3%)	-0.01
Internal medicine/family medicine visits (30 days prior) v2; n (%)	1,469 (52.7%)	1,468 (52.6%)	0.00	7,381 (52.9%)	7,282 (52.2%)	0.01	11,348 (50.8%)	11,109 (49.8%)	0.02	20198 (51.7%)	19859 (50.8%)	0.02
Internal medicine/family medicine visits (31 to 180 days prior) v2; n (%)	2,048 (73.4%)	2,033 (72.9%)	0.01	9,897 (70.9%)	9,621 (68.9%)	0.04	14,888 (66.7%)	15,277 (68.4%)	-0.04	26833 (68.7%)	26931 (68.9%)	0.00
Cardiologist visit; n (%)	1,715 (61.5%)	1,844 (66.1%)	-0.10	8,643 (61.9%)	8,241 (59.0%)	0.06	15,939 (71.4%)	16,749 (75.0%)	-0.08	26297 (67.3%)	26834 (68.7%)	-0.03
Number of Cardiologist visits (30 days prior); n (%)	1,278 (45.8%)	1,272 (45.6%)	0.00	6,331 (45.4%)	6,217 (44.5%)	0.02	12,337 (55.3%)	12,208 (54.7%)	0.01	19946 (51.1%)	19697 (50.4%)	0.01
Number of Cardiologist visits (31 to 180 days prior); n (%)	1,089 (39.0%)	1,170 (41.9%)	-0.06	5,859 (42.0%)	5,354 (38.4%)	0.07	9,733 (43.6%)	10,383 (46.5%)	-0.06	16681 (42.7%)	16907 (43.3%)	-0.01
Electrocardiogram v2; n (%)	1,897 (68.0%)	1,931 (69.2%)	-0.03	9,862 (70.6%)	10,320 (73.9%)	-0.07	16,644 (74.6%)	16,887 (75.7%)	-0.03	28403 (72.7%)	29138 (74.6%)	-0.04
Use of glucose test strips; n (%)	26 (0.9%)	30 (1.1%)	-0.02	97 (0.7%)	101 (0.7%)	0.00	241 (1.1%)	229 (1.0%)	0.01	364 (0.9%)	360 (0.9%)	0.00
Dialysis; n (%)	1 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!	1 (0.0%)	0 (0.0%)	#DIV/0!
number of different/distinct medication prescriptions												
...mean (sd)	8.18 (4.00)	8.05 (4.04)	0.03	9.29 (4.50)	9.24 (4.56)	0.01	8.57 (3.98)	8.52 (4.04)	0.01	8.80 (4.17)	8.74 (4.23)	0.01
...median [IQR]	8.00 [5.00, 10.00]	7.00 [5.00, 10.00]	0.25	9.00 [6.00, 12.00]	9.00 [6.00, 12.00]	0.00	8.00 [6.00, 11.00]	8.00 [6.00, 11.00]	0.00	6.65 (4.66)	6.57 (4.73)	0.02
Number of Hospitalizations												
...mean (sd)	0.00 (0.00)	0.00 (0.00)	#DIV/0!	0.35 (0.55)	0.34 (0.54)	0.02	0.21 (0.47)	0.21 (0.46)	0.00	0.25 (0.48)	0.24 (0.47)	0.02
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	#DIV/0!	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	0.00	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 (0.55)	0.00 (0.54)	0.00
Number of hospital days												
...mean (sd)	0.00 (0.00)	0.00 (0.00)	#DIV/0!	1.59 (3.38)	1.50 (3.34)	0.03	0.88 (2.32)	0.85 (2.52)	0.01	1.07 (2.68)	1.02 (2.76)	0.02
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	#DIV/0!	0.00 [0.00, 3.00]	0.00 [0.00, 2.00]	0.00	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 (3.10)	0.00 (3.16)	0.00
Number of Emergency Department (ED) visits v3												
...mean (sd)	0.40 (0.94)	0.40 (0.99)	0.00	0.44 (1.54)	0.44 (1.72)	0.00	0.64 (1.46)	0.63 (1.26)	0.01	0.55 (1.46)	0.55 (1.43)	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, 1.00]	0.00 [0.00, 1.00]	0.00	0.00 (1.62)	0.00 (1.63)	0.00
Number of Office visits												
...mean (sd)	5.25 (3.98)	5.16 (3.64)	0.02	5.89 (4.47)	5.77 (4.32)	0.03	11.61 (10.64)	11.48 (9.99)	0.01	9.11 (8.54)	8.99 (8.04)	0.01
...median [IQR]	4.00 [3.00, 7.00]	4.00 [3.00, 7.00]	0.00	5.00 [3.00, 8.00]	5.00 [3.00, 8.00]	0.00	9.00 [5.00, 15.00]	9.00 [5.00, 15.00]	0.00	5.29 (8.79)	5.29 (8.28)	0.00
Number of Endocrinologist visits												
...mean (sd)	0.09 (0.81)	0.09 (0.86)	0.00	0.13 (1.13)	0.11 (0.87)	0.02	0.17 (1.45)	0.15 (1.39)	0.01	0.15 (1.31)	0.13 (1.19)	0.02
...median [IQR]	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	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 (1.41)	0.00 (1.26)	0.00
Number of internal medicine/family medicine visits												
...mean (sd)	8.11 (10.84)	8.19 (12.81)	-0.01	6.56 (9.62)	6.46 (9.25)	0.01	6.41 (8.10)	6.38 (7.75)	0.00	6.58 (8.88)	6.54 (8.75)	0.00
...median [IQR]	5.00 [2.00, 10.00]	5.00 [1.00, 10.00]	0.00	4.00 [1.00, 8.00]	4.00 [1.00, 8.00]	0.00	4.00 [1.00, 9.00]	4.00 [1.00, 9.00]	0.00	3.22 (9.94)	3.22 (9.74)	0.00
Number of Cardiologist visits												
...mean (sd)	3.29 (4.91)	3.30 (4.42)	0.00	3.35 (4.99)	3.29 (5.01)	0.01	4.52 (6.31)	4.46 (5.54)	0.01	4.01 (5.78)	3.96 (5.28)	0.01
...median [IQR]	2.00 [0.00, 5.00]	2.00 [0.00, 5.00]	0.00	2.00 [0.00, 5.00]	1.50 [0.00, 5.00]	0.10	2.00 [0.00, 6.00]	3.00 [1.00, 6.00]	-0.17	1.57 (6.22)	1.75 (5.77)	-0.03
Number electrocardiograms received v2												
...mean (sd)	1.56 (2.08)	1.54 (1.79)	0.01	1.77 (2.23)	1.72 (1.91)	0.02	1.82 (2.02)	1.80 (1.87)	0.01	1.78 (2.10)	1.75 (1.88)	0.02
...median [IQR]	1.00 [0.00, 2.00]	1.00 [0.00, 2.00]	0.00	1.00 [0.00, 2.00]	1.00 [0.00, 2.00]	0.00	1.00 [0.00, 2.00]	1.00 [1.00, 2.00]	0.00	0.79 (2.34)	0.79 (2.08)	0.00
Number of HbA1c tests ordered												
...mean (sd)	0.39 (0.69)	0.39 (0.69)	0.00	0.14 (0.45)	0.15 (0.46)	-0.02	0.40 (0.71)	0.40 (0.70)	0.00	0.31 (0.63)	0.31 (0.62)	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, 1.00]	0.00 [0.00, 1.00]	0.00	0.00 (0.66)	0.00 (0.66)	0.00
Number of glucose tests ordered												
...mean (sd)	0.13 (0.58)	0.16 (0.96)	-0.04	0.10 (0.54)	0.11 (0.58)	-0.02	0.13 (0.61)	0.12 (0.48)	0.02	0.12 (0.58)	0.12 (0.56)	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, 0.00]	0.00	0.00 (0.63)	0.00 (0.62)	0.00
Number of lipid tests ordered												

Appendix B

...mean (sd)	0.67 (0.86)	0.68 (0.84)	-0.01	0.25 (0.70)	0.24 (0.63)	0.02	0.68 (0.76)	0.68 (0.74)	0.00	0.53 (0.75)	0.52 (0.71)	0.01
...median [IQR]	0.00 [0.00, 1.00]	1.00 [0.00, 1.00]	-1.18	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	1.00 [0.00, 1.00]	1.00 [0.00, 1.00]	0.00	0.36 (0.81)	0.43 (0.77)	-0.09
Number of creatinine tests ordered												
...mean (sd)	0.07 (0.33)	0.07 (0.32)	0.00	0.05 (0.28)	0.05 (0.27)	0.00	0.10 (0.39)	0.09 (0.37)	0.03	0.08 (0.35)	0.07 (0.33)	0.03
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 (0.37)	0.00 (0.36)	0.00
Number of BUN tests ordered												
...mean (sd)	0.04 (0.23)	0.05 (0.25)	-0.04	0.03 (0.22)	0.03 (0.22)	0.00	0.06 (0.30)	0.05 (0.28)	0.03	0.05 (0.27)	0.04 (0.26)	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, 0.00]	0.00	0.00 (0.29)	0.00 (0.28)	0.00
Number of tests for microalbuminuria												
...mean (sd)	0.21 (0.70)	0.19 (0.64)	0.03	0.07 (0.37)	0.07 (0.37)	0.00	0.12 (0.41)	0.12 (0.39)	0.00	0.11 (0.42)	0.11 (0.41)	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, 0.00]	0.00	0.00 (0.46)	0.00 (0.44)	0.00
Total N distinct ICD9/ICD10 diagnoses at the 3rd digit level Copy												
...mean (sd)	3.02 (4.95)	3.04 (5.12)	0.00	2.23 (4.87)	2.21 (4.87)	0.00	4.18 (6.62)	4.08 (6.51)	0.02	3.40 (5.94)	3.34 (5.88)	0.01
...median [IQR]	0.00 [0.00, 5.00]	0.00 [0.00, 5.00]	0.00	0.00 [0.00, 2.00]	0.00 [0.00, 2.00]	0.00	0.00 [0.00, 6.00]	0.00 [0.00, 6.00]	0.00	0.00 (6.35)	0.00 (6.30)	0.00
For PS												
Hemorrhagic stroke+Other cerebrovascular disease+Cerebrovascular procedure (for PS); n (%)	45 (1.6%)	52 (1.9%)	-0.02	297 (2.1%)	316 (2.3%)	-0.01	416 (1.9%)	398 (1.8%)	0.01	758 (1.9%)	766 (2.0%)	-0.01
Occurrence of creatinine tests ordered (for PS); n (%)												
Occurrence of BUN tests ordered (for PS); n (%)	148 (5.3%)	154 (5.5%)	-0.01	495 (3.5%)	495 (3.5%)	0.00	1,648 (7.4%)	1,562 (7.0%)	0.02	2291 (5.9%)	2211 (5.7%)	0.01
Occurrence of chronic renal insufficiency w/o CKD (for PS) v2; n (%)	95 (3.4%)	103 (3.7%)	-0.02	311 (2.2%)	333 (2.4%)	-0.01	1,063 (4.8%)	1,001 (4.5%)	0.01	1469 (3.8%)	1437 (3.7%)	0.01
Chronic kidney disease Stage 1-2 (for PS); n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!
Chronic kidney disease Stage 3-6 (for PS); n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!	0	0	#VALUE!	#VALUE!	#VALUE!	#VALUE!
Bladder stones+Kidney stones (for PS); n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!
Diabetes with peripheral circulatory disorders+Gangrene+Osteomyelitis(for PS) v3 with ICD10 Copy; n (%)	35 (1.3%)	35 (1.3%)	0.00	191 (1.4%)	229 (1.6%)	-0.02	283 (1.3%)	274 (1.2%)	0.01	509 (1.3%)	538 (1.4%)	-0.01
Alcohol abuse or dependence+Drug abuse or dependence (for PS); n (%)	75 (2.7%)	49 (1.8%)	0.06	285 (2.0%)	269 (1.9%)	0.01	408 (1.8%)	430 (1.9%)	-0.01	768 (2.0%)	748 (1.9%)	0.01
Diabetes with other ophthalmic manifestations+Retinal detachment, vitreous hemorrhage, vitrectomy+Retinal laser coagulation therapy (for PS); n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!
Other atherosclerosis+Cardiac conduction disorders+Other CVD (for PS) v2 Copy; n (%)	11 (0.4%)	11 (0.4%)	0.00	204 (1.5%)	168 (1.2%)	0.03	224 (1.0%)	191 (0.9%)	0.01	439 (1.1%)	370 (0.9%)	0.02
Previous cardiac procedure (CABG or PTCA or Stent) + History of CABG or PTCA (for PS) v3; n (%)	515 (18.5%)	505 (18.1%)	0.01	4,706 (33.7%)	4,661 (33.4%)	0.01	3,619 (16.2%)	3,549 (15.9%)	0.01	8840 (22.6%)	8715 (22.3%)	0.01
Hyperthyroidism + Hypothyroidism + Other disorders of thyroid gland (for PS); n (%)	153 (5.5%)	141 (5.1%)	0.02	730 (5.2%)	700 (5.0%)	0.01	1,780 (8.0%)	1,772 (7.9%)	0.00	2663 (6.8%)	2613 (6.7%)	0.00
Delirium + Psychosis (for PS); n (%)	430 (15.4%)	454 (16.3%)	-0.02	1,697 (12.2%)	1,748 (12.5%)	-0.01	3,078 (13.8%)	3,045 (13.6%)	0.01	5205 (13.3%)	5247 (13.4%)	0.00
Any use of Meglitinides (for PS); n (%)	28 (1.0%)	27 (1.0%)	0.00	190 (1.4%)	207 (1.5%)	-0.01	285 (1.3%)	264 (1.2%)	0.01	503 (1.3%)	498 (1.3%)	0.00
Any use of AGIs (for PS); n (%)	4 (0.1%)	3 (0.1%)	0.00	76 (0.5%)	69 (0.5%)	0.00	72 (0.3%)	57 (0.3%)	0.00	152 (0.4%)	129 (0.3%)	0.02
CKD stage 3-6 + dialysis (for PS); n (%)	2 (0.1%)	4 (0.1%)	0.00	17 (0.1%)	27 (0.2%)	-0.03	18 (0.1%)	28 (0.1%)	0.00	37 (0.1%)	59 (0.2%)	-0.03
Use of thiazide; n (%)	1 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!	1 (0.0%)	0 (0.0%)	#DIV/0!
Use of beta blockers; n (%)	319 (11.4%)	332 (11.9%)	-0.02	1,447 (10.4%)	1,514 (10.8%)	-0.01	2,908 (13.0%)	2,867 (12.8%)	0.01	4674 (12.0%)	4713 (12.1%)	0.00
Use of calcium channel blockers; n (%)	1,727 (61.9%)	1,731 (62.0%)	0.00	9,487 (68.0%)	9,422 (67.5%)	0.01	14,583 (65.3%)	14,638 (65.6%)	-0.01	25797 (66.0%)	25791 (66.0%)	0.00
All antidiabetic medications except Insulin; n (%)	1,068 (38.3%)	1,010 (36.2%)	0.04	5,367 (38.4%)	5,347 (38.3%)	0.00	8,746 (39.2%)	8,649 (38.8%)	0.01	15181 (38.9%)	15006 (38.4%)	0.01
DM Medications - Insulin Copy; n (%)	603 (21.6%)	585 (21.0%)	0.01	2,704 (19.4%)	2,727 (19.5%)	0.00	4,497 (20.1%)	4,460 (20.0%)	0.00	7804 (20.0%)	7772 (19.9%)	0.00
Use of Low Intensity Statins; n (%)	126 (4.5%)	119 (4.3%)	0.01	695 (5.0%)	733 (5.3%)	-0.01	1,030 (4.6%)	802 (3.6%)	0.05	1851 (4.7%)	1654 (4.2%)	0.02
Use of High Intensity Statins; n (%)	960 (34.4%)	925 (33.2%)	0.03	4,415 (31.6%)	4,638 (33.2%)	-0.03	7,800 (34.9%)	7,804 (35.0%)	0.00	13175 (33.7%)	13367 (34.2%)	-0.01
Malignant hypertension; n (%)	553 (19.8%)	586 (21.0%)	-0.03	3,170 (22.7%)	2,952 (21.1%)	0.04	4,696 (21.0%)	4,665 (20.9%)	0.00	8419 (21.5%)	8203 (21.0%)	0.01
Cardiovascular stress test; n (%)	108 (3.9%)	103 (3.7%)	0.01	6,144 (44.0%)	5,989 (42.9%)	0.02	3,405 (15.3%)	3,554 (15.9%)	-0.02	9657 (24.7%)	9646 (24.7%)	0.00
Echocardiogram; n (%)	6 (0.2%)	13 (0.5%)	-0.05	96 (0.7%)	63 (0.5%)	0.03	105 (0.5%)	85 (0.4%)	0.01	207 (0.5%)	161 (0.4%)	0.01
Number of BNP tests	655 (23.5%)	781 (28.0%)	-0.10	6,201 (44.4%)	6,865 (49.2%)	-0.10	7,094 (31.8%)	8,024 (35.9%)	-0.09	13950 (35.7%)	15670 (40.1%)	-0.09
...mean (sd)	0.09 (0.43)	0.09 (0.36)	0.00	0.07 (0.32)	0.07 (0.33)	0.00	0.12 (0.40)	0.13 (0.42)	-0.02	0.10 (0.38)	0.11 (0.39)	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, 0.00]	0.00	0.00 (0.40)	0.00 (0.42)	0.00
Number of Cardiac biomarkers tests (troponin, CK-MBs, Myoglobin, CPK)												
...mean (sd)	0.31 (1.08)	0.35 (1.15)	-0.04	0.27 (1.16)	0.30 (1.23)	-0.03	0.24 (0.54)	0.25 (0.55)	-0.02	0.26 (0.85)	0.28 (0.90)	0.00
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 (1.01)	0.00 (1.06)	0.00
Number of Ambulatory Blood pressure monitoring tests												
...mean (sd)	0.00 (0.02)	0.00 (0.02)	0.00	0.00 (0.03)	0.00 (0.04)	0.00	0.00 (0.02)	0.00 (0.03)	0.00	0.00 (0.02)	0.00 (0.03)	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, 0.00]	0.00	0.00 (0.03)	0.00 (0.04)	0.00
N of days on antihypertensive medications during baseline												
...mean (sd)	131.24 (67.61)	130.11 (66.94)	0.02	132.77 (67.41)	132.32 (67.50)	0.01	137.09 (64.11)	136.78 (64.52)	0.00	135.13 (65.56)	134.71 (65.77)	0.00
...median [IQR]	170.00 [94.75, 181.00]	169.00 [92.00, 181.00]	0.01	172.00 [97.00, 181.00]	171.00 [96.00, 181.00]	0.01	173.00 [118.00, 181.00]	173.00 [116.00, 181.00]	0.00	135.41 (72.60)	134.98 (72.81)	0.00
N of days in database anytime prior												
...mean (sd)	1,737.28 (1,168.84)	1,752.47 (1,196.68)	-0.01	2,106.30 (1,213.13)	2,104.50 (1,207.54)	0.00	860.39 (497.95)	859.94 (468.49)	0.00	1368.18 (874.66)	1368.37 (865.24)	0.00
...median [IQR]	1,578.00 [699.75, 2,481.50]	1,600.00 [708.75, 2,508.25]	-0.02	185.0 [1,036.00, 3,090.75]	2,144.00 [1,017.00, 3,097.00]	-0.03	775.00 [499.00, 1,074.75]	775.00 [511.00, 1,085.00]	0.00	1142.98 (1039.21)	1157.24 (1029.89)	0.00
Mean Copay for per prescription cost (charges in U.S. \$) (180-1 day prior)												
...mean (sd)	32.13 (39.93)	31.29 (40.47)	0.02	22.72 (21.47)	22.59 (23.48)	0.01	113.35 (101.72)	115.02 (120.71)	-0.01	75.17 (78.67)	76.01 (92.94)	0.00
...median [IQR]	19.94 [8.75, 41.24]	20.38 [9.47, 39.44]	-0.01	18.19 [8.85, 30.64]	17.21 [8.61, 29.98]	0.04	90.00 [62.27, 132.46]	90.94 [63.10, 132.85]	-0.01	40.08 (79.30)	40.10 (93.57)	0.00
...Missing; n (%)	56 (2.0%)	61 (2.2%)	-0.01	420 (3.0%)	422 (3.0%)	0.00	482 (2.2%)	502 (2.2%)	0.00	958 (2.5%)	985 (2.5%)	0.00
Colonoscopy; n (%)	96 (3.4%)	86 (3.1%)	0.02	468 (3.4%)	459 (3.3%)	0.01	621 (2.8%)	639 (2.9%)	-0.01	1185 (3.0%)	1184 (3.0%)	0.00
Fecal occult blood (FOB) test; n (%)	112 (4.0%)	111 (4.0%)	0.00	316 (2.3%)	303 (2.2%)	0.01	621 (2.8%)	603 (2.7%)	0.01	1049 (2.7%)	1017 (2.6%)	0.01
Flu vaccine; n (%)	525 (18.8%)	549 (19.0%)	-0.02	1,463 (10.5%)	1,461 (10.5%)	0.00	7,309 (32.7%)	7,390 (33.1%)	-0.01	9297 (23.8%)	9400 (24.1%)	-0.01
Mammogram; n (%)	227 (8.1%)	220 (7.9%)	0.01	782 (5.6%)	732 (5.2%)	0.02	1,723 (7.7%)	1,707 (7.6%)	0.00	2732 (7.0%)	2659 (6.8%)	0.01

Appendix B

Pap smear; n (%)	42 (1.5%)	41 (1.5%)	0.00	236 (1.7%)	221 (1.6%)	0.01	446 (2.0%)	438 (2.0%)	0.00	724 (1.9%)	700 (1.8%)	0.01
Pneumonia vaccine; n (%)	256 (9.2%)	263 (9.4%)	-0.01	419 (3.0%)	438 (3.1%)	-0.01	2,807 (12.6%)	2,800 (12.5%)	0.00	3482 (8.9%)	3501 (9.0%)	0.00
PSA test or Prostate exam for DRE; n (%)	483 (17.3%)	471 (16.9%)	0.01	1,011 (7.2%)	980 (7.0%)	0.01	3,880 (17.4%)	3,854 (17.3%)	0.00	5374 (13.8%)	5305 (13.6%)	0.01
Bone mineral density; n (%)	104 (3.7%)	103 (3.7%)	0.00	250 (1.8%)	257 (1.8%)	0.00	739 (3.3%)	724 (3.2%)	0.01	1093 (2.8%)	1084 (2.8%)	0.00
Use of Sympathomimetic agents; n (%)	10 (0.4%)	8 (0.3%)	0.02	70 (0.5%)	79 (0.6%)	-0.01	48 (0.2%)	53 (0.2%)	0.00	128 (0.3%)	140 (0.4%)	-0.02
Use of CNS stimulants; n (%)	4 (0.1%)	3 (0.1%)	0.00	78 (0.6%)	73 (0.5%)	0.01	28 (0.1%)	30 (0.1%)	0.00	110 (0.3%)	106 (0.3%)	0.00
Use of estrogens, progestins, androgens; n (%)	73 (2.6%)	78 (2.8%)	-0.01	625 (4.5%)	617 (4.4%)	0.00	657 (2.9%)	703 (3.1%)	-0.01	1355 (3.5%)	1398 (3.6%)	-0.01
Use of Angiogenesis inhibitors; n (%)	0 (0.0%)	1 (0.0%)	#DIV/0!	13 (0.1%)	4 (0.0%)	0.04	**	**	#VALUE!	#VALUE!	#VALUE!	#VALUE!
Use of Oral Immunosuppressants; n (%)	2 (0.1%)	1 (0.0%)	0.04	14 (0.1%)	7 (0.1%)	0.00	**	**	#VALUE!	#VALUE!	#VALUE!	#VALUE!
Use of fondaparinux or Bivalirudin; n (%)	0 (0.0%)	1 (0.0%)	#DIV/0!	12 (0.1%)	10 (0.1%)	0.00	**	**	#VALUE!	#VALUE!	#VALUE!	#VALUE!
Use of other direct thrombin inhibitors (lepirudin, des	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!
Use of Ticagrelor ON CED; n (%)	0 (0.0%)	1 (0.0%)	#DIV/0!	14 (0.1%)	12 (0.1%)	0.00	6 (0.0%)	6 (0.0%)	#DIV/0!	20 (0.1%)	19 (0.0%)	0.04
Use of Ticagrelor; n (%)	1 (0.0%)	2 (0.1%)	-0.04	19 (0.1%)	18 (0.1%)	0.00	43 (0.2%)	36 (0.2%)	0.00	63 (0.2%)	56 (0.1%)	0.03
Number of D-dimer tests												
...mean (sd)	0.02 (0.14)	0.02 (0.14)	0.00	0.02 (0.15)	0.02 (0.15)	0.00	0.03 (0.18)	0.03 (0.18)	0.00	0.03 (0.17)	0.03 (0.17)	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, 0.00]	0.00	0.00 [0.18]	0.00 [0.18]	0.00
Numbe of CRP, high-sensitivity CRP tests												
...mean (sd)	0.06 (0.33)	0.06 (0.32)	0.00	0.02 (0.20)	0.02 (0.19)	0.00	0.07 (0.36)	0.07 (0.34)	0.00	0.05 (0.31)	0.05 (0.29)	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, 0.00]	0.00	0.00 (0.32)	0.00 (0.31)	0.00
Number of PT or aPTT tests												
...mean (sd)	0.51 (1.32)	0.46 (1.53)	0.03	0.45 (1.36)	0.38 (1.44)	0.05	0.47 (1.25)	0.43 (1.37)	0.03	0.47 (1.30)	0.41 (1.41)	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, 1.00]	0.00 [0.00, 0.00]	0.00	0.00 (1.44)	0.00 (1.56)	0.00
Number of Bleeding time tests												
...mean (sd)	0.00 (0.00)	0.00 (0.00)	#DIV/0!	0.00 (0.02)	0.00 (0.01)	0.00	0.00 (0.01)	0.00 (0.02)	0.00	0.00 (0.01)	0.00 (0.02)	0.00
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	#DIV/0!	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 (0.02)	0.00 (0.02)	0.00
HAS-BLED Score (ICD-9 and ICD-10), 180 days												
...mean (sd)	3.25 (0.70)	3.23 (0.67)	0.03	3.25 (0.74)	3.25 (0.74)	0.00	3.28 (0.63)	3.28 (0.62)	0.00	3.27 (0.68)	3.27 (0.67)	0.00
...median [IQR]	3.00 [3.00, 4.00]	3.00 [3.00, 4.00]	0.00	3.00 [3.00, 4.00]	3.00 [3.00, 4.00]	0.00	3.00 [3.00, 4.00]	3.00 [3.00, 4.00]	0.00	2.36 (0.76)	2.36 (0.75)	0.00
N of Generic name drugs												
...mean (sd)	14.73 (11.91)	14.51 (12.77)	0.02	12.44 (8.50)	12.33 (9.55)	0.01	14.78 (10.66)	14.67 (11.77)	0.01	13.94 (10.04)	13.82 (11.11)	0.00
...median [IQR]	12.00 [7.00, 19.00]	11.00 [6.00, 19.00]	0.08	11.00 [6.00, 16.00]	10.00 [6.00, 16.00]	0.11	12.00 [8.00, 19.00]	12.00 [7.00, 19.00]	0.00	9.07 (10.79)	8.65 (11.95)	0.00
N of Brand name drugs												
...mean (sd)	4.80 (6.60)	4.49 (4.60)	0.05	5.59 (5.92)	5.53 (4.85)	0.01	4.64 (5.86)	4.56 (4.70)	0.02	4.99 (5.94)	4.90 (4.75)	0.00
...median [IQR]	3.00 [0.00, 6.00]	3.00 [1.00, 6.00]	0.00	4.00 [2.00, 8.00]	4.00 [2.00, 7.00]	0.00	3.00 [1.00, 6.00]	3.00 [1.00, 6.00]	0.00	2.72 (6.54)	2.72 (5.25)	0.00
Use of clopidogrel ; n (%)	180 (6.5%)	177 (6.3%)	0.01	1,663 (11.9%)	1,623 (11.6%)	0.01	2,096 (9.4%)	2,122 (9.5%)	0.00	3939 (10.1%)	3922 (10.0%)	0.00
Systemic embolism; n (%)	13 (0.5%)	11 (0.4%)	0.01	50 (0.4%)	58 (0.4%)	0.00	77 (0.3%)	80 (0.4%)	-0.02	140 (0.4%)	149 (0.4%)	0.00
DVT; n (%)	35 (1.3%)	32 (1.1%)	0.02	207 (1.5%)	213 (1.5%)	0.00	245 (1.1%)	272 (1.2%)	-0.01	487 (1.2%)	517 (1.3%)	-0.01
PE; n (%)	5 (0.2%)	4 (0.1%)	0.03	92 (0.7%)	91 (0.7%)	0.00	84 (0.4%)	73 (0.3%)	0.02	181 (0.5%)	168 (0.4%)	0.01
Diabetes: 1 inpatient or 2 outpatient claims within 18	780 (28.0%)	749 (26.8%)	0.03	3,371 (24.1%)	3,331 (23.9%)	0.00	5,636 (25.3%)	5,630 (25.2%)	0.00	9787 (25.0%)	9710 (24.9%)	0.00
Intracranial or retroperitoneal hemorrhage: 1 inpatient	0 (0.0%)	1 (0.0%)	#DIV/0!	9 (0.1%)	8 (0.1%)	0.00	20 (0.1%)	17 (0.1%)	0.00	29 (0.1%)	26 (0.1%)	0.00
Peptic Ulcer Disease; n (%)	203 (7.3%)	208 (7.5%)	-0.01	901 (6.5%)	844 (6.0%)	0.02	1,652 (7.4%)	1,633 (7.3%)	0.00	2756 (7.1%)	2685 (6.9%)	0.01
Upper GI bleed; n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	5 (0.0%)	4 (0.0%)	#DIV/0!	0 (0.0%)	**	#VALUE!	5 (0.0%)	#VALUE!	#VALUE!
Lower/ unspecified GI bleed; n (%)	21 (0.8%)	24 (0.9%)	-0.01	104 (0.7%)	98 (0.7%)	0.00	116 (0.5%)	132 (0.6%)	-0.01	241 (0.6%)	254 (0.7%)	-0.01
Urogenital bleed; n (%)	91 (3.3%)	85 (3.0%)	0.02	441 (3.2%)	429 (3.1%)	0.01	671 (3.0%)	628 (2.8%)	0.01	1203 (3.1%)	1142 (2.9%)	0.01
Other bleeds; n (%)	29 (1.0%)	27 (1.0%)	0.00	167 (1.2%)	157 (1.1%)	0.01	229 (1.0%)	243 (1.1%)	-0.01	425 (1.1%)	427 (1.1%)	0.00
Prior cancer; n (%)	285 (10.2%)	289 (10.4%)	-0.01	1,288 (9.2%)	1,288 (10.5%)	0.00	2,427 (10.9%)	2,334 (10.5%)	0.01	4000 (10.2%)	3911 (10.0%)	0.01
Aspirin; n (%)	13 (0.5%)	11 (0.4%)	0.01	164 (1.2%)	161 (1.2%)	0.00	105 (0.5%)	97 (0.4%)	0.01	282 (0.7%)	269 (0.7%)	0.00
Aspirin/dipyridamole; n (%)	9 (0.3%)	9 (0.3%)	0.00	79 (0.6%)	71 (0.5%)	0.01	90 (0.4%)	84 (0.4%)	0.00	178 (0.5%)	164 (0.4%)	0.01
Other antiplatelet agents; n (%)	17 (0.6%)	13 (0.5%)	0.01	68 (0.5%)	77 (0.6%)	-0.01	134 (0.6%)	125 (0.6%)	0.00	219 (0.6%)	215 (0.6%)	0.00
PGP inhibitors; n (%)	1,098 (39.4%)	1,087 (39.0%)	0.01	6,825 (48.9%)	6,727 (48.2%)	0.01	9,742 (43.6%)	9,629 (43.1%)	0.01	17665 (45.2%)	17443 (44.6%)	0.01
Other gastroprotective agents; n (%)	19 (0.7%)	16 (0.6%)	0.01	131 (0.9%)	125 (0.9%)	0.00	165 (0.7%)	156 (0.7%)	0.00	315 (0.8%)	297 (0.8%)	0.00
Number of lipid tests ordered												
...mean (sd)	0.67 (0.86)	0.68 (0.84)	-0.01	0.25 (0.70)	0.24 (0.63)	0.02	0.71 (0.86)	0.71 (0.81)	0.00	0.54 (0.81)	0.54 (0.75)	0.00
...median [IQR]	0.00 [0.00, 1.00]	1.00 [0.00, 1.00]	-1.18	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	1.00 [0.00, 1.00]	1.00 [0.00, 1.00]	0.00	0.36 (0.87)	0.43 (0.81)	0.00
Proton pump inhibitor; n (%)	470 (16.8%)	440 (15.8%)	0.03	2,736 (19.6%)	2,724 (19.5%)	0.00	4,221 (18.9%)	4,253 (19.1%)	-0.01	7427 (19.0%)	7417 (19.0%)	0.00
H2 receptor antagonist; n (%)	91 (3.3%)	93 (3.3%)	0.00	384 (2.8%)	399 (2.9%)	-0.01	917 (4.1%)	890 (4.0%)	0.01	1392 (3.6%)	1382 (3.5%)	0.01
Vitamin K therapy; n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	11 (0.1%)	8 (0.1%)	0.00	4 (0.0%)	4 (0.0%)	#DIV/0!	15 (0.0%)	12 (0.0%)	#DIV/0!
Number of neurologist visits												
...mean (sd)	0.16 (0.98)	0.16 (0.97)	0.00	0.20 (1.18)	0.20 (1.00)	0.00	0.24 (1.44)	0.23 (1.23)	0.01	0.22 (1.32)	0.21 (1.14)	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, 0.00]	0.00	0.00 (1.43)	0.00 (1.23)	0.00
Number of INR (prothrombin) tests ordered												
...mean (sd)	0.41 (1.13)	0.36 (1.33)	0.04	0.36 (1.18)	0.30 (1.28)	0.05	0.45 (1.21)	0.41 (1.34)	0.03	0.41 (1.19)	0.37 (1.32)	0.00
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 [0.00, 1.00]	0.00 [0.00, 0.00]	0.00	0.00 (1.31)	0.00 (1.45)	0.00
Treating prescriber - Cardiologist; n (%)	1,281 (45.9%)	1,280 (45.9%)	0.00	7,610 (54.5%)	7,447 (53.3%)	0.02	12,337 (55.3%)	12,208 (54.7%)	0.01	21228 (54.3%)	20935 (53.6%)	0.01
Treating prescriber - Primary Care Physician; n (%)	1,575 (56.5%)	1,574 (56.4%)	0.00	4,213 (30.2%)	4,147 (29.7%)	0.01	5,306 (23.8%)	5,332 (23.9%)	0.00	11094 (28.4%)	11053 (28.3%)	0.00
Treating prescriber - Other; n (%)	1,997 (71.6%)	2,025 (72.6%)	-0.02	10,745 (77.0%)	10,635 (76.2%)	0.02	17,177 (77.0%)	17,046 (76.4%)	0.01	29919 (76.6%)	29706 (76.0%)	0.01
Alpha blockers; n (%)	400 (14.3%)	399 (14.3%)	0.00	1,835 (13.1%)	1,839 (13.2%)	0.00	3,188 (14.3%)	3,078 (13.8%)	0.01	5423 (13.9%)	5316 (13.6%)	0.01
CHADS2 score, 180 days, V												
...mean (sd)	1.88 (1.05)	1.87 (1.00)	0.01	1.91 (1.09)	1.90 (1.07)	0.01	2.90 (1.27)	2.92 (1.26)	-0.02	2.47 (1.19)	2.48 (1.18)	0.00
...median [IQR]	2.00 [1.00, 2.00]	2.00 [1.00, 2.00]	0.00	2.00 [1.00, 3.00]	2.00 [1.00, 2.00]	0.00	3.00 [2.00, 4.00]	3.00 [2.00, 4.00]	0.00	1.93 (1.30)	1.93 (1.28)	0.00
Use of Prasugrel; n (%)	5 (0.2%)	4 (0.1%)	0.03	56 (0.4%)	61 (0.4%)	0.00	**	**	#VALUE!	#VALUE!	#VALUE!	#VALUE!
Use of Loop Diuretics+other diuretics+other hypertens	669 (24.0%)	668 (23.9%)	0.00	4,208 (30.1%)	4,198 (30.1%)	0.00	5,853 (26.2%)	5,880 (26.3%)	0.00	10730 (27.5%)	10746 (27.5%)	0.00
Commercial vs Medicare Advantage- Business Type Code - CORRECT ONE - OPTUM							0	0				
...Commercial; n (%)	543 (19.5%)	550 (19.7%)	-0.01	11,890 (85.2%)	11,934 (85.5%)	-0.01	-	-	#VALUE!	12,433 (74.2%)	12,484 (74.5%)	-0.01
...Medicare Advantage; n (%)	2,247 (80.5%)	2240 (80.3%)	0.01	2,070 (14.8%)	2,026 (14.5%)	0.01	-	-	#VALUE!	4,317 (25.8%)	4,266 (25.5%)	0.01

Appendix B

Commercial vs Medicare Advantage- Business Type Code												
...COM = COMMERCIAL; n (%)	543 (19.5%)	550 (19.7%)	-0.01	-	-	#VALUE!	-	-	#VALUE!	543 (19.5%)	550 (19.7%)	-0.01
...MCR = MEDICARE; n (%)	2,247 (80.5%)	2,240 (80.3%)	0.01	-	-	#VALUE!	-	-	#VALUE!	2,247 (80.5%)	2,240 (80.3%)	0.01
...MCD = MEDICAID; n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	-	-	#VALUE!	-	-	#VALUE!	0 (0.0%)	0 (0.0%)	#DIV/0!
...NONE = NO BUSINESS LINE CODE (added in 2015); n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	-	-	#VALUE!	-	-	#VALUE!	0 (0.0%)	0 (0.0%)	#DIV/0!
...UNK = UNKNOWN (added in 2015); n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	-	-	#VALUE!	-	-	#VALUE!	0 (0.0%)	0 (0.0%)	#DIV/0!
Commercial vs Medicare Advantage- Data Type												
...1 - Fee For Service; n (%)	-	-		1,842 (13.2%)	1,816 (13.0%)	-	-	-		1,842 (13.2%)	1,816 (13.0%)	0.00
...2 - Encounter; n (%)	-	-		228 (1.6%)	210 (1.5%)	-	-	-		228 (1.6%)	210 (1.5%)	0.00
...3 - Medicare; n (%)	-	-		11,016 (78.9%)	11,069 (79.3%)	-	-	-		11,016 (78.9%)	11,069 (79.3%)	0.00
...4 - Medicare Encounter; n (%)	-	-		874 (6.3%)	865 (6.2%)	-	-	-		874 (6.3%)	865 (6.2%)	0.00
Metropolitan Statistical Area - Urban (any MSA) vs Rural (non-MSA)												
...Urban; n (%)	-	-		11,038 (79.1%)	11,101 (79.5%)	-	-	-		11,038 (79.1%)	11,101 (79.5%)	0.00
...Rural; n (%)	-	-		101 (0.7%)	111 (0.8%)	-	-	-		101 (0.7%)	111 (0.8%)	0.00
...Unknown/Missing; n (%)	-	-		2,821 (20.2%)	2,748 (19.7%)	-	-	-		2,821 (20.2%)	2,748 (19.7%)	0.00

Due to CMS cell suppression policy, all values less than 11 are denoted with **