

# Replication of the EINSTEIN-DVT Anticoagulant Trial in Healthcare Claims Data

NCT04736420

September 14 2021

## 1. RCT Details

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

### 1.1 Title

**Oral Rivaroxaban for Symptomatic Venous Thromboembolism ([EINSTEIN DVT](#))**

### 1.2 Intended aim(s)

To compare the risk of symptomatic, recurrent venous thromboembolism (VTE) in patients with acute, symptomatic deep vein thrombosis (DVT) for rivaroxaban versus standard therapy of warfarin.

### 1.3 Primary endpoint for replication

The primary outcome of the study was symptomatic, recurrent VTE

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

Assuming a noninferiority margin of 2.0, it was determined that about 3,000 patients would be needed to achieve 90% power to conclude noninferiority of rivaroxaban over standard therapy at two-sided alpha of 0.05.

### 1.5 Secondary endpoint for replication (assay sensitivity) and RCT finding

Major bleeding; RR = 0.65 (95% CI 0.33–1.30)

### 1.6 Trial estimate

RR = 0.68 (95% CI 0.44-1.04) comparing rivaroxaban vs standard therapy (Agnelli et al., 2010)

## 2. Person responsible for implementation of replication in Aetion

Dureshahwar Jawaid, MPH implemented the study design in the Aetion Evidence Platform. She is not responsible for the validity of the design and analytic choices. All implementation steps are recorded and the implementation history is archived in the platform.

## 3. Data Source(s)

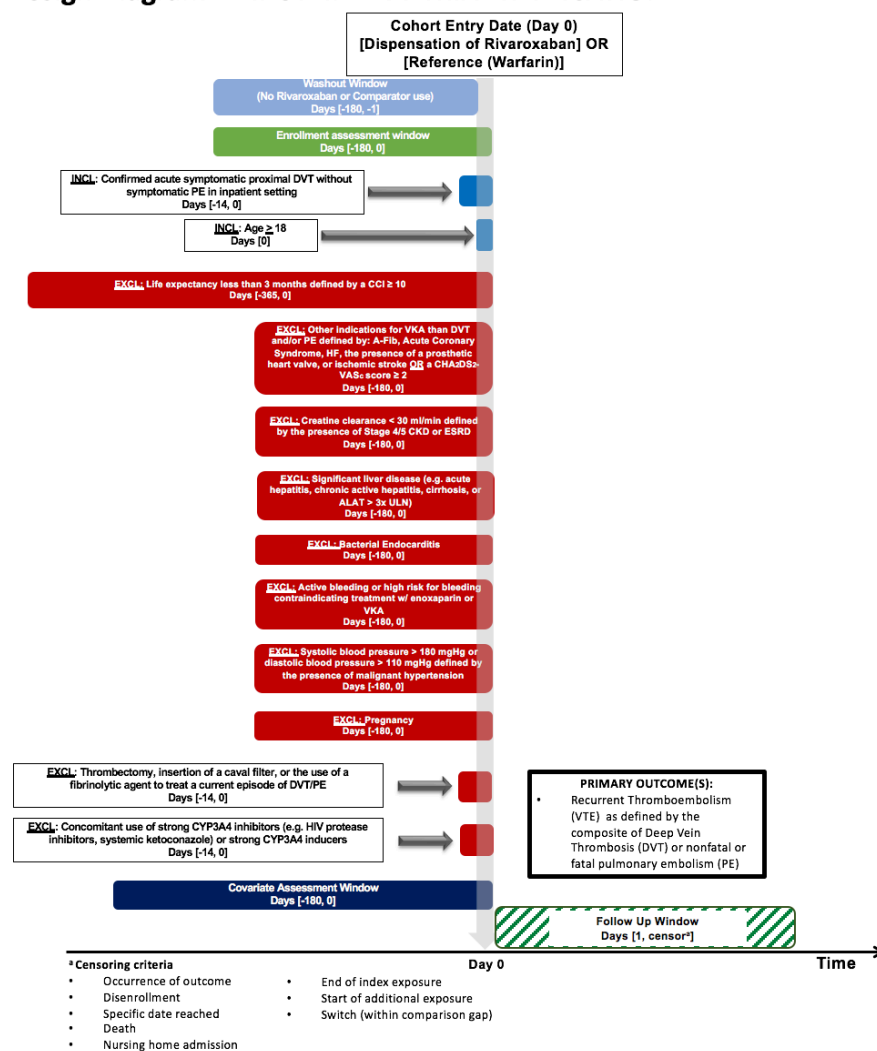
Optum, MarketScan, Medicare

#### 4. Study Design Diagram

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

Figure 1.

#### Design Diagram – EINSTEIN-DVT 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 rivaroxaban to warfarin users. The patients will be required to have continuous enrollment during a baseline period of 180 days before initiation of rivaroxaban or warfarin (index date). We will restrict the analyses to patients with a diagnosis of proximal DVT without symptomatic PE.

### 5.2 Important steps for cohort formation

New use of rivaroxaban, exposure, and warfarin, comparator, is defined as no use of either therapy in 180 days prior to index date.

#### 5.2.1 Eligible cohort entry dates

Market availability of rivaroxaban in the U.S. prevention of venous thromboembolism after orthopedic surgery started on July 30, 2008

- For Medicare: July 30, 2008– December 31, 2017 (end of available data)
- For Marketscan: July 30, 2008 – December 31, 2018 (end of available data)
- For Optum: July 30, 2008 – March 31, 2020 (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

	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

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Did not meet cohort entry criteria	-76,678,873	994,766	-199,008,369	1,195,539	-1,964,276	4,922,632
Excluded due to insufficient enrollment	-118,721	876,045	-99,207	1,096,332	-232,358	4,690,274
Excluded due to prior use of referent	-516,528	359,517	-684,176	412,156	-3,197,338	1,492,936
Excluded due to prior use of exposure and because patient qualified in >1 exposure category	-221,490	138,027	-216,501	195,655	-834,065	658,871
Excluded based on Age (<65 - Medicare only)	-	-	-	-	-72456	586,415
Excluded based on Age (missing)	0	138,027	0	195,655	-214	586,201
Excluded based on Gender	0	138,027	0	195,655	0	586,201
Excluded based on Use of other NOACs (dabigatran, apixaban, edoxaban)	-5421	132,606	-4267	191,388	-21987	564,214
Excluded based on Inclusion # 1 - DVT w/o Symptomatic PE and based on Exclusion # 1 - Age <=18	-117,812	14,794	-168,633	22,755	-499,609	64,605
Excluded based on Exclusion # 2 - Thrombectomy, Caval Filter	-210	14,584	-335	22,420	-903	63,702
Excluded based on Exclusion # 3 - other indications for VKA	-1721	12,863	-2,053	20,367	-9,815	53,887
Excluded based on Exclusion # 6 - CKD stage 4/5/ESRD	-114	12,749	-121	20,246	-496	53,391
Excluded based on Exclusion # 7 - Liver Disease and based on Exclusion # 8 - Bacterial Endocarditis	-497	12,252	-767	19,479	-1,320	52,071
Excluded based on Exclusion # 9 - CCI	-184	12,068	-155	19,324	-348	51,723
Excluded based on Exclusion # 10 - Active Bleeding/High Risk for Bleeding	-295	11,773	-478	18,846	-1,156	50,567
Excluded based on Exclusion # 11 - Malignant Hypertension and based on Exclusion # 12 - Pregnancy	-39	11,734	-116	18,730	-120	50,447
Excluded based on Exclusion # 14 - CYP3A4 Inhibitors	-12	11,722	-28	18,702	-72	50,375
Excluded based on Exclusion # 15 - Symptomatic Pulmonary Embolism	-369	11,353	-817	17,885	-1008	49,367
<b>Final cohort</b>		<b>11353</b>		<b>17885</b>		<b>49367</b>

## 6. Variables

### 6.1 Exposure-related variables:

#### Study drug:

The study exposure of interest is initiation of rivaroxaban. New initiation will be defined by no use of rivaroxaban or warfarin in the prior 6 months before treatment initiation (washout period).

#### Comparator:

New initiators of warfarin, defined by no use of rivaroxaban or warfarin in the prior 6 months.

### 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:** VTE

Safety outcomes of interest:

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 rivaroxaban 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 (rivaroxaban 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 rivaroxaban 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

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:

Optum- <https://bwh-dope.aetion.com/projects/details/1482/results/64422/result/0>

MarketScan- <https://bwh-dope.aetion.com/projects/details/1480/results/64423/result/0>

Medicare- <https://bwh-dope.aetion.com/projects/details/1479/results/64424/result/0>

Date conducted: 1/15/2021

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 rivaroxaban vs. warfarin

Optum- <https://bwh-dope.aetion.com/projects/details/1482/results/63169/result/0>

MarketScan- <https://bwh-dope.aetion.com/projects/details/1480/results/63168/result/0>

Medicare- <https://bwh-dope.aetion.com/projects/details/1479/results/63200/result/0>

Date conducted: 12/22/2020 (Medicare 12/23/20)

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 2 covariates: age 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 balance and final power assessment are reviewed by primary investigators, FDA, and assigned members of advisory board.

Reviewed by PI:	Jessica Franklin	Date reviewed:	11/18/2020
Reviewed by FDA:	Ken Quinto	Date reviewed:	11/29/2020
Reasons for stopping analysis (if required):			

## 9. Balance Assessment

### Aetion report links:

Optum: <https://bwh-dope.aetion.com/projects/details/1482/results/63187/result/0>

Marketscan: <https://bwh-dope.aetion.com/projects/details/1480/results/63178/result/0>

Medicare: <https://bwh-dope.aetion.com/projects/details/1479/results/63202/result/0>

Date conducted: 12/23/20

After review of initial feasibility and power analyses, complete creation of the remaining covariates from Section 6.2. 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.

- 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	326 (1.04%)	175 (1.11%)	151 (0.96%)
Death	698 (2.22%)	345 (2.20%)	353 (2.25%)
Start of an additional exposure	1,548 (4.93%)	983 (6.26 %)	565 (3.60%)
End of index exposure	23,549 (74.98%)	11,297 (71.94%)	12,252 (78.02%)
Specified date reached	1,374 (4.37%)	711 (4.53%)	663 (4.22%)
End of patient enrollment	925 (2.95%)	503 (3.20%)	422 (2.69%)
Switch to other NOACs (for censoring) + nursing home admission	2,988 (9.51%)	1,690 (10.76%)	1,298 (8.27%)

- Report follow-up time by treatment group.

Median Follow-Up Time (Days) [IQR]			
Patient Group	Optum	Marketscan	Medicare
Overall Patient Population	59 [29-131]	73 [38-146]	73 [38-154]
Referent	64 [28-138]	78 [38-150]	82 [38-165]
Exposure	54 [29-126]	67 [38-141]	65 [38-139]

- Report overall risk of the primary outcome.

	Optum	Marketscan	Medicare	Pooled
Risk per 1,000 patients	17.57	18.15	18.96	18.54

## 10. Final Power Assessment

Date conducted: 12/23/20

- 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.

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○ Pooled

Superiority Analysis		Non-inferiority Analysis	
Number of patients matched	25,970	Number of patients matched	25,970
Reference	12,985	Reference	12,985
Exposed	12,985	Exposed	12,985
Risk per 1,000 patients	18.54	Risk per 1,000 patients	18.54
Desired HR from RCT	0.68	Assumed HR from RCT	1
Alpha (2-sided)	0.05	Alpha (2-sided)	0.05
		Non-inferiority margin	2
Number of events expected	481.4838	Number of events expected	481.4838
Power	0.988435033	Power	0.999999992

○ Optum

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Superiority Analysis		Non-inferiority Analysis	
Number of patients matched	3,150	Number of patients matched	3,150
Reference	1,575	Reference	1,575
Exposed	1,575	Exposed	1,575
Risk per 1,000 patients	17.57	Risk per 1,000 patients	17.57
Desired HR from RCT	0.68	Assumed HR from RCT	1
Alpha (2-sided)	0.05	Alpha (2-sided)	0.05
		Non-inferiority margin	2
Number of events expected	55.3455	Number of events expected	55.3455
Power	0.299994744	Power	0.731829277

○ Marketscan

Superiority Analysis		Non-inferiority Analysis	
Number of patients matched	5,798	Number of patients matched	5,798
Reference	2,899	Reference	2,899
Exposed	2,899	Exposed	2,899
Risk per 1,000 patients	18.15	Risk per 1,000 patients	18.15
Desired HR from RCT	0.68	Assumed HR from RCT	1
Alpha (2-sided)	0.05	Alpha (2-sided)	0.05
		Non-inferiority margin	2
Number of events expected	105.2337	Number of events expected	105.2337
Power	0.507287833	Power	0.944678362

○ Medicare

Superiority Analysis		Non-inferiority Analysis	
Number of patients matched	17,022	Number of patients matched	17,022
Reference	8,511	Reference	8,511
Exposed	8,511	Exposed	8,511
Risk per 1,000 patients	18.96	Risk per 1,000 patients	18.96
Desired HR from RCT	0.68	Assumed HR from RCT	1
Alpha (2-sided)	0.05	Alpha (2-sided)	0.05
		Non-inferiority margin	2
Number of events expected	322.73712	Number of events expected	322.73712
Power	0.933738593	Power	0.999990058

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

Reviewed by PI:	Shirley Wang	Date reviewed:	12/24/2020
Reviewed by FDA:	Ken Quinto	Date reviewed:	01/18/2020
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](#) 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
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**

Agnelli G, Berkowitz S, Bounameaux H, et al. Oral Rivaroxaban for Symptomatic Venous Thromboembolism. N Engl J Med. 2010; 363:2499-2510

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



Appendix A

#	EINSTEIN DVT trial definitions	Implementation in routine care	Please see the following Google Drive for further details or any missing information: <a href="https://drive.google.com/drive/folders/1WD618wrywYlEaXfLTCuK-VCcnb6b-gV7usp=sharing">https://drive.google.com/drive/folders/1WD618wrywYlEaXfLTCuK-VCcnb6b-gV7usp=sharing</a>	
	Trial details- Primary approval; Unintended S with label change		Some 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: <a href="https://www.nber.org/data/icd9-icd10-cm-and-pcs-crosswalk-general-equivalence-mapping.html">https://www.nber.org/data/icd9-icd10-cm-and-pcs-crosswalk-general-equivalence-mapping.html</a>	
	EXPOSURE vs. COMPARISON		References/Rationale	Color coding
	Rivaroxaban (15mg twice daily for 3 wks followed by 20 mg once daily) vs Warfarin (or acenocoumarol)	Rivaroxaban vs. Warfarin		Criteria
	PRIMARY OUTCOME			Adequate mapping in claims
	Recurrent thromboembolism defined as the composite of (Deep vein thrombosis) DVT or nonfatal or fatal pulmonary embolism (PE)	Measured 1 day after drug initiation in any diagnosis position and in an inpatient care setting  Recurrent VTE (composite of DVT or PE): See 'VTE' sheet for codes	Fang MC, Fan D, Sung SH, et al. Validity of Using Inpatient and Outpatient Administrative Codes to Identify Acute Venous Thromboembolism: The CVRN VTE Study. Med Care. 2017;55(12):e137-e143.	Intermediate mapping in claims
	INCLUSION CRITERIA			Poor mapping or cannot be measured in claims
	1 Confirmed acute symptomatic proximal DVT without symptomatic PE	Measured 14 days prior to and including the day of drug initiation in any diagnosis position and in an inpatient or ED care setting as defined below:  DVT: ICD-9 Dx: 451.1x, 451.2x, 451.81, 451.9x, 453.1x, 453.2x, 453.8x, 453.9x, 453.40, 453.41, 453.42, 453.0 ICD-10 Dx: I80.1*, I80.2, I80.3, I80.9, I82.0, I82.1, I82.2* EXCEPT I82.2*1, I82.4*, I82.6*, I82.890, I82.90, I82.A1*, I82.B1*, I82.C1*, T800XXA (and I26.90 or I26.99), T81718A (and I26.90 or I26.99), T8172XA (and I26.90 or I26.99), T82817A (and I26.90 or I26.99), T82818A (and I26.90 or I26.99)	We will apply PE as exclusion criteria.	Can't be measured in claims but not important for the analysis
	2 Written informed consent	N/A		
	EXCLUSION CRITERIA			
	1 Legal lower age limitations	Measured on day of drug initiation Age ≤ 18		
	2 Thrombolectomy, insertion of a caval filter, or use of a fibrinolytic agent to treat the current episode of DVT or PE	Measured 14 days prior to and including the day of drug initiation in any diagnosis position and in an inpatient or outpatient care setting as defined below:  Thrombolectomy: ICD-9 Px: 39.74 ICD-10 Px: O3CG3ZZ, O3CG4ZZ, O3CH3ZZ, O3CH4ZZ, O3CJ3ZZ, O3CJ4ZZ, O3CK3ZZ, O3CK4ZZ, O3CL3ZZ, O3CL4ZZ, O3CM3ZZ, O3CM4ZZ, O3CN3ZZ, O3CN4ZZ, O3CP3ZZ, O3CP4ZZ, O3CQ3ZZ, O3CQ4ZZ, O3CR3ZZ, O3CR4ZZ, O3CS3ZZ, O3CS4ZZ, O3CT3ZZ, O3CT4ZZ, O3CU3ZZ, O3CU4ZZ, O3CV3ZZ, O3CV4ZZ HCPCS: C1757  Caval filter: CPT: 37191, 37192 HCPCS: C1880		
	3 Other indications for VKA than DVT and/or PE	Measured 180 days prior to drug initiation in any diagnosis position and inpatient or outpatient care setting as defined below:  Atrial fibrillation: ICD-9 Dx: 427.3x  Acute coronary syndrome: ICD-9 Dx: 411.xx ICD-10 Dx: I24.9  Heart failure: ICD-9 Dx: 428.x, 398.91, 402.01, 402.11, 402.91, 404.01, 404.11, 404.91, 404.03, 404.13, 404.93  Prosthetic heart valve: ICD-9 Dx: V43.3 ICD-10 Dx: Z95.2  Ischemic Stroke: ICD-9 Dx: 433.xx, 434.xx, 436.xx		
	4 More than 48 hours pre-randomization treatment with therapeutic dosages of anti-coagulant treatment or more than a single dose of VKA prior to randomization	N/A		

# Appendix A

5	Participation in another pharmacotherapeutic study within 30 days	N/A		
6	Creatinine clearance <30 ml/min	<p>Measured 180 days prior to and including the day of drug initiation in any diagnosis position and in an inpatient or outpatient care setting as defined below:</p> <p><u>CKD stage 4/5/ESRD:</u>  <u>ICD-9 Dx:</u>            585.4x, 585.5x, 585.6x  <u>ICD-10 Dx:</u>            N18.4x, N18.5x, N18.6x</p>		
7	Significant liver disease (e.g. acute hepatitis, chronic active hepatitis, cirrhosis) or ALAT>3x ULN	<p>Measured 180 days prior to and including the day of drug initiation in any diagnosis position and in an inpatient or outpatient care setting as defined below:</p> <p><u>Moderate/severe liver disease:</u>  <u>ICD-9 Dx:</u>            070.xx, 570.xx-573.xx, 456.0x-456.2x, 576.8x, 782.4x, 789.5x  <u>ICD-9 Px:</u>            39.1x and 42.91</p>		
8	Bacterial endocarditis	<p>Measured 180 days prior to and including the day of drug initiation in any diagnosis position and in an inpatient or outpatient care setting as defined below:</p> <p><u>Bacterial endocarditis:</u>  <u>ICD-9 Dx:</u>            421.x  <u>ICD-10 Dx:</u>            I33.x</p>		
9	Life expectancy <3 months	<p>Measured over 365 days prior to drug initiation:</p> <p>CCI ≥10</p>		
10	Active bleeding or high risk for bleeding contraindicating treatment with enoxaparin or VKA	<p>Measured 180 days prior to and including the day of drug initiation in any diagnosis position and in an inpatient or outpatient care setting as defined below:</p> <p>Active bleeding or bleeding history-- see 'Major Bleeding' sheet</p>		
11	Systolic blood pressure >180 mgHg or diastolic blood pressure >110mgHg	<p>Measured 180 days prior to and including the day of drug initiation in any diagnosis position and in an inpatient or outpatient care setting as defined below:</p> <p><u>Malignant Hypertension:</u>  <u>ICD-9 Dx:</u>            401.0, 402.0, 402.00, 402.01, 403.0, 403.00, 403.01, 404.0, 404.00, 404.01, 404.02, 404.03, 405.0, 405.01, 405.09</p>		
12	Childbearing potential without proper contraceptive measures, pregnancy or breastfeeding	<p>Measured 180 days prior to and including they day of drug initiation in any diagnosis position and in an inpatient or outpatient care setting as defined below:</p> <p>Pregnancy or lactation-- see 'Pregnancy' sheet</p>		
13	Any other contraindication listed in the local labeling of enoxaparin, warfarin, or acenocoumarol	N/A		
14	Concomitant use of strong CYP3A4 inhibitors (e.g. HIV protease inhibitors, systemic ketoconazole) or strong CYP3A4 inducers rifampin	<p>Prescription claim for following CYP3A inhibitors or strong CYP3A inducers</p> <p>Measured 14 days prior to and also <b>on</b> the drug initiation date</p> <p>Inhibitors: Ketoconazole, itraconazole, voriconazole, telithromycin, clarithromycin, nefazodone, ritonavir, saquinavir, neffinavir, indinavir, atazanavir            Inducers: Rifampin, rifampicin/rifampin, phenytoin, carbamazepine</p>		
15	Symptomatic pulmonary embolism	<p>Measured 14 days prior to and including the day of drug initiation in any diagnosis position and in an inpatient care setting as defined below:</p> <p><u>Pulmonary embolism:</u>  <u>ICD-9 Dx:</u>            415.1x  <u>ICD-10 Dx:</u>            I26.* EXCEPT I26.90</p>		

# Appendix A

<b><u>Trial Category</u></b>	Secondary initiation
<b><u>RCT Category</u></b>	5a- Successful NI with label change
<b><u>Trial Name (with web links)</u></b>	<a href="#">EINSTEIN DVT</a>
<b><u>Study Batch</u></b>	NOACs
<b><u>NCT</u></b>	<a href="#">NCT00440193</a>
<b><u>Therapeutic Area</u></b>	Cardiology/Vascular Diseases
<b><u>Brand Name</u></b>	Xarelto
<b><u>Generic Name</u></b>	Rivaroxaban
<b><u>Sponsor</u></b>	Bayer
<b><u>Year</u></b>	2010
<b><u>Measurable endpoint</u></b>	Percentage of Participants With Symptomatic Recurrent Venous Thromboembolism [VTE] (i.e. the Composite of Recurrent Deep Vein Thrombosis [DVT] or Fatal or Non-fatal Pulmonary Embolism [PE]) Until the Intended End of Study Treatment
<b><u>Exposure</u></b>	Rivaroxaban
<b><u>Comparator</u></b>	Enoxaparin/VKA
<b><u>Trial finding</u></b>	HR = 0.68 (95% CI 0.44–1.04)
<b><u>No. of Patients</u></b>	3,449
<b><u>Non-inferiority margin</u></b>	HR = 2.0
<b><u>Finding for potential Assay Sens. Outcome from trial-</u></b>	HR 0.72, 95% CI 0.53-0.99
<b><u>Assay Sens. Finding</u></b>	Percentage of Participants With the Composite Variable Comprising Recurrent DVT, Non-fatal PE <b><u>and All Cause Mortality</u></b> Until the Intended End of Study Treatment
<b><u>Power</u></b>	0.90. Assuming equal efficacy, a total of 88 events was calculated to give a power of 90% to prove that rivaroxaban is at least as effective as the comparator, considering a non-inferiority upper CI margin for the hazard ratio of 2.0 (two-sided $\alpha=0.05$ ). A mean incidence for the primary efficacy outcome of 3% was expected and at least 1465 participants per group were determined to be necessary. This number was to be adjusted based on the observed overall incidence of symptomatic recurrent VTE.

# Appendix A

Title	
Venous Thromboembolism (VTE)	
<b>ICD-9 Dx inpatient primary position</b>	
<b>PE</b>	
415.1	PULMONARY EMBOLISM AND INFARCTION
415.11	IATROGENIC PULMONARY EMBOLISM AND INFARCTION
415.19	OTHER PULMONARY EMBOLISM AND INFARCTION
<b>DVT</b>	
451.1	PHLEBITIS AND THROMBOPHLEBITIS OF DEEP VEINS OF LOWER EXTREMITIES
451.11	PHLEBITIS AND THROMBOPHLEBITIS OF FEMORAL VEIN (DEEP) (SUPERFICIAL)
451.19	PHLEBITIS AND THROMBOPHLEBITIS OF OTHER
451.2	PHLEBITIS AND THROMBOPHLEBITIS OF LOWER EXTREMITIES UNSPECIFIED
451.81	PHLEBITIS AND THROMBOPHLEBITIS OF ILIAC VEIN
451.9	PHLEBITIS AND THROMBOPHLEBITIS OF UNSPECIFIED SITE
453	BUDD-CHIARI SYNDROME
453.1	THROMBOPHLEBITIS MIGRANS
453.2	EMBOLISM AND THROMBOSIS OF INFERIOR VENA CAVA
453.4	ACUTE VENOUS EMBOLISM AND THROMBOSIS OF DEEP VESSELS OF LOWER EXTREMITY
453.4	ACUTE VENOUS EMBOLISM AND THROMBOSIS OF UNSPECIFIED DEEP VESSELS OF LOWER EXTREMITY
453.41	ACUTE VENOUS EMBOLISM AND THROMBOSIS OF DEEP VESSELS OF PROXIMAL LOWER EXTREMITY
453.42	ACUTE VENOUS EMBOLISM AND THROMBOSIS OF DEEP VESSELS OF DISTAL LOWER EXTREMITY
453.5	CHRONIC VENOUS EMBOLISM AND THROMBOSIS OF DEEP VESSELS OF LOWER EXTREMITY
453.5	CHRONIC VENOUS EMBOLISM AND THROMBOSIS OF UNSPECIFIED DEEP VESSELS OF LOWER EXTREMITY
453.51	CHRONIC VENOUS EMBOLISM AND THROMBOSIS OF DEEP VESSELS OF PROXIMAL LOWER EXTREMITY
453.52	CHRONIC VENOUS EMBOLISM AND THROMBOSIS OF DEEP VESSELS OF DISTAL LOWER EXTREMITY
453.8	ACUTE VENOUS EMBOLISM AND THROMBOSIS OF OTHER SPECIFIED VEINS
453.82	ACUTE VENOUS EMBOLISM AND THROMBOSIS OF DEEP VEINS OF UPPER EXTREMITY
453.83	ACUTE VENOUS EMBOLISM AND THROMBOSIS OF UPPER EXTREMITY UNSPECIFIED
453.84	ACUTE VENOUS EMBOLISM AND THROMBOSIS OF AXILLARY VEINS
453.85	ACUTE VENOUS EMBOLISM AND THROMBOSIS OF SUBCLAVIAN VEINS
453.86	ACUTE VENOUS EMBOLISM AND THROMBOSIS OF INTERNAL JUGULAR VEINS
453.87	ACUTE VENOUS EMBOLISM AND THROMBOSIS OF OTHER THORACIC VEINS
453.89	ACUTE VENOUS EMBOLISM AND THROMBOSIS OF OTHER SPECIFIED VEINS

# Appendix A

453.9	EMBOLISM AND THROMBOSIS OF UNSPECIFIED SITE
<b>ICD-10 Dx inpatient primary position</b>	
<b>PE</b>	
I26.0	Pulmonary embolism with acute cor pulmonale
I26.01	Septic pulmonary embolism with acute cor pulmonale
I26.02	Saddle embolus of pulmonary artery with acute cor pulmonale
I26.09	Other pulmonary embolism with acute cor pulmonale
I26.9	Pulmonary embolism without acute cor pulmonale
I26.99	Other pulmonary embolism without acute cor pulmonale
<b>DVT</b>	
I80.1	Phlebitis and thrombophlebitis of femoral vein
I80.10	Phlebitis and thrombophlebitis of unspecified femoral vein
I80.11	Phlebitis and thrombophlebitis of right femoral vein
I80.12	Phlebitis and thrombophlebitis of left femoral vein
I80.13	Phlebitis and thrombophlebitis of femoral vein, bilateral
I80.2	Phlebitis and thrombophlebitis of other and unspecified deep vessels of lower extremities
I80.20	Phlebitis and thrombophlebitis of unspecified deep vessels of lower extremities
I80.201	Phlebitis and thrombophlebitis of unspecified deep vessels of right lower extremity
I80.202	Phlebitis and thrombophlebitis of unspecified deep vessels of left lower extremity
I80.203	Phlebitis and thrombophlebitis of unspecified deep vessels of lower extremities, bilateral
I80.209	Phlebitis and thrombophlebitis of unspecified deep vessels of unspecified lower extremity
I80.21	Phlebitis and thrombophlebitis of iliac vein
I80.211	Phlebitis and thrombophlebitis of right iliac vein
I80.212	Phlebitis and thrombophlebitis of left iliac vein
I80.213	Phlebitis and thrombophlebitis of iliac vein, bilateral
I80.219	Phlebitis and thrombophlebitis of unspecified iliac vein
I80.22	Phlebitis and thrombophlebitis of popliteal vein
I80.221	Phlebitis and thrombophlebitis of right popliteal vein
I80.222	Phlebitis and thrombophlebitis of left popliteal vein
I80.223	Phlebitis and thrombophlebitis of popliteal vein, bilateral
I80.229	Phlebitis and thrombophlebitis of unspecified popliteal vein
I80.23	Phlebitis and thrombophlebitis of tibial vein
I80.231	Phlebitis and thrombophlebitis of right tibial vein

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I80.232	Phlebitis and thrombophlebitis of left tibial vein
I80.233	Phlebitis and thrombophlebitis of tibial vein, bilateral
I80.239	Phlebitis and thrombophlebitis of unspecified tibial vein
I80.29	Phlebitis and thrombophlebitis of other deep vessels of lower extremities
I80.291	Phlebitis and thrombophlebitis of other deep vessels of right lower extremity
I80.292	Phlebitis and thrombophlebitis of other deep vessels of left lower extremity
I80.293	Phlebitis and thrombophlebitis of other deep vessels of lower extremity, bilateral
I80.299	Phlebitis and thrombophlebitis of other deep vessels of unspecified lower extremity
I80.3	Phlebitis and thrombophlebitis of lower extremities, unspecified
I80.9	Phlebitis and thrombophlebitis of unspecified site
I82.0	Exposure) Rivaroxaban+E+E6
I82.1	Thrombophlebitis migrans
I80.3	Phlebitis and thrombophlebitis of lower extremities, unspecified
I82.4	Acute embolism and thrombosis of deep veins of lower extremity
I82.40	Acute embolism and thrombosis of unspecified deep veins of lower extremity
I82.401	Acute embolism and thrombosis of unspecified deep veins of right lower extremity
I82.402	Acute embolism and thrombosis of unspecified deep veins of left lower extremity
I82.403	Acute embolism and thrombosis of unspecified deep veins of lower extremity, bilateral
I82.409	Acute embolism and thrombosis of unspecified deep veins of unspecified lower extremity
I82.41	Acute embolism and thrombosis of femoral vein
I82.411	Acute embolism and thrombosis of right femoral vein
I82.412	Acute embolism and thrombosis of left femoral vein
I82.413	Acute embolism and thrombosis of femoral vein, bilateral
I82.419	Acute embolism and thrombosis of unspecified femoral vein
I82.42	Acute embolism and thrombosis of iliac vein
I82.421	Acute embolism and thrombosis of right iliac vein
I82.422	Acute embolism and thrombosis of left iliac vein
I82.423	Acute embolism and thrombosis of iliac vein, bilateral
I82.429	Acute embolism and thrombosis of unspecified iliac vein
I82.43	Acute embolism and thrombosis of popliteal vein
I82.431	Acute embolism and thrombosis of right popliteal vein
I82.432	Acute embolism and thrombosis of left popliteal vein
I82.433	Acute embolism and thrombosis of popliteal vein, bilateral
I82.439	Acute embolism and thrombosis of unspecified popliteal vein
I82.44	Acute embolism and thrombosis of tibial vein

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I82.441	Acute embolism and thrombosis of right tibial vein
I82.442	Acute embolism and thrombosis of left tibial vein
I82.443	Acute embolism and thrombosis of tibial vein, bilateral
I82.449	Acute embolism and thrombosis of unspecified tibial vein
I82.49	Acute embolism and thrombosis of other specified deep vein of lower extremity
I82.491	Acute embolism and thrombosis of other specified deep vein of right lower extremity
I82.492	Acute embolism and thrombosis of other specified deep vein of left lower extremity
I82.493	Acute embolism and thrombosis of other specified deep vein of lower extremity, bilateral
I82.499	Acute embolism and thrombosis of other specified deep vein of unspecified lower extremity
I82.4Y	Acute embolism and thrombosis of unspecified deep veins of proximal lower extremity
I82.4Y1	Acute embolism and thrombosis of unspecified deep veins of right proximal lower extremity
I82.4Y2	Acute embolism and thrombosis of unspecified deep veins of left proximal lower extremity
I82.4Y3	Acute embolism and thrombosis of unspecified deep veins of proximal lower extremity, bilateral
I82.4Y9	Acute embolism and thrombosis of unspecified deep veins of unspecified proximal lower extremity
I82.4Z	Acute embolism and thrombosis of unspecified deep veins of distal lower extremity
I82.4Z1	Acute embolism and thrombosis of unspecified deep veins of right distal lower extremity
I82.4Z2	Acute embolism and thrombosis of unspecified deep veins of left distal lower extremity
I82.4Z3	Acute embolism and thrombosis of unspecified deep veins of distal lower extremity, bilateral
I82.4Z9	Acute embolism and thrombosis of unspecified deep veins of unspecified distal lower extremity
I82.5	Chronic embolism and thrombosis of deep veins of lower extremity
I82.50	Chronic embolism and thrombosis of unspecified deep veins of lower extremity
I82.501	Chronic embolism and thrombosis of unspecified deep veins of right lower extremity
I82.502	Chronic embolism and thrombosis of unspecified deep veins of left lower extremity
I82.503	Chronic embolism and thrombosis of unspecified deep veins of lower extremity, bilateral
I82.509	Chronic embolism and thrombosis of unspecified deep veins of unspecified lower extremity
I82.51	Chronic embolism and thrombosis of femoral vein
I82.511	Chronic embolism and thrombosis of right femoral vein
I82.512	Chronic embolism and thrombosis of left femoral vein
I82.513	Chronic embolism and thrombosis of femoral vein, bilateral
I82.519	Chronic embolism and thrombosis of unspecified femoral vein
I82.52	Chronic embolism and thrombosis of iliac vein
I82.521	Chronic embolism and thrombosis of right iliac vein
I82.522	Chronic embolism and thrombosis of left iliac vein
I82.523	Chronic embolism and thrombosis of iliac vein, bilateral
I82.529	Chronic embolism and thrombosis of unspecified iliac vein

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I82.53	Chronic embolism and thrombosis of popliteal vein
I82.531	Chronic embolism and thrombosis of right popliteal vein
I82.532	Chronic embolism and thrombosis of left popliteal vein
I82.533	Chronic embolism and thrombosis of popliteal vein, bilateral
I82.539	Chronic embolism and thrombosis of unspecified popliteal vein
I82.54	Chronic embolism and thrombosis of tibial vein
I82.541	Chronic embolism and thrombosis of right tibial vein
I82.542	Chronic embolism and thrombosis of left tibial vein
I82.543	Chronic embolism and thrombosis of tibial vein, bilateral
I82.549	Chronic embolism and thrombosis of unspecified tibial vein
I82.59	Chronic embolism and thrombosis of other specified deep vein of lower extremity
I82.591	Chronic embolism and thrombosis of other specified deep vein of right lower extremity
I82.592	Chronic embolism and thrombosis of other specified deep vein of left lower extremity
I82.593	Chronic embolism and thrombosis of other specified deep vein of lower extremity, bilateral
I82.599	Chronic embolism and thrombosis of other specified deep vein of unspecified lower extremity
I82.5Y	Chronic embolism and thrombosis of unspecified deep veins of proximal lower extremity
I82.5Y1	Chronic embolism and thrombosis of unspecified deep veins of right proximal lower extremity
I82.5Y2	Chronic embolism and thrombosis of unspecified deep veins of left proximal lower extremity
I82.5Y3	Chronic embolism and thrombosis of unspecified deep veins of proximal lower extremity, bilateral
I82.5Y9	Chronic embolism and thrombosis of unspecified deep veins of unspecified proximal lower extremity
I82.5Z	Chronic embolism and thrombosis of unspecified deep veins of distal lower extremity
I82.5Z1	Chronic embolism and thrombosis of unspecified deep veins of right distal lower extremity
I82.5Z2	Chronic embolism and thrombosis of unspecified deep veins of left distal lower extremity
I82.5Z3	Chronic embolism and thrombosis of unspecified deep veins of distal lower extremity, bilateral
I82.5Z9	Chronic embolism and thrombosis of unspecified deep veins of unspecified distal lower extremity
I82.6	Acute embolism and thrombosis of veins of upper extremity
I82.60	Acute embolism and thrombosis of unspecified veins of upper extremity
I82.601	Acute embolism and thrombosis of unspecified veins of right upper extremity
I82.602	Acute embolism and thrombosis of unspecified veins of left upper extremity
I82.603	Acute embolism and thrombosis of unspecified veins of upper extremity, bilateral
I82.609	Acute embolism and thrombosis of unspecified veins of unspecified upper extremity
I82.62	Acute embolism and thrombosis of deep veins of upper extremity
I82.621	Acute embolism and thrombosis of deep veins of right upper extremity
I82.622	Acute embolism and thrombosis of deep veins of left upper extremity
I82.623	Acute embolism and thrombosis of deep veins of upper extremity, bilateral



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I82.629	Acute embolism and thrombosis of deep veins of unspecified upper extremity
I82.890	Acute embolism and thrombosis of other specified veins
I82.90	Acute embolism and thrombosis of unspecified vein
I82.A1	Acute embolism and thrombosis of axillary vein
I82.A11	Acute embolism and thrombosis of right axillary vein
I82.A12	Acute embolism and thrombosis of left axillary vein
I82.A13	Acute embolism and thrombosis of axillary vein, bilateral
I82.A19	Acute embolism and thrombosis of unspecified axillary vein
I82.B1	Acute embolism and thrombosis of subclavian vein
I82.B11	Acute embolism and thrombosis of right subclavian vein
I82.B12	Acute embolism and thrombosis of left subclavian vein
I82.B13	Acute embolism and thrombosis of subclavian vein, bilateral
I82.B19	Acute embolism and thrombosis of unspecified subclavian vein
I82.C1	Acute embolism and thrombosis of internal jugular vein
I82.C11	Acute embolism and thrombosis of right internal jugular vein
I82.C12	Acute embolism and thrombosis of left internal jugular vein
I82.C13	Acute embolism and thrombosis of internal jugular vein, bilateral
I82.C19	Acute embolism and thrombosis of unspecified internal jugular vein

# Appendix A

Title	
Major Bleeding	
<b>ICD-9 Dx: 1 inpatient or 2 outpatient</b>	
562.02	DIVERTICULOSIS OF SMALL INTESTINE WITH HEMORRHAGE
562.03	DIVERTICULITIS OF SMALL INTESTINE WITH HEMORRHAGE
562.12	DIVERTICULOSIS OF COLON WITH HEMORRHAGE
562.13	DIVERTICULITIS OF COLON WITH HEMORRHAGE
568.81	HEMOPERITONEUM (NONTRAUMATIC
569.3	HEMORRHAGE OF RECTUM AND ANUS
569.83	PERFORATION OF INTESTINE
569.85	ANGIODYSPLASIA OF INTESTINE WITH HEMORRHAGE OF INTESTINE
569.86	DIEULAFOY LESION (HEMORRHAGIC
578	HEMATEMESIS
578.9	HEMORRHAGE OF GASTROINTESTINAL TRACT UNSPECIFIED
423	HEMOPERICARDIUM
432	NONTRAUMATIC EXTRADURAL HEMORRHAGE
432.1	SUBDURAL HEMORRHAGE
432.9	UNSPECIFIED INTRACRANIAL HEMORRHAGE
459	HEMORRHAGE UNSPECIFIED
531	ACUTE GASTRIC ULCER WITH HEMORRHAGE
531	ACUTE GASTRIC ULCER WITH HEMORRHAGE WITHOUT OBSTRUCTION
531.01	ACUTE GASTRIC ULCER WITH HEMORRHAGE WITH OBSTRUCTION
531.2	ACUTE GASTRIC ULCER WITH HEMORRHAGE AND PERFORATION
531.2	ACUTE GASTRIC ULCER WITH HEMORRHAGE AND PERFORATION WITHOUT OBSTRUCTION
531.21	ACUTE GASTRIC ULCER WITH HEMORRHAGE AND PERFORATION WITH OBSTRUCTION
531.4	CHRONIC OR UNSPECIFIED GASTRIC ULCER WITH HEMORRHAGE
531.4	CHRONIC OR UNSPECIFIED GASTRIC ULCER WITH HEMORRHAGE WITHOUT OBSTRUCTION
531.41	CHRONIC OR UNSPECIFIED GASTRIC ULCER WITH HEMORRHAGE WITH OBSTRUCTION
531.6	CHRONIC OR UNSPECIFIED GASTRIC ULCER WITH HEMORRHAGE AND PERFORATION
531.6	CHRONIC OR UNSPECIFIED GASTRIC ULCER WITH HEMORRHAGE AND PERFORATION WITHOUT OBSTRUCTION
531.61	CHRONIC OR UNSPECIFIED GASTRIC ULCER WITH HEMORRHAGE AND PERFORATION WITH OBSTRUCTION
532	ACUTE DUODENAL ULCER WITH HEMORRHAGE
532	ACUTE DUODENAL ULCER WITH HEMORRHAGE WITHOUT OBSTRUCTION
532.01	ACUTE DUODENAL ULCER WITH HEMORRHAGE WITH OBSTRUCTION
532.2	ACUTE DUODENAL ULCER WITH HEMORRHAGE AND PERFORATION
532.2	ACUTE DUODENAL ULCER WITH HEMORRHAGE AND PERFORATION WITHOUT OBSTRUCTION
532.21	ACUTE DUODENAL ULCER WITH HEMORRHAGE AND PERFORATION WITH OBSTRUCTION
532.4	CHRONIC OR UNSPECIFIED DUODENAL ULCER WITH HEMORRHAGE
532.4	CHRONIC OR UNSPECIFIED DUODENAL ULCER WITH HEMORRHAGE WITHOUT OBSTRUCTION
532.41	CHRONIC OR UNSPECIFIED DUODENAL ULCER WITH HEMORRHAGE WITH OBSTRUCTION

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532.6	CHRONIC OR UNSPECIFIED DUODENAL ULCER WITH HEMORRHAGE AND PERFORATION
532.6	CHRONIC OR UNSPECIFIED DUODENAL ULCER WITH HEMORRHAGE AND PERFORATION WITHOUT OBSTRUCTION
532.61	CHRONIC OR UNSPECIFIED DUODENAL ULCER WITH HEMORRHAGE AND PERFORATION WITH OBSTRUCTION
533	ACUTE PEPTIC ULCER OF UNSPECIFIED SITE WITH HEMORRHAGE
533	ACUTE PEPTIC ULCER OF UNSPECIFIED SITE WITH HEMORRHAGE WITHOUT OBSTRUCTION
533.01	ACUTE PEPTIC ULCER OF UNSPECIFIED SITE WITH HEMORRHAGE WITH OBSTRUCTION
533.2	ACUTE PEPTIC ULCER OF UNSPECIFIED SITE WITH HEMORRHAGE AND PERFORATION
533.2	ACUTE PEPTIC ULCER OF UNSPECIFIED SITE WITH HEMORRHAGE AND PERFORATION WITHOUT OBSTRUCTION
533.21	ACUTE PEPTIC ULCER OF UNSPECIFIED SITE WITH HEMORRHAGE AND PERFORATION WITH OBSTRUCTION
533.4	CHRONIC OR UNSPECIFIED PEPTIC ULCER OF UNSPECIFIED SITE WITH HEMORRHAGE
533.4	CHRONIC OR UNSPECIFIED PEPTIC ULCER OF UNSPECIFIED SITE WITH HEMORRHAGE WITHOUT OBSTRUCTION
533.41	CHRONIC OR UNSPECIFIED PEPTIC ULCER OF UNSPECIFIED SITE WITH HEMORRHAGE WITH OBSTRUCTION
533.6	CHRONIC OR UNSPECIFIED PEPTIC ULCER OF UNSPECIFIED SITE WITH HEMORRHAGE AND PERFORATION
533.6	CHRONIC OR UNSPECIFIED PEPTIC ULCER OF UNSPECIFIED SITE WITH HEMORRHAGE AND PERFORATION WITHOUT OBSTRUCTION
533.61	CHRONIC OR UNSPECIFIED PEPTIC ULCER OF UNSPECIFIED SITE WITH HEMORRHAGE AND PERFORATION WITH OBSTRUCTION
534	ACUTE GASTROJEJUNAL ULCER WITH HEMORRHAGE
534	ACUTE GASTROJEJUNAL ULCER WITH HEMORRHAGE WITHOUT OBSTRUCTION
534.01	ACUTE GASTROJEJUNAL ULCER WITH HEMORRHAGE WITH OBSTRUCTION
534.2	ACUTE GASTROJEJUNAL ULCER WITH HEMORRHAGE AND PERFORATION
534.2	ACUTE GASTROJEJUNAL ULCER WITH HEMORRHAGE AND PERFORATION WITHOUT OBSTRUCTION
534.21	ACUTE GASTROJEJUNAL ULCER WITH HEMORRHAGE AND PERFORATION WITH OBSTRUCTION
534.4	CHRONIC OR UNSPECIFIED GASTROJEJUNAL ULCER WITH HEMORRHAGE
534.4	CHRONIC OR UNSPECIFIED GASTROJEJUNAL ULCER WITH HEMORRHAGE WITHOUT OBSTRUCTION
534.41	CHRONIC OR UNSPECIFIED GASTROJEJUNAL ULCER WITH HEMORRHAGE WITH OBSTRUCTION
534.6	CHRONIC OR UNSPECIFIED GASTROJEJUNAL ULCER WITH HEMORRHAGE AND PERFORATION
534.6	CHRONIC OR UNSPECIFIED GASTROJEJUNAL ULCER WITH HEMORRHAGE AND PERFORATION WITHOUT OBSTRUCTION
534.61	CHRONIC OR UNSPECIFIED GASTROJEJUNAL ULCER WITH HEMORRHAGE AND PERFORATION WITH OBSTRUCTION
578.1	BLOOD IN STOOL
719.1	HEMARTHROSIS
719.1	HEMARTHROSIS SITE UNSPECIFIED
719.11	HEMARTHROSIS INVOLVING SHOULDER REGION
719.12	HEMARTHROSIS INVOLVING UPPER ARM
719.13	HEMARTHROSIS INVOLVING FOREARM
719.14	HEMARTHROSIS INVOLVING HAND
719.15	HEMARTHROSIS INVOLVING PELVIC REGION AND THIGH
719.16	HEMARTHROSIS INVOLVING LOWER LEG
719.17	HEMARTHROSIS INVOLVING ANKLE AND FOOT
719.18	HEMARTHROSIS INVOLVING OTHER SPECIFIED SITES
719.19	HEMARTHROSIS INVOLVING MULTIPLE SITES
430	SUBARACHNOID HEMORRHAGE
431	INTRACEREBRAL HEMORRHAGE

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784.7	EPISTAXIS
784.8	HEMORRHAGE FROM THROAT
599.7	HEMATURIA
599.7	HEMATURIA UNSPECIFIED
599.71	GROSS HEMATURIA
599.72	MICROSCOPIC HEMATURIA
786.3	HEMOPTYSIS
786.3	HEMOPTYSIS UNSPECIFIED
786.31	ACUTE IDIOPATHIC PULMONARY HEMORRHAGE IN INFANTS
786.39	OTHER HEMOPTYSIS
<b>ICD-10 Dx: 1 inpatient or 2 outpatient</b>	
I31.2	Hemopericardium, not elsewhere classified
I60.00	Nontraumatic subarachnoid hemorrhage from unspecified carotid siphon and bifurcation
I60.01	Nontraumatic subarachnoid hemorrhage from right carotid siphon and bifurcation
I60.02	Nontraumatic subarachnoid hemorrhage from left carotid siphon and bifurcation
I60.10	Nontraumatic subarachnoid hemorrhage from unspecified middle cerebral artery
I60.11	Nontraumatic subarachnoid hemorrhage from right middle cerebral artery
I60.12	Nontraumatic subarachnoid hemorrhage from left middle cerebral artery
I60.2	Nontraumatic subarachnoid hemorrhage from anterior communicating artery
I60.30	Nontraumatic subarachnoid hemorrhage from unspecified posterior communicating artery
I60.31	Nontraumatic subarachnoid hemorrhage from right posterior communicating artery
I60.32	Nontraumatic subarachnoid hemorrhage from left posterior communicating artery
I60.4	Nontraumatic subarachnoid hemorrhage from basilar artery
I60.50	Nontraumatic subarachnoid hemorrhage from unspecified vertebral artery
I60.51	Nontraumatic subarachnoid hemorrhage from right vertebral artery
I60.52	Nontraumatic subarachnoid hemorrhage from left vertebral artery
I60.6	Nontraumatic subarachnoid hemorrhage from other intracranial arteries
I60.7	Nontraumatic subarachnoid hemorrhage from unspecified intracranial artery
I60.8	Other nontraumatic subarachnoid hemorrhage
I60.9	Nontraumatic subarachnoid hemorrhage, unspecified
I61.0	Nontraumatic intracerebral hemorrhage in hemisphere, subcortical
I61.1	Nontraumatic intracerebral hemorrhage in hemisphere, cortical
I61.2	Nontraumatic intracerebral hemorrhage in hemisphere, unspecified
I61.3	Nontraumatic intracerebral hemorrhage in brain stem
I61.4	Nontraumatic intracerebral hemorrhage in cerebellum
I61.5	Nontraumatic intracerebral hemorrhage, intraventricular
I61.6	Nontraumatic intracerebral hemorrhage, multiple localized
I61.8	Other nontraumatic intracerebral hemorrhage
I61.9	Nontraumatic intracerebral hemorrhage, unspecified
I62.00	Nontraumatic subdural hemorrhage, unspecified

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I62.01	Nontraumatic acute subdural hemorrhage
I62.02	Nontraumatic subacute subdural hemorrhage
I62.03	Nontraumatic chronic subdural hemorrhage
I62.1	Nontraumatic extradural hemorrhage
I62.9	Nontraumatic intracranial hemorrhage, unspecified
K25.0	Acute gastric ulcer with hemorrhage
K25.2	Acute gastric ulcer with both hemorrhage and perforation
K25.4	Chronic or unspecified gastric ulcer with hemorrhage
K25.6	Chronic or unspecified gastric ulcer with both hemorrhage and perforation
K26.0	Acute duodenal ulcer with hemorrhage
K26.2	Acute duodenal ulcer with both hemorrhage and perforation
K26.4	Chronic or unspecified duodenal ulcer with hemorrhage
K26.6	Chronic or unspecified duodenal ulcer with both hemorrhage and perforation
K27.0	Acute peptic ulcer, site unspecified, with hemorrhage
K27.2	Acute peptic ulcer, site unspecified, with both hemorrhage and perforation
K27.4	Chronic or unspecified peptic ulcer, site unspecified, with hemorrhage
K27.6	Chronic or unspecified peptic ulcer, site unspecified, with both hemorrhage and perforation
K28.0	Acute gastrojejunal ulcer with hemorrhage
K28.2	Acute gastrojejunal ulcer with both hemorrhage and perforation
K28.4	Chronic or unspecified gastrojejunal ulcer with hemorrhage
K28.6	Chronic or unspecified gastrojejunal ulcer with both hemorrhage and perforation
K55.21	Angiodysplasia of colon with hemorrhage
K56.60	Unspecified intestinal obstruction
K57.01	Diverticulitis of small intestine with perforation and abscess with bleeding
K57.11	Diverticulosis of small intestine without perforation or abscess with bleeding
K57.13	Diverticulitis of small intestine without perforation or abscess with bleeding
K57.21	Diverticulitis of large intestine with perforation and abscess with bleeding
K57.31	Diverticulosis of large intestine without perforation or abscess with bleeding
K57.33	Diverticulitis of large intestine without perforation or abscess with bleeding
K57.41	Diverticulitis of both small and large intestine with perforation and abscess with bleeding
K57.51	Diverticulosis of both small and large intestine without perforation or abscess with bleeding
K57.53	Diverticulitis of both small and large intestine without perforation or abscess with bleeding
K57.81	Diverticulitis of intestine, part unspecified, with perforation and abscess with bleeding
K57.91	Diverticulosis of intestine, part unspecified, without perforation or abscess with bleeding
K57.93	Diverticulitis of intestine, part unspecified, without perforation or abscess with bleeding
K62.5	Hemorrhage of anus and rectum
K63.1	Perforation of intestine (nontraumatic)
K63.81	Dieulafoy lesion of intestine
K66.1	Hemoperitoneum
K92.0	Hematemesis
K92.1	Melena

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K92.2	Gastrointestinal hemorrhage, unspecified
M25.00	Hemarthrosis, unspecified joint
M25.011	Hemarthrosis, right shoulder
M25.012	Hemarthrosis, left shoulder
M25.019	Hemarthrosis, unspecified shoulder
M25.021	Hemarthrosis, right elbow
M25.022	Hemarthrosis, left elbow
M25.029	Hemarthrosis, unspecified elbow
M25.031	Hemarthrosis, right wrist
M25.032	Hemarthrosis, left wrist
M25.039	Hemarthrosis, unspecified wrist
M25.041	Hemarthrosis, right hand
M25.042	Hemarthrosis, left hand
M25.049	Hemarthrosis, unspecified hand
M25.051	Hemarthrosis, right hip
M25.052	Hemarthrosis, left hip
M25.059	Hemarthrosis, unspecified hip
M25.061	Hemarthrosis, right knee
M25.062	Hemarthrosis, left knee
M25.069	Hemarthrosis, unspecified knee
M25.071	Hemarthrosis, right ankle
M25.072	Hemarthrosis, left ankle
M25.073	Hemarthrosis, unspecified ankle
M25.074	Hemarthrosis, right foot
M25.075	Hemarthrosis, left foot
M25.076	Hemarthrosis, unspecified foot
M25.08	Hemarthrosis, other specified site
R58	Hemorrhage, not elsewhere classified
R04	Hemorrhage from respiratory passages
R04.0	Epistaxis
R04.1	Hemorrhage from throat
R04.2	Hemoptysis
R04.8	Hemorrhage from other sites in respiratory passages
R04.81	Acute idiopathic pulmonary hemorrhage in infants
R04.89	Hemorrhage from other sites in respiratory passages
R04.9	Hemorrhage from respiratory passages, unspecified
R31	Hematuria
R31.0	Gross hematuria
R31.1	Benign essential microscopic hematuria
R31.2	Other microscopic hematuria
R31.21	Asymptomatic microscopic hematuria

# Appendix A

R31.29	Other microscopic hematuria
R31.9	Hematuria, unspecified
<b>ICD-9 Px</b>	
44.43	ENDOSCOPIC CONTROL OF GASTRIC OF DUODENAL BLEEDING
<b>ICD-10 Px</b>	
OW3P8ZZ	Control Bleeding in Gastrointestinal Tract, Via Natural or Artificial Opening Endoscopic
<b>HCPCS</b>	
43255	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

# Appendix A

## Pregnancy

### Dx codes

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

### Procedure codes

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



# Appendix A

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

# Appendix A

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

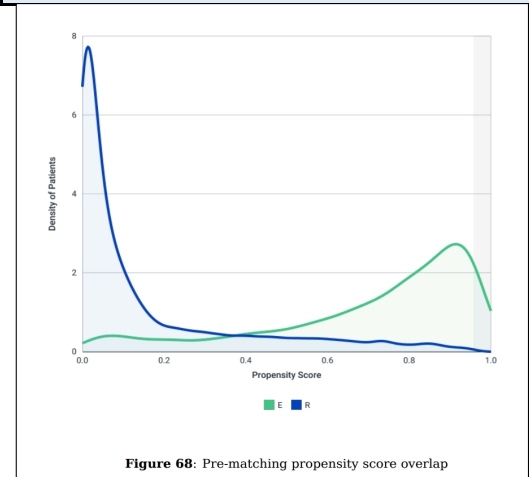
Appendix B

Optum

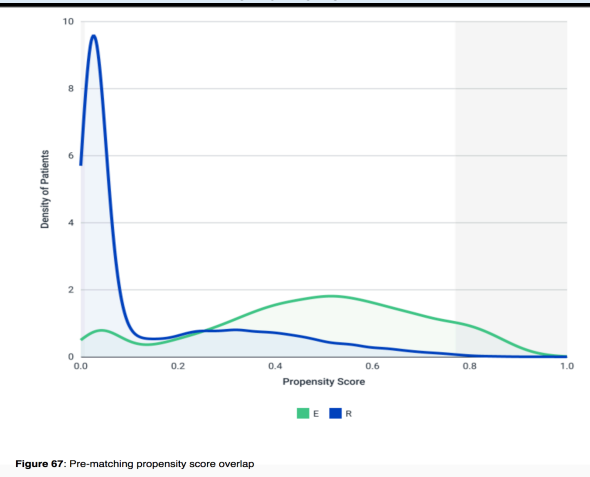
MarketScan

Medicare

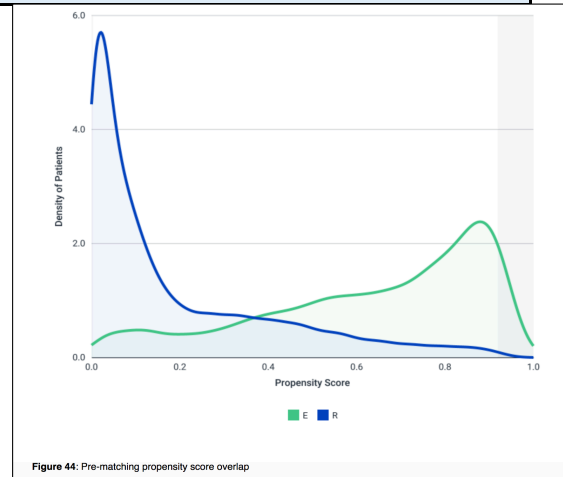
BEFORE PS MATCHING



The c-statistics for the propensity score model, pre-matching was 0.925. The postmatching c-statistic was 0.568

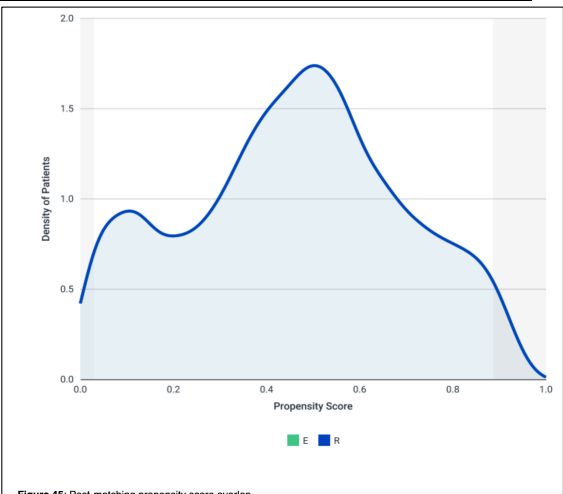
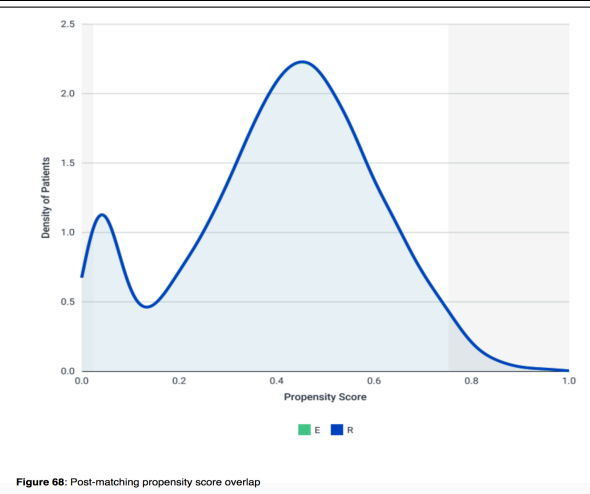
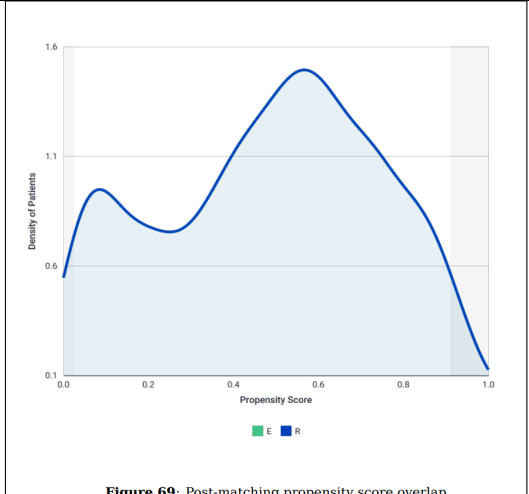


The c-statistics for the propensity score model, pre-matching was 0.873. The post-matching c-statistic was 0.557.



The c-statistics for the propensity score model, pre-matching was 0.89. The post-matching c-statistic was 0.536.

AFTER PS MATCHING



Appendix B

Unmatched											
Variable	Optum			MarketScan			Medicare			POOLED	
	Reference- warfarin Copy	Exposure - rivaroxaban (15 or 20 mg) Copy	St. Diff.	Reference- warfarin Copy	Exposure - rivaroxaban (15 or 20 mg) Copy	St. Diff.	Reference- warfarin Copy	Exposure - rivaroxaban (15 or 20 mg) Copy	St. Diff.	Reference- warfarin Copy	Exposure - rivaroxaban (15 or 20 mg) Copy
Number of patients	7,413	3,940		13,977	3,908		32,619	16,748		54,009	24,596
Age											
...mean (sd)	64.55 (15.26)	64.30 (15.26)	0.02	56.88 (15.95)	54.05 (15.64)	0.18	77.01 (8.04)	75.83 (7.74)	0.15	70.09 (11.70)	70.52 (10.81)
Age categories without zero category											
...18 - 54; n (%)	1,823 (24.6%)	938 (23.8%)	0.02	6,009 (43.0%)	1,966 (50.3%)	-0.15	0 (0.0%)	0 (0.0%)	#DIV/0!	7,832 (14.5%)	2904 (11.8%)
...55 - 64; n (%)	1,258 (17.0%)	646 (16.4%)	0.02	4,046 (28.9%)	1,128 (28.9%)	0.00	0 (0.0%)	0 (0.0%)	#DIV/0!	5,304 (9.8%)	1,774 (7.2%)
...65 - 74; n (%)	2,057 (27.7%)	1,289 (32.7%)	-0.11	1,840 (13.2%)	415 (10.6%)	0.08	14,321 (43.9%)	8,365 (49.9%)	-0.12	18,218 (33.7%)	10,069 (40.9%)
...≥ 75; n (%)	2,275 (30.7%)	1,067 (27.1%)	0.08	2,082 (14.9%)	399 (10.2%)	0.14	18,298 (56.1%)	8,383 (50.1%)	0.12	22,655 (41.9%)	9,849 (40.0%)
Gender without zero category- United											
...Males; n (%)	3,360 (45.3%)	1,804 (45.8%)	-0.01	6,838 (48.9%)	1,898 (48.6%)	0.01	11,768 (36.1%)	6,573 (39.2%)	-0.06	21,966 (40.7%)	10,275 (41.8%)
...Females; n (%)	4,052 (54.7%)	2,136 (54.2%)	0.01	7,139 (51.1%)	2,010 (51.4%)	-0.01	20,851 (63.9%)	10,175 (60.8%)	0.06	32,042 (59.3%)	14,321 (58.2%)
Race											
...White; n (%)							27,361 (83.9%)	14,167 (84.6%)		27,361 (83.9%)	14,167 (84.6%)
...Black; n (%)							3,680 (11.3%)	1,731 (10.3%)		3,680 (11.3%)	1,731 (10.3%)
...Asian; n (%)							255 (0.8%)	138 (0.8%)		255 (0.8%)	138 (0.8%)
...Hispanic; n (%)							699 (2.1%)	351 (2.1%)		699 (2.1%)	351 (2.1%)
...North American Native; n (%)							147 (0.5%)	51 (0.3%)		147 (0.5%)	51 (0.3%)
...Other/Unknown; n (%)							477 (1.5%)	310 (1.9%)		477 (1.5%)	310 (1.9%)
...Missing; n (%)											
Region without zero category- United v3 (lumping missing&other category with West)	0	0	#VALUE!	2,574 (18.4%)	668 (17.1%)	0.03	6,317 (19.4%)	3,229 (19.3%)	0.00	#VALUE!	#VALUE!
...Northeast; n (%)	831 (11.2%)	501 (12.7%)	-0.05	4,295 (30.7%)	1,033 (26.4%)	0.10	11,948 (36.6%)	7,062 (42.2%)	-0.11	17,074 (31.6%)	8,596 (34.9%)
...South; n (%)	3,054 (41.2%)	1,714 (43.5%)	-0.05	5,245 (37.5%)	1,760 (45.0%)	-0.15	8,837 (27.1%)	3,639 (21.7%)	0.13	17,136 (31.7%)	7,113 (28.9%)
...Midwest; n (%)	1,858 (25.1%)	930 (23.6%)	0.03	1,684 (12.0%)	407 (10.4%)	0.05	5,432 (16.7%)	2,794 (16.7%)	0.00	8,974 (16.6%)	4,131 (16.8%)
...Unknown-missing; n (%)	N/A	N/A	#VALUE!	179 (1.3%)	40 (1.0%)	0.03	N/A	N/A	#VALUE!	179 (1.3%)	40 (1.0%)
CV Covariates											
Ischemic heart disease; n (%)	1,075 (14.5%)	527 (13.4%)	0.03	1,607 (11.5%)	375 (9.6%)	0.06	6,992 (21.4%)	3,153 (18.8%)	0.06	9,674 (17.9%)	4,055 (16.5%)
Acute MI; n (%)	76 (1.0%)	45 (1.1%)	-0.01	185 (1.3%)	59 (1.5%)	-0.02	443 (1.4%)	201 (1.2%)	0.02	704 (1.3%)	305 (1.2%)
ACS/unstable angina; n (%)	24 (0.3%)	17 (0.4%)	-0.02	27 (0.2%)	** (0.2%)	0.00	119 (0.4%)	100 (0.6%)	-0.03	170 (0.3%)	#VALUE!
Old MI; n (%)	221 (3.0%)	97 (2.5%)	0.03	212 (1.5%)	45 (1.2%)	0.03	1,484 (4.5%)	688 (4.1%)	0.02	1917 (3.5%)	830 (3.4%)
Stable angina; n (%)	127 (1.7%)	74 (1.9%)	-0.02	164 (1.2%)	53 (1.4%)	-0.02	554 (1.7%)	288 (1.7%)	0.00	845 (1.6%)	415 (1.7%)
Coronary atherosclerosis and other forms of chronic ischemic heart disease; n (%)	958 (12.9%)	448 (11.4%)	0.05	1,407 (10.1%)	304 (7.8%)	0.08	6,404 (19.6%)	2,807 (16.8%)	0.07	8,769 (16.2%)	3,559 (14.5%)
Other atherosclerosis with ICD10 v2 Copy; n (%)	76 (1.0%)	38 (1.0%)	0.00	132 (0.9%)	19 (0.5%)	0.05	473 (1.5%)	161 (1.0%)	0.05	681 (1.3%)	218 (0.9%)
Previous cardiac procedure (CABG or PTCA or Stent) v4; n (%)	43 (0.6%)	** (0.2%)	0.06	77 (0.6%)	16 (0.4%)	0.03	171 (0.5%)	53 (0.3%)	0.03	291 (0.5%)	#VALUE!
History of CABG or PTCA; n (%)	300 (4.0%)	153 (3.9%)	0.01	253 (1.5%)	57 (1.5%)	0.02	2,547 (7.8%)	1,061 (6.3%)	0.06	3,100 (5.7%)	1,271 (5.2%)
Any stroke; 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%)
Ischemic stroke (w and w/o mention of cerebral infarction); 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%)
Hemorrhagic stroke; 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%)
TIA; n (%)	74 (1.0%)	29 (0.7%)	0.03	110 (0.8%)	31 (0.8%)	0.00	400 (1.2%)	174 (1.0%)	0.02	584 (1.1%)	234 (1.0%)
Other cerebrovascular disease; n (%)	135 (1.8%)	41 (1.0%)	0.07	195 (1.4%)	31 (0.8%)	0.06	748 (2.3%)	309 (1.8%)	0.04	1078 (2.0%)	381 (1.5%)
Cerebrovascular procedure; n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	** (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!	#VALUE!	0 (0.0%)
Heart failure(CHF); n (%)	** (0.1%)	0 (0.0%)	0.04	** (0.1%)	** (0.1%)	0.00	13 (0.0%)	** (0.0%)	#DIV/0!	#VALUE!	#VALUE!
Peripheral Vascular Disease (PVD) or PVD Surgery v2; n (%)	868 (11.7%)	403 (10.2%)	0.05	1,462 (10.5%)	394 (10.1%)	0.01	4,144 (12.7%)	1,860 (11.1%)	0.05	6,474 (12.0%)	2,657 (10.8%)
Atrial fibrillation; 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%)
Other cardiac dysrhythmia; n (%)	835 (11.3%)	424 (10.8%)	0.02	1,471 (10.5%)	377 (9.6%)	0.03	4,288 (13.1%)	1,861 (11.1%)	0.06	6,594 (12.2%)	2,662 (10.8%)
Cardiac conduction disorders; n (%)	307 (4.1%)	174 (4.4%)	-0.01	391 (2.8%)	115 (2.9%)	-0.01	1,807 (5.5%)	932 (5.6%)	0.00	2505 (4.6%)	1221 (5.0%)
Other CVD; n (%)	1,128 (15.2%)	591 (15.0%)	0.01	2,126 (15.2%)	587 (15.0%)	0.01	5,129 (15.7%)	2,459 (14.7%)	0.03	8,383 (15.5%)	3,637 (14.8%)
Diabetes-related complications											
Occurrence of Diabetic Neuropathy v2 Copy; n (%)	430 (5.8%)	242 (6.1%)	-0.01	438 (3.1%)	121 (3.1%)	0.00	1,714 (5.3%)	819 (4.9%)	0.02	2582 (4.8%)	1182 (4.8%)
Occurrence of diabetic nephropathy V3 with ICD10 Copy; n (%)	235 (3.2%)	139 (3.5%)	-0.02	210 (1.5%)	52 (1.3%)	0.02	813 (2.5%)	382 (2.3%)	0.01	1,258 (2.3%)	573 (2.3%)
Hypoglycemia v2; n (%)	125 (1.7%)	34 (0.9%)	0.07	202 (1.4%)	37 (0.9%)	0.05	846 (2.6%)	389 (2.3%)	0.02	1173 (2.2%)	460 (1.9%)
Hyperglycemia; n (%)	432 (5.8%)	266 (6.8%)	-0.04	536 (3.8%)	179 (4.6%)	-0.04	2,248 (6.9%)	1,306 (7.8%)	-0.03	3216 (6.0%)	1751 (7.1%)
Diabetic ketoacidosis; n (%)	43 (0.6%)	15 (0.4%)	0.03	76 (0.5%)	23 (0.6%)	-0.01	93 (0.3%)	47 (0.3%)	0.00	212 (0.4%)	85 (0.3%)
Hypertension: 1 inpatient or 2 outpatient claims within 365 days; n (%)	4,752 (64.1%)	2,425 (61.5%)	0.05	7,213 (51.6%)	1,912 (48.9%)	0.05	26,154 (80.2%)	12,823 (76.6%)	0.09	38,119 (70.6%)	17,160 (69.8%)
Hyperlipidemia v2; n (%)	3,522 (47.5%)	1,740 (44.2%)	0.07	4,709 (33.7%)	1,254 (32.1%)	0.03	17,566 (53.9%)	8,658 (51.7%)	0.04	25,797 (47.8%)	11,652 (47.4%)
Edema; n (%)	2,328 (31.4%)	1,209 (30.7%)	0.02	3,008 (21.5%)	981 (25.1%)	-0.09	8,516 (26.1%)	4,346 (25.9%)	0.00	13852 (25.6%)	6536 (26.6%)
Renal Dysfunction (non-diabetic) v2; n (%)	1,752 (23.6%)	762 (19.3%)	0.10	2,250 (16.1%)	585 (15.0%)	0.03	8,823 (27.0%)	3,546 (21.2%)	0.14	12,825 (23.7%)	4,893 (19.9%)
Occurrence of acute renal disease v2; n (%)	785 (10.6%)	321 (8.1%)	0.09	1,104 (7.9%)	319 (8.2%)	-0.01	3,945 (12.1%)	1,484 (8.9%)	0.10	5834 (10.8%)	2124 (8.6%)
Occurrence of chronic renal insufficiency; n (%)	1,035 (14.0%)	403 (10.2%)	0.12	990 (7.1%)	188 (4.8%)	0.10	5,734 (17.6%)	1,950 (11.6%)	0.17	7,759 (14.4%)	2,541 (10.3%)
Chronic kidney disease v2; n (%)	1,002 (13.5%)	387 (9.8%)	0.12	941 (6.7%)	164 (4.2%)	0.11	5,447 (16.7%)	1,859 (11.1%)	0.16	7,390 (13.7%)	2,410 (9.8%)
CKD Stage 3-4; n (%)	597 (8.1%)	245 (6.2%)	0.07	515 (3.7%)	82 (2.1%)	0.10	3,238 (9.9%)	1,103 (6.6%)	0.12	4,350 (8.1%)	1,430 (5.8%)
Occurrence of hypertensive nephropathy; n (%)	637 (8.6%)	240 (6.1%)	0.10	508 (3.6%)	80 (2.0%)	0.10	4,290 (13.2%)	1,327 (7.9%)	0.17	5,435 (10.1%)	1,647 (6.7%)
Occurrence of miscellaneous renal insufficiency v2; n (%)	677 (9.1%)	300 (7.6%)	0.05	945 (6.8%)	248 (6.3%)	0.02	2,885 (8.8%)	1,275 (7.6%)	0.04	4,507 (8.3%)	1,823 (7.4%)
Other Covariates											
Liver disease; n (%)	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%)	#VALUE!
Osteoarthritis; n (%)	2,271 (30.6%)	1,234 (31.3%)	-0.02	3,146 (22.5%)	820 (21.0%)	0.04	11,828 (36.3%)	5,866 (35.0%)	0.03	17245 (31.9%)	7920 (32.2%)

Appendix B

Other arthritis, arthropathies and musculoskeletal pain; n (%)	6,356 (85.7%)	3,246 (82.4%)	0.09	10,836 (77.5%)	3,049 (78.0%)	-0.01	24,897 (76.3%)	12,838 (76.7%)	-0.01	42089 (77.9%)	19133 (77.8%)	0.00
Dorsopathies; n (%)	2,513 (33.9%)	1,389 (35.3%)	-0.03	4,111 (29.4%)	1,236 (31.6%)	-0.05	10,374 (31.8%)	5,330 (31.8%)	0.00	16998 (31.5%)	7955 (32.3%)	-0.02
Fractures; n (%)	869 (11.7%)	404 (10.3%)	0.04	1,433 (10.3%)	423 (10.8%)	-0.02	4,020 (12.3%)	2,047 (12.2%)	0.00	6322 (11.7%)	2874 (11.7%)	0.00
Falls v2; n (%)	692 (9.3%)	396 (10.1%)	-0.03	370 (2.6%)	139 (3.6%)	-0.06	1,680 (5.2%)	735 (4.4%)	0.04	2742 (5.1%)	1270 (5.2%)	0.00
Osteoporosis; n (%)	728 (9.8%)	343 (8.7%)	0.04	704 (5.0%)	155 (4.0%)	0.05	5,102 (15.6%)	2,328 (13.9%)	0.05	6534 (12.1%)	2826 (11.5%)	0.02
Depression; n (%)	1,346 (18.2%)	655 (16.6%)	0.04	1,914 (13.7%)	561 (14.4%)	-0.02	5,417 (16.6%)	2,468 (14.7%)	0.05	8677 (16.1%)	3684 (15.0%)	0.03
Anxiety; n (%)	1,083 (14.6%)	689 (17.5%)	-0.08	1,527 (10.9%)	569 (14.6%)	-0.11	4,262 (13.1%)	2,240 (13.4%)	-0.01	6872 (12.7%)	3498 (14.2%)	-0.04
Sleep_Disorder; n (%)	777 (10.5%)	252 (6.4%)	0.15	1,462 (10.5%)	352 (9.0%)	0.05	2,779 (8.5%)	938 (5.6%)	0.11	5018 (9.3%)	1542 (6.3%)	0.11
Dementia; n (%)	706 (9.5%)	355 (9.0%)	0.02	574 (4.1%)	167 (4.3%)	-0.01	5,539 (17.0%)	2,441 (14.6%)	0.07	6819 (12.6%)	2963 (12.0%)	0.02
Delirium; n (%)	281 (3.8%)	120 (3.0%)	0.04	387 (2.8%)	113 (2.9%)	-0.01	1,560 (4.8%)	754 (4.5%)	0.01	2228 (4.1%)	987 (4.0%)	0.01
Psychosis; n (%)	215 (2.9%)	91 (2.3%)	0.04	238 (1.7%)	58 (1.5%)	0.02	1,203 (3.7%)	553 (3.3%)	0.02	1656 (3.1%)	702 (2.9%)	0.01
Obesity; n (%)	1,498 (20.2%)	943 (23.9%)	-0.09	2,456 (17.6%)	930 (23.8%)	-0.15	5,202 (15.9%)	2,677 (16.0%)	0.00	9156 (17.0%)	4550 (18.5%)	-0.04
Overweight; n (%)	244 (3.3%)	249 (6.3%)	-0.14	205 (1.5%)	132 (3.4%)	-0.12	1,125 (3.4%)	739 (4.4%)	-0.05	1574 (2.9%)	1120 (4.6%)	-0.09
Smoking; n (%)	1,951 (26.3%)	1,206 (30.6%)	-0.10	2,266 (16.2%)	697 (17.8%)	-0.04	8,893 (27.3%)	5,096 (30.4%)	-0.07	13110 (24.3%)	6999 (28.5%)	-0.10
Alcohol abuse or dependence; n (%)	210 (2.8%)	111 (2.8%)	0.00	281 (2.0%)	99 (2.5%)	-0.03	243 (0.7%)	190 (1.1%)	-0.04	734 (1.4%)	400 (1.6%)	-0.02
Drug abuse or dependence; n (%)	210 (2.8%)	166 (4.2%)	-0.08	289 (2.1%)	124 (3.2%)	-0.07	251 (0.8%)	201 (1.2%)	-0.04	750 (1.4%)	491 (2.0%)	-0.05
COPD; n (%)	1,066 (14.4%)	502 (12.7%)	0.05	1,214 (8.7%)	299 (7.7%)	0.04	5,389 (16.5%)	2,517 (15.0%)	0.04	7669 (14.2%)	3318 (13.5%)	0.02
Asthma; n (%)	710 (9.6%)	418 (10.6%)	-0.03	1,139 (8.1%)	344 (8.8%)	-0.03	2,725 (8.4%)	1,431 (8.5%)	0.00	4574 (8.5%)	2193 (8.9%)	-0.01
Obstructive sleep apnea; n (%)	555 (7.5%)	363 (9.2%)	-0.06	1,037 (7.4%)	347 (8.9%)	-0.05	1,809 (5.5%)	955 (5.7%)	-0.01	3401 (6.3%)	1665 (6.8%)	-0.02
Pneumonia; n (%)	574 (7.7%)	267 (6.8%)	0.03	1,026 (7.3%)	303 (7.8%)	-0.02	2,850 (8.7%)	1,307 (7.8%)	0.03	4450 (8.2%)	1877 (7.6%)	0.02
Other Medications												
Use of ACE inhibitors; n (%)	1,874 (25.3%)	878 (22.3%)	0.07	2,969 (21.2%)	706 (18.1%)	0.08	9,840 (30.2%)	4,570 (27.3%)	0.06	14683 (27.2%)	6154 (25.0%)	0.05
Use of ARBs; n (%)	899 (12.1%)	585 (14.8%)	-0.08	1,741 (12.5%)	472 (12.1%)	0.01	5,634 (17.3%)	3,141 (18.8%)	-0.04	8274 (15.3%)	4198 (17.1%)	-0.05
Use of Loop Diuretics - United; n (%)	824 (11.1%)	366 (9.3%)	0.06	1,262 (9.0%)	284 (7.3%)	0.06	5,787 (17.7%)	2,453 (14.6%)	0.08	7873 (14.6%)	3103 (12.6%)	0.06
Use of other diuretics- United; n (%)	100 (1.3%)	68 (1.7%)	-0.03	181 (1.3%)	56 (1.4%)	-0.01	710 (2.2%)	308 (1.8%)	0.03	991 (1.8%)	432 (1.8%)	0.00
Use of nitrates-United; n (%)	171 (2.3%)	88 (2.2%)	0.01	327 (2.3%)	62 (1.6%)	0.05	1,485 (4.6%)	622 (3.7%)	0.05	1983 (3.7%)	772 (3.1%)	0.03
Use of other hypertension drugs; n (%)	336 (4.5%)	147 (3.7%)	0.04	577 (4.1%)	123 (3.1%)	0.05	2,141 (6.6%)	909 (5.4%)	0.05	3054 (5.7%)	1179 (4.8%)	0.04
Use of Anti-arrhythmics; n (%)	19 (0.3%)	** (0.2%)	0.02	59 (0.4%)	** (0.3%)	0.02	160 (0.5%)	70 (0.4%)	0.01	238 (0.4%)	#VALUE!	#VALUE!
Use of COPD/asthma meds- United; n (%)	1,097 (14.8%)	625 (15.9%)	-0.03	2,035 (14.6%)	606 (15.5%)	-0.03	5,862 (18.0%)	3,203 (19.1%)	-0.03	8994 (16.7%)	4434 (18.0%)	-0.03
Use of statins; n (%)	2,353 (31.7%)	1,257 (31.9%)	0.00	3,676 (26.3%)	877 (22.4%)	0.09	13,267 (40.7%)	6,840 (40.8%)	0.00	19296 (35.7%)	8974 (36.5%)	-0.02
Use of other lipid-lowering drugs; n (%)	391 (5.3%)	177 (4.5%)	0.04	851 (6.1%)	167 (4.3%)	0.08	2,075 (6.4%)	1,096 (6.5%)	0.00	3317 (6.1%)	1440 (5.9%)	0.01
Use of antiplatelet agents; n (%)	414 (5.6%)	204 (5.2%)	0.02	881 (6.3%)	222 (5.7%)	0.03	2,761 (8.5%)	1,341 (8.0%)	0.02	4056 (7.5%)	1767 (7.2%)	0.01
Use of heparin and other low-molecular weight heparins; n (%)	3,868 (52.2%)	211 (5.2%)	1.21	25 (0.2%)	** (0.1%)	0.03	16,176 (49.6%)	909 (5.4%)	1.14	20069 (37.2%)	#VALUE!	#VALUE!
Use of NSAIDs; n (%)	1,503 (20.3%)	908 (23.0%)	-0.07	3,060 (21.9%)	932 (23.8%)	-0.05	5,871 (18.0%)	3,345 (20.0%)	-0.05	10434 (19.3%)	5185 (21.1%)	-0.04
Use of oral corticosteroids; n (%)	1,930 (26.0%)	1,065 (27.0%)	-0.02	3,566 (25.5%)	1,121 (28.7%)	-0.07	9,326 (28.6%)	4,915 (29.3%)	-0.02	14822 (27.4%)	7101 (28.9%)	-0.03
Use of bisphosphonate (United); n (%)	283 (3.8%)	123 (3.1%)	0.04	321 (2.3%)	57 (1.5%)	0.06	1,786 (5.5%)	824 (4.9%)	0.03	2390 (4.4%)	1004 (4.1%)	0.01
Use of opioids- United; n (%)	4,042 (54.5%)	1,932 (49.0%)	0.11	8,355 (59.8%)	2,318 (59.3%)	0.01	15,563 (47.7%)	7,860 (46.9%)	0.02	27960 (51.8%)	12110 (49.2%)	0.05
Use of antidepressants; n (%)	1,919 (25.9%)	1,055 (26.8%)	-0.02	3,269 (23.4%)	937 (24.0%)	-0.01	9,282 (28.5%)	4,711 (28.1%)	0.01	14470 (26.8%)	6703 (27.3%)	-0.01
Use of antipsychotics; n (%)	351 (4.7%)	194 (4.9%)	-0.01	507 (3.6%)	154 (3.9%)	-0.02	2,139 (6.6%)	1,110 (6.6%)	0.00	2997 (5.5%)	1458 (5.8%)	-0.02
Labs												
Lab values- HbA1c (%) v3; n (%)	651 (8.8%)	506 (12.8%)	-0.13	130 (0.9%)	46 (1.2%)	-0.03	N/A	N/A	#VALUE!	781 (3.7%)	552 (7.0%)	-0.15
Lab values- HbA1c (%) (within 3 months) v3; n (%)	390 (5.3%)	315 (8.0%)	-0.11	88 (0.6%)	27 (0.7%)	-0.01	N/A	N/A	#VALUE!	478 (2.2%)	342 (4.4%)	-0.12
Lab values- HbA1c (%) (within 6 months) v3; n (%)	651 (8.8%)	506 (12.8%)	-0.13	130 (0.9%)	46 (1.2%)	-0.03	N/A	N/A	#VALUE!	781 (3.7%)	552 (7.0%)	-0.15
Lab values- BNP; n (%)	29 (0.4%)	23 (0.6%)	-0.03	** (0.0%)	** (0.1%)	-0.04	N/A	N/A	#VALUE!	#VALUE!	#VALUE!	#VALUE!
Lab values- BNP (within 3 months); n (%)	24 (0.3%)	18 (0.5%)	-0.03	** (0.0%)	** (0.1%)	-0.04	N/A	N/A	#VALUE!	#VALUE!	#VALUE!	#VALUE!
Lab values- BNP (within 6 months); n (%)	29 (0.4%)	23 (0.6%)	-0.03	** (0.0%)	** (0.1%)	-0.04	N/A	N/A	#VALUE!	#VALUE!	#VALUE!	#VALUE!
Lab values- BUN (mg/dl); n (%)	1,719 (23.2%)	1,143 (29.0%)	-0.13	155 (1.1%)	78 (2.0%)	-0.07	N/A	N/A	#VALUE!	1,874 (8.8%)	1,221 (15.6%)	-0.21
Lab values- BUN (mg/dl) (within 3 months); n (%)	1,189 (16.0%)	815 (20.7%)	-0.12	106 (0.8%)	56 (1.4%)	-0.06	N/A	N/A	#VALUE!	1,295 (6.1%)	871 (11.1%)	-0.18
Lab values- BUN (mg/dl) (within 6 months); n (%)	1,719 (23.2%)	1,143 (29.0%)	-0.13	155 (1.1%)	78 (2.0%)	-0.07	N/A	N/A	#VALUE!	1,874 (8.8%)	1,221 (15.6%)	-0.21
Lab values- Creatinine (mg/dl) v2; n (%)	1,753 (23.6%)	1,179 (29.9%)	-0.14	165 (1.2%)	83 (2.1%)	-0.07	N/A	N/A	#VALUE!	1,918 (9.0%)	1,262 (16.1%)	-0.22
Lab values- Creatinine (mg/dl) (within 3 months) v2; n (%)	1,211 (16.3%)	846 (21.5%)	-0.13	114 (0.8%)	60 (1.5%)	-0.07	N/A	N/A	#VALUE!	1,325 (6.2%)	906 (11.5%)	-0.19
Lab values- Creatinine (mg/dl) (within 6 months) v2; n (%)	1,753 (23.6%)	1,179 (29.9%)	-0.14	165 (1.2%)	83 (2.1%)	-0.07	N/A	N/A	#VALUE!	1,918 (9.0%)	1,262 (16.1%)	-0.22
Lab values- HDL level (mg/dl); n (%)	962 (13.0%)	693 (17.6%)	-0.13	96 (0.7%)	46 (1.2%)	-0.05	N/A	N/A	#VALUE!	1,058 (4.9%)	739 (9.4%)	-0.18
Lab values- HDL level (mg/dl) (within 3 months); n (%)	542 (7.3%)	396 (10.1%)	-0.10	55 (0.4%)	25 (0.6%)	-0.03	N/A	N/A	#VALUE!	597 (2.8%)	421 (5.4%)	-0.13
Lab values- HDL level (mg/dl) (within 6 months); n (%)	962 (13.0%)	693 (17.6%)	-0.13	96 (0.7%)	46 (1.2%)	-0.05	N/A	N/A	#VALUE!	1,058 (4.9%)	739 (9.4%)	-0.18
Lab values- LDL level (mg/dl) v2; n (%)	966 (13.0%)	700 (17.8%)	-0.13	111 (0.8%)	46 (1.2%)	-0.04	N/A	N/A	#VALUE!	1,077 (5.0%)	746 (9.5%)	-0.17
Lab values- LDL level (mg/dl) (within 3 months) v2; n (%)	547 (7.4%)	399 (10.1%)	-0.10	66 (0.5%)	24 (0.6%)	-0.01	N/A	N/A	#VALUE!	613 (2.9%)	423 (5.4%)	-0.13
Lab values- LDL level (mg/dl) (within 6 months) v2; n (%)	966 (13.0%)	700 (17.8%)	-0.13	111 (0.8%)	46 (1.2%)	-0.04	N/A	N/A	#VALUE!	1,077 (5.0%)	746 (9.5%)	-0.17
Lab values- NT-proBNP; n (%)	** (0.1%)	** (0.2%)	-0.03	0 (0.0%)	0 (0.0%)	#DIV/0!	N/A	N/A	#VALUE!	#VALUE!	#VALUE!	#VALUE!
Lab values- NT-proBNP (within 3 months); n (%)	** (0.0%)	** (0.2%)	-0.06	0 (0.0%)	0 (0.0%)	#DIV/0!	N/A	N/A	#VALUE!	#VALUE!	#VALUE!	-
Lab values- NT-proBNP (within 6 months); n (%)	** (0.1%)	** (0.2%)	-0.03	0 (0.0%)	0 (0.0%)	#DIV/0!	N/A	N/A	#VALUE!	#VALUE!	#VALUE!	-
Lab values- Total cholesterol (mg/dl) v2; n (%)	972 (13.1%)	702 (17.8%)	-0.13	99 (0.7%)	46 (1.2%)	-0.05	N/A	N/A	#VALUE!	1,071 (5.0%)	748 (9.5%)	-0.17
Lab values- Total cholesterol (mg/dl) (within 3 months) v2; n (%)	549 (7.4%)	401 (10.2%)	-0.10	55 (0.4%)	25 (0.6%)	-0.03	N/A	N/A	#VALUE!	604 (2.8%)	426 (5.4%)	-0.13
Lab values- Total cholesterol (mg/dl) (within 6 months) v2; n (%)	972 (13.1%)	702 (17.8%)	-0.13	99 (0.7%)	46 (1.2%)	-0.05	N/A	N/A	#VALUE!	1,071 (5.0%)	748 (9.5%)	-0.17
Lab values- Triglyceride level (mg/dl); n (%)	964 (13.0%)	696 (17.7%)	-0.13	100 (0.7%)	46 (1.2%)	-0.05	N/A	N/A	#VALUE!	1,064 (5.0%)	742 (9.5%)	-0.17
Lab values- Triglyceride level (mg/dl) (within 3 months); n (%)	544 (7.3%)	397 (10.1%)	-0.10	57 (0.4%)	24 (0.6%)	-0.03	N/A	N/A	#VALUE!	601 (2.8%)	421 (5.4%)	-0.13

Appendix B

Lab values- Triglyceride level (mg/dl) (within 6 months); n (%)	964 (13.0%)	696 (17.7%)	-0.13	100 (0.7%)	46 (1.2%)	-0.05	N/A	N/A	#VALUE!	1,064 (5.0%)	742 (9.5%)	-0.17
Lab result number- HbA1c (%) mean (only 2 to 20 included) v4	650	505		112	45		N/A	N/A		762	550	
...mean (sd)	6.79 (1.57)	6.72 (1.73)	0.04	7.26 (1.63)	7.18 (1.48)	0.05	N/A	N/A	#VALUE!	6.86 (1.58)	6.76 (1.71)	0.06
...Missing; n (%)	6,763 (91.2%)	3,435 (87.2%)	0.13	13,865 (99.2%)	3,863 (98.8%)	0.04	N/A	N/A	#VALUE!	20,628 (96.4%)	7,298 (93.0%)	0.15
Lab result number- BNP mean v2	29	23		4	5		N/A	N/A		33	28	
...mean (sd)	74.87 (72.49)	96.03 (235.14)	-0.12	19.25 (8.96)	161.20 (119.25)	-1.68	N/A	N/A	#VALUE!	68.13 (70.09)	107.67 (225.68)	-0.24
...Missing; n (%)	7,384 (99.6%)	3,917 (99.4%)	0.03	13,973 (100.0%)	3,903 (99.9%)	0.04	N/A	N/A	#VALUE!	21,357 (99.8%)	7,820 (99.6%)	0.04
Lab result number- BUN (mg/dl) mean v2	1,719	1,143		155	78		N/A	N/A		1,874	1,221	
...mean (sd)	18.02 (7.51)	17.09 (6.74)	0.13	1,436.31 (17,669.46)	17.18 (6.52)	0.11	N/A	N/A	#VALUE!	135.33 (5069.29)	17.10 (6.73)	0.03
...Missing; n (%)	5,694 (76.8%)	2,797 (71.0%)	0.13	13,822 (98.9%)	3,830 (98.0%)	0.07	N/A	N/A	#VALUE!	19,516 (91.2%)	6,627 (84.4%)	0.21
Lab result number- Creatinine (mg/dl) mean (only 0.1 to 15 included) v3	1,741	1,168		160	81		N/A	N/A		1,901	1,249	
...mean (sd)	1.00 (0.34)	0.96 (0.29)	0.13	0.98 (0.31)	0.97 (0.29)	0.03	N/A	N/A	#VALUE!	1.00 (0.34)	0.96 (0.29)	0.13
...Missing; n (%)	5,672 (76.5%)	2,772 (70.4%)	0.14	13,817 (98.9%)	3,827 (97.9%)	0.08	N/A	N/A	#VALUE!	19,489 (91.1%)	6,599 (84.1%)	0.21
Lab result number- HDL level (mg/dl) mean (only <=5000 included) v2	962	693		95	46		N/A	N/A		1,057	739	
...mean (sd)	53.64 (17.08)	53.25 (17.87)	0.02	46.65 (12.95)	48.63 (14.03)	-0.15	N/A	N/A	#VALUE!	53.01 (16.76)	52.96 (17.67)	0.00
...Missing; n (%)	6,451 (87.0%)	3,247 (82.4%)	0.13	13,882 (99.3%)	3,862 (98.8%)	0.05	N/A	N/A	#VALUE!	20,333 (95.1%)	7,109 (90.6%)	0.18
Lab result number- LDL level (mg/dl) mean (only <=5000 included) v2	942	692		97	44		N/A	N/A		1,039	736	
...mean (sd)	102.51 (34.84)	101.93 (36.29)	0.02	96.33 (37.96)	92.61 (31.60)	0.11	N/A	N/A	#VALUE!	101.93 (35.16)	101.37 (36.06)	0.02
...Missing; n (%)	6,471 (87.3%)	3,248 (82.4%)	0.14	13,880 (99.3%)	3,864 (98.9%)	0.04	N/A	N/A	#VALUE!	20,351 (95.1%)	7,112 (90.6%)	0.18
Lab result number- Total cholesterol (mg/dl) mean (only <=5000 included) v2	971	702		98	46		N/A	N/A		1,069	748	
...mean (sd)	184.17 (40.78)	183.48 (41.96)	0.02	176.51 (45.32)	181.96 (42.96)	-0.12	N/A	N/A	#VALUE!	183.47 (41.23)	183.39 (42.05)	0.00
...Missing; n (%)	6,442 (86.9%)	3,238 (82.2%)	0.13	13,879 (99.3%)	3,862 (98.8%)	0.05	N/A	N/A	#VALUE!	20,321 (95.0%)	7,100 (90.5%)	0.17
Lab result number- Triglyceride level (mg/dl) mean (only <=5000 included) v2	964	696		99	46		N/A	N/A		1,063	742	
...mean (sd)	136.73 (77.90)	140.13 (102.33)	-0.04	159.89 (94.35)	179.18 (110.20)	-0.19	N/A	N/A	#VALUE!	138.89 (79.60)	142.55 (102.90)	-0.04
...Missing; n (%)	6,449 (87.0%)	3,244 (82.3%)	0.13	13,878 (99.3%)	3,862 (98.8%)	0.05	N/A	N/A	#VALUE!	20,327 (95.0%)	7,106 (90.5%)	0.17
Lab result number- Hemoglobin mean (only >0 included)	1,393	952		106	71		N/A	N/A		1,499	1,023	
...mean (sd)	13.28 (1.90)	13.37 (1.86)	-0.05	1,408.80 (14,373.80)	12.85 (2.78)	0.14	N/A	N/A	#VALUE!	111.96 (3808.03)	13.33 (1.94)	0.04
...Missing; n (%)	6,020 (81.2%)	2,988 (75.8%)	0.13	13,871 (99.2%)	3,837 (98.2%)	0.09	N/A	N/A	#VALUE!	19,891 (93.0%)	6,825 (87.0%)	0.20
Lab result number- Serum sodium mean (only > 90 and <190 included)	1,691	1,116		143	77		N/A	N/A		1,834	1,193	
...mean (sd)	139.91 (2.74)	140.29 (2.71)	-0.14	139.13 (2.43)	139.00 (3.00)	0.05	N/A	N/A	#VALUE!	139.85 (2.72)	140.21 (2.73)	-0.13
...Missing; n (%)	5,722 (77.2%)	2,824 (71.7%)	0.13	13,834 (99.0%)	3,831 (98.0%)	0.08	N/A	N/A	#VALUE!	19,556 (91.4%)	6,655 (84.8%)	0.20
Lab result number- Albumin mean (only >0 and <=10 included)	1,536	1,006		116	66		N/A	N/A		1,652	1,072	
...mean (sd)	4.08 (0.39)	4.12 (0.40)	-0.10	3.95 (0.78)	3.98 (0.64)	-0.04	N/A	N/A	#VALUE!	4.07 (0.43)	4.11 (0.42)	-0.09
...Missing; n (%)	5,877 (79.3%)	2,934 (74.5%)	0.11	13,861 (99.2%)	3,842 (98.3%)	0.08	N/A	N/A	#VALUE!	19,738 (92.3%)	6,776 (86.3%)	0.20
Lab result number- Glucose (fasting or random) mean (only 10-1000 included)	1,667	1,111		131	78		N/A	N/A		1,798	1,189	
...mean (sd)	111.25 (46.51)	113.95 (43.40)	-0.06	136.41 (56.48)	147.32 (75.50)	-0.16	N/A	N/A	#VALUE!	113.08 (47.32)	116.14 (46.18)	-0.07
...Missing; n (%)	5,746 (77.5%)	2,829 (71.8%)	0.13	13,846 (99.1%)	3,830 (98.0%)	0.09	N/A	N/A	#VALUE!	19,592 (91.6%)	6,659 (84.8%)	0.21
Lab result number- Potassium mean (only 1-7 included)	1,721	1,153		155	75		N/A	N/A		1,876	1,228	
...mean (sd)	4.31 (0.43)	4.35 (0.44)	-0.09	4.23 (0.41)	4.33 (0.40)	-0.25	N/A	N/A	#VALUE!	4.30 (0.43)	4.35 (0.44)	-0.11
...Missing; n (%)	5,692 (76.8%)	2,787 (70.7%)	0.14	13,822 (98.9%)	3,833 (98.1%)	0.07	N/A	N/A	#VALUE!	19,514 (91.2%)	6,620 (84.4%)	0.21
<b>Comorbidity Scores</b>												
Combined comorbidity score, 365 days Copy												
...mean (sd)	1.91 (2.34)	2.06 (2.35)	-0.06	1.39 (2.10)	1.58 (2.23)	-0.09	2.20 (2.56)	2.04 (2.57)	0.06	1.95 (2.42)	1.97 (2.48)	-0.01
Non-Frillity; n (%)	3,500 (47.2%)	1,973 (50.1%)	-0.06	5,638 (40.3%)	1,646 (42.1%)	-0.04	854 (2.6%)	263 (1.6%)	0.07	9,992 (18.5%)	3,882 (15.8%)	0.07
Frailty Score (mean): Empirical Version 365 days, v2												
...mean (sd)	0.19 (0.07)	0.18 (0.07)	0.14	0.17 (0.06)	0.17 (0.06)	0.00	0.11 (0.08)	0.09 (0.08)	0.25	0.14 (0.07)	0.12 (0.08)	0.27
<b>Healthcare Utilization</b>												
Any hospitalization; n (%)	5,944 (80.2%)	2,390 (60.7%)	0.44	13,968 (99.9%)	3,908 (100.0%)	-0.04	24,871 (76.2%)	9,527 (56.9%)	0.42	44,783 (82.9%)	15,825 (64.3%)	0.43
Any hospitalization within prior 30 days; n (%)	5,565 (75.1%)	2,178 (55.3%)	0.42	13,769 (98.5%)	3,866 (98.9%)	-0.04	23,580 (72.3%)	8,440 (50.4%)	0.46	42914 (79.5%)	14484 (58.9%)	0.46
Any hospitalization during prior 31-180 days; n (%)	1,176 (15.9%)	491 (12.5%)	0.10	1,855 (13.3%)	517 (13.2%)	0.00	5,754 (17.6%)	2,725 (16.3%)	0.03	8785 (16.3%)	3733 (15.2%)	0.03
Internal medicine/family medicine visits; n (%)	6,578 (88.7%)	3,420 (86.8%)	0.06	10,624 (76.0%)	3,112 (79.6%)	-0.09	30,337 (93.0%)	15,307 (91.4%)	0.06	47539 (88.0%)	21839 (88.8%)	-0.02
Internal medicine/family medicine visits (30 days prior) v2; n (%)	5,853 (79.0%)	2,941 (74.6%)	0.10	7,601 (54.4%)	2,169 (55.5%)	-0.02	27,977 (85.8%)	13,422 (80.1%)	0.15	41431 (76.7%)	18532 (75.3%)	0.03
Internal medicine/family medicine visits (31 to 180 days prior) v2; n (%)	5,044 (68.0%)	2,627 (66.7%)	0.03	8,752 (62.6%)	2,499 (63.9%)	-0.03	23,788 (72.9%)	12,139 (72.5%)	0.01	37584 (69.6%)	17265 (70.2%)	-0.01
Cardiologist visit; n (%)	3,053 (41.2%)	1,683 (42.7%)	-0.03	3,042 (21.8%)	883 (22.6%)	-0.02	15,604 (47.8%)	7,724 (46.1%)	0.03	21699 (40.2%)	10290 (41.8%)	-0.03
Number of Cardiologist visits (30 days prior); n (%)	2,224 (30.0%)	1,248 (31.7%)	-0.04	1,698 (12.1%)	502 (12.8%)	-0.02	11,149 (34.2%)	5,410 (32.3%)	0.04	15071 (27.9%)	7160 (29.1%)	-0.03
Number of Cardiologist visits (31 to 180 days prior); n (%)	1,404 (18.9%)	730 (18.5%)	0.01	1,797 (12.9%)	489 (12.5%)	0.01	8,231 (25.2%)	4,091 (24.4%)	0.02	11432 (21.2%)	5310 (21.6%)	-0.01
Electrocardiogram v2; n (%)	4,088 (55.1%)	2,158 (54.8%)	0.01	5,377 (38.5%)	1,410 (36.1%)	0.05	19,760 (60.6%)	10,095 (60.3%)	0.01	29225 (54.1%)	13663 (55.5%)	-0.03
Use of glucose test strips; n (%)	126 (1.7%)	54 (1.4%)	0.02	168 (1.2%)	40 (1.0%)	0.02	535 (1.6%)	273 (1.6%)	0.00	829 (1.5%)	367 (1.5%)	0.00
Dialysis; n (%)	12 (0.2%)	0 (0.0%)	0.06	34 (0.2%)	** (0.2%)	0.00	50 (0.2%)	** (0.0%)	0.06	96 (0.2%)	#VALUE!	#VALUE!
number of different/distinct medication prescriptions												
...mean (sd)	9.27 (5.24)	8.77 (5.41)	0.09	9.24 (5.40)	8.81 (5.72)	0.08	10.13 (5.09)	9.52 (5.21)	0.12	9.78 (5.19)	9.29 (5.33)	0.00
Number of Hospitalizations												
...mean (sd)	1.04 (0.77)	0.78 (0.80)	0.33	1.29 (0.66)	1.30 (0.66)	-0.02	1.07 (0.89)	0.80 (0.91)	0.30	1.12 (0.82)	0.88 (0.86)	0.00

Appendix B

Number of hospital days												
...mean (sd)	5.40 (6.24)	3.51 (5.41)	0.32	7.63 (8.24)	6.53 (7.92)	0.14	6.13 (7.52)	3.90 (6.63)	0.31	6.42 (7.55)	4.26 (6.68)	0.00
Number of Emergency Department (ED) visits v3												
...mean (sd)	1.85 (2.17)	2.24 (2.08)	-0.18	1.92 (4.54)	2.74 (6.70)	-0.14	2.04 (2.04)	2.42 (2.17)	-0.18	1.98 (2.91)	2.44 (3.32)	0.00
Number of Office visits												
...mean (sd)	5.48 (4.83)	5.64 (4.79)	-0.03	5.53 (5.19)	5.62 (5.12)	-0.02	12.84 (14.53)	13.84 (15.97)	-0.07	9.94 (11.73)	11.22 (13.47)	0.00
Number of internal medicine/family medicine visits												
...mean (sd)	10.84 (15.87)	9.07 (12.25)	0.12	6.06 (11.94)	5.97 (10.44)	0.01	11.66 (12.16)	10.09 (12.41)	0.13	10.10 (12.68)	9.27 (12.09)	0.00
Number of Cardiologist visits												
...mean (sd)	1.39 (3.30)	1.36 (3.07)	0.01	0.61 (2.29)	0.62 (2.33)	0.00	1.79 (3.80)	1.63 (3.45)	0.04	1.43 (3.40)	1.43 (3.24)	0.00
Number electrocardiograms received v2												
...mean (sd)	1.16 (1.68)	1.22 (1.70)	-0.04	0.65 (1.11)	0.65 (1.16)	0.00	1.32 (1.64)	1.36 (1.67)	-0.02	1.12 (1.53)	1.22 (1.60)	0.00
Number of HbA1c tests ordered												
...mean (sd)	0.31 (0.64)	0.36 (0.68)	-0.08	0.20 (0.53)	0.22 (0.54)	-0.04	0.37 (0.70)	0.39 (0.71)	-0.03	0.32 (0.65)	0.36 (0.68)	0.00
Number of glucose tests ordered												
...mean (sd)	0.27 (2.73)	0.37 (4.22)	-0.03	0.16 (0.98)	0.16 (0.96)	0.00	0.18 (0.72)	0.18 (0.72)	0.00	0.19 (1.26)	0.21 (1.83)	0.00
Number of lipid tests ordered												
...mean (sd)	0.49 (0.77)	0.48 (0.78)	0.01	0.34 (0.75)	0.36 (0.85)	-0.02	0.52 (0.72)	0.54 (0.73)	-0.03	0.47 (0.73)	0.50 (0.76)	0.00
Total N distinct ICD9/ICD10 diagnoses at the 3rd digit level Copy												
...mean (sd)	6.61 (10.06)	10.92 (12.43)	-0.38	5.13 (9.89)	8.02 (11.79)	-0.27	9.35 (12.17)	11.79 (13.06)	-0.19	7.88 (11.34)	11.05 (12.77)	0.00
For PS												
Hemorrhagic stroke+Other cerebrovascular diseases+Cerebrovascular procedure (for PS); n (%)	135 (1.8%)	41 (1.0%)	0.07	199 (1.4%)	31 (0.8%)	0.06	748 (2.3%)	309 (1.8%)	0.04	1082 (2.0%)	381 (1.5%)	0.04
immobilization; n (%)	766 (10.3%)	378 (9.6%)	#DIV/0!	1,385 (9.9%)	417 (10.7%)	#DIV/0!	2,774 (8.5%)	1,488 (8.9%)	#DIV/0!	1,385 (9.9%)	417 (10.7%)	-0.03
Occurrence of creatinine tests ordered (for PS); n (%)	592 (8.0%)	317 (8.0%)	0.00	926 (6.6%)	247 (6.3%)	0.01	3,559 (10.9%)	1,774 (10.6%)	0.01	5077 (9.4%)	2338 (9.5%)	0.00
Occurrence of BUN tests ordered (for PS); n (%)	350 (4.7%)	160 (4.1%)	0.03	597 (4.3%)	140 (3.6%)	0.04	2,099 (6.4%)	998 (6.0%)	0.02	3046 (5.6%)	1298 (5.3%)	0.01
Occurrence of chronic renal insufficiency w/o CKD (for PS) v2; n (%)	593 (8.0%)	179 (4.5%)	0.14	599 (4.3%)	109 (2.8%)	0.08	3,259 (10.0%)	967 (5.8%)	0.16	4451 (8.2%)	1255 (5.1%)	0.12
Chronic kidney disease Stage 1-2 (for PS); n (%)	154 (2.1%)	66 (1.7%)	0.03	124 (0.9%)	29 (0.7%)	0.02	566 (1.7%)	262 (1.6%)	0.01	844 (1.6%)	357 (1.5%)	0.01
Chronic kidney disease Stage 3-6 (for PS); n (%)	597 (8.1%)	245 (6.2%)	0.07	515 (3.7%)	82 (2.1%)	0.10	3,238 (9.9%)	1,103 (6.6%)	0.12	4350 (8.1%)	1430 (5.8%)	0.09
Acute kidney injury; n (%)	818 (11.0%)	329 (8.4%)	#DIV/0!	1,167 (8.3%)	331 (8.5%)	#DIV/0!	4,121 (12.6%)	1,533 (9.2%)	#DIV/0!	1,167 (8.3%)	331 (8.5%)	-0.01
Bladder stones+Kidney stones (for PS); n (%)	243 (3.3%)	140 (3.6%)	-0.02	397 (2.8%)	120 (3.1%)	-0.02	1,013 (3.1%)	500 (3.0%)	0.01	1653 (3.1%)	760 (3.1%)	0.00
Alcohol abuse or dependence+Drug abuse or dependence (for PS); n (%)	394 (5.3%)	260 (6.6%)	-0.05	528 (3.8%)	206 (5.3%)	-0.07	471 (1.4%)	376 (2.2%)	-0.06	1393 (2.6%)	842 (3.4%)	-0.05
Other atherosclerosis+Cardiac conduction disorders+Other CVD (for PS) v2 Copy; n (%)	1,386 (18.7%)	738 (18.7%)	0.00	2,467 (17.7%)	684 (17.5%)	0.01	6,719 (20.6%)	3,222 (19.2%)	0.04	10572 (19.6%)	4644 (18.9%)	0.02
Previous cardiac procedure (CABG or PTCA or Stent) + History of CABG or PTCA (for PS) v3; n (%)	312 (4.2%)	154 (3.9%)	0.02	303 (2.2%)	69 (1.8%)	0.03	2,603 (8.0%)	1,073 (6.4%)	0.06	3218 (6.0%)	1296 (5.3%)	0.03
Diabetes with complication; n (%)	812 (11.0%)	438 (11.1%)	#DIV/0!	1,013 (7.2%)	311 (8.0%)	#DIV/0!	3,661 (11.2%)	1,716 (10.2%)	#DIV/0!	1,013 (7.2%)	311 (8.0%)	-0.03
Delirium + Psychosis (for PS); n (%)	433 (5.8%)	186 (4.7%)	0.05	551 (3.9%)	154 (3.9%)	0.00	2,441 (7.5%)	1,151 (6.9%)	0.02	3425 (6.3%)	1491 (6.1%)	0.01
Any use of Meglitinides (for PS); n (%)	13 (0.2%)	** (0.3%)	-0.02	30 (0.2%)	** (0.1%)	0.03	108 (0.3%)	48 (0.3%)	0.00	151 (0.3%)	#VALUE!	#VALUE!
Any use of AGIs (for PS); n (%)	** (0.1%)	** (0.1%)	0.00	** (0.0%)	** (0.1%)	-0.04	32 (0.1%)	** (0.0%)	0.04	#VALUE!	#VALUE!	#VALUE!
CKD stage 3-6 + dialysis (for PS); n (%)	609 (8.2%)	247 (6.3%)	0.07	546 (3.9%)	89 (2.3%)	0.09	3,272 (10.0%)	1,110 (6.6%)	0.12	4427 (8.2%)	1446 (5.9%)	0.09
Use of thiazide- United; n (%)	671 (9.1%)	365 (9.3%)	-0.01	1,101 (7.9%)	246 (6.3%)	0.06	3,945 (12.1%)	1,768 (10.6%)	0.05	5717 (10.6%)	2379 (9.7%)	0.03
Use of beta blockers; n (%)	1,762 (23.8%)	811 (20.6%)	0.08	3,041 (21.8%)	707 (18.1%)	0.09	11,260 (34.5%)	5,254 (31.4%)	0.07	16063 (29.7%)	6772 (27.5%)	0.05
Use of calcium channel blockers; n (%)	1,415 (19.1%)	722 (18.3%)	0.02	2,267 (16.2%)	545 (13.9%)	0.06	8,772 (26.9%)	4,060 (24.2%)	0.06	12454 (23.1%)	5327 (21.7%)	0.03
All antidiabetic medications except insulin; n (%)	1,120 (15.1%)	574 (14.6%)	0.01	1,771 (12.7%)	458 (11.7%)	0.03	5,547 (17.0%)	2,680 (16.0%)	0.03	8438 (15.6%)	3712 (15.1%)	0.01
DM Medications - Insulin Copy; n (%)	441 (5.9%)	217 (5.5%)	0.02	779 (5.6%)	196 (5.0%)	0.03	1,692 (5.2%)	734 (4.4%)	0.04	2912 (5.4%)	1147 (4.7%)	0.03
Use of Low Intensity Statins; n (%)	1,617 (21.8%)	763 (19.4%)	0.06	2,357 (16.9%)	521 (13.3%)	0.10	9,199 (28.2%)	4,445 (26.5%)	0.04	13173 (24.4%)	5729 (23.3%)	0.03
Use of High Intensity Statins; n (%)	769 (10.4%)	503 (12.8%)	-0.08	1,328 (9.5%)	365 (9.3%)	0.01	4,205 (12.9%)	2,477 (14.8%)	-0.06	6302 (11.7%)	3345 (13.6%)	-0.06
Malignant hypertension; n (%)	771 (10.4%)	206 (5.2%)	0.19	6,113 (43.7%)	1,154 (29.5%)	0.30	13,959 (42.8%)	4,636 (27.7%)	0.32	20843 (38.6%)	5996 (24.4%)	0.31
Cardiovascular stress test; n (%)	29 (0.4%)	** (0.2%)	0.04	51 (0.4%)	15 (0.4%)	0.00	174 (0.5%)	81 (0.5%)	0.00	254 (0.5%)	#VALUE!	#VALUE!
Echocardiogram; n (%)	1,217 (16.4%)	712 (18.1%)	-0.05	2,591 (18.5%)	783 (20.0%)	-0.04	6,200 (19.0%)	3,177 (19.0%)	0.00	10008 (18.5%)	4672 (19.0%)	-0.01
Number of BNP tests												
...mean (sd)	0.06 (0.28)	0.11 (0.38)	-0.15	0.03 (0.20)	0.05 (0.25)	-0.09	0.09 (0.33)	0.12 (0.37)	-0.09	0.07 (0.29)	0.11 (0.36)	-0.12
Number of Cardiac biomarkers tests (troponin, CK-MBs, Myoglobin, CPK)												
...mean (sd)	0.32 (1.21)	0.40 (1.19)	-0.07	0.22 (0.95)	0.28 (1.06)	-0.06	0.22 (0.55)	0.27 (0.62)	-0.09	0.23 (0.79)	0.29 (0.82)	0.00
Number of Ambulatory Blood pressure monitoring tests												
...mean (sd)	0.00 (0.04)	0.00 (0.00)	0.00	0.00 (0.04)	0.00 (0.04)	0.00	0.00 (0.03)	0.00 (0.04)	0.00	0.00 (0.03)	0.00 (0.04)	0.00
N of days on antihypertensive medications during baseline							0	0				
...mean (sd)	78.67 (79.06)	79.51 (80.27)	-0.01	67.34 (78.33)	58.24 (75.77)	0.12	107.82 (76.83)	104.35 (78.11)	0.04	93.34 (77.53)	93.04 (78.09)	0.00
N of days in database anytime prior							0	0				
...mean (sd)	1,629.27 (1,170.61)	1,681.72 (1,331.40)	-0.04	1,747.51 (1,223.63)	2,037.38 (1,445.60)	-0.22	619.84 (384.70)	645.09 (368.82)	-0.07	1050.22 (815.43)	1032.36 (841.75)	0.00
Mean Copay for per prescription cost (charges in U.S. \$) (180-1 day prior)							0	0				
...mean (sd)	24.96 (37.89)	23.57 (44.39)	0.03	17.03 (20.99)	14.53 (58.71)	0.06	108.59 (118.97)	107.60 (113.33)	0.01	73.42 (94.13)	79.35 (98.03)	0.00
...Missing; n (%)	471 (6.4%)	263 (6.7%)	-0.01	1,064 (7.6%)	305 (7.8%)	-0.01	1,114 (3.4%)	643 (3.8%)	-0.02	2649 (4.9%)	1211 (4.9%)	0.00
Colonoscopy; n (%)	293 (4.0%)	150 (3.8%)	0.01	631 (4.5%)	158 (4.0%)	0.02	1,423 (4.4%)	690 (4.1%)	0.01	2347 (4.3%)	998 (4.1%)	0.01
Fecal occult blood (FOB) test; n (%)	275 (3.7%)	117 (3.0%)	0.04	517 (3.7%)	97 (2.5%)	0.07	879 (2.7%)	487 (2.9%)	-0.01	1671 (3.1%)	701 (2.9%)	0.01
Flu vaccine; n (%)	1,060 (14.3%)	612 (15.5%)	-0.03	1,272 (9.1%)	355 (9.1%)	0.00	9,282 (28.5%)	4,854 (29.0%)	-0.01	11614 (21.5%)	5821 (23.7%)	-0.05
Mammogram; n (%)	745 (10.0%)	421 (10.7%)	-0.02	1,269 (9.1%)	351 (9.0%)	0.00	3,468 (10.6%)	1,907 (11.4%)	-0.03	5482 (10.2%)	2679 (10.9%)	-0.02
Pap smear; n (%)	353 (4.8%)	171 (4.3%)	0.02	991 (7.1%)	291 (7.4%)	-0.01	841 (2.6%)	453 (2.7%)	-0.01	2185 (4.0%)	915 (3.7%)	0.02
Pneumonia vaccine; n (%)	693 (9.3%)	688 (17.5%)	-0.24	499 (3.6%)	264 (6.8%)	-0.14	4,756 (14.6%)	3,881 (23.2%)	-0.22	5948 (11.0%)	4833 (19.6%)	-0.24

## Appendix B

PAS test or Prostate exam for DRE; n (%)	738 (10.0%)	433 (11.0%)	-0.03	1,136 (8.1%)	325 (8.3%)	-0.01	3,297 (10.1%)	1,947 (11.6%)	-0.05	5171 (9.6%)	2705 (11.0%)	-0.03
Bone mineral density; n (%)	289 (3.9%)	143 (3.6%)	0.02	283 (2.0%)	76 (1.9%)	0.01	1,395 (4.3%)	793 (4.7%)	-0.02	1967 (3.6%)	1012 (4.1%)	-0.03
Use of CNS stimulants; n (%)	52 (0.7%)	26 (0.7%)	0.00	188 (1.3%)	72 (1.8%)	-0.04	95 (0.3%)	68 (0.4%)	-0.02	335 (0.6%)	166 (0.7%)	-0.01
Use of estrogens, progestins, and androgens; n (%)	469 (6.3%)	238 (6.0%)	0.01	1,441 (10.3%)	456 (11.7%)	-0.04	1,116 (3.4%)	615 (3.7%)	-0.02	3026 (5.6%)	1309 (5.3%)	0.01
Use of Angiogenesis inhibitors; n (%)	** (0.0%)	** (0.1%)	-0.04	** (0.1%)	** (0.2%)	-0.03	29 (0.1%)	16 (0.1%)	0.00	#VALUE!	#VALUE!	#VALUE!
Use of Oral Immunosuppressants; n (%)	35 (0.5%)	** (0.3%)	0.03	132 (0.9%)	14 (0.4%)	0.06	41 (0.1%)	16 (0.1%)	0.00	208 (0.4%)	#VALUE!	#VALUE!
Use of fondaparinux or Bivalirudin; n (%)	120 (1.6%)	** (0.2%)	0.15	240 (1.7%)	16 (0.4%)	0.13	387 (1.2%)	24 (0.1%)	0.14	747 (1.4%)	#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 (%)	** (0.0%)	** (0.1%)	-0.04	** (0.0%)	** (0.1%)	-0.04	** (0.0%)	** (0.0%)	#DIV/0!	#VALUE!	#VALUE!	#VALUE!
Use of Ticagrelor; n (%)	** (0.0%)	** (0.1%)	-0.04	** (0.1%)	** (0.1%)	0.00	24 (0.1%)	22 (0.1%)	0.00	#VALUE!	#VALUE!	#VALUE!
Number of D-dimer tests												
...mean (sd)	0.06 (0.27)	0.11 (0.36)	-0.16	0.06 (0.26)	0.07 (0.29)	-0.04	0.08 (0.30)	0.11 (0.34)	-0.09	0.07 (0.29)	0.10 (0.34)	-0.05
Numbe of CRP, high-sensitivity CRP tests												
...mean (sd)	0.14 (0.66)	0.18 (0.85)	-0.05	0.12 (0.62)	0.17 (0.72)	-0.07	0.15 (0.72)	0.17 (0.67)	-0.03	0.14 (0.69)	0.17 (0.71)	0.00
Number of PT or aPTT tests												
...mean (sd)	1.04 (2.19)	0.96 (1.60)	0.04	0.72 (1.79)	0.70 (1.51)	0.01	0.62 (1.10)	0.61 (0.89)	0.01	0.70 (1.49)	0.68 (1.15)	0.00
Number of Bleeding time tests												
...mean (sd)	0.00 (0.02)	0.00 (0.00)	0.00	0.00 (0.03)	0.00 (0.03)	0.00	0.00 (0.02)	0.00 (0.02)	0.00	0.00 (0.02)	0.00 (0.02)	0.00
HAS-BLED Score (ICD-9 and ICD-10), 180 days												
...mean (sd)	2.86 (1.05)	2.80 (1.04)	0.06	2.41 (1.01)	2.32 (0.98)	0.09	3.46 (0.81)	3.40 (0.82)	0.07	3.11 (0.90)	3.13 (0.89)	0.00
N of Generic name drugs												
...mean (sd)	18.04 (16.90)	16.55 (17.28)	0.09	14.06 (11.77)	13.04 (12.54)	0.08	19.33 (15.03)	17.38 (15.17)	0.13	17.79 (14.54)	16.56 (15.15)	0.00
N of Brand name drugs												
...mean (sd)	3.33 (5.27)	3.81 (4.55)	-0.10	3.46 (4.75)	3.79 (3.90)	-0.08	3.58 (5.38)	4.07 (4.63)	-0.10	3.51 (5.21)	3.98 (4.51)	0.00
Use of clopidogrel ; n (%)	295 (4.0%)	130 (3.3%)	0.04	556 (4.0%)	126 (3.2%)	0.04	2,006 (6.1%)	928 (5.5%)	0.03	2857 (5.3%)	1184 (4.8%)	0.02
Systemic embolism; n (%)	263 (3.5%)	100 (2.5%)	0.06	764 (5.5%)	191 (4.9%)	0.03	834 (2.6%)	367 (2.2%)	0.03	1861 (3.4%)	658 (2.7%)	0.04
DVT; n (%)	7,411 (100.0%)	3,936 (99.9%)	0.04	13,970 (99.9%)	3,906 (100.0%)	0.00	32,605 (99.9%)	16,737 (99.9%)	0.04	53986 (100.0%)	24579 (99.9%)	0.04
Post-thrombotic syndrome; n (%)	21 (0.3%)	13 (0.3%)	#DIV/0!	21 (0.2%)	14 (0.4%)	#DIV/0!	87 (0.3%)	28 (0.2%)	#DIV/0!	21 (0.2%)	14 (0.4%)	-0.04
PE; n (%)	575 (7.8%)	410 (10.4%)	-0.09	570 (4.1%)	233 (6.0%)	-0.09	1,930 (5.9%)	1,268 (7.6%)	-0.07	3075 (5.7%)	1911 (7.8%)	-0.08
Coagulation defects; n (%)	252 (3.4%)	86 (2.2%)	#DIV/0!	501 (3.6%)	130 (3.3%)	#DIV/0!	632 (1.9%)	214 (1.3%)	0.00	501 (3.6%)	130 (3.3%)	0.02
Diabetes: 1 inpatient or 2 outpatient claims within 183 days; n (%)	1,806 (24.4%)	910 (23.1%)	0.03	2,635 (18.9%)	692 (17.7%)	0.03	9,089 (27.9%)	4,176 (24.9%)	0.07	13530 (25.1%)	5778 (23.5%)	0.04
Intracranial or retroperitoneal hemorrhage: 1 inpatient or 2 outpatient claims within 183 days; n (%)												
...mean (sd)	** (0.1%)	** (0.1%)	0.00	12 (0.1%)	0 (0.0%)	-0.04	42 (0.1%)	12 (0.1%)	0.00	#VALUE!	#VALUE!	#VALUE!
Peptic Ulcer Disease; n (%)	1,859 (25.1%)	979 (24.8%)	0.01	2,501 (17.9%)	762 (19.5%)	-0.04	9,584 (29.4%)	4,607 (27.5%)	0.04	13944 (25.8%)	6348 (25.8%)	0.00
Major Surgery ; n (%)	566 (7.6%)	355 (9.0%)	#DIV/0!	1,309 (9.4%)	327 (8.4%)	#DIV/0!	2,682 (8.2%)	1,655 (9.9%)	#DIV/0!	1,309 (9.4%)	327 (8.4%)	0.04
Upper GI bleed; 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!
Lower/ unspecified GI bleed; 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!
Urogenital bleed; n (%)	30 (0.4%)	13 (0.3%)	0.02	85 (0.6%)	42 (1.1%)	-0.05	** (0.0%)	** (0.0%)	#DIV/0!	#VALUE!	#VALUE!	#VALUE!
Other bleeds; n (%)	430 (5.8%)	200 (5.1%)	0.03	796 (5.7%)	218 (5.6%)	0.00	1,841 (5.6%)	769 (4.6%)	0.05	3067 (5.7%)	1187 (4.8%)	0.04
Prior cancer; n (%)	922 (12.4%)	707 (17.9%)	-0.15	1,383 (9.9%)	519 (13.3%)	-0.11	4,862 (14.9%)	3,362 (20.1%)	-0.14	7167 (13.3%)	4588 (18.7%)	-0.15
Antibiotics; n (%)	3,535 (47.7%)	1,930 (49.0%)	#DIV/0!	7,040 (50.4%)	2,046 (52.4%)	#DIV/0!	17,449 (53.5%)	9,034 (53.9%)	#DIV/0!	7,040 (50.4%)	2,046 (52.4%)	-0.04
Aspirin; n (%)	44 (0.6%)	31 (0.8%)	-0.02	160 (1.1%)	63 (1.6%)	-0.04	146 (0.4%)	67 (0.4%)	0.00	350 (0.6%)	161 (0.7%)	-0.01
Aspirin/dipyridamole; n (%)	** (0.1%)	** (0.1%)	0.00	22 (0.2%)	** (0.1%)	0.03	113 (0.3%)	45 (0.3%)	0.00	#VALUE!	#VALUE!	#VALUE!
Other antiplatelet agents; n (%)	21 (0.3%)	** (0.3%)	0.00	67 (0.5%)	** (0.3%)	0.03	181 (0.6%)	100 (0.6%)	0.00	269 (0.5%)	#VALUE!	#VALUE!
PGP inhibitors; n (%)	1,375 (18.5%)	667 (16.9%)	0.04	2,756 (19.7%)	720 (18.4%)	0.03	7,501 (23.0%)	3,737 (22.3%)	0.02	11632 (21.5%)	5124 (20.8%)	0.02
Other gastroprotective agents; n (%)	100 (1.3%)	58 (1.5%)	-0.02	215 (1.5%)	78 (2.0%)	-0.04	554 (1.7%)	258 (1.5%)	0.02	869 (1.6%)	394 (1.6%)	0.00
Number of lipid tests ordered												
...mean (sd)	0.49 (0.77)	0.48 (0.78)	0.01	0.34 (0.75)	0.36 (0.85)	-0.02	0.54 (0.79)	0.56 (0.80)	-0.03	0.48 (0.78)	0.52 (0.81)	0.00
Proton pump inhibitor; n (%)	1,695 (22.9%)	892 (22.6%)	0.01	3,099 (22.2%)	825 (21.1%)	0.03	10,056 (30.8%)	4,868 (29.1%)	0.04	14850 (27.5%)	6585 (26.8%)	0.02
H2 receptor antagonist; n (%)	312 (4.2%)	174 (4.4%)	-0.01	497 (3.6%)	175 (4.5%)	-0.05	2,157 (6.6%)	1,010 (6.0%)	0.02	2966 (5.5%)	1359 (5.5%)	0.00
Vitamin K therapy; n (%)	** (0.1%)	** (0.0%)	0.04	22 (0.2%)	0 (0.0%)	0.06	** (0.0%)	** (0.0%)	#DIV/0!	#VALUE!	#VALUE!	#VALUE!
Number of INR (prothrombin) tests ordered												
...mean (sd)	0.73 (1.63)	0.53 (0.88)	0.15	0.53 (1.22)	0.46 (0.98)	0.06	0.58 (1.01)	0.56 (0.77)	0.02	0.59 (1.17)	0.54 (0.82)	0.00
Treating prescriber - Cardiologist; n (%)	2,275 (30.7%)	1,282 (32.5%)	-0.04	4,338 (31.0%)	1,372 (35.1%)	-0.09	11,149 (34.2%)	5,410 (32.3%)	0.04	17762 (32.9%)	8064 (32.8%)	0.00
Treating prescriber - Primary Care Physician; n (%)	6,535 (88.2%)	3,215 (81.6%)	0.19	5,771 (41.3%)	1,695 (43.4%)	-0.04	13,113 (40.2%)	6,308 (37.7%)	0.05	25419 (47.1%)	11218 (45.6%)	0.03
Treating prescriber - Other; n (%)	7,407 (99.9%)	3,938 (99.9%)	0.00	13,310 (95.2%)	3,732 (95.5%)	-0.01	32,361 (99.2%)	16,705 (99.7%)	-0.07	53078 (98.3%)	24375 (99.1%)	-0.07
Alpha blockers; n (%)	527 (7.1%)	295 (7.5%)	-0.02	872 (6.2%)	204 (5.2%)	0.04	3,226 (9.9%)	1,744 (10.4%)	-0.02	4625 (8.6%)	2243 (9.1%)	-0.02
CHA2DS2 VASc score, 180 days, V												
...mean (sd)	3.72 (1.81)	2.57 (1.68)	0.66	3.50 (1.56)	2.64 (1.73)	0.52	4.65 (1.70)	3.61 (1.83)	0.59	4.22 (1.68)	3.29 (1.79)	0.01
Use of Prasugrel; n (%)	13 (0.2%)	** (0.1%)	0.03	27 (0.2%)	** (0.3%)	-0.02	** (0.0%)	** (0.0%)	#DIV/0!	#VALUE!	#VALUE!	#VALUE!
Use of Loop Diuretics+other diuretics+other hypertension drugs; n (%)	1,136 (15.3%)	532 (13.5%)	0.05	1,808 (12.9%)	427 (10.9%)	0.06	7,645 (23.4%)	3,294 (19.7%)	0.09	10589 (19.6%)	4253 (17.3%)	0.06
Commercial vs Medicare Advantage- Business Type Code - CORRECT ONE - OPTUM												
...Commercial; n (%)	2,640 (35.6%)	1277 (32.4%)	0.07	3,998 (28.6%)	835 (21.4%)	0.17	-	-	#VALUE!	6,638 (31.0%)	2112 (26.9%)	0.09
...Medicare Advantage; n (%)	4,773 (64.4%)	2663 (67.6%)	-0.07	9,979 (71.4%)	3073 (78.6%)	-0.17	-	-	#VALUE!	14,752 (69.0%)	5736 (73.1%)	-0.09
Commercial vs Medicare Advantage- Business Type Code												
...COM = COMMERCIAL; n (%)	2,640 (35.6%)	1,277 (32.4%)	0.07	-	-	-	-	-	#VALUE!	2,640 (35.6%)	1,277 (32.4%)	0.07
...MCR = MEDICARE; n (%)	4,773 (64.4%)	2,663 (67.6%)	-0.07	-	-	-	-	-	#VALUE!	4,773 (64.4%)	2,663 (67.6%)	-0.07
...MCD = MEDICAID; n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	-	-	-	-	#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												



# Appendix B

...1 - Fee For Service; n (%)	-	-	8,838 (63.2%)	2,764 (70.7%)	-0.16	-	-	8,838 (63.2%)	2,764 (70.7%)	-0.16
...2 - Encounter; n (%)	-	-	1,141 (8.2%)	309 (7.9%)	0.01	-	-	1,141 (8.2%)	309 (7.9%)	0.01
...3 - Medicare; n (%)	-	-	3,608 (25.8%)	750 (19.2%)	0.16	-	-	3,608 (25.8%)	750 (19.2%)	0.16
...4 - Medicare Encounter; n (%)	-	-	390 (2.8%)	85 (2.2%)	0.04	-	-	390 (2.8%)	85 (2.2%)	0.04
Metropolitan Statistical Area - Urban (any MSA) vs Rural (non-MSA)										
...Urban; n (%)	-	-	11,109 (79.5%)	2,903 (74.3%)	0.12	-	-	11,109 (79.5%)	2,903 (74.3%)	0.12
...Rural; n (%)	-	-	151 (1.1%)	145 (3.7%)	-0.17	-	-	151 (1.1%)	145 (3.7%)	-0.17
...Unknown/Missing; n (%)	-	-	2,717 (19.4%)	860 (22.0%)	-0.06	-	-	2,717 (19.4%)	860 (22.0%)	-0.06

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

Appendix B

PS-matched											
	Optum			MarketScan			Medicare			POOLED	
Variable	Reference- warfarin Copy	oxaban (15 or 20 mg) Copy	St. Diff.	Reference- warfarin Copy	oxaban (15 or 20 mg) Copy	St. Diff.	Reference- warfarin Copy	oxaban (15 or 20 mg) Copy	St. Diff.	Reference- warfarin Copy	Exposure - rivaroxaban (15 or 20 mg) Copy
Number of patients	1,575	1,575		2,899	2,899		8,511	8,511		12,985	12,985
Age											
...mean (sd)	65.29 (15.26)	65.87 (14.42)	-0.04	55.03 (16.16)	55.22 (15.70)	-0.01	76.35 (7.86)	76.58 (7.93)	-0.03	70.25 (11.27)	70.51 (11.02)
Age categories without zero category											
...18 - 54; n (%)	373 (23.7%)	319 (20.3%)	0.08	1,394 (48.1%)	1,388 (47.9%)	0.00	0 (0.0%)	0 (0.0%)	#DIV/0!	1767 (13.6%)	1707 (13.1%)
...55 - 64; n (%)	269 (17.1%)	268 (17.0%)	0.00	821 (28.3%)	827 (28.5%)	0.00	0 (0.0%)	0 (0.0%)	#DIV/0!	1,090 (8.4%)	1,095 (8.4%)
...65 - 74; n (%)	424 (26.9%)	512 (32.5%)	-0.12	313 (10.8%)	338 (11.7%)	-0.03	4,015 (47.2%)	3,893 (45.7%)	0.03	4,752 (36.6%)	4,743 (36.5%)
...≥ 75; n (%)	509 (32.3%)	476 (30.2%)	0.05	371 (12.8%)	346 (11.9%)	0.03	4,496 (52.8%)	4,618 (54.3%)	-0.03	5,376 (41.4%)	5,440 (41.9%)
Gender without zero category- United											
...Males; n (%)	718 (45.6%)	703 (44.6%)	0.02	1,383 (47.7%)	1,412 (48.7%)	-0.02	3,166 (37.2%)	3,136 (36.8%)	0.01	5,267 (40.6%)	5,251 (40.4%)
...Females; n (%)	857 (54.4%)	872 (55.4%)	-0.02	1,516 (52.3%)	1,487 (51.3%)	0.02	5,345 (62.8%)	5,375 (63.2%)	-0.01	7,718 (59.4%)	7,734 (59.6%)
Race											
...White; n (%)							7,144 (83.9%)	7,136 (83.8%)		7,144 (83.9%)	7,136 (83.8%)
...Black; n (%)							932 (11.0%)	947 (11.1%)		932 (11.0%)	947 (11.1%)
...Asian; n (%)							81 (1.0%)	77 (0.9%)		81 (1.0%)	77 (0.9%)
...Hispanic; n (%)							188 (2.2%)	192 (2.3%)		188 (2.2%)	192 (2.3%)
...North American Native; n (%)							33 (0.4%)	31 (0.4%)		33 (0.4%)	31 (0.4%)
...Other/Unknown; n (%)							133 (1.6%)	128 (1.5%)		133 (1.6%)	128 (1.5%)
Region without zero category-United v3 (lumping missing&other category with West)											
...Northeast; n (%)	182 (11.6%)	189 (12.0%)	-0.01	490 (16.9%)	522 (18.0%)	-0.03	1,623 (19.1%)	1,606 (18.9%)	0.01	2,295 (17.7%)	2,317 (17.8%)
...South; n (%)	662 (42.0%)	664 (42.2%)	0.00	808 (27.9%)	829 (28.6%)	-0.02	3,508 (41.2%)	3,470 (40.8%)	0.01	4,978 (38.3%)	4,963 (38.2%)
...Midwest; n (%)	391 (24.8%)	383 (24.3%)	0.01	1,249 (43.1%)	1,191 (41.1%)	0.04	2,049 (24.1%)	2,086 (24.5%)	-0.01	3,689 (28.4%)	3,660 (28.2%)
...West; n (%)	340 (21.6%)	339 (21.5%)	0.00	309 (10.7%)	320 (11.0%)	-0.01	1,331 (15.6%)	1,349 (15.9%)	-0.01	1,980 (15.2%)	2,008 (15.5%)
...Unknown+missing; n (%)	N/A	N/A	#VALUE!	37 (1.3%)	37 (1.3%)	0.02	N/A	N/A	#VALUE!	43 (1.5%)	37 (1.3%)
CV Covariates											
Ischemic heart disease; n (%)	225 (14.3%)	234 (14.9%)	-0.02	309 (10.7%)	296 (10.2%)	0.02	1,805 (21.2%)	1,799 (21.1%)	0.00	2,339 (18.0%)	2,329 (17.9%)
Acute MI; n (%)	15 (1.0%)	19 (1.2%)	-0.02	51 (1.8%)	41 (1.4%)	0.03	129 (1.5%)	123 (1.4%)	0.01	195 (1.5%)	183 (1.4%)
ACS/unstable angina; n (%)	** (0.6%)	** (0.3%)	0.00	** (0.2%)	** (0.3%)	-0.02	55 (0.6%)	55 (0.6%)	0.00	#VALUE!	#VALUE!
Old MI; n (%)	48 (3.0%)	42 (2.7%)	0.02	44 (1.5%)	38 (1.3%)	0.02	402 (4.7%)	389 (4.6%)	0.00	494 (3.8%)	469 (3.6%)
Stable angina; n (%)	28 (1.8%)	34 (2.2%)	-0.03	46 (1.6%)	39 (1.3%)	0.03	155 (1.8%)	162 (1.9%)	-0.01	229 (1.8%)	235 (1.8%)
Coronary atherosclerosis and other forms of chronic ischemic heart disease; n (%)	196 (12.4%)	204 (13.0%)	-0.02	256 (8.8%)	242 (8.3%)	0.02	1,624 (19.1%)	1,620 (19.0%)	0.00	2,076 (16.0%)	2,066 (15.9%)
Other atherosclerosis with ICD10 v2 Copy; n (%)	16 (1.0%)	17 (1.1%)	-0.01	31 (1.1%)	15 (0.5%)	0.07	124 (1.5%)	84 (1.0%)	0.05	171 (1.3%)	116 (0.9%)
Previous cardiac procedure (CABG or PTCA or Stent) v4; n (%)	** (0.5%)	** (0.3%)	0.03	17 (0.6%)	12 (0.4%)	0.03	54 (0.6%)	35 (0.4%)	0.03	#VALUE!	#VALUE!
History of CABG or PTCA; n (%)	56 (3.6%)	74 (4.7%)	-0.06	42 (1.4%)	43 (1.5%)	-0.01	618 (7.3%)	639 (7.5%)	-0.01	716 (5.5%)	756 (5.8%)
Any stroke; 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%)	000 (0.0%)
Ischemic stroke (w and w/o mention of cerebral infarction); 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%)	000 (0.0%)
Hemorrhagic stroke; 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!	000 (0.0%)	0 (0.0%)
TIA; n (%)	12 (0.8%)	15 (1.0%)	-0.02	28 (1.0%)	25 (0.9%)	0.01	95 (1.1%)	103 (1.2%)	-0.01	135 (1.0%)	143 (1.1%)
Other cerebrovascular disease; n (%)	22 (1.4%)	29 (1.8%)	-0.03	23 (0.8%)	29 (1.0%)	-0.02	178 (2.1%)	183 (2.2%)	-0.01	223 (1.7%)	241 (1.9%)
Cerebrovascular procedure; 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!	000 (0.0%)	0 (0.0%)
Heart failure(CHF); n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	** (0.1%)	** (0.0%)	0.04	<11 (0.0%)	<11 (0.0%)	#DIV/0!	#VALUE!	#VALUE!
Peripheral Vascular Disease (PVD) or PVD Surgery v2; n (%)	183 (11.6%)	189 (12.0%)	-0.01	329 (11.3%)	325 (11.2%)	0.00	1,107 (13.0%)	1,097 (12.9%)	0.00	1,619 (12.5%)	1,611 (12.4%)
Atrial fibrillation; 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%)	000 (0.0%)
Other cardiac dysrhythmia; n (%)	174 (11.0%)	182 (11.6%)	-0.02	305 (10.5%)	296 (10.2%)	0.01	1,118 (13.1%)	1,099 (12.9%)	0.01	1,597 (12.3%)	1,577 (12.1%)
Cardiac conduction disorders; n (%)	64 (4.1%)	64 (4.1%)	0.00	86 (3.0%)	87 (3.0%)	0.00	466 (5.5%)	523 (6.1%)	-0.03	616 (4.7%)	674 (5.2%)
Other CVD; n (%)	272 (17.3%)	261 (16.6%)	0.02	430 (14.8%)	454 (15.7%)	-0.03	1,402 (16.5%)	1,367 (16.1%)	0.01	2,104 (16.2%)	2,082 (16.0%)
Diabetes-related complications											
Occurrence of Diabetic Neuropathy v2 Copy; n (%)	104 (6.6%)	117 (7.4%)	-0.03	95 (3.3%)	88 (3.0%)	0.02	474 (5.6%)	451 (5.3%)	0.01	673 (5.2%)	656 (5.1%)
Occurrence of diabetic nephropathy V3 with ICD10 Copy; n (%)	54 (3.4%)	64 (4.1%)	-0.04	45 (1.6%)	44 (1.5%)	0.01	249 (2.9%)	217 (2.5%)	0.02	348 (2.7%)	325 (2.5%)
Hypoglycemia v2; n (%)	20 (1.3%)	26 (1.7%)	-0.03	33 (1.1%)	31 (1.1%)	0.00	241 (2.8%)	216 (2.5%)	0.02	294 (2.3%)	273 (2.1%)
Hyperglycemia; n (%)	103 (6.5%)	101 (6.4%)	0.00	137 (4.7%)	134 (4.6%)	0.00	644 (7.6%)	648 (7.6%)	0.00	884 (6.8%)	883 (6.8%)
Diabetic ketoacidosis; n (%)	13 (0.8%)	** (0.4%)	0.05	** (0.4%)	15 (0.5%)	-0.01	28 (0.3%)	29 (0.3%)	0.00	#VALUE!	#VALUE!
Hypertension: 1 inpatient or 2 outpatient claims within 365 days; n (%)	1,009 (64.1%)	1,044 (66.3%)	-0.05	1,471 (50.7%)	1,490 (51.4%)	-0.01	6,804 (79.9%)	6,845 (80.4%)	-0.01	9,284 (71.5%)	9,379 (72.2%)
Hyperlipidemia v2; n (%)	725 (46.0%)	766 (48.6%)	-0.05	952 (32.8%)	964 (33.3%)	-0.01	4,628 (54.4%)	4,625 (54.3%)	0.00	6,305 (48.6%)	6,355 (48.9%)
Edema; n (%)	491 (31.2%)	509 (32.3%)	-0.02	701 (24.2%)	707 (24.4%)	0.00	2,208 (25.9%)	2,213 (26.0%)	0.00	3400 (26.2%)	3429 (26.4%)
Renal Dysfunction (non-diabetic) v2; n (%)	363 (23.0%)	378 (24.0%)	-0.02	452 (15.6%)	470 (16.2%)	-0.02	2,153 (25.3%)	2,230 (26.2%)	-0.02	2968 (22.9%)	3078 (23.7%)
Occurrence of acute renal disease v2; n (%)	176 (11.2%)	185 (11.7%)	-0.02	229 (7.9%)	254 (8.8%)	-0.03	1,009 (11.9%)	1,028 (12.1%)	-0.01	1414 (10.9%)	1467 (11.3%)
Occurrence of chronic renal insufficiency; n (%)	200 (12.7%)	209 (13.3%)	-0.02	160 (5.5%)	167 (5.8%)	-0.01	1,274 (15.0%)	1,293 (15.2%)	-0.01	1634 (12.6%)	1669 (12.9%)
Chronic kidney disease v2; n (%)	193 (12.3%)	199 (12.6%)	-0.01	150 (5.2%)	148 (5.1%)	0.00	1,205 (14.2%)	1,224 (14.4%)	-0.01	1548 (11.9%)	1571 (11.9%)
CKD Stage 3-4; n (%)	117 (7.4%)	132 (8.4%)	-0.04	73 (2.5%)	79 (2.7%)	-0.01	724 (8.5%)	715 (8.4%)	0.00	914 (7.0%)	926 (7.1%)
Occurrence of hypertensive nephropathy; n (%)	117 (7.4%)	129 (8.2%)	-0.03	67 (2.3%)	73 (2.5%)	-0.01	922 (10.8%)	937 (11.0%)	-0.01	1106 (8.5%)	1139 (8.8%)
Occurrence of miscellaneous renal insufficiency v2; n (%)	123 (7.8%)	133 (8.4%)	-0.02	195 (6.7%)	199 (6.9%)	-0.01	765 (9.0%)	733 (8.6%)	0.01	1083 (8.3%)	1065 (8.2%)
Other Covariates											
Liver disease; 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%)
Osteoarthritis; n (%)	506 (32.1%)	515 (32.7%)	-0.01	656 (22.6%)	651 (22.5%)	0.00	3,140 (36.9%)	3,181 (37.4%)	-0.01	4302 (33.1%)	4347 (33.5%)

Appendix B

Other arthritis, arthropathies and musculoskeletal pain; n (%)	1,330 (84.4%)	1,329 (84.4%)	0.00	2,280 (78.6%)	2,265 (78.1%)	0.01	6,544 (76.9%)	6,553 (77.0%)	0.00	10154 (78.2%)	10147 (78.1%)	0.00
Dorsopathies; n (%)	563 (35.7%)	552 (35.0%)	0.01	948 (32.7%)	909 (31.4%)	0.03	2,792 (32.8%)	2,816 (33.1%)	-0.01	4303 (33.1%)	4277 (32.9%)	0.00
Fractures; n (%)	200 (12.7%)	197 (12.5%)	0.01	321 (11.1%)	299 (10.3%)	0.03	1,177 (13.8%)	1,110 (13.0%)	-0.02	1698 (13.1%)	1606 (12.4%)	0.02
Falls v2; n (%)	178 (11.3%)	184 (11.7%)	-0.01	106 (3.7%)	104 (3.6%)	0.01	427 (5.0%)	439 (5.2%)	-0.01	711 (5.5%)	727 (5.6%)	0.00
Osteoporosis; n (%)	148 (9.4%)	154 (9.8%)	-0.01	120 (4.1%)	119 (4.1%)	0.00	1,301 (15.3%)	1,287 (15.1%)	0.01	1569 (12.1%)	1560 (12.0%)	0.00
Depression; n (%)	296 (18.8%)	315 (20.0%)	-0.03	417 (14.4%)	407 (14.0%)	0.01	1,407 (16.5%)	1,395 (16.4%)	0.00	2120 (16.3%)	2117 (16.3%)	0.00
Anxiety; n (%)	278 (17.7%)	285 (18.1%)	-0.01	412 (14.2%)	398 (13.7%)	0.01	1,230 (14.5%)	1,230 (14.5%)	0.00	1920 (14.8%)	1913 (14.7%)	0.00
Sleep_Disorder; n (%)	137 (8.7%)	152 (9.7%)	-0.03	301 (10.4%)	293 (10.1%)	0.01	602 (7.1%)	616 (7.2%)	0.00	1040 (8.0%)	1061 (8.2%)	-0.01
Dementia; n (%)	175 (11.1%)	173 (11.0%)	0.00	142 (4.9%)	131 (4.5%)	0.02	1,430 (16.8%)	1,386 (16.3%)	0.01	1747 (13.5%)	1690 (13.0%)	0.01
Delirium; n (%)	70 (4.4%)	71 (4.5%)	0.00	86 (3.0%)	86 (3.0%)	0.00	492 (5.8%)	464 (5.5%)	0.01	648 (5.0%)	621 (4.8%)	0.01
Psychosis; n (%)	51 (3.2%)	44 (2.8%)	0.02	51 (1.8%)	50 (1.7%)	0.01	346 (4.1%)	311 (3.7%)	0.02	448 (3.5%)	405 (3.1%)	0.02
Obesity; n (%)	372 (23.6%)	383 (24.3%)	-0.02	665 (22.9%)	664 (22.9%)	0.00	1,485 (17.4%)	1,452 (17.1%)	0.01	2522 (19.4%)	2499 (19.2%)	0.01
Overweight; n (%)	82 (5.2%)	78 (5.0%)	0.01	84 (2.9%)	76 (2.6%)	0.02	368 (4.3%)	383 (4.5%)	-0.01	534 (4.1%)	537 (4.1%)	0.00
Smoking; n (%)	464 (29.5%)	469 (29.8%)	-0.01	512 (17.7%)	522 (18.0%)	-0.01	2,580 (30.3%)	2,587 (30.4%)	0.00	3556 (27.4%)	3578 (27.6%)	0.00
Alcohol abuse or dependence; n (%)	52 (3.3%)	53 (3.4%)	-0.01	61 (2.1%)	59 (2.0%)	0.01	100 (1.2%)	86 (1.0%)	0.02	213 (1.6%)	198 (1.5%)	0.01
Drug abuse or dependence; n (%)	68 (4.3%)	58 (3.7%)	0.03	77 (2.7%)	78 (2.7%)	0.00	96 (1.1%)	103 (1.2%)	-0.01	241 (1.9%)	239 (1.8%)	0.01
COPD; n (%)	215 (13.7%)	228 (14.5%)	-0.02	237 (8.2%)	234 (8.1%)	0.00	1,454 (17.1%)	1,433 (16.8%)	0.01	1906 (14.7%)	1895 (14.6%)	0.00
Asthma; n (%)	156 (9.9%)	154 (9.8%)	0.00	258 (8.9%)	262 (9.0%)	0.00	765 (9.0%)	746 (8.8%)	0.01	1179 (9.1%)	1162 (8.9%)	0.01
Obstructive sleep apnea; n (%)	137 (8.7%)	145 (9.2%)	-0.02	274 (9.5%)	268 (9.2%)	0.01	485 (5.7%)	464 (5.5%)	0.01	896 (6.9%)	877 (6.8%)	0.00
Pneumonia; n (%)	133 (8.4%)	136 (8.6%)	-0.01	242 (8.3%)	232 (8.0%)	0.01	843 (9.9%)	805 (9.5%)	0.01	1218 (9.4%)	1173 (9.0%)	0.01
Other Medications												
Use of ACE inhibitors; n (%)	385 (24.4%)	394 (25.0%)	-0.01	559 (19.3%)	548 (18.9%)	0.01	2,410 (28.3%)	2,442 (28.7%)	-0.01	3354 (25.8%)	3384 (26.1%)	-0.01
Use of ARBs; n (%)	215 (13.7%)	218 (13.8%)	0.00	353 (12.2%)	369 (12.7%)	-0.02	1,572 (18.5%)	1,589 (18.7%)	-0.01	2140 (16.5%)	2176 (16.8%)	-0.01
Use of Loop Diuretics - United; n (%)	177 (11.2%)	174 (11.0%)	0.01	230 (7.9%)	241 (8.3%)	-0.01	1,423 (16.7%)	1,427 (16.8%)	0.00	1830 (14.1%)	1842 (14.2%)	0.00
Use of other diuretics- United; n (%)	19 (1.2%)	26 (1.7%)	-0.04	47 (1.6%)	45 (1.6%)	0.00	176 (2.1%)	170 (2.0%)	0.01	242 (1.9%)	241 (1.9%)	0.00
Use of nitrates-United; n (%)	35 (2.2%)	38 (2.4%)	-0.01	57 (2.0%)	47 (1.6%)	0.03	382 (4.5%)	367 (4.3%)	0.01	474 (3.7%)	452 (3.5%)	0.01
Use of other hypertension drugs; n (%)	66 (4.2%)	70 (4.4%)	-0.01	117 (4.0%)	91 (3.3%)	0.05	522 (6.1%)	528 (6.2%)	0.00	705 (5.4%)	689 (5.3%)	0.00
Use of Anti-arrhythmics; n (%)	** (0.3%)	** (0.3%)	0.00	** (0.4%)	** (0.3%)	0.02	37 (0.4%)	40 (0.5%)	-0.01	#VALUE!	#VALUE!	#VALUE!
Use of COPD/asthma meds- United; n (%)	259 (16.4%)	230 (14.6%)	0.05	414 (14.3%)	484 (16.7%)	-0.07	1,627 (19.1%)	1,601 (18.8%)	0.01	2300 (17.7%)	2315 (17.8%)	0.00
Use of statins; n (%)	498 (31.6%)	529 (33.6%)	-0.04	680 (23.5%)	699 (24.1%)	-0.01	3,519 (41.3%)	3,513 (41.3%)	0.00	4697 (36.2%)	4741 (36.5%)	-0.01
Use of other lipid-lowering drugs; n (%)	86 (5.5%)	80 (5.1%)	0.02	130 (4.5%)	146 (5.0%)	-0.02	563 (6.6%)	571 (6.7%)	0.00	779 (6.0%)	797 (6.1%)	0.00
Use of antiplatelet agents; n (%)	87 (5.5%)	86 (5.5%)	0.00	167 (5.8%)	172 (5.9%)	0.00	766 (9.0%)	749 (8.8%)	0.01	1020 (7.9%)	1007 (7.8%)	0.00
Use of heparin and other low-molecular weight heparins; n (%)	245 (15.6%)	210 (13.3%)	0.07	** (0.2%)	** (0.1%)	0.03	986 (11.6%)	906 (10.6%)	0.03	#VALUE!	#VALUE!	#VALUE!
Use of NSAIDs; n (%)	338 (21.5%)	335 (21.3%)	0.00	686 (23.7%)	669 (23.1%)	0.01	1,714 (20.1%)	1,677 (19.7%)	0.01	2738 (21.1%)	2681 (20.6%)	0.01
Use of oral corticosteroids; n (%)	416 (26.4%)	420 (26.7%)	-0.01	748 (25.8%)	872 (30.1%)	-0.10	2,555 (30.0%)	2,516 (29.6%)	0.01	3719 (28.6%)	3808 (29.3%)	-0.02
Use of bisphosphonate (United); n (%)	54 (3.4%)	54 (3.4%)	0.00	44 (1.5%)	49 (1.7%)	-0.02	424 (5.0%)	429 (5.0%)	0.00	522 (4.0%)	532 (4.1%)	-0.01
Use of opioids- United; n (%)	830 (52.7%)	829 (52.6%)	0.00	1,743 (60.1%)	1,733 (59.8%)	0.01	4,168 (49.0%)	4,215 (49.5%)	-0.01	6741 (51.9%)	6777 (52.2%)	-0.01
Use of antidepressants; n (%)	460 (29.2%)	448 (28.4%)	0.02	717 (24.7%)	709 (24.5%)	0.00	2,420 (28.4%)	2,431 (28.6%)	0.00	3597 (27.7%)	3588 (27.6%)	0.00
Use of antipsychotics; n (%)	85 (5.4%)	81 (5.1%)	0.01	115 (4.0%)	115 (4.0%)	0.00	579 (6.8%)	570 (6.7%)	0.00	779 (6.0%)	766 (5.9%)	0.00
Labs												
Lab values- HbA1c (%) v3; n (%)	190 (12.1%)	169 (10.7%)	0.04	29 (1.0%)	29 (1.0%)	0.00	N/A	N/A	#VALUE!	219 (4.9%)	198 (4.4%)	0.02
Lab values- HbA1c (%) (within 3 months) v3; n (%)	110 (7.0%)	103 (6.5%)	0.02	17 (0.6%)	19 (0.7%)	-0.01	N/A	N/A	#VALUE!	127 (2.8%)	122 (2.7%)	0.01
Lab values- HbA1c (%) (within 6 months) v3; n (%)	190 (12.1%)	169 (10.7%)	0.04	29 (1.0%)	29 (1.0%)	0.00	N/A	N/A	#VALUE!	219 (4.9%)	198 (4.4%)	0.02
Lab values- BNP; n (%)	** (0.4%)	** (0.4%)	-0.01	0 (0.0%)	** (0.1%)	-0.04	N/A	N/A	#VALUE!	#VALUE!	#VALUE!	#VALUE!
Lab values- BNP (within 3 months); n (%)	** (0.4%)	** (0.4%)	0.00	0 (0.0%)	** (0.1%)	-0.04	N/A	N/A	#VALUE!	#VALUE!	#VALUE!	#VALUE!
Lab values- BNP (within 6 months); n (%)	** (0.4%)	** (0.5%)	-0.01	0 (0.0%)	** (0.1%)	-0.04	N/A	N/A	#VALUE!	#VALUE!	#VALUE!	#VALUE!
Lab values- BUN (mg/dl); n (%)	437 (27.7%)	449 (28.5%)	-0.02	35 (1.2%)	55 (1.9%)	-0.06	N/A	N/A	#VALUE!	472 (10.5%)	504 (11.3%)	-0.03
Lab values- BUN (mg/dl) (within 3 months); n (%)	290 (18.4%)	322 (20.4%)	-0.05	23 (0.8%)	39 (1.3%)	-0.05	N/A	N/A	#VALUE!	313 (7.0%)	361 (8.1%)	-0.04
Lab values- BUN (mg/dl) (within 6 months); n (%)	437 (27.7%)	449 (28.5%)	-0.02	35 (1.2%)	55 (1.9%)	-0.06	N/A	N/A	#VALUE!	472 (10.5%)	504 (11.3%)	-0.03
Lab values- Creatinine (mg/dl) v2; n (%)	452 (28.7%)	466 (29.6%)	-0.02	38 (1.3%)	59 (2.0%)	-0.05	N/A	N/A	#VALUE!	490 (11.0%)	525 (11.7%)	-0.02
Lab values- Creatinine (mg/dl) (within 3 months) v2; n (%)	301 (19.1%)	337 (21.4%)	-0.06	25 (0.9%)	42 (1.4%)	-0.05	N/A	N/A	#VALUE!	326 (7.3%)	379 (8.5%)	-0.04
Lab values- Creatinine (mg/dl) (within 6 months) v2; n (%)	452 (28.7%)	466 (29.6%)	-0.02	38 (1.3%)	59 (2.0%)	-0.05	N/A	N/A	#VALUE!	490 (11.0%)	525 (11.7%)	-0.02
Lab values- HDL level (mg/dl); n (%)	242 (15.4%)	263 (16.7%)	-0.04	21 (0.7%)	32 (1.1%)	-0.04	N/A	N/A	#VALUE!	263 (5.9%)	295 (6.6%)	-0.03
Lab values- HDL level (mg/dl) (within 3 months); n (%)	123 (7.8%)	146 (9.3%)	-0.05	** (0.2%)	19 (0.7%)	-0.07	N/A	N/A	#VALUE!	#VALUE!	165 (3.7%)	#VALUE!
Lab values- HDL level (mg/dl) (within 6 months); n (%)	242 (15.4%)	263 (16.7%)	-0.04	21 (0.7%)	32 (1.1%)	-0.04	N/A	N/A	#VALUE!	263 (5.9%)	295 (6.6%)	-0.03
Lab values- LDL level (mg/dl) v2; n (%)	244 (15.5%)	264 (16.8%)	-0.04	24 (0.8%)	32 (1.1%)	-0.03	N/A	N/A	#VALUE!	268 (6.0%)	296 (6.6%)	-0.02
Lab values- LDL level (mg/dl) (within 3 months) v2; n (%)	128 (8.1%)	145 (9.2%)	-0.04	** (0.3%)	18 (0.6%)	-0.04	N/A	N/A	#VALUE!	#VALUE!	163 (3.6%)	#VALUE!
Lab values- LDL level (mg/dl) (within 6 months) v2; n (%)	244 (15.5%)	264 (16.8%)	-0.04	24 (0.8%)	32 (1.1%)	-0.03	N/A	N/A	#VALUE!	268 (6.0%)	296 (6.6%)	-0.02
Lab values- NT-proBNP; n (%)	** (0.1%)	** (0.1%)	0.00	0 (0.0%)	0 (0.0%)	#DIV/0!	N/A	N/A	#VALUE!	#VALUE!	#VALUE!	#VALUE!
Lab values- NT-proBNP (within 3 months); n (%)	** (0.1%)	** (0.1%)	0.00	0 (0.0%)	0 (0.0%)	#DIV/0!	N/A	N/A	#VALUE!	#VALUE!	#VALUE!	#VALUE!
Lab values- NT-proBNP (within 6 months); n (%)	** (0.1%)	** (0.1%)	0.00	0 (0.0%)	0 (0.0%)	#DIV/0!	N/A	N/A	#VALUE!	#VALUE!	#VALUE!	#VALUE!
Lab values- Total cholesterol (mg/dl) v2; n (%)	245 (15.6%)	263 (16.7%)	-0.03	20 (0.7%)	32 (1.1%)	-0.04	N/A	N/A	#VALUE!	265 (5.9%)	295 (6.6%)	-0.03
Lab values- Total cholesterol (mg/dl) (within 3 months) v2; n (%)	125 (7.9%)	145 (9.2%)	-0.05	** (0.2%)	19 (0.7%)	-0.07	N/A	N/A	#VALUE!	#VALUE!	164 (3.7%)	#VALUE!
Lab values- Total cholesterol (mg/dl) (within 6 months) v2; n (%)	245 (15.6%)	263 (16.7%)	-0.03	20 (0.7%)	32 (1.1%)	-0.04	N/A	N/A	#VALUE!	265 (5.9%)	295 (6.6%)	-0.03
Lab values- Triglyceride level (mg/dl); n (%)	244 (15.5%)	265 (16.8%)	-0.04	21 (0.7%)	32 (1.1%)	-0.04	N/A	N/A	#VALUE!	265 (5.9%)	297 (6.6%)	-0.03
Lab values- Triglyceride level (mg/dl) (within 3 months); n (%)	126 (8.0%)	146 (9.3%)	-0.05	** (0.2%)	18 (0.6%)	-0.06	N/A	N/A	#VALUE!	#VALUE!	164 (3.7%)	#VALUE!

Appendix B

Lab values- Triglyceride level (mg/dl) (within 6 months); n (%)	244 (15.5%)	265 (16.8%)	-0.04	21 (0.7%)	32 (1.1%)	-0.04	N/A	N/A	#VALUE!	265 (5.9%)	297 (6.6%)	-0.03
Lab result number- HbA1c (%) mean (only 2 to 20 included) v4	189	169		27	28		N/A	N/A	#VALUE!	216	197	
...mean (sd)	6.88 (1.71)	6.69 (1.48)	0.12	7.17 (1.18)	7.17 (1.32)	0.00	N/A	N/A	#VALUE!	6.92 (1.66)	6.76 (1.46)	0.10
...Missing; n (%)	1,386 (88.0%)	1,406 (89.3%)	-0.04	2,872 (99.1%)	2,871 (99.0%)	0.01	N/A	N/A	#VALUE!	4,258 (95.2%)	4,277 (95.6%)	-0.02
Lab result number- BNP mean v2	7	8		-	2		N/A	N/A	#VALUE!	7	10	
...mean (sd)	94.99 (97.03)	197.30 (393.25)	-0.36	- (-)	32.00 (28.28)	#VALUE!	N/A	N/A	#VALUE!	#VALUE!	164.24 (393.40)	#VALUE!
...Missing; n (%)	1,568 (99.6%)	1,567 (99.5%)	0.01	2,899 (100.0%)	2,897 (99.9%)	0.04	N/A	N/A	#VALUE!	4,467 (99.8%)	4,464 (99.8%)	0.00
Lab result number- BUN (mg/dl) mean v2	437	449		35	55		N/A	N/A	#VALUE!	472	504	
...mean (sd)	18.11 (8.11)	17.57 (7.17)	0.07	17.18 (8.16)	16.40 (6.60)	0.11	N/A	N/A	#VALUE!	18.04 (8.12)	17.44 (7.12)	0.08
...Missing; n (%)	1,138 (72.3%)	1,126 (71.5%)	0.02	2,864 (98.8%)	2,844 (98.1%)	0.06	N/A	N/A	#VALUE!	4,002 (89.5%)	3,970 (88.7%)	0.03
Lab result number- Creatinine (mg/dl) mean (only 0.1 to 15 included) v3	447	460		37	57		N/A	N/A	#VALUE!	484	517	
...mean (sd)	0.99 (0.36)	0.97 (0.28)	0.06	0.95 (0.32)	0.95 (0.28)	0.00	N/A	N/A	#VALUE!	0.99 (0.36)	0.97 (0.28)	0.06
...Missing; n (%)	1,128 (71.6%)	1,115 (70.8%)	0.02	2,862 (98.7%)	2,842 (98.0%)	0.05	N/A	N/A	#VALUE!	3,990 (89.2%)	3,957 (88.4%)	0.03
Lab result number- HDL level (mg/dl) mean (only <=5000 included) v2	242	263		21	32		N/A	N/A	#VALUE!	263	295	
...mean (sd)	52.41 (17.47)	53.27 (16.64)	-0.05	48.62 (13.24)	44.83 (11.26)	0.31	N/A	N/A	#VALUE!	52.11 (17.22)	52.35 (16.18)	-0.01
...Missing; n (%)	1,333 (84.6%)	1,312 (83.3%)	0.04	2,878 (99.3%)	2,867 (98.9%)	0.04	N/A	N/A	#VALUE!	4,211 (94.1%)	4,179 (93.4%)	0.03
Lab result number- LDL level (mg/dl) mean (only <=5000 included) v2	239	262		21	30		N/A	N/A	#VALUE!	260	292	
...mean (sd)	101.44 (33.15)	100.96 (36.42)	0.01	103.33 (25.48)	94.27 (29.11)	0.33	N/A	N/A	#VALUE!	101.59 (32.68)	100.27 (35.82)	0.04
...Missing; n (%)	1,336 (84.8%)	1,313 (83.4%)	0.04	2,878 (99.3%)	2,869 (99.0%)	0.03	N/A	N/A	#VALUE!	4,214 (94.2%)	4,182 (93.5%)	0.03
Lab result number- Total cholesterol (mg/dl) mean (only <=5000 included) v2	245	263		20	32		N/A	N/A	#VALUE!	265	295	
...mean (sd)	180.67 (41.98)	181.58 (40.29)	-0.02	180.45 (27.83)	180.69 (46.88)	-0.01	N/A	N/A	#VALUE!	180.65 (41.20)	181.48 (41.11)	-0.02
...Missing; n (%)	1,330 (84.4%)	1,312 (83.3%)	0.03	2,879 (99.3%)	2,867 (98.9%)	0.04	N/A	N/A	#VALUE!	4,209 (94.1%)	4,179 (93.4%)	0.03
Lab result number- Triglyceride level (mg/dl) mean (only <=5000 included) v2	244	265		21	32		N/A	N/A	#VALUE!	265	297	
...mean (sd)	134.91 (69.13)	136.25 (69.41)	-0.02	143.67 (74.18)	177.70 (98.70)	-0.39	N/A	N/A	#VALUE!	135.60 (69.66)	140.72 (73.17)	-0.07
...Missing; n (%)	1,331 (84.5%)	1,310 (83.2%)	0.04	2,878 (99.3%)	2,867 (98.9%)	0.04	N/A	N/A	#VALUE!	4,209 (94.1%)	4,177 (93.4%)	0.03
Lab result number- Hemoglobin mean (only >0 included)	368	376		25	49		N/A	N/A	#VALUE!	393	425	
...mean (sd)	13.18 (1.94)	13.23 (1.89)	-0.03	12.30 (3.19)	12.67 (3.06)	-0.12	N/A	N/A	#VALUE!	13.12 (2.04)	13.17 (2.06)	-0.02
...Missing; n (%)	1,207 (76.6%)	1,199 (76.1%)	0.01	2,874 (99.1%)	2,850 (98.3%)	0.07	N/A	N/A	#VALUE!	4,081 (91.2%)	4,049 (90.5%)	0.02
Lab result number- Serum sodium mean (only >90 and <190 included)	431	438		35	53		N/A	N/A	#VALUE!	466	491	
...mean (sd)	140.16 (2.94)	140.09 (2.65)	0.03	139.41 (2.22)	138.69 (3.08)	0.27	N/A	N/A	#VALUE!	140.10 (2.90)	139.94 (2.70)	0.06
...Missing; n (%)	1,144 (72.6%)	1,137 (72.2%)	0.01	2,864 (98.8%)	2,846 (98.2%)	0.05	N/A	N/A	#VALUE!	4,008 (89.6%)	3,983 (89.0%)	0.02
Lab result number- Albumin mean (only >0 and <=10 included)	393	384		27	45		N/A	N/A	#VALUE!	420	429	
...mean (sd)	4.07 (0.42)	4.06 (0.44)	0.02	3.88 (0.89)	3.96 (0.75)	-0.10	N/A	N/A	#VALUE!	4.06 (0.46)	4.05 (0.48)	0.02
...Missing; n (%)	1,182 (75.0%)	1,191 (75.6%)	-0.01	2,872 (99.1%)	2,854 (98.4%)	0.06	N/A	N/A	#VALUE!	4,054 (90.6%)	4,045 (90.4%)	0.01
Lab result number- Glucose (fasting or random) mean (only 10-1000 included)	430	438		33	54		N/A	N/A	#VALUE!	463	492	
...mean (sd)	114.69 (54.46)	113.20 (40.43)	0.03	141.69 (58.99)	149.10 (79.94)	-0.11	N/A	N/A	#VALUE!	116.61 (54.85)	117.14 (46.40)	-0.01
...Missing; n (%)	1,145 (72.7%)	1,137 (72.2%)	0.01	2,866 (98.9%)	2,845 (98.1%)	0.07	N/A	N/A	#VALUE!	4,011 (89.7%)	3,982 (89.0%)	0.02
Lab result number- Potassium mean (only 1-7 included)	439	451		34	52		N/A	N/A	#VALUE!	473	503	
...mean (sd)	4.36 (0.43)	4.32 (0.43)	0.09	4.11 (0.33)	4.32 (0.38)	-0.59	N/A	N/A	#VALUE!	4.34 (0.42)	4.32 (0.43)	0.05
...Missing; n (%)	1,136 (72.1%)	1,124 (71.4%)	0.02	2,865 (98.8%)	2,847 (98.2%)	0.05	N/A	N/A	#VALUE!	4,001 (89.4%)	3,971 (88.8%)	0.02
Comorbidity Scores												
CCI (180 days)- ICD9 and ICD10 v2												
...mean (sd)	2.24 (2.49)	2.23 (2.44)	0.00	1.54 (2.15)	1.51 (2.17)	0.01	2.33 (2.65)	2.27 (2.61)	0.02	2.14 (2.53)	2.10 (2.50)	0.02
Non-Frailty; n (%)	758 (48.1%)	742 (47.1%)	0.02	1,188 (41.0%)	1,206 (41.6%)	-0.01	227 (2.7%)	162 (1.9%)	0.05	2,173 (16.7%)	2,110 (16.2%)	0.01
Frailty Score (mean); Empirical Version 365 days, v2												
...mean (sd)	0.20 (0.07)	0.20 (0.07)	0.00	0.17 (0.06)	0.17 (0.06)	0.00	0.11 (0.08)	0.11 (0.08)	0.00	0.13 (0.07)	0.13 (0.07)	0.00
Healthcare Utilization												
Any hospitalization; n (%)	1,171 (74.3%)	1,168 (74.2%)	0.00	2,898 (100.0%)	2,899 (100.0%)	#DIV/0!	6,540 (76.8%)	6,597 (77.5%)	-0.02	10,609 (81.7%)	10,664 (82.1%)	-0.01
Any hospitalization within prior 30 days; n (%)	1,051 (66.7%)	1,076 (68.3%)	-0.03	2,867 (98.9%)	2,861 (98.7%)	0.02	6,186 (72.7%)	6,226 (73.2%)	-0.01	10104 (77.8%)	10163 (78.3%)	-0.01
Any hospitalization during prior 31-180 days; n (%)	285 (18.1%)	260 (16.5%)	0.04	345 (11.9%)	385 (13.3%)	-0.04	1,609 (18.9%)	1,500 (17.6%)	0.03	2239 (17.2%)	2145 (16.5%)	0.02
Internal medicine/family medicine visits; n (%)	1,414 (89.8%)	1,433 (91.0%)	-0.04	2,306 (79.5%)	2,292 (79.1%)	0.01	7,909 (92.9%)	8,030 (94.3%)	-0.06	11629 (89.6%)	11755 (90.5%)	-0.03
Internal medicine/family medicine visits (30 days prior) v2; n (%)	1,257 (79.8%)	1,288 (81.8%)	-0.05	1,654 (57.1%)	1,591 (54.9%)	0.04	7,300 (85.8%)	7,400 (86.9%)	-0.03	10211 (78.6%)	10279 (79.2%)	-0.01
Internal medicine/family medicine visits (31 to 180 days prior) v2; n (%)	1,105 (70.2%)	1,103 (70.0%)	0.00	1,893 (65.3%)	1,870 (64.5%)	0.02	6,307 (74.1%)	6,289 (73.9%)	0.00	9305 (71.7%)	9262 (71.3%)	0.01
Cardiologist visit; n (%)	681 (43.2%)	702 (44.6%)	-0.03	626 (21.6%)	642 (22.1%)	-0.01	4,247 (49.9%)	4,211 (49.5%)	0.01	5554 (42.8%)	5555 (42.8%)	0.00
Number of Cardiologist visits (30 days prior); n (%)	496 (31.5%)	500 (31.7%)	0.00	377 (13.0%)	359 (12.4%)	0.02	3,097 (36.4%)	3,041 (35.7%)	0.01	3970 (30.6%)	3900 (30.0%)	0.01
Number of Cardiologist visits (31 to 180 days prior); n (%)	315 (20.0%)	327 (20.8%)	-0.02	351 (12.1%)	355 (12.2%)	0.00	2,225 (26.1%)	2,169 (25.5%)	0.01	2891 (22.3%)	2851 (22.0%)	0.01
Electrocardiogram v2; n (%)	897 (57.0%)	888 (56.4%)	0.01	1,056 (36.4%)	1,062 (36.6%)	0.00	5,347 (62.8%)	5,402 (63.5%)	-0.01	7300 (56.2%)	7352 (56.6%)	-0.01
Use of glucose test strips; n (%)	27 (1.7%)	21 (1.3%)	0.03	31 (1.1%)	30 (1.0%)	0.01	131 (1.5%)	130 (1.5%)	0.00	189 (1.5%)	181 (1.4%)	0.01
Dialysis; n (%)	** (0.1%)	0 (0.0%)	0.04	** (0.2%)	** (0.2%)	0.00	<11 (0.1%)	<11 (0.1%)	0.00	#VALUE!	#VALUE!	#VALUE!
number of different/distinct medication prescriptions												
...mean (sd)	9.11 (5.28)	9.12 (5.40)	0.00	9.08 (5.24)	9.08 (5.82)	0.00	9.99 (5.30)	9.94 (5.25)	0.01	9.68 (5.28)	9.65 (5.40)	0.01
Number of Hospitalizations												
...mean (sd)	0.97 (0.80)	0.99 (0.84)	-0.02	1.29 (0.70)	1.29 (0.64)	0.00	1.11 (0.92)	1.10 (0.89)	0.01	1.13 (0.86)	1.13 (0.83)	0.00

Appendix B

Number of hospital days												
...mean (sd)	5.10 (5.19)	5.11 (7.06)	0.00	7.00 (6.55)	6.98 (8.63)	0.00	6.22 (6.56)	6.04 (8.07)	0.02	6.26 (6.41)	6.14 (8.08)	0.02
Number of Emergency Department (ED) visits v3												
...mean (sd)	2.07 (2.62)	2.04 (1.86)	0.01	2.58 (5.38)	2.66 (7.21)	-0.01	2.15 (2.27)	2.12 (1.90)	0.01	2.24 (3.27)	2.23 (3.79)	0.00
Number of Office visits												
...mean (sd)	5.47 (4.54)	5.63 (4.70)	-0.03	5.58 (5.27)	5.57 (5.04)	0.00	13.86 (15.96)	13.58 (15.05)	0.02	10.99 (13.25)	10.83 (12.52)	0.01
Number of internal medicine/family medicine visits												
...mean (sd)	11.72 (18.22)	9.93 (12.31)	0.12	6.37 (11.98)	6.10 (10.85)	0.02	12.38 (12.28)	11.56 (12.82)	0.07	10.96 (13.08)	10.14 (12.34)	0.06
Number of Cardiologist visits												
...mean (sd)	1.41 (3.19)	1.57 (3.56)	-0.05	0.60 (1.92)	0.57 (1.90)	0.02	1.91 (4.01)	1.88 (3.85)	0.01	1.56 (3.55)	1.55 (3.47)	0.00
Number electrocardiograms received v2												
...mean (sd)	1.26 (1.97)	1.25 (1.69)	0.01	0.65 (1.20)	0.66 (1.17)	-0.01	1.42 (1.74)	1.40 (1.64)	0.01	1.23 (1.67)	1.22 (1.55)	0.01
Number of HbA1c tests ordered												
...mean (sd)	0.36 (0.67)	0.34 (0.65)	0.03	0.21 (0.57)	0.22 (0.55)	-0.02	0.38 (0.71)	0.37 (0.70)	0.01	0.34 (0.68)	0.33 (0.66)	0.01
Number of glucose tests ordered												
...mean (sd)	0.41 (5.52)	0.41 (5.16)	0.00	0.14 (0.62)	0.15 (0.64)	-0.02	0.19 (0.89)	0.18 (0.69)	0.01	0.21 (2.07)	0.20 (1.91)	0.01
Number of lipid tests ordered												
...mean (sd)	0.49 (0.78)	0.47 (0.74)	0.03	0.35 (0.80)	0.34 (0.78)	0.01	0.53 (0.77)	0.53 (0.75)	0.00	0.48 (0.78)	0.48 (0.76)	0.00
Total N distinct ICD9/ICD10 diagnoses at the 3rd digit level Copy												
...mean (sd)	9.94 (12.57)	10.03 (12.80)	-0.01	7.61 (11.53)	7.46 (11.79)	0.01	12.03 (13.75)	11.42 (13.25)	0.05	10.79 (13.14)	10.37 (12.88)	0.03
For PS												
Hemorrhagic stroke+Other cerebrovascular disease+Cerebrovascular procedure (for PS); n (%)	22 (1.4%)	29 (1.8%)	-0.03	23 (0.8%)	29 (1.0%)	-0.02	178 (2.1%)	183 (2.2%)	-0.01	223 (1.7%)	241 (1.9%)	-0.02
Major trauma potentially causing prolonged immobili	189 (12.0%)	189 (12.0%)	#DIV/0!	313 (10.8%)	301 (10.4%)	#DIV/0!	836 (9.8%)	771 (9.1%)	#DIV/0!	313 (10.8%)	301 (10.4%)	0.01
Occurrence of creatinine tests ordered (for PS); n (%)	112 (7.1%)	133 (8.4%)	-0.05	183 (6.3%)	194 (6.7%)	-0.02	898 (10.6%)	898 (10.6%)	0.00	1193 (9.2%)	1225 (9.4%)	-0.01
Occurrence of BUN tests ordered (for PS); n (%)	63 (4.0%)	58 (3.7%)	0.02	109 (3.8%)	115 (4.0%)	-0.01	514 (6.0%)	500 (5.9%)	0.00	686 (5.3%)	673 (5.2%)	0.00
Occurrence of chronic renal insufficiency w/o CKD (for PS) v2; n (%)	106 (6.7%)	105 (6.7%)	0.00	96 (3.3%)	97 (3.3%)	0.00	656 (7.7%)	687 (8.1%)	-0.01	858 (6.6%)	889 (6.8%)	-0.01
Chronic kidney disease Stage 1-2 (for PS); n (%)	27 (1.7%)	30 (1.9%)	-0.02	21 (0.7%)	22 (0.8%)	-0.01	153 (1.8%)	155 (1.8%)	0.00	201 (1.5%)	207 (1.6%)	-0.01
Chronic kidney disease Stage 3-6 (for PS); n (%)	117 (7.4%)	132 (8.4%)	-0.04	73 (2.5%)	79 (2.7%)	-0.01	724 (8.5%)	715 (8.4%)	0.00	914 (7.0%)	926 (7.1%)	0.00
Acute kidney injury; n (%)	180 (11.4%)	191 (12.1%)	#DIV/0!	239 (8.2%)	264 (9.1%)	#DIV/0!	1,052 (12.4%)	1,062 (12.5%)	#DIV/0!	239 (8.2%)	264 (9.1%)	-0.03
Bladder stones+Kidney stones (for PS); n (%)	52 (3.3%)	49 (3.1%)	0.01	83 (2.9%)	89 (3.1%)	-0.01	302 (3.5%)	260 (3.1%)	0.02	437 (3.4%)	398 (3.1%)	0.02
Alcohol abuse or dependence+Drug abuse or dependence (for PS); n (%)	114 (7.2%)	105 (6.7%)	0.02	132 (4.6%)	129 (4.4%)	0.01	186 (2.2%)	179 (2.1%)	0.01	432 (3.3%)	413 (3.2%)	0.01
Other atherosclerosis+Cardiac conduction disorders+Other CVD (for PS) v2 Copy; n (%)	327 (20.8%)	310 (19.7%)	0.03	506 (17.5%)	526 (18.1%)	-0.02	1,794 (21.1%)	1,779 (20.9%)	0.00	2627 (20.2%)	2615 (20.1%)	0.00
Previous cardiac procedure (CABG or PTCA or Stent) + History of CABG or PTCA (for PS) v3; n (%)	59 (3.7%)	74 (4.7%)	-0.05	54 (1.9%)	51 (1.8%)	0.01	631 (7.4%)	648 (7.6%)	-0.01	744 (5.7%)	773 (6.0%)	-0.01
Diabetes with complication; n (%)	192 (12.2%)	203 (12.9%)	#DIV/0!	230 (7.9%)	233 (8.0%)	#DIV/0!	1,003 (11.8%)	973 (11.4%)	#DIV/0!	230 (7.9%)	233 (8.0%)	0.00
Delirium + Psychosis (for PS); n (%)	107 (6.8%)	100 (6.3%)	0.02	123 (4.2%)	121 (4.2%)	0.00	729 (8.6%)	682 (8.0%)	0.02	959 (7.4%)	903 (7.0%)	0.02
Any use of Meglitinides (for PS); n (%)	** (0.1%)	** (0.3%)	-0.04	** (0.1%)	** (0.1%)	0.00	22 (0.3%)	33 (0.4%)	-0.02	#VALUE!	#VALUE!	#VALUE!
Any use of AGIs (for PS); n (%)	0 (0.0%)	** (0.2%)	-0.06	0 (0.0%)	** (0.1%)	-0.04	<11 (0.1%)	<11 (0.1%)	0.00	#VALUE!	#VALUE!	#VALUE!
CKD stage 3-6 + dialysis (for PS); n (%)	120 (7.6%)	133 (8.4%)	-0.03	78 (2.7%)	85 (2.9%)	-0.01	730 (8.6%)	721 (8.5%)	0.00	928 (7.1%)	939 (7.2%)	0.00
Use of thiazide; n (%)	149 (9.5%)	147 (9.3%)	0.01	211 (7.3%)	195 (6.7%)	0.02	907 (10.7%)	938 (11.0%)	-0.01	1267 (9.8%)	1280 (9.9%)	0.00
Use of beta blockers; n (%)	366 (23.2%)	379 (24.1%)	-0.02	562 (19.4%)	546 (18.8%)	0.02	2,831 (33.3%)	2,870 (33.7%)	-0.01	3759 (28.9%)	3795 (29.2%)	-0.01
Use of calcium channel blockers; n (%)	297 (18.9%)	313 (19.9%)	-0.03	447 (15.1%)	441 (15.2%)	0.00	2,270 (26.7%)	2,240 (26.3%)	0.01	3004 (23.1%)	2994 (23.1%)	0.00
All antidiabetic medications except insulin; n (%)	241 (15.3%)	239 (15.2%)	0.00	337 (11.6%)	359 (12.4%)	-0.02	1,433 (16.8%)	1,454 (17.1%)	-0.01	2011 (15.5%)	2052 (15.8%)	-0.01
DM Medications - Insulin Copy; n (%)	96 (6.1%)	96 (6.1%)	0.00	141 (4.9%)	153 (5.3%)	-0.02	380 (4.5%)	421 (4.9%)	-0.02	617 (4.8%)	670 (5.2%)	-0.02
Use of Low Intensity Statins; n (%)	312 (19.8%)	344 (21.8%)	-0.05	391 (13.5%)	430 (14.8%)	-0.04	2,353 (27.6%)	2,373 (27.9%)	-0.01	3056 (23.5%)	3147 (24.2%)	-0.02
Use of High Intensity Statins; n (%)	190 (12.1%)	190 (12.1%)	0.00	284 (9.8%)	271 (9.3%)	0.02	1,202 (14.1%)	1,200 (14.1%)	0.00	1676 (12.9%)	1661 (13.8%)	0.00
Malignant hypertension; n (%)	107 (6.8%)	152 (9.7%)	-0.11	966 (33.3%)	1,037 (35.8%)	-0.05	2,872 (33.7%)	3,118 (36.6%)	-0.06	3945 (30.4%)	4307 (33.2%)	-0.06
Cardiovascular stress test; n (%)	** (0.4%)	** (0.1%)	0.06	** (0.2%)	12 (0.4%)	-0.04	58 (0.7%)	37 (0.4%)	0.04	#VALUE!	#VALUE!	#VALUE!
Echocardiogram; n (%)	278 (17.7%)	320 (20.3%)	-0.07	544 (18.8%)	574 (19.8%)	-0.03	1,743 (20.5%)	1,815 (21.3%)	-0.02	2565 (19.8%)	2709 (20.9%)	-0.03
Number of BNP tests												
...mean (sd)	0.08 (0.35)	0.08 (0.30)	0.00	0.04 (0.21)	0.05 (0.25)	-0.04	0.09 (0.34)	0.09 (0.34)	0.00	0.08 (0.32)	0.08 (0.32)	0.00
Number of Cardiac biomarkers tests (troponin, CK-MBs, Myoglobin, CPK)												
...mean (sd)	0.31 (1.04)	0.37 (1.19)	-0.05	0.24 (0.91)	0.26 (0.93)	-0.02	0.23 (0.59)	0.23 (0.58)	0.00	0.24 (0.74)	0.25 (0.77)	0.00
Number of Ambulatory Blood pressure monitoring tests												
...mean (sd)	0.00 (0.05)	0.00 (0.00)	0.00	0.00 (0.02)	0.00 (0.03)	0.00	0.00 (0.03)	0.00 (0.06)	0.00	0.00 (0.03)	0.00 (0.05)	0.00
N of days on antihypertensive medications during baseline												
...mean (sd)	80.03 (79.04)	83.44 (80.30)	-0.04	62.02 (76.84)	61.63 (76.67)	0.01	105.69 (77.60)	106.89 (77.05)	-0.02	92.83 (77.61)	93.94 (77.37)	0.00
N of days in database anytime prior												
...mean (sd)	1,668.43 (1,266.59)	1,713.11 (1,303.00)	-0.03	1,982.39 (1,383.61)	2,031.47 (1,419.09)	-0.04	628.51 (384.70)	605.19 (348.57)	0.06	1056.91 (847.86)	1058.00 (857.35)	0.00
Mean Copay for per prescription cost (charges in U.S. \$) (180-1 day prior)												
...mean (sd)	23.17 (31.74)	23.95 (33.91)	-0.02	14.78 (20.67)	14.89 (66.84)	0.00	108.61 (103.27)	109.54 (113.72)	-0.01	77.30 (84.90)	78.03 (98.05)	0.00
...Missing; n (%)	94 (6.0%)	90 (5.7%)	0.01	210 (7.2%)	221 (7.6%)	-0.02	286 (3.4%)	297 (3.5%)	-0.01	590 (4.5%)	608 (4.7%)	-0.01
Colonoscopy; n (%)	61 (3.9%)	61 (3.9%)	0.00	127 (4.4%)	121 (4.2%)	0.01	353 (4.1%)	333 (3.9%)	0.01	541 (4.2%)	515 (4.0%)	0.01
Fecal occult blood (FOB) test; n (%)	52 (3.3%)	54 (3.4%)	-0.01	76 (2.6%)	76 (2.6%)	0.00	244 (2.9%)	224 (2.6%)	0.02	372 (2.9%)	354 (2.7%)	0.01
Flu vaccine; n (%)	253 (16.1%)	238 (15.1%)	0.03	270 (9.3%)	279 (9.6%)	-0.01	2,434 (28.6%)	2,417 (28.4%)	0.00	2957 (22.8%)	2934 (22.6%)	0.00
Mammogram; n (%)	154 (9.8%)	155 (9.8%)	0.00	262 (9.0%)	253 (8.7%)	0.01	898 (10.6%)	887 (10.4%)	0.01	1314 (10.1%)	1295 (10.0%)	0.00
Pap smear; n (%)	62 (3.9%)	51 (3.2%)	0.04	199 (6.9%)	195 (6.7%)	0.01	215 (2.5%)	206 (2.4%)	0.01	476 (3.7%)	452 (3.5%)	0.01
Pneumonia vaccine; n (%)	213 (13.5%)	220 (14.0%)	-0.01	173 (6.0%)	164 (5.7%)	0.01	1,654 (19.4%)	1,602 (18.8%)	0.02	2040 (15.7%)	1986 (15.3%)	0.01

Appendix B

PSA test or Prostate exam for DRE; n (%)	157 (10.0%)	154 (9.8%)	0.01	234 (8.1%)	237 (8.2%)	0.00	886 (10.4%)	872 (10.2%)	0.01	1277 (9.8%)	1263 (9.7%)	0.00
Bone mineral density; n (%)	67 (4.3%)	60 (3.8%)	0.03	51 (1.8%)	49 (1.7%)	0.01	382 (4.5%)	381 (4.5%)	0.00	500 (3.9%)	490 (3.8%)	0.01
Use of CNS stimulants; n (%)	15 (1.0%)	** (0.6%)	0.04	47 (1.6%)	59 (2.0%)	-0.03	35 (0.4%)	34 (0.4%)	0.00	97 (0.7%)	#VALUE!	#VALUE!
Use of estrogens, progestins, androgens; n (%)	86 (5.5%)	78 (5.0%)	0.02	355 (12.2%)	323 (11.1%)	0.03	311 (3.7%)	299 (3.5%)	0.01	752 (5.8%)	700 (5.4%)	0.02
Use of Angiogenesis inhibitors; n (%)	0 (0.0%)	** (0.1%)	-0.04	** (0.1%)	** (0.2%)	-0.03	10 (0.1%)	8 (0.1%)	0.00	#VALUE!	#VALUE!	#VALUE!
Use of Oral Immunosuppressants; n (%)	** (0.6%)	** (0.3%)	0.04	27 (0.9%)	13 (0.4%)	0.06	6 (0.1%)	12 (0.1%)	0.00	#VALUE!	#VALUE!	#VALUE!
Use of fondaparinux or Bivalirudin; n (%)	** (0.5%)	** (0.4%)	0.01	20 (0.7%)	16 (0.6%)	0.01	19 (0.2%)	24 (0.3%)	-0.02	#VALUE!	#VALUE!	#VALUE!
Use of other direct thrombin inhibitors (Ilepirudin, 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%)	0 (0.0%)	#DIV/0!	** (0.1%)	** (0.1%)	0.00	1 (0.0%)	1 (0.0%)	#DIV/0!	#VALUE!	#VALUE!	#VALUE!
Use of Ticagrelor; n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	** (0.1%)	** (0.1%)	0.00	14 (0.2%)	12 (0.1%)	0.03	#VALUE!	#VALUE!	#VALUE!
Number of D-dimer tests												
...mean (sd)	0.08 (0.29)	0.07 (0.31)	0.03	0.07 (0.29)	0.06 (0.29)	0.03	0.08 (0.30)	0.09 (0.30)	-0.03	0.08 (0.30)	0.08 (0.30)	0.00
Numbe of CRP, high-sensitivity CRP tests												
...mean (sd)	0.17 (0.67)	0.16 (0.70)	0.01	0.14 (0.61)	0.14 (0.58)	0.00	0.16 (0.86)	0.16 (0.69)	0.00	0.16 (0.79)	0.16 (0.67)	0.00
Number of PT or aPTT tests												
...mean (sd)	1.03 (2.00)	1.02 (1.76)	0.01	0.71 (1.58)	0.72 (1.57)	-0.01	0.56 (0.92)	0.55 (1.01)	0.01	0.65 (1.26)	0.64 (1.26)	0.00
Number of Bleeding time tests												
...mean (sd)	0.00 (0.00)	0.00 (0.00)	#DIV/0!	0.00 (0.03)	0.00 (0.03)	0.00	0.00 (0.02)	0.00 (0.02)	0.00	0.00 (0.02)	0.00 (0.02)	0.00
HAS-BLED Score (ICD-9 and ICD-10), 180 days												
...mean (sd)	2.89 (1.02)	2.93 (1.07)	-0.04	2.37 (1.00)	2.37 (0.99)	0.00	3.49 (0.82)	3.48 (0.81)	0.01	3.17 (0.89)	3.17 (0.89)	0.00
N of Generic name drugs												
...mean (sd)	18.54 (17.31)	18.70 (19.99)	-0.01	13.69 (11.34)	13.71 (12.94)	0.00	18.66 (14.45)	18.74 (16.05)	-0.01	17.54 (14.21)	17.61 (15.96)	0.00
N of Brand name drugs												
...mean (sd)	3.61 (6.03)	3.61 (4.03)	0.00	3.54 (5.26)	3.63 (3.55)	-0.02	3.99 (6.55)	3.97 (4.25)	0.00	3.84 (6.22)	3.85 (4.08)	0.00
Use of clopidogrel ; n (%)	60 (3.8%)	63 (4.0%)	-0.01	91 (3.1%)	100 (3.4%)	-0.02	539 (6.3%)	543 (6.4%)	0.00	690 (5.3%)	706 (5.4%)	0.00
Systemic embolism; n (%)	62 (3.9%)	53 (3.4%)	0.03	145 (5.0%)	156 (5.4%)	-0.02	216 (2.5%)	210 (2.5%)	0.00	423 (3.2%)	419 (3.2%)	0.01
DVT; n (%)	1,575 (100.0%)	1,575 (100.0%)	#DIV/0!	2,897 (99.9%)	2,898 (100.0%)	-0.04	8,504 (99.9%)	8,503 (99.9%)	0.00	12976 (99.9%)	12976 (99.9%)	0.00
Post-thrombotic syndrome; n (%)	** (0.3%)	** (0.3%)	#DIV/0!	** (0.2%)	** (0.2%)	#DIV/0!	23 (0.3%)	20 (0.2%)	#DIV/0!	** (0.2%)	** (0.2%)	0.00
PE; n (%)	163 (10.3%)	158 (10.0%)	0.01	141 (4.9%)	132 (4.6%)	0.01	599 (7.0%)	612 (7.2%)	-0.01	903 (7.0%)	902 (6.9%)	0.00
Coagulation defects; n (%)	43 (2.7%)	46 (2.9%)	#DIV/0!	110 (3.8%)	110 (3.8%)	#DIV/0!	159 (1.9%)	141 (1.7%)	#DIV/0!	110 (3.8%)	110 (3.8%)	0.00
Diabetes: 1 inpatient or 2 outpatient claims within 18	391 (24.8%)	393 (25.0%)	0.00	516 (17.8%)	543 (18.7%)	-0.02	2,342 (27.5%)	2,351 (27.6%)	0.00	3249 (25.0%)	3287 (25.3%)	-0.01
Intracranial or retroperitoneal hemorrhage: 1 inpatier	** (0.1%)	** (0.1%)	0.00	0 (0.0%)	0 (0.0%)	#DIV/0!	12 (0.1%)	10 (0.1%)	0.00	#VALUE!	#VALUE!	#VALUE!
Peptic Ulcer Disease; n (%)	399 (25.3%)	407 (25.8%)	-0.01	574 (19.8%)	571 (19.7%)	0.00	2,559 (30.1%)	2,560 (30.1%)	0.00	3532 (27.2%)	3538 (27.2%)	0.00
Major Surgery ; n (%)	154 (9.8%)	147 (9.3%)	#DIV/0!	262 (9.0%)	261 (9.0%)	#DIV/0!	854 (10.0%)	835 (9.8%)	#DIV/0!	262 (9.0%)	261 (9.0%)	0.00
Upper GI bleed; 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!
Lower/ unspecified GI bleed; 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!
Urogenital bleed; n (%)	** (0.3%)	** (0.3%)	0.00	27 (0.9%)	30 (1.0%)	-0.01	1 (0.0%)	0 (0.0%)	#DIV/0!	#VALUE!	#VALUE!	#VALUE!
Other bleeds; n (%)	106 (6.7%)	110 (7.0%)	-0.01	170 (5.9%)	170 (5.9%)	0.00	512 (6.0%)	490 (5.8%)	0.01	788 (6.1%)	770 (5.9%)	0.01
Prior cancer; n (%)	237 (15.0%)	228 (14.5%)	0.01	351 (12.1%)	331 (11.4%)	0.02	1,577 (18.5%)	1,523 (17.9%)	0.02	2165 (16.7%)	2082 (16.0%)	0.02
Antibiotics; n (%)	751 (47.7%)	774 (49.1%)	#DIV/0!	1,526 (52.6%)	1,514 (52.2%)	#DIV/0!	4,722 (55.5%)	4,673 (54.9%)	#DIV/0!	1,526 (52.6%)	1,514 (52.2%)	0.01
Aspirin; n (%)	** (0.6%)	** (0.6%)	0.00	51 (1.8%)	48 (1.7%)	0.01	37 (0.4%)	42 (0.5%)	-0.01	#VALUE!	#VALUE!	#VALUE!
Aspirin/dipyridamole; n (%)	** (0.2%)	** (0.2%)	0.00	** (0.1%)	** (0.1%)	0.00	26 (0.3%)	30 (0.4%)	-0.02	#VALUE!	#VALUE!	#VALUE!
Other antiplatelet agents; n (%)	** (0.3%)	** (0.3%)	0.00	** (0.1%)	** (0.3%)	-0.04	53 (0.6%)	50 (0.6%)	0.00	#VALUE!	#VALUE!	#VALUE!
PGP inhibitors; n (%)	280 (17.8%)	281 (17.8%)	0.00	546 (18.8%)	548 (18.9%)	0.00	1,954 (23.0%)	1,957 (23.0%)	0.00	2780 (21.4%)	2786 (21.5%)	0.00
Other gastroprotective agents; n (%)	24 (1.5%)	26 (1.7%)	-0.02	56 (1.9%)	49 (1.7%)	0.02	141 (1.7%)	143 (1.7%)	0.00	221 (1.7%)	218 (1.7%)	0.00
Number of lipid tests ordered												
...mean (sd)	0.49 (0.78)	0.47 (0.74)	0.03	0.35 (0.80)	0.34 (0.78)	0.01	0.55 (0.84)	0.56 (0.83)	-0.01	0.50 (0.82)	0.50 (0.81)	0.00
Proton pump inhibitor; n (%)	380 (24.1%)	379 (24.1%)	0.00	618 (21.3%)	633 (21.8%)	-0.01	2,625 (30.8%)	2,667 (31.3%)	-0.01	3623 (27.9%)	3679 (28.3%)	-0.01
H2 receptor antagonist; n (%)	73 (4.6%)	66 (4.2%)	0.02	117 (4.0%)	119 (4.1%)	-0.01	578 (6.8%)	546 (6.4%)	0.02	768 (5.9%)	731 (5.6%)	0.01
Vitamin K therapy; n (%)	** (0.1%)	** (0.1%)	0.00	0 (0.0%)	0 (0.0%)	#DIV/0!	2 (0.0%)	1 (0.0%)	#DIV/0!	#VALUE!	#VALUE!	#VALUE!
Number of INR (prothrombin) tests ordered												
...mean (sd)	0.73 (1.55)	0.58 (1.00)	0.12	0.52 (1.11)	0.47 (1.03)	0.05	0.53 (0.86)	0.50 (0.85)	0.04	0.55 (1.03)	0.50 (0.91)	0.00
Treating prescriber - Cardiologist; n (%)	508 (32.3%)	509 (32.3%)	0.00	1,002 (34.6%)	994 (34.3%)	0.01	3,097 (36.4%)	3,041 (35.7%)	0.01	4607 (35.5%)	4544 (35.0%)	0.01
Treating prescriber - Primary Care Physician; n (%)	1,368 (86.9%)	1,399 (88.8%)	-0.06	1,243 (42.9%)	1,247 (43.0%)	0.00	3,431 (40.3%)	3,422 (40.2%)	0.00	6042 (46.5%)	6068 (46.7%)	0.00
Treating prescriber - Other; n (%)	1,574 (99.9%)	1,574 (99.9%)	0.00	2,754 (95.0%)	2,761 (95.2%)	-0.01	8,475 (99.6%)	8,483 (99.7%)	-0.02	12803 (98.6%)	12818 (98.7%)	-0.01
Alpha blockers; n (%)	121 (7.7%)	124 (7.9%)	-0.01	162 (5.6%)	159 (5.5%)	0.00	868 (10.2%)	862 (10.1%)	0.00	1151 (8.9%)	1145 (8.8%)	0.00
CHA2DS2 VASc score, 180 days, V												
...mean (sd)	3.13 (1.81)	3.22 (1.79)	-0.05	2.90 (1.70)	2.98 (1.68)	-0.05	4.08 (1.83)	4.17 (1.82)	-0.05	3.70 (1.80)	3.79 (1.79)	0.00
Use of Prasugrel; n (%)	** (0.1%)	0 (0.0%)	0.04	** (0.1%)	** (0.1%)	0.00	1 (0.0%)	1 (0.0%)	#DIV/0!	#VALUE!	#VALUE!	#VALUE!
Use of Loop Diuretics+other diuretics+other hyperten:	237 (15.0%)	247 (15.7%)	-0.02	351 (12.1%)	349 (12.0%)	0.00	1,864 (21.9%)	1,901 (22.3%)	-0.01	2452 (18.9%)	2497 (19.2%)	-0.01
Commercial vs Medicare Advantage- Business Type Code - CORRECT ONE - OPTUM							0	0				
...Commercial; n (%)	495 (31.4%)	471 (29.9%)	0.03	688 (23.7%)	708 (24.4%)	-0.02	-	-	#VALUE!	1,183 (26.4%)	1,179 (26.4%)	0.00
...Medicare Advantage; n (%)	1,080 (68.6%)	1104 (70.1%)	-0.03	2211 (76.3%)	2191 (75.6%)	0.02	-	-	#VALUE!	3,291 (73.6%)	3,295 (73.6%)	0.00
Commercial vs Medicare Advantage- Business Type Code												
...COM = COMMERCIAL; n (%)	495 (31.4%)	471 (29.9%)	0.03	-	-	#VALUE!	-	-	#VALUE!	495 (31.4%)	471 (29.9%)	0.03
...MCR = MEDICARE; n (%)	1,080 (68.6%)	1,104 (70.1%)	-0.03	-	-	#VALUE!	-	-	#VALUE!	1,080 (68.6%)	1,104 (70.1%)	-0.03
...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	-	-		0	0		-	-				

# Appendix B

...1 - Fee For Service; n (%)	-	-	1,985 (68.5%)	1,967 (67.9%)	-	-	1,985 (68.5%)	1,967 (67.9%)	0.00
...2 - Encounter; n (%)	-	-	226 (7.8%)	224 (7.7%)	-	-	226 (7.8%)	224 (7.7%)	0.00
...3 - Medicare; n (%)	-	-	625 (21.6%)	643 (22.2%)	-	-	625 (21.6%)	643 (22.2%)	0.00
...4 - Medicare Encounter; n (%)	-	-	63 (2.2%)	65 (2.2%)	-	-	63 (2.2%)	65 (2.2%)	0.00
Metropolitan Statistical Area - Urban (any MSA) vs Rural (non-MSA)							0	0	0.00
...Urban; n (%)	-	-	2,156 (74.4%)	2,161 (74.5%)	-	-	2,156 (74.4%)	2,161 (74.5%)	
...Rural; n (%)	-	-	100 (3.4%)	95 (3.3%)	-	-	100 (3.4%)	95 (3.3%)	
...Unknown/Missing; n (%)	-	-	643 (22.2%)	643 (22.2%)	-	-	643 (22.2%)	643 (22.2%)	