

Replication of the AMPLIFY Anticoagulant Trial in Healthcare Claims Data

NCT 00643201

May 25, 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 Apixaban for the Treatment of Acute Venous Thromboembolism ([AMPLIFY](#))

1.2 Intended aim(s)

To compare the risk of symptomatic, recurrent venous thromboembolism (VTE) in patients with symptomatic deep vein thrombosis (DVT), pulmonary embolism (PE), or both for apixaban versus standard therapy of warfarin.

1.3 Primary endpoint for replication

The primary outcome of the study was symptomatic, recurrent VTE or death related to VTE

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

Assuming a non-inferiority margin of 1.80, it was determined that 4,094 patients would be needed to achieve 90% power to conclude noninferiority of apixaban over standard therapy at one-sided alpha level of 0.025.

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

Major bleeding; RR= 0.31 (95% CI 0.17–0.55)

1.6 Trial estimate

RR = 0.84 (95% CI 0.60-1.18) comparing apixaban vs standard therapy (Agnelli et al., 2013)

2. Person responsible for implementation of replication in Aetion

Dureshahwar Jawaidd, 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)

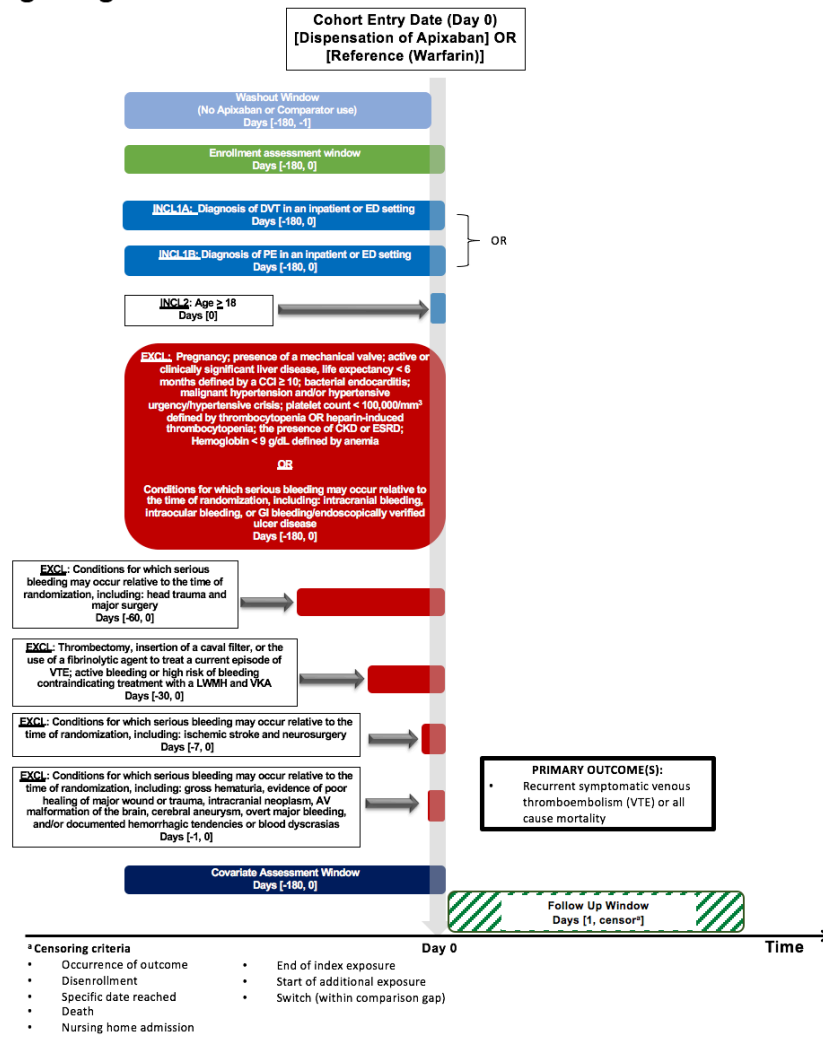
Optum, MarketScan, Medicare

4. Study Design Diagram

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

Figure 1.

Design Diagram – AMPLIFY 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 apixaban to warfarin users. The patients will be required to have continuous enrollment during a baseline period of 180 days before initiation of apixaban or warfarin (index date). We will restrict the analyses to patients with a diagnosis of proximal DVT, PE, or both.

5.2 Important steps for cohort formation

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

5.2.1 Eligible cohort entry dates

Market availability of apixaban in the U.S. for treatment of deep vein thrombosis and pulmonary embolism started on August 21, 2014

- For Medicare: August 21, 2014 – December 31, 2017 (end of available data)
- For Marketscan: August 21, 2014 – December 31, 2018 (end of available data)
- For Optum: August 21, 2014 – 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		Marketscan		Medicare	
	Less Excluded Patients	Remaining Patients	Less Excluded Patients	Remaining Patients	Less Excluded Patients	Remaining Patients
All patients		77,673,639		200,203,908		6,886,908
Did not meet cohort entry criteria	-76,868,532	805,107	-199,645,422	558,486	-4,150,733	2,736,175

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Excluded due to insufficient enrollment	-101,912	703,195	-39,077	519,409	-53,978	2,682,197
Excluded due to prior use of referent	-347,539	355,656	-307,198	212,211	-1,789,291	892,906
Excluded due to prior use of exposure and because patient qualified in >1 exposure category	-254,675	100,981	-137,453	74,763	-554,606	338,300
Excluded based on Age	0	100,981	0	74,758	-104	338,196
Excluded based on Gender	0	100,981	0	74,758	0	338,196
Excluded based on Use of other NOACs (rivaroxaban, dabigatran, edoxaban)	-5,094	95,887	-3118	71,640	-19004	319,192
Excluded based on Inclusion # 3a - Acute Symptomatic Proximal DVT	-82,653	13,234	-60406	11,234	-277,170	42,022
Excluded based on Inclusion # 3b - Acute Symptomatic PE and based on Inclusion # 4 - Age	-4,641	8,593	-2852	8,382	-21,229	20,793
Excluded based on Exclusion # 1 - pregnancy	-14	8,579	-42	8,340	-22	20,771
Excluded based on Exclusion # 6 - Thrombectomy, Insertion of Caval Filter, or Use of Fibrinolytic Agent	-211	8,368	-143	8,197	-24	20,747
Excluded based on Exclusion # 7 - Active bleeding (HAS_BLED Score >=3), based on Exclusion # 10A - Mechanical Valve, and based on Exclusion # 11.1 - Intracranial Bleeding	-3,708	4,660	-1447	6,750	-11,558	9,189
Excluded based on Exclusion # 11.2 - Intraocular Bleeding	0	4,660	0	6,750	0	9,189
Excluded based on Exclusion # 11.3 - Gastrointestinal Bleeding	-12	4,648	-52	6,698	-78	9,111
Excluded based on Exclusion # 11.4 - Head Trauma or Other Major Trauma	-60	4,588	-65	6,633	-96	9,015
Excluded based on Exclusion # 11.5 - Major Surgery, Exclusion # 11.6 - Ischemic Stroke, Exclusion # 11.7 - Neurosurgery, Exclusion # 11.8 - Gross Hematuria, Exclusion # 11.9 - Non - healing surgical wound, Exclusion # 11.10 - Intracranial neoplasm, arteriovenous malformation or aneurysm, and Exclusion # 11.11 - Overt Major Bleeding	-57	4,531	-33	6,600	-111	8,904
Excluded based on Exclusion # 11.12 - Coagulation defects or malignant neoplasm of tissue	-36	4,495	-20	6,580	-33	8,871
Excluded based on Exclusion # 12 - active liver disease	-133	4,362	-142	6,438	-226	8,645
Excluded based on Exclusion # 13 - CCI >= 10 and based on Exclusion # 14 - Bacterial Endocarditis	-39	4,323	-33	6,405	-28	8,617

Excluded based on Exclusion # 15 - Uncontrolled Hypertension and based on Exclusion # 16 - thrombocytopenia	-26	4,297	-36	6,369	-78	8,539
Excluded based on Exclusion # 17 – anemia, Exclusion # 18 - CKD/ESRD, and Exclusion # 22 - Heparin-induced thrombocytopenia	-33	4,264	-31	6,338	-139	8,400
Excluded based on Exclusion # 27 - aspirin (ASA) >165 mg	0	4,264	0	6,338	0	8,400
Excluded based on Exclusion # 28 - ASA plus clopidogrel or ASA plus ticlopidine	0	4,264	0	6,338	0	8,400
Final cohort		4,264		6,338		8,400

6. Variables

6.1 Exposure-related variables:

Study drug:

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

Comparator:

New initiators of warfarin, defined by no use of apixaban 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 and cause-specific mortality
- **Secondary Outcome:** Individual components
 - Hospital admission for VTE (principal diagnosis position)
 - Cause-specific mortality
 - Inpatient mortality identified using discharge status codes from hospitalization for VTE

Safety outcome 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 apixaban and comparator and will continue until the earliest date of the following events:

- The first occurrence of the outcome of interest, unless otherwise specified for selected outcomes,
- The date of end of continuous registration in the database,
- End of the study period,
- Measured death event occurs,
- Nursing home admission

- Nursing home admissions are considered a censoring event because the data sources utilized typically provide little to no data on a patient, particularly on drug utilization, after admission. We will utilize this as an exclusion reason for cohorts for the same reason.
- The date of drug discontinuation, defined as the date of the last continuous treatment episode of the index drug (apixaban 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 apixaban to rivaroxaban 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
- Treatment of current episode of VTE with thrombectomy, insertion of caval filter, or use of fibrinolytic agent (streptokinase, alteplase, reteplase, tenecteplase)

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

7. Initial Feasibility Analysis

Action report name:

For apixaban vs. warfarin

Optum- <https://bwh-dope.aetion.com/projects/details/1484/results/64537/result/0>

Marketscan- <https://bwh-dope.aetion.com/projects/details/1481/results/64536/result/0>

Medicare- <https://bwh-dope.aetion.com/projects/details/1483/results/64535/result/0>

Date conducted: 1/19/21

Complete Action 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 apixaban vs. warfarin

Optum- <https://bwh-dope.aetion.com/projects/details/1484/results/64538/result/0>

Marketscan- <https://bwh-dope.aetion.com/projects/details/1481/results/64539/result/0>

Medicare- <https://bwh-dope.aetion.com/projects/details/1483/results/64540/result/0>

Date conducted: 1/19/2021

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

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

Action report links:

Optum: <https://bwh-dope.aetion.com/projects/details/1484/results/64541/result/0>

Marketscan: <https://bwh-dope.aetion.com/projects/details/1481/results/64542/result/0>

Medicare: <https://bwh-dope.aetion.com/projects/details/1483/results/64543/result/0>

Date conducted: 1/19/2021

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
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Dummy outcome	67 (0.94%)	25 (0.70%)	42 (1.18%)
Death	103 (1.44%)	49 (1.37%)	54 (1.51%)
Start of an additional exposure	232 (3.25%)	175 (4.90%)	57 (1.60%)
End of index exposure	4,701 (65.84%)	2,202 (61.68%)	2,499 (70.00%)
Specified date reached	857 (12.00%)	424 (11.88%)	433 (12.13%)
End of patient enrollment	425 (5.95%)	198 (5.55%)	227 (6.36%)
Switch to NOACs (for censoring) + nursing home admission + thrombectomy, insertion of caval filter, use of fibrinolytic agent	755 (10.57%)	497 (13.92%)	258 (7.23%)

- Report follow-up time by treatment group.

Median Follow-Up Time (Days) [IQR]			
Patient Group	Optum	Marketscan	Medicare
Overall Patient Population	82.5 [38-174.5]	96 [38-186]	74 [38-170]
Referent	72 [37-189]	88 [38-171]	73 [38-161]
Exposure	96.5 [38-155]	100 [38-195]	78 [38-183]

- Report overall risk of the primary outcome.

	Optum	Marketscan	Medicare	Pooled
Risk per 1,000 patients	12.93	13.13	14.66	13.74

10. Final Power Assessment

Date conducted: 12/16/20

- 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.
 - Pooled

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Non-inferiority Analysis	
Number of patients matched	7,140
Reference	3,570
Exposed	3,570
Risk per 1,000 patients	13.74
HR from RCT	0.84
Alpha (2-sided)	0.05
Non-inferiority margin	1.8
Number of events expected	98.1036
Power	0.965194245

- Optum

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

Non-inferiority Analysis	
Number of patients matched	980
Reference	490
Exposed	490
Risk per 1,000 patients	12.93
HR from RCT	0.84
Alpha (2-sided)	0.05
Non-inferiority margin	1.8
Number of events expected	12.6714
Power	0.273097221

○ Marketscan

Non-inferiority Analysis	
Number of patients matched	2,762
Reference	1,381
Exposed	1,381
Risk per 1,000 patients	13.13
Assumed HR from RCT	0.84
Alpha (2-sided)	0.05
Non-inferiority margin	1.8
Number of events expected	36.26506
Power	0.631133873

○ Medicare

Non-inferiority Analysis	
Number of patients matched	3,398
Reference	1,699
Exposed	1,699
Risk per 1,000 patients	14.66
Assumed HR from RCT	0.84
Alpha (2-sided)	0.05
Non-inferiority margin	1.8
Number of events expected	49.81468
Power	0.767185633

- 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](https://clinicaltrials.gov) and upload this document.

13. Comparative Analyses

Action report name:

Date conducted:

13.1 For primary analysis:

13.2 For sensitivity analyses:

14. Requested Results

14.1 Table 1: Baseline characteristics before and after adjustment

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

14.2 Table 2: Follow-up time

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

14.3 Table 3: Censoring events

	Overall	Referent	Exposure
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, Buller HR, Cohen A, et al. Oral Apixaban for the Treatment of Acute Venous Thromboembolism. *N Engl J Med*. 2013; 369:799-808.

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

Appendix A

AMPLIFY trial definitions	Implementation in routine care	Please see the following Google Drive for further details or any missing information: https://drive.google.com/drive/folders/1WD618wrywYfEaXzILTCuK-VCcnb6b-gV7usp-sharing	
Trial details- Secondary approval, Successful NI with label change		ICD-10 codes are not listed in this document because of excel cell size limitations and excessive number of ICD-10 codes. Full ICD-10 code lists will be available in the above Google Drive Folder (link above). ICD-9 to ICD-10 code conversions were completed using a SAS macro that implements forward/backward mapping based on the CMS ICD-9 to ICD-10 mapping: https://www.nber.org/data/icd9-icd-10-cm-and-pcs-crosswalk-general-equivalence-mapping.html	
EXPOSURE vs. COMPARISON		References/Rationale	Color coding
Apixaban (dose of 10 mg twice daily for 7 days, followed by 5 mg twice daily for 6 months) versus conventional therapy (subcutaneous enoxaparin, followed by warfarin)	Apixaban vs. Warfarin		Criteria
PRIMARY OUTCOME			Can be replicated in claims
The primary efficacy outcome was recurrent symptomatic venous thromboembolism or death related to venous thromboembolism.	Measured 1 day after drug initiation <u>Venous thromboembolism:</u> 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.	Can be intermediately measured in claims
INCLUSION CRITERIA			Can't be measured in claims
Signed Written Informed Consent	N/A		Can't be measured in claims but not important for the analysis
Subjects whose index event was either unprovoked OR provoked with a risk for recurrence as described in the eligibility checklist	N/A		
Either of the following:			
• Acute symptomatic proximal deep vein thrombosis (DVT) with evidence of proximal thrombosis that involves at least the popliteal vein or a more proximal vein, demonstrated by imaging with: - compression ultrasound (CUS), including grey-scale or color-coded Doppler, OR - ascending contrast venography	Measured 180 days prior to and including day of drug initiation in any diagnosis position and in an inpatient or ED care setting <u>Deep vein thrombosis (DVT):</u> ICD-9 Dx: 451.xx, 453.xx ICD-10 Dx: I26.xx, I80.xx, I81.xx, I82.xx, I26.xx		
• Acute symptomatic PE with evidence of thrombosis demonstrated by imaging as follows: - an intraluminal filling defect in segmental or more proximal branches on spiral computed tomography (CT) scan; or - an intraluminal filling defect or a sudden cutoff of vessels more than 2.5 mm in diameter on the pulmonary angiogram; or - a perfusion defect of at least 75% of a segment with a local normal ventilation result (high probability) on ventilation/perfusion lung scan (VPLS)	Measured 180 days prior to and including day of drug initiation in any diagnosis position and in an inpatient or ED care setting <u>Pulmonary embolism (PE):</u> ICD-9 Dx: 415.xx ICD-10 Dx: I26.xx		
Men and women, ages 18 years or greater	Measured at day of drug initiation Age >= 18		
Women of childbearing potential (WOCBP) must be using an adequate method of contraception to avoid pregnancy throughout the study in such a manner that the risk of pregnancy is minimized. (Additional details in Supplementary Appendix)	N/A	Criteria captured as an exclusion criteria in the Pregnancy measure	
WOCBP must have a negative serum or urine pregnancy test (minimum sensitivity 25 IU/L or equivalent units of human chorionic gonadotropin [HCG]) within 24 hours prior to the start of investigational product.			
EXCLUSION CRITERIA			
WOCBP who are unwilling or unable to use an acceptable method of birth control (such as oral contraceptives, other hormonal contraceptives [vaginal products, skin patches, or implanted or injectable products], or mechanical products such as an intrauterine device or barrier methods [diaphragm, condoms, spermicides]) to avoid pregnancy for the entire study.	Measured 180 days prior to and including day of drug initiation in any diagnosis position and in an inpatient or outpatient care setting See 'Pregnancy' sheet for codes		
Women who are pregnant or breastfeeding.			
Women with a positive pregnancy test on enrollment or prior to investigational product administration.			
Subjects with a provoked index event without the existence of a persistent risk factor for recurrence as described in the eligibility checklist	N/A		
Less than 6 months of anticoagulation planned for the most recent DVT or pulmonary embolism (PE) (index event)	N/A		

Appendix A

Thrombectomy, insertion of a caval filter, or use of a fibrinolytic agent to treat the current episode of venous thromboembolism (VTE).	<p>Measured 30 days prior and including the day of drug initiation in any diagnosis position in an inpatient or ED care setting</p> <p><u>Thrombectomy:</u> CPT codes: 37184, 37185, 37186, 37187, 37188 HCPCS codes: C1757</p> <p><u>Caval filter:</u> CPT codes: 37191, 37192, 37193 HCPCS codes: C1880</p> <p><u>Fibrinolytic agent:</u> streptokinase, alteplase, reteplase, tenecteplase</p>	Components will act as both exclusion criterion and censoring events	
Active bleeding or high risk for bleeding contraindicating treatment with low-molecularweight heparin (LMWH) and a vitamin K antagonist (VKA)	<p>Measured 30 days prior to and including the day of drug initiation</p> <p>HAS-BLED score >=3</p>	<p>Major bleeding risk 5.8% per year for score 3</p> <p>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4407886/</p>	
Subjects with cancer who will be treated for 6 months or more with LMWH therapy	N/A		
Subjects with contraindications according to the local prescribing information of enoxaparin or warfarin	N/A		
Subjects with an indication, other than VTE, intended for long-term treatment with a VKA such as:	N/A		
Mechanical valve	<p>Measured 180 days prior to and including the drug initiation in any diagnosis position and in an inpatient or outpatient care setting</p> <p><u>Mechanical valve</u> ICD-9 Dx: V43.3x ICD-10 Dx: Z95.2x, Z95.3x, Z95.4x ICD-9 Px: 35.0x, 35.2x, 35.3x ICD-10 Px: 02RGxxx, 02RFxxx, 02RHxxx, 02RJxxx, 02QGxxx, 02QFxxx, 02QHxxx, 02QJxxx</p>		
Atrial fibrillation or atrial flutter with moderate to high risk of systemic thromboembolism. Subjects with atrial fibrillation that appears to be associated with acute PE may participate.	N/A		
Conditions for which serious bleeding may occur and the time of exclusion relative to the time of randomization:			
• 6 months			
Intracranial bleeding	<p>Measured 180 days prior to and including the day of drug initiation in any diagnosis position and in an inpatient care setting</p> <p><u>Intracranial hemorrhage:</u> ICD-9 Dx: 430.xx, 431.xx, 432.xx ICD-10 Dx: I60.xx, I61.xx, I62.xx</p>		
Intraocular bleeding	<p>Measured 180 days prior to and including the day of drug initiation in any diagnosis position and in an inpatient care setting</p> <p><u>Vitreous hemorrhage:</u> ICD-9 Dx: 379.23 ICD-10 Dx: H43.1x</p> <p><u>Retinal hemorrhage</u> ICD-9 Dx: 362.81 ICD-10 Dx: H35.6x, H35.73</p> <p><u>Hemophthalmos</u> ICD-9 Dx: 360.43, 459.0x, 364.41 ICD-10 Dx: H44.8xx</p>		

Appendix A

Gastrointestinal bleeding and/or endoscopically verified ulcer disease	<p>Measured 180 days prior to and including day of drug initiation in any diagnosis position and in an inpatient care setting</p> <p><u>Gastrointestinal bleeding:</u> ICD-9 Dx: 531.0x gastric ulcer w/ hemorrhage, 531.2x gastric ulcer w/ hemorrhage and perforation 531.4x 531.6x chronic / unspecified ulcer w/ hemorrhage 532.0x, 532.2x, 532.4x, 532.6x, 533.0x, 533.2x, 533.4x, 533.6x, 534.0x, 534.2x, 534.4x, 534.6x, 562.0x, 562.1x, 568.8x, 569.3x, 569.8x 578.x Gastrointestinal hemorrhage</p> <p>ICD-10 Dx: K25.0x, K25.2x, K25.6x, K26.0x, K26.2x, K26.4x, K26.6x, K27.0x, K27.2x, K27.4x, K27.6x, K28.0x, K28.2x, K28.4x, K28.6x, K55.21, K57.xx, K62.5x, K63.1x, K63.81, K66.1x, K92.0x, K92.1x, K92.2x</p> <p>ICD-9 Px: 44.43 ICD-10 Px: OW3P8ZZ</p>		
• 2 months			
Head trauma or other major trauma	<p>Measured 60 days prior to and including the day of drug initiation in any diagnosis position and in an inpatient or outpatient care setting</p> <p>See 'Major Trauma' sheet for codes</p>		
Major surgery	<p>Measured 60 days prior to and including the day of drug initiation in any diagnosis position and in an inpatient or outpatient care setting</p> <p>Major surgery selected from codes range 35.x-84.x</p>		
• 1 week			
- Ischemic stroke	<p>Measured 7 days prior to and including the day of drug initiation in any diagnosis position and in an inpatient care setting</p> <p><u>Ischemic stroke:</u> ICD-9 Dx: 433.x, 434. x, 436.xx</p>		
- Neurosurgery	<p>Measured 7 days prior to and including the day of drug initiation in any diagnosis position and in an inpatient care setting</p> <p><u>Neurosurgery:</u> ICD-9 Px: 01.xx, 02.xx, 03.xx, 04.xx, 05.xx ICD-10 Px: 00xxxx</p>		
• Time of randomization			
- Gross hematuria	<p>Measured 1 day prior to and including the of drug initiation in any diagnosis position in an inpatient or outpatient care setting</p> <p><u>Gross hematuria:</u> ICD-9 Dx: 599.71 (not 599.7x) ICD-10 Dx: R31.0</p>		
- Evidence of poor healing of a major wound or major trauma	<p>Measured 1 day prior and including the day of drug initiation in any diagnosis position in an inpatient or outpatient care setting</p> <p><u>Non-healing surgical wound</u> ICD-9 Dx: 998.33 ICD-10 Dx: T81.33XA</p>		
- Planned major surgery	N/A		

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- Intracranial neoplasm, arteriovenous malformation or aneurysm	<p>Measured 1 day prior to and including the day of drug initiation in any diagnosis position and in an inpatient or outpatient care setting</p> <p><u>Intracranial neoplasm:</u> ICD-9 Dx: 239.6x, 191.xx, 225.xx ICD-10 Dx: D49.6x, C71.x, D33.0x, D33.1x, D33.2x</p> <p><u>AV malformation of brain:</u> ICD-9 Dx: 747.81 ICD-10 Dx: Q28.2x, Q28.3x</p> <p><u>Cerebral aneurysm</u> ICD-9 Dx: 437.3x ICD-10 Dx: I67.1x</p>		
- Overt major bleeding	<p>Measured 1 day prior and including the day of drug initiation in any diagnosis position and in an inpatient or outpatient care setting</p> <p>See 'Major Bleeding' sheet for codes</p>		
- Documented hemorrhagic tendencies or blood dyscrasias	<p>Measured 1 day prior and including the day of drug initiation in any diagnosis position in an inpatient or outpatient care setting</p> <p><u>Coagulation defects</u> ICD-9 Dx: 286.x ICD-10 Dx: D65.x, D66.x, D67.xx, D68.xx, D69.xx</p> <p><u>Malignant Neoplasm Of Lymphatic And Hematopoietic Tissue</u> ICD-9 Dx: 200.xx to 209.xx ICD-10 Dx: C81.xx to C96.xx</p>		
Active and clinically significant liver disease (eg, hepatorenal syndrome)	<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</p> <p><u>Liver disease:</u> ICD-9 Dx: 070.xx, 570.xx-573.xx 456.0x-456.2x, 576.8x, 782.4x, 789.5x ICD-9 Px: 39.1x, 42.91</p> <p><u>Hepatorenal syndrome:</u> ICD-9 Dx: 572.4 ICD-10 Dx: K76.7</p>		
Life expectancy <6 months	<p>Measured 180 days prior to drug initiation in any diagnosis position and in an inpatient or outpatient care setting</p> <p>CC1>=10</p>		
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</p> <p><u>Bacterial endocarditis:</u> ICD-9 Dx: 421.0x ICD-10 Dx: I33.0x</p>		
Uncontrolled hypertension: systolic blood pressure >180 mm Hg or diastolic blood pressure >100 mm Hg; (subjects who have a transient, higher blood pressure elevation associated with acute PE [upper limit: systolic blood pressure 200 mm Hg or diastolic blood pressure 100 mm Hg] may enter the study); elevated blood pressure that is persistent 1-2 days after the index DVT or PE should be treated according to local guidelines.	<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</p> <p><u>Malignant hypertension:</u> ICD-9 Dx: 401.0x <u>Hypertensive urgency/Hypertensive crisis:</u> ICD-10 Dx: I16.xx</p>		
Platelet count <100,000/mm3	<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</p> <p><u>Thrombocytopenia:</u> ICD-9 Dx: 287.3x, 287.4x, 287.5x ICD-10 Dx: D69.3x, D69.4x, D69.5x, D69.6x</p>		

Appendix A

Hemoglobin <9 g/dL	Measured 180 days prior to and including the day of drug initiation in any diagnosis position and in an inpatient or outpatient care setting <u>Anemia:</u> ICD 9 Dx: 282.x (hereditary hemolytic anemias) 283.x (acquired hemolytic anemias, autoimmune etc) 284.x (aplastic anemia and other bone marrow failure syndromes)		
Serum creatinine >2.5 mg/dL (221 umol/L)	Measured 180 days prior to and including the day of drug initiation in any diagnosis position and in an inpatient or an outpatient care setting <u>CKD, ESRD:</u> ICD-9 Dx: 585.4x, 585.5x, 585.6x: CKD 4, 5, ESRD 586.xx: renal failure ICD-10 Dx: N19.xx N18.4x Chronic kidney disease, stage 4 (severe) N18.5x Chronic kidney disease, stage 5 N18.6x End stage renal disease N18.9x Chronic kidney disease, unspecified		
Calculated creatinine clearance <25 ml/min			
ALT or AST >2 times upper limit of normal	N/A (Incorporated into moderate/severe liver disease above)		
Total bilirubin >1.5 times upper limit of normal (unless an alternative causative factor is identified [eg, Gilbert's syndrome]).			
Heparin-induced thrombocytopenia;	Measured 180 days prior to and including the day of drug initiation in any position and in an inpatient or outpatient care setting <u>Heparin induced thrombocytopenia (HIT)</u> ICD-9 Dx: 289.84 ICD-10 Dx: D75.82		
Allergic reaction to unfractionated heparin, LMWH, fondaparinux, or any VKA.	N/A		
DVT or PE treatment with more than two doses of fondaparinux or a LMWH that is labeled for once-daily dosing, or more than three doses of a LMWH that is labeled for twice-daily dosing, or continuous infusion of unfractionated heparin for more than 36 hours, before the first administration of study drug; and/or --	N/A		
DVT or PE treatment with more than two doses of oral VKA therapy before the first administration of study drug.	N/A		
Treatment with apixaban in a previous clinical trial.	N/A		
Subjects requiring aspirin (ASA) >165 mg/day at randomization.	Measured 1 day prior to and including the day of drug initiation in any diagnosis position and in an inpatient our outpatient care setting Aspirin (prescription only) dose greater than >165 mg		
Subjects requiring dual antiplatelet therapy (ASA plus clopidogrel or ASA plus ticlopidine) at randomization. Subjects who transition from dual antiplatelet therapy to monotherapy prior to randomization will be eligible for the trial.	Measured 1 day prior to and including the day of drug initiation in any diagnosis position and in an inpatient or outpatient care setting (both concurrent prescription and combination products) Aspirin + clopidogrel or Aspirin + ticlopidine		
Prisoners or subjects who are involuntarily incarcerated	N/A		
Subjects who are compulsorily detained for treatment of either a psychiatric or physical (eg, infectious disease) illness	N/A		
Receiving concurrent investigational agents or has received an investigational agent within the past 30 days prior to the first dose of study treatment (with the exception of approved medications being used for an approved indication, eg, investigating a new dosing regimen for an approved indication)	N/A		
Any condition, which in the opinion of the investigator, would put the subject at an unacceptable risk from participating in the study	N/A		
Any other medical, social, logistical, or psychological reason, which in the opinion of the investigator, would preclude compliance with, or successful completion of, the study protocol.	N/A		

Appendix A

<u>Trial ID</u>	
<u>Trial Name (with web links)</u>	AMPLIFY
<u>Trial Name (with pdf links)</u>	
<u>NCT</u>	NCT00643201
<u>Therapeutic Area</u>	Cardiology/Vascular Diseases
<u>Brand Name</u>	Eliquis
<u>Generic Name</u>	Apixaban
<u>Sponsor</u>	Bristol-Myers Squibb
<u>Year</u>	2013
<u>Measurable endpoint</u>	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
<u>Exposure</u>	Apixaban
<u>Comparator</u>	Enoxaparin, Warfarin
<u>Population</u>	
<u>Trial finding</u>	HR = 0.84 (95%CI 0.60–1.18)
<u>Notes</u>	
<u>No. of Patients</u>	5,395
<u>Non-inferiority margin</u>	HR = 1.8
<u>Assay Sens. Endpoint</u>	
<u>Assay Sens. Finding</u>	
<u>Power</u>	0.90; With the use of an estimated incidence of the primary efficacy outcome of 3% at 6 months with conventional therapy and a noninferiority margin of 1.80 for the relative risk, we calculated that we would need to enroll 4094 patients for the study to have 90% power to show the noninferiority of apixaban, at a one sided alpha level of 0.025. This sample was increased to 4816 patients to account for up to 15% of patients discontinuing treatment early.

Appendix A

Title	
Major Bleeding	
ICD-9 Dx	
423	HEMOPERICARDIUM
430	SUBARACHNOID HEMORRHAGE
431	INTRACEREBRAL HEMORRHAGE
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
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

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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
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
569.86	DIEULAFOY LESION (HEMORRHAGIC) OF INTESTINE
578	HEMATEMESIS
578.1	BLOOD IN STOOL

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578.9	HEMORRHAGE OF GASTROINTESTINAL TRACT UNSPECIFIED
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
ICD-10 Dx	
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

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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
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

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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
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

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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
R31.9	Heaturia, unspecified in inpatient confinement
R31.9	Heaturia, unspecified in inpatient confinement
R04.2	Hemoptysis
R04.9	Hemorrhage from respiratory passages, unspecified
R04.81	Acute idiopathic pulmonary hemorrhage in infants
R04.89	Hemorrhage from other sites in respiratory passages
R31.0	Gross hematuria
R31.1	Benign essential microscopic hematuria
R31.2	Other microscopic hematuria
ICD-9 and 10 Px	
OW.3P8ZZ	Control Bleeding in Gastrointestinal Tract, Via Natural or Artificial Opening Endoscopic
44.43	ENDOSCOPIC CONTROL OF GASTRIC OR DUODENAL BLEEDING

Appendix A

Pregnancy

Dx codes

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

Procedure codes

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

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

Appendix A

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

Appendix A

Title	
Venous Thromboembolism (VTE)	
ICD-9 Dx inpatient primary position	
PE	
415.1	PULMONARY EMBOLISM AND INFARCTION
415.11	IATROGENIC PULMONARY EMBOLISM AND INFARCTION
415.19	OTHER PULMONARY EMBOLISM AND INFARCTION
DVT	
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

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453.9	EMBOLISM AND THROMBOSIS OF UNSPECIFIED SITE
ICD-10 Dx inpatient primary position	
PE	
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
DVT	
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	Budd-Chiari syndrome
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 B

Optum

MarketScan

Medicare

BEFORE PS MATCHING

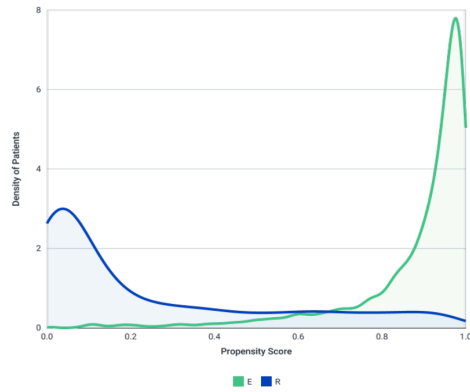


Figure 68: Pre-matching propensity score overlap

The c-statistics for the propensity score model, pre-matching was 0.938. The postmatching c-statistic was 0.684.

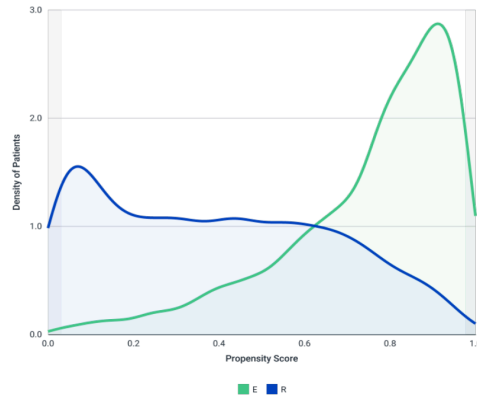


Figure 67: Pre-matching propensity score overlap

The c-statistics for the propensity score model, pre-matching was 0.848. The postmatching c-statistic was 0.572.

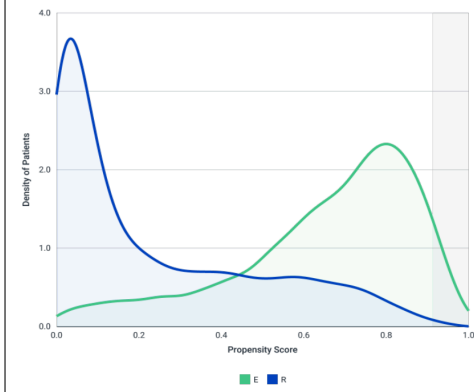


Figure 44: Pre-matching propensity score overlap

The c-statistics for the propensity score model, pre-matching was 0.874. The postmatching c-statistic was 0.566.

AFTER PS MATCHING

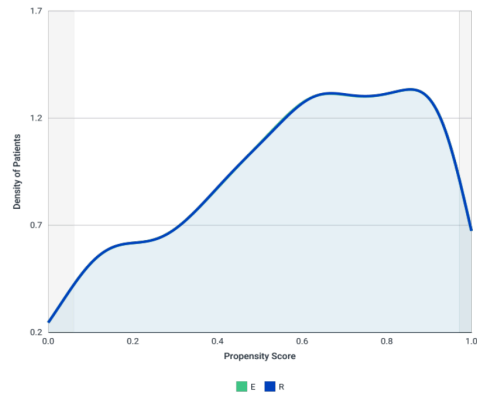


Figure 69: Post-matching propensity score overlap

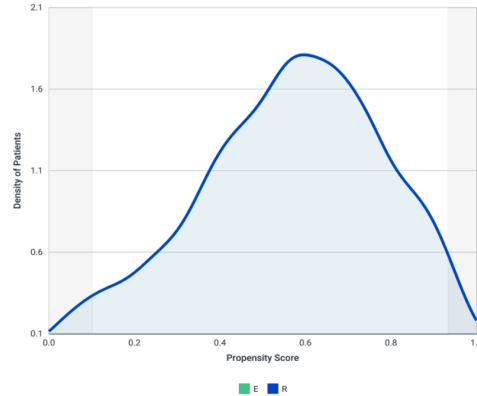


Figure 68: Post-matching propensity score overlap

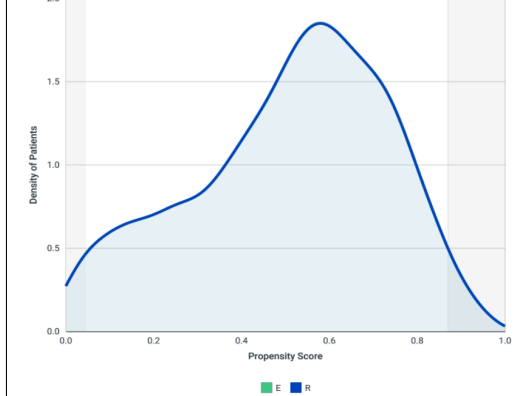


Figure 45: Post-matching propensity score overlap

Appendix B

Unmatched														
	Optum				MarketScan			Medicare				POOLED		
Variable	Reference - Warfarin	Exposure - Apixaban	St. Diff.	Reference - Warfarin	Exposure - Apixaban	St. Diff.	Reference - Warfarin	Exposure - Apixaban	St. Diff.	Reference - Warfarin	Exposure - Apixaban	St. Diff.		
Number of patients	1,472	2,783		2,464	3,874		4,983	3,406		8,919	10,063			
Age														
...mean (sd)	56.64 (14.48)	56.04 (14.74)	0.04	51.80 (12.29)	50.99 (12.53)	0.07	62.86 (14.56)	63.42 (13.81)	-0.04	58.78 (13.96)	56.59 (13.60)	0.16		
Age categories without zero category														
...18 - 54; n (%)	605 (41.1%)	1,207 (43.4%)	-0.05	1,318 (53.5%)	2,133 (55.1%)	-0.03	1,326 (26.6%)	852 (25.0%)	0.04	3,249 (36.4%)	4192 (41.7%)	-0.11		
...55 - 64; n (%)	500 (34.0%)	878 (31.5%)	0.05	989 (40.1%)	1,531 (39.5%)	0.01	1,364 (27.4%)	856 (25.1%)	0.05	2,853 (32.0%)	3,265 (32.4%)	-0.01		
...65 - 74; n (%)	185 (12.6%)	398 (14.3%)	-0.05	86 (3.5%)	118 (3.0%)	0.03	1,233 (24.7%)	998 (29.3%)	-0.10	1,504 (16.9%)	1,514 (15.0%)	0.05		
...≥ 75; n (%)	182 (12.4%)	300 (10.8%)	0.05	71 (2.9%)	92 (2.4%)	0.03	1,060 (21.3%)	700 (20.6%)	0.02	1,313 (14.7%)	1,092 (10.9%)	0.11		
Gender without zero category- United														
...Males; n (%)	747 (50.7%)	1,386 (49.8%)	0.02	1,324 (53.7%)	1,972 (50.9%)	0.06	2,339 (46.9%)	1,571 (46.1%)	0.02	4,410 (49.4%)	4,929 (49.0%)	0.01		
...Females; n (%)	725 (49.3%)	1,397 (50.2%)	-0.02	1,140 (46.3%)	1,902 (49.1%)	-0.06	2,644 (53.1%)	1,835 (53.9%)	-0.02	4,509 (50.6%)	5,134 (51.0%)	-0.01		
Race														
...White; n (%)							4,106 (82.4%)	2,789 (81.9%)		4,106 (82.4%)	2,789 (81.9%)	0.00		
...Black; n (%)							630 (12.6%)	470 (13.8%)		630 (12.6%)	470 (13.8%)	0.00		
...Asian; n (%)							24 (0.5%)	13 (0.4%)		24 (0.5%)	13 (0.4%)	0.00		
...Hispanic; n (%)							98 (2.0%)	46 (1.4%)		98 (2.0%)	46 (1.4%)	0.00		
...North American Native; n (%)							24 (0.5%)	18 (0.5%)		24 (0.5%)	18 (0.5%)	0.00		
...Other/Unknown; n (%)							101 (2.0%)	70 (2.1%)		101 (2.0%)	70 (2.1%)	0.00		
Region without zero category- United v3 (lumping missing&other category with West)														
...Northeast; n (%)	156 (10.6%)	262 (9.4%)	0.04	452 (18.3%)	622 (16.1%)	0.06	1,000 (20.1%)	644 (18.9%)	0.03	1608 (18.0%)	1,528 (15.2%)	0.08		
...South; n (%)	414 (28.1%)	1,333 (47.9%)	-0.42	749 (30.4%)	869 (22.4%)	0.18	1,368 (27.5%)	1,425 (41.8%)	-0.30	2,531 (28.4%)	3,627 (36.0%)	-0.16		
...Midwest; n (%)	503 (34.2%)	658 (23.6%)	0.24	802 (32.5%)	1,978 (51.1%)	-0.38	1,556 (31.2%)	795 (23.3%)	0.18	2,861 (32.1%)	3,431 (34.1%)	-0.04		
...West; n (%)	399 (27.1%)	530 (19.0%)	0.19	456 (18.5%)	394 (10.2%)	0.24	1,059 (21.3%)	542 (15.9%)	0.14	1,914 (21.5%)	1,466 (14.6%)	0.18		
...Unknown+missing; n (%)	N/A	N/A	#VALUE!	** (0.2%)	** (0.3%)	-0.02	N/A	N/A	#VALUE!	** (0.2%)	** (0.3%)	-0.02		
CV Covariates														
Ischemic heart disease; n (%)	226 (15.4%)	459 (16.5%)	-0.03	305 (12.4%)	499 (12.9%)	-0.02	968 (19.4%)	714 (21.0%)	-0.04	1,499 (16.8%)	1,672 (16.6%)	0.01		
Acute MI; n (%)	67 (4.6%)	123 (4.4%)	0.01	106 (4.3%)	169 (4.4%)	0.00	210 (4.2%)	168 (4.9%)	-0.03	383 (4.3%)	460 (4.6%)	-0.01		
ACS/unstable angina; n (%)	40 (2.7%)	99 (3.6%)	-0.05	71 (2.9%)	129 (3.3%)	-0.02	178 (3.6%)	131 (3.8%)	-0.01	289 (3.2%)	359 (3.6%)	-0.02		
Old MI; n (%)	36 (2.4%)	72 (2.6%)	-0.01	31 (1.3%)	47 (1.2%)	0.01	269 (5.4%)	171 (5.0%)	0.02	336 (3.8%)	290 (2.9%)	0.05		
Stable angina; n (%)	19 (1.3%)	70 (2.5%)	-0.09	27 (1.1%)	82 (2.1%)	-0.08	92 (1.8%)	81 (2.4%)	-0.04	138 (1.5%)	233 (2.3%)	-0.06		
Coronary atherosclerosis and other forms of chronic ischemic heart disease; n (%)	137 (9.3%)	278 (10.0%)	-0.02	165 (6.7%)	260 (6.7%)	0.00	683 (13.7%)	516 (15.1%)	-0.04	985 (11.0%)	1,054 (10.5%)	0.02		
Other atherosclerosis with ICD10 v2 Copy; n (%)	** (0.5%)	12 (0.4%)	0.01	12 (0.5%)	** (0.2%)	0.05	38 (0.8%)	18 (0.5%)	0.04	#VALUE!	#VALUE!	#VALUE!		
Previous cardiac procedure (CABG or PTCA or Stent) v4; n (%)	** (0.3%)	** (0.1%)	0.04	** (0.2%)	21 (0.5%)	-0.05	20 (0.4%)	13 (0.4%)	0.00	#VALUE!	#VALUE!	#VALUE!		
History of CABG or PTCA; n (%)	40 (2.7%)	66 (2.4%)	0.02	19 (0.8%)	32 (0.8%)	0.00	226 (4.5%)	165 (4.8%)	-0.01	285 (3.2%)	263 (2.6%)	0.04		
Any stroke; n (%)	** (0.7%)	37 (1.3%)	-0.06	25 (1.0%)	34 (0.9%)	0.01	158 (3.2%)	103 (3.0%)	0.01	#VALUE!	174 (1.7%)	#VALUE!		
Ischemic stroke (w and w/o mention of cerebral infarction); n (%)	** (0.7%)	37 (1.3%)	-0.06	25 (1.0%)	33 (0.9%)	0.01	146 (2.9%)	100 (2.9%)	0.00	#VALUE!	170 (1.7%)	#VALUE!		
Hemorrhagic stroke; n (%)	0 (0.0%)	** (0.1%)	-0.04	0 (0.0%)	** (0.0%)	#DIV/0!	12 (0.2%)	** (0.1%)	0.03	012 (0.1%)	#VALUE!	#VALUE!		
TIA; n (%)	** (0.3%)	** (0.4%)	-0.02	** (0.3%)	12 (0.3%)	0.00	44 (0.9%)	19 (0.6%)	0.03	#VALUE!	#VALUE!	#VALUE!		
Other cerebrovascular disease; n (%)	** (0.7%)	15 (0.5%)	0.03	20 (0.8%)	22 (0.6%)	0.02	72 (1.4%)	53 (1.6%)	-0.02	#VALUE!	90 (0.9%)	#VALUE!		
Cerebrovascular procedure; n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!	** (0.0%)	** (0.0%)	#DIV/0!	#VALUE!	#VALUE!	#VALUE!		
Heart failure (CHF); n (%)	145 (9.9%)	273 (9.8%)	0.00	197 (8.0%)	326 (8.4%)	-0.01	805 (16.2%)	506 (14.9%)	0.04	1147 (12.9%)	1,105 (11.0%)	0.06		
Peripheral Vascular Disease (PVD) or PVD Surgery v2; n (%)	52 (3.5%)	92 (3.3%)	0.01	65 (2.6%)	67 (1.7%)	0.06	315 (6.3%)	206 (6.0%)	0.01	432 (4.8%)	365 (3.6%)	0.06		
Atrial fibrillation; n (%)	104 (7.1%)	173 (6.2%)	0.04	131 (5.3%)	247 (6.4%)	-0.05	503 (10.1%)	309 (9.1%)	0.03	738 (8.3%)	729 (7.2%)	0.04		
Other cardiac dysrhythmia; n (%)	263 (17.9%)	433 (15.6%)	0.06	409 (16.6%)	635 (16.4%)	0.01	1,028 (20.6%)	668 (19.6%)	0.02	1,700 (19.1%)	1,736 (17.3%)	0.05		
Cardiac conduction disorders; n (%)	94 (6.4%)	176 (6.3%)	0.00	136 (5.5%)	169 (4.4%)	0.05	366 (7.3%)	234 (6.9%)	0.02	596 (6.7%)	579 (5.8%)	0.04		
Other CVD; n (%)	396 (26.9%)	811 (29.1%)	-0.05	579 (23.5%)	1,035 (26.7%)	-0.07	1,178 (23.6%)	852 (25.0%)	-0.03	2,153 (24.1%)	2,698 (26.8%)	-0.06		
Diabetes-related complications														
Occurrence of Diabetic Neuropathy v2 Copy; n (%)	31 (2.1%)	123 (4.4%)	-0.13	46 (1.9%)	74 (1.9%)	0.00	291 (5.8%)	154 (4.5%)	0.06	368 (4.1%)	351 (3.5%)	0.03		
Occurrence of diabetic nephropathy V3 with ICD10 Copy; n (%)	21 (1.4%)	51 (1.8%)	-0.03	34 (1.4%)	37 (1.0%)	0.04	110 (2.2%)	51 (1.5%)	0.05	165 (1.8%)	139 (1.4%)	0.03		
Hypoglycemia v2; n (%)	** (0.4%)	** (0.1%)	0.06	** (0.3%)	** (0.1%)	0.04	131 (2.6%)	83 (2.4%)	0.01	#VALUE!	#VALUE!	#VALUE!		
Hyperglycemia; n (%)	131 (8.9%)	230 (8.3%)	0.02	117 (4.7%)	208 (5.4%)	-0.03	452 (9.1%)	301 (8.8%)	0.01	700 (7.8%)	739 (7.3%)	0.02		
Diabetic ketoacidosis; n (%)	** (0.3%)	16 (0.6%)	-0.04	** (0.3%)	19 (0.5%)	-0.03	27 (0.5%)	15 (0.4%)	0.01	#VALUE!	50 (0.5%)	#VALUE!		
Hypertension: 1 inpatient or 2 outpatient claims within 365 days; n (%)	588 (39.9%)	996 (35.8%)	0.08	974 (39.5%)	1,599 (41.3%)	-0.04	2,258 (45.3%)	1,402 (41.2%)	0.08	3,820 (42.8%)	3,997 (39.7%)	0.06		
Hyperlipidemia v2; n (%)	508 (34.5%)	964 (34.6%)	0.00	705 (28.6%)	1,203 (31.1%)	-0.05	1,995 (40.0%)	1,423 (41.8%)	-0.04	3,208 (36.0%)	3,590 (35.7%)	0.01		
Edema; n (%)	243 (16.5%)	444 (16.0%)	0.01	335 (13.6%)	550 (14.2%)	-0.02	789 (15.8%)	506 (14.9%)	0.02	1367 (15.3%)	1500 (14.9%)	0.01		
Renal Dysfunction (non-diabetic) v2; n (%)	213 (14.5%)	407 (14.6%)	0.00	307 (12.5%)	486 (12.5%)	0.00	916 (18.4%)	580 (17.0%)	0.04	1,436 (16.1%)	1,473 (14.6%)	0.04		
Occurrence of acute renal disease v2; n (%)	86 (5.8%)	202 (7.3%)	-0.06	159 (6.5%)	265 (6.8%)	-0.01	513 (10.3%)	284 (8.3%)	0.07	758 (8.5%)	751 (7.5%)	0.04		
Occurrence of chronic renal insufficiency; n (%)	87 (5.9%)	124 (4.5%)	0.06	84 (3.4%)	113 (2.9%)	0.03	359 (7.2%)	197 (5.8%)	0.06	530 (5.9%)	434 (4.3%)	0.07		

Appendix B

Chronic kidney disease v2; n (%)	80 (5.4%)	116 (4.2%)	0.06	76 (3.1%)	102 (2.6%)	0.03	345 (6.9%)	189 (5.5%)	0.06	501 (5.6%)	407 (4.0%)	0.07
CKD Stage 3-4; n (%)	48 (3.3%)	90 (3.2%)	0.01	56 (2.3%)	75 (1.9%)	0.03	249 (5.0%)	143 (4.2%)	0.04	353 (4.0%)	308 (3.1%)	0.05
Occurrence of hypertensive nephropathy; n (%)	41 (2.8%)	51 (1.8%)	0.07	53 (2.2%)	69 (1.8%)	0.03	213 (4.3%)	98 (2.9%)	0.08	307 (3.4%)	218 (2.2%)	0.07
Occurrence of miscellaneous renal insufficiency v2; n (%)	92 (6.2%)	163 (5.9%)	0.01	132 (5.4%)	192 (5.0%)	0.02	326 (6.5%)	229 (6.7%)	-0.01	550 (6.2%)	584 (5.8%)	0.02
Other Covariates												
Liver disease; n (%)	** (0.5%)	** (0.1%)	0.07	0 (0.0%)	** (0.1%)	-0.04	28 (0.6%)	** (0.2%)	0.06	#VALUE!	#VALUE!	#VALUE!
Osteoarthritis; n (%)	283 (19.2%)	553 (19.9%)	-0.02	397 (16.1%)	570 (14.7%)	0.04	1,164 (23.4%)	836 (24.5%)	-0.03	1844 (20.7%)	1959 (19.5%)	0.03
Other arthritis, arthropathies and musculoskeletal pain; n (%)	868 (59.0%)	1,587 (57.0%)	0.04	1,414 (57.4%)	2,100 (54.2%)	0.06	2,917 (58.5%)	1,938 (56.9%)	0.03	5199 (58.3%)	5625 (55.9%)	0.05
Dorsopathies; n (%)	440 (29.9%)	894 (32.1%)	-0.05	634 (25.7%)	995 (25.7%)	0.00	1,702 (34.2%)	1,139 (33.4%)	0.02	2776 (31.1%)	3028 (30.1%)	0.02
Fractures; n (%)	62 (4.2%)	99 (3.6%)	0.03	78 (3.2%)	114 (2.9%)	0.02	347 (7.0%)	227 (6.7%)	0.01	487 (5.5%)	440 (4.4%)	0.05
Falls v2; n (%)	88 (6.0%)	140 (5.0%)	0.04	47 (1.9%)	98 (2.5%)	-0.04	241 (4.8%)	124 (3.6%)	0.06	376 (4.2%)	362 (3.6%)	0.03
Osteoporosis; n (%)	66 (4.5%)	115 (4.1%)	0.02	53 (2.2%)	68 (1.8%)	0.03	400 (8.0%)	306 (9.0%)	-0.04	519 (5.8%)	489 (4.9%)	0.04
Depression; n (%)	286 (19.4%)	455 (16.3%)	0.08	334 (13.6%)	495 (12.8%)	0.02	1,352 (27.1%)	888 (26.1%)	0.02	1972 (22.1%)	1838 (18.3%)	0.09
Anxiety; n (%)	305 (20.7%)	617 (22.2%)	-0.04	407 (16.5%)	699 (18.0%)	-0.04	1,372 (27.5%)	959 (28.2%)	-0.02	2084 (23.4%)	2275 (22.6%)	0.02
Sleep_Disorder; n (%)	74 (5.0%)	81 (2.9%)	0.11	196 (8.0%)	109 (2.8%)	0.23	376 (7.5%)	105 (3.1%)	0.20	646 (7.2%)	295 (2.9%)	0.20
Dementia; n (%)	73 (5.0%)	136 (4.9%)	0.00	49 (2.0%)	70 (1.8%)	0.01	577 (11.6%)	375 (11.0%)	0.02	699 (7.8%)	581 (5.8%)	0.08
Delirium; n (%)	34 (2.3%)	80 (2.9%)	-0.04	42 (1.7%)	55 (1.4%)	0.02	345 (6.9%)	203 (6.0%)	0.04	421 (4.7%)	338 (3.4%)	0.07
Psychosis; n (%)	25 (1.7%)	51 (1.8%)	-0.01	25 (1.0%)	37 (1.0%)	0.00	418 (8.4%)	305 (9.0%)	-0.02	468 (5.2%)	393 (3.9%)	0.06
Obesity; n (%)	561 (38.1%)	974 (35.0%)	0.06	869 (35.3%)	1,303 (33.6%)	0.04	1,465 (29.4%)	837 (24.6%)	0.11	2895 (32.5%)	3114 (30.9%)	0.03
Overweight; n (%)	64 (4.3%)	193 (6.9%)	-0.11	74 (3.0%)	212 (5.5%)	-0.12	175 (3.5%)	165 (4.8%)	-0.07	313 (3.5%)	570 (5.7%)	-0.11
Smoking; n (%)	538 (36.5%)	1,004 (36.1%)	0.01	444 (18.0%)	742 (19.2%)	-0.03	2,380 (47.8%)	1,651 (48.5%)	-0.01	3362 (37.7%)	3397 (33.8%)	0.08
Alcohol abuse or dependence; n (%)	25 (1.7%)	56 (2.0%)	-0.02	33 (1.3%)	45 (1.2%)	0.01	102 (2.0%)	80 (2.3%)	-0.02	160 (1.8%)	181 (1.8%)	0.00
Drug abuse or dependence; n (%)	75 (5.1%)	163 (5.9%)	-0.04	50 (2.0%)	87 (2.2%)	-0.01	319 (6.4%)	228 (6.7%)	-0.01	444 (5.0%)	478 (4.8%)	0.01
COPD; n (%)	256 (17.4%)	430 (15.5%)	0.05	219 (8.9%)	306 (7.9%)	0.04	1,312 (26.3%)	902 (26.5%)	0.00	1787 (20.0%)	1638 (16.3%)	0.10
Asthma; n (%)	203 (13.8%)	348 (12.5%)	0.04	284 (11.5%)	441 (11.4%)	0.00	773 (15.5%)	484 (14.2%)	0.04	1260 (14.1%)	1273 (12.7%)	0.04
Obstructive sleep apnea; n (%)	261 (17.7%)	405 (14.6%)	0.08	375 (15.2%)	538 (13.9%)	0.04	748 (15.0%)	465 (13.7%)	0.04	1384 (15.5%)	1408 (14.0%)	0.04
Pneumonia; n (%)	258 (17.5%)	513 (18.4%)	-0.02	363 (14.7%)	651 (16.8%)	-0.06	1,074 (21.6%)	748 (22.0%)	-0.01	1695 (19.0%)	1912 (19.0%)	0.00
Other Medications												
Use of ACE inhibitors; n (%)	223 (15.1%)	334 (12.0%)	0.09	392 (15.9%)	614 (15.8%)	0.00	751 (15.1%)	437 (12.8%)	0.07	1366 (15.3%)	1385 (13.8%)	0.04
Use of ARBs; n (%)	94 (6.4%)	200 (7.2%)	-0.03	218 (8.8%)	364 (9.4%)	-0.02	233 (4.7%)	163 (4.8%)	0.00	545 (6.1%)	727 (7.2%)	-0.04
Use of Loop Diuretics - United; n (%)	117 (7.9%)	190 (6.8%)	0.04	166 (6.7%)	232 (6.0%)	0.03	677 (13.6%)	383 (11.2%)	0.07	960 (10.8%)	805 (8.0%)	0.10
Use of other diuretics-United; n (%)	34 (2.3%)	60 (2.2%)	0.01	52 (2.1%)	78 (2.0%)	0.01	138 (2.8%)	74 (2.2%)	0.04	224 (2.5%)	212 (2.1%)	0.03
Use of nitrates-United; n (%)	20 (1.4%)	42 (1.5%)	-0.01	33 (1.3%)	43 (1.1%)	0.02	158 (3.2%)	123 (3.6%)	-0.02	211 (2.4%)	208 (2.1%)	0.02
Use of other hypertension drugs; n (%)	33 (2.2%)	69 (2.5%)	-0.02	65 (2.6%)	89 (2.3%)	0.02	235 (4.7%)	147 (4.3%)	0.02	333 (3.7%)	305 (3.0%)	0.04
Use of Anti-arrhythmics; n (%)	16 (1.1%)	34 (1.2%)	-0.01	25 (1.0%)	59 (1.5%)	-0.05	57 (1.1%)	53 (1.6%)	-0.04	98 (1.1%)	146 (1.5%)	-0.04
Use of COPD/asthma meds- United; n (%)	243 (16.5%)	463 (16.6%)	0.00	359 (14.6%)	635 (16.4%)	-0.05	1,077 (21.6%)	815 (23.9%)	-0.05	1679 (18.8%)	1913 (19.0%)	-0.01
Use of statins; n (%)	288 (19.6%)	557 (20.1%)	-0.01	459 (18.6%)	739 (19.1%)	-0.01	1,330 (26.7%)	935 (27.5%)	-0.02	2077 (23.3%)	2231 (22.2%)	0.03
Use of other lipid-lowering drugs; n (%)	47 (3.2%)	95 (3.4%)	-0.01	94 (3.8%)	153 (3.9%)	-0.01	236 (4.7%)	155 (4.6%)	0.00	377 (4.2%)	403 (4.0%)	0.01
Use of antiplatelet agents; n (%)	24 (1.6%)	43 (1.5%)	0.01	53 (2.2%)	92 (2.4%)	-0.01	235 (4.7%)	161 (4.7%)	0.00	312 (3.5%)	296 (2.9%)	0.03
Use of heparin and other low-molecular weight heparins; n (%)	840 (57.1%)	122 (4.4%)	1.39	** (0.1%)	** (0.0%)	0.04	2,098 (42.1%)	154 (4.5%)	0.99	#VALUE!	#VALUE!	#VALUE!
Use of NSAIDs; n (%)	156 (10.6%)	344 (12.4%)	-0.06	348 (14.1%)	620 (16.0%)	-0.05	542 (10.9%)	385 (11.3%)	-0.01	1046 (11.7%)	1349 (13.4%)	-0.05
Use of opioids-United; n (%)	589 (40.0%)	1,111 (39.9%)	0.00	1,127 (45.7%)	1,713 (44.2%)	0.03	2,163 (43.4%)	1,464 (43.0%)	0.01	3879 (43.5%)	4288 (42.6%)	0.02
Use of antidepressants; n (%)	385 (26.2%)	715 (25.7%)	0.01	560 (22.7%)	915 (23.6%)	-0.02	1,907 (38.3%)	1,309 (38.4%)	0.00	2852 (32.0%)	2939 (29.2%)	0.06
Use of antipsychotics; n (%)	69 (4.7%)	147 (5.3%)	-0.03	94 (3.8%)	144 (3.7%)	0.01	763 (15.3%)	544 (16.0%)	-0.02	926 (10.4%)	835 (8.3%)	0.07
Labs												
Lab values- HbA1c (%) v3; n (%)	129 (8.8%)	284 (10.2%)	-0.05	** (0.4%)	35 (0.9%)	-0.06	N/A	N/A	#VALUE!	3,936 #VALUE!	6,657 #VALUE!	#VALUE!
Lab values- HbA1c (%) (within 3 months) v3; n (%)	75 (5.1%)	179 (6.4%)	-0.06	** (0.3%)	23 (0.6%)	-0.04	N/A	N/A	#VALUE!	#VALUE!	202 (3.0%)	#VALUE!
Lab values- HbA1c (%) (within 6 months) v3; n (%)	129 (8.8%)	284 (10.2%)	-0.05	** (0.4%)	35 (0.9%)	-0.06	N/A	N/A	#VALUE!	#VALUE!	319 (4.8%)	#VALUE!
Lab values- BNP; n (%)	22 (1.5%)	37 (1.3%)	0.02	0 (0.0%)	** (0.2%)	-0.06	N/A	N/A	#VALUE!	022 (0.6%)	#VALUE!	#VALUE!
Lab values- BNP (within 3 months); n (%)	21 (1.4%)	35 (1.3%)	0.01	0 (0.0%)	** (0.2%)	-0.06	N/A	N/A	#VALUE!	021 (0.5%)	#VALUE!	#VALUE!
Lab values- BNP (within 6 months); n (%)	22 (1.5%)	37 (1.3%)	0.02	0 (0.0%)	** (0.2%)	-0.06	N/A	N/A	#VALUE!	022 (0.6%)	#VALUE!	#VALUE!
Lab values- BUN (mg/dl); n (%)	290 (19.7%)	642 (23.1%)	-0.08	18 (0.7%)	49 (1.3%)	-0.06	N/A	N/A	#VALUE!	308 (7.8%)	691 (10.4%)	-0.09
Lab values- BUN (mg/dl) (within 3 months); n (%)	203 (13.8%)	452 (16.2%)	-0.07	** (0.4%)	32 (0.8%)	-0.05	N/A	N/A	#VALUE!	#VALUE!	484 (7.3%)	#VALUE!
Lab values- BUN (mg/dl) (within 6 months); n (%)	290 (19.7%)	642 (23.1%)	-0.08	18 (0.7%)	49 (1.3%)	-0.06	N/A	N/A	#VALUE!	308 (7.8%)	691 (10.4%)	-0.09
Lab values- Creatinine (mg/dl) v2; n (%)	297 (20.2%)	679 (24.4%)	-0.10	20 (0.8%)	52 (1.3%)	-0.05	N/A	N/A	#VALUE!	317 (8.1%)	731 (11.0%)	-0.10
Lab values- Creatinine (mg/dl) (within 3 months) v2; n (%)	206 (14.0%)	483 (17.4%)	-0.09	12 (0.5%)	34 (0.9%)	-0.05	N/A	N/A	#VALUE!	218 (5.5%)	517 (7.8%)	-0.09
Lab values- Creatinine (mg/dl) (within 6 months) v2; n (%)	297 (20.2%)	679 (24.4%)	-0.10	20 (0.8%)	52 (1.3%)	-0.05	N/A	N/A	#VALUE!	317 (8.1%)	731 (11.0%)	-0.10
Lab values- HDL level (mg/dl); n (%)	164 (11.1%)	376 (13.5%)	-0.07	12 (0.5%)	37 (1.0%)	-0.06	N/A	N/A	#VALUE!	176 (4.5%)	413 (6.2%)	-0.08
Lab values- HDL level (mg/dl) (within 3 months); n (%)	90 (6.1%)	211 (7.6%)	-0.06	** (0.3%)	23 (0.6%)	-0.04	N/A	N/A	#VALUE!	#VALUE!	234 (3.5%)	#VALUE!
Lab values- HDL level (mg/dl) (within 6 months); n (%)	164 (11.1%)	376 (13.5%)	-0.07	12 (0.5%)	37 (1.0%)	-0.06	N/A	N/A	#VALUE!	176 (4.5%)	413 (6.2%)	-0.08
Lab values- LDL level (mg/dl) v2; n (%)	167 (11.3%)	387 (13.9%)	-0.08	13 (0.5%)	37 (1.0%)	-0.06	N/A	N/A	#VALUE!	180 (4.6%)	424 (6.4%)	-0.08

Appendix B

Lab values- LDL level (mg/dl) (within 3 months) v2; n (%)	91 (6.2%)	217 (7.8%)	-0.06	** (0.3%)	24 (0.6%)	-0.04	N/A	N/A	#VALUE!	#VALUE!	241 (3.6%)	#VALUE!
Lab values- LDL level (mg/dl) (within 6 months) v2; n (%)	167 (11.3%)	387 (13.9%)	-0.08	13 (0.5%)	37 (1.0%)	-0.06	N/A	N/A	#VALUE!	180 (4.6%)	424 (6.4%)	-0.08
Lab values- NT-proBNP; n (%)	** (0.6%)	** (0.2%)	0.06	0 (0.0%)	0 (0.0%)	#DIV/0!	N/A	N/A	#VALUE!	#VALUE!	#VALUE!	#VALUE!
Lab values- NT-proBNP (within 3 months); n (%)	** (0.5%)	** (0.1%)	0.07	0 (0.0%)	0 (0.0%)	#DIV/0!	N/A	N/A	#VALUE!	#VALUE!	#VALUE!	-
Lab values- NT-proBNP (within 6 months); n (%)	** (0.6%)	** (0.2%)	0.06	0 (0.0%)	0 (0.0%)	#DIV/0!	N/A	N/A	#VALUE!	#VALUE!	#VALUE!	-
Lab values- Total cholesterol (mg/dl) v2; n (%)	169 (11.5%)	386 (13.9%)	-0.07	** (0.4%)	38 (1.0%)	-0.07	N/A	N/A	#VALUE!	#VALUE!	424 (6.4%)	#VALUE!
Lab values- Total cholesterol (mg/dl) (within 3 months) v2; n (%)	92 (6.2%)	215 (7.7%)	-0.06	** (0.3%)	24 (0.6%)	-0.04	N/A	N/A	#VALUE!	#VALUE!	239 (3.6%)	#VALUE!
Lab values- Total cholesterol (mg/dl) (within 6 months) v2; n (%)	169 (11.5%)	386 (13.9%)	-0.07	** (0.4%)	38 (1.0%)	-0.07	N/A	N/A	#VALUE!	#VALUE!	424 (6.4%)	#VALUE!
Lab values- Triglyceride level (mg/dl); n (%)	167 (11.3%)	382 (13.7%)	-0.07	12 (0.5%)	36 (0.9%)	-0.05	N/A	N/A	#VALUE!	179 (4.5%)	418 (6.3%)	-0.08
Lab values- Triglyceride level (mg/dl) (within 3 months); n (%)	90 (6.1%)	212 (7.6%)	-0.06	** (0.3%)	22 (0.6%)	-0.04	N/A	N/A	#VALUE!	#VALUE!	234 (3.5%)	#VALUE!
Lab values- Triglyceride level (mg/dl) (within 6 months); n (%)	167 (11.3%)	382 (13.7%)	-0.07	12 (0.5%)	36 (0.9%)	-0.05	N/A	N/A	#VALUE!	179 (4.5%)	418 (6.3%)	-0.08
Lab result number- HbA1c (%) mean (only 2 to 20 included) v4	129	283		11	35		N/A	N/A		140	318	
...mean (sd)	6.38 (1.65)	6.67 (1.84)	-0.17	7.09 (1.28)	7.19 (1.62)	-0.07	N/A	N/A	#VALUE!	6.44 (1.63)	6.73 (1.82)	-0.17
...Missing; n (%)	1,343 (91.2%)	2,500 (89.8%)	0.05	2,453 (99.6%)	3,839 (99.1%)	0.06	N/A	N/A	#VALUE!	3,796 (96.4%)	6,339 (95.2%)	0.06
Lab result number- BNP mean v2	22	37		-	6		N/A	N/A		22	43	
...mean (sd)	188.71 (481.48)	211.85 (716.09)	-0.04	- (-)	821.82 (1,746.63)	#VALUE!	N/A	N/A	#VALUE!	#VALUE!	296.96 (918.07)	#VALUE!
...Missing; n (%)	1,450 (98.5%)	2,746 (98.7%)	-0.02	2,464 (100.0%)	3,868 (99.8%)	0.06	N/A	N/A	#VALUE!	3,914 (99.4%)	6,614 (99.4%)	0.00
Lab result number- BUN (mg/dl) mean v2	290	642		18	49		N/A	N/A		308	691	
...mean (sd)	14.97 (5.67)	14.75 (4.93)	0.04	11,126.96 (35,122.84)	14.95 (5.16)	0.45	N/A	N/A	#VALUE!	664.37 (8292.09)	14.76 (4.95)	0.11
...Missing; n (%)	1,182 (80.3%)	2,141 (76.9%)	0.08	2,446 (99.3%)	3,825 (98.7%)	0.06	N/A	N/A	#VALUE!	3,628 (92.2%)	5,966 (89.6%)	0.09
Lab result number- Creatinine (mg/dl) mean (only 0.1 to 15 included) v3	292	674		18	52		N/A	N/A		310	726	
...mean (sd)	0.91 (0.29)	0.92 (0.23)	-0.04	1.05 (0.31)	0.95 (0.19)	0.39	N/A	N/A	#VALUE!	0.92 (0.29)	0.92 (0.23)	0.00
...Missing; n (%)	1,180 (80.2%)	2,109 (75.8%)	0.11	2,446 (99.3%)	3,822 (98.7%)	0.06	N/A	N/A	#VALUE!	3,626 (92.1%)	5,931 (89.1%)	0.10
Lab result number- HDL level (mg/dl) mean (only <=5000 included) v2	164	376		11	37		N/A	N/A		175	413	
...mean (sd)	54.89 (18.99)	49.89 (16.20)	0.28	48.00 (11.92)	42.95 (12.24)	0.42	N/A	N/A	#VALUE!	54.46 (18.71)	49.27 (15.91)	0.30
...Missing; n (%)	1,308 (88.9%)	2,407 (86.5%)	0.07	2,453 (99.6%)	3,837 (99.0%)	0.07	N/A	N/A	#VALUE!	3,761 (95.6%)	6,244 (93.8%)	0.08
Lab result number- LDL level (mg/dl) mean (only <=5000 included) v2	164	385		11	34		N/A	N/A		175	419	
...mean (sd)	108.72 (37.92)	112.46 (39.24)	-0.10	92.09 (39.78)	94.24 (30.60)	-0.06	N/A	N/A	#VALUE!	107.67 (38.14)	110.98 (38.67)	-0.09
...Missing; n (%)	1,308 (88.9%)	2,398 (86.2%)	0.08	2,453 (99.6%)	3,840 (99.1%)	0.06	N/A	N/A	#VALUE!	3,761 (95.6%)	6,238 (93.7%)	0.08
Lab result number- Total cholesterol (mg/dl) mean (only <=5000 included) v2	169	386		10	38		N/A	N/A		179	424	
...mean (sd)	191.79 (42.02)	191.77 (43.11)	0.00	176.40 (28.15)	173.63 (53.27)	0.07	N/A	N/A	#VALUE!	190.93 (41.54)	190.14 (44.15)	0.02
...Missing; n (%)	1,303 (88.5%)	2,397 (86.1%)	0.07	2,454 (99.6%)	3,836 (99.0%)	0.07	N/A	N/A	#VALUE!	3,757 (95.5%)	6,233 (93.6%)	0.08
Lab result number- Triglyceride level (mg/dl) mean (only <=5000 included) v2	167	382		11	36		N/A	N/A		178	418	
...mean (sd)	132.55 (72.17)	147.15 (76.74)	-0.20	163.09 (137.89)	220.01 (535.52)	-0.15	N/A	N/A	#VALUE!	134.44 (77.63)	153.43 (172.03)	-0.14
...Missing; n (%)	1,305 (88.7%)	2,401 (86.3%)	0.07	2,453 (99.6%)	3,838 (99.1%)	0.06	N/A	N/A	#VALUE!	3,758 (95.5%)	6,239 (93.7%)	0.08
Lab result number- Hemoglobin mean (only >0 included)	255	568		13	41		N/A	N/A		268	609	
...mean (sd)	13.68 (1.85)	13.90 (1.82)	-0.12	18,472.91 (45,243.58)	14.22 (1.44)	0.58	N/A	N/A	#VALUE!	909.09 (9627.75)	13.92 (1.80)	0.13
...Missing; n (%)	1,217 (82.7%)	2,215 (79.6%)	0.08	2,451 (99.5%)	3,833 (98.9%)	0.07	N/A	N/A	#VALUE!	3,668 (93.2%)	6,048 (90.9%)	0.09
Lab result number- Serum sodium mean (only >90 and < 190 included)	283	641		16	50		N/A	N/A		299	691	
...mean (sd)	140.35 (2.52)	140.27 (2.65)	0.03	138.74 (3.71)	139.42 (2.77)	-0.21	N/A	N/A	#VALUE!	140.26 (2.60)	140.21 (2.66)	0.02
...Missing; n (%)	1,189 (80.8%)	2,142 (77.0%)	0.09	2,448 (99.4%)	3,824 (98.7%)	0.07	N/A	N/A	#VALUE!	3,637 (92.4%)	5,966 (89.6%)	0.10
Lab result number- Albumin mean (only >0 and <=10 included)	254	602		14	41		N/A	N/A		268	643	
...mean (sd)	4.05 (0.45)	4.16 (0.37)	-0.27	4.10 (0.28)	4.09 (0.41)	0.03	N/A	N/A	#VALUE!	4.05 (0.44)	4.16 (0.37)	-0.27
...Missing; n (%)	1,218 (82.7%)	2,181 (78.4%)	0.11	2,450 (99.4%)	3,833 (98.9%)	0.05	N/A	N/A	#VALUE!	3,668 (93.2%)	6,014 (90.3%)	0.11
Lab result number- Glucose (fasting or random) mean (only 10-1000 included)	282	638		17	52		N/A	N/A		299	690	
...mean (sd)	107.08 (33.93)	111.43 (45.57)	-0.11	140.46 (83.78)	142.00 (79.78)	-0.02	N/A	N/A	#VALUE!	108.98 (38.37)	113.73 (48.97)	-0.11
...Missing; n (%)	1,190 (80.8%)	2,145 (77.1%)	0.09	2,447 (99.3%)	3,822 (98.7%)	0.06	N/A	N/A	#VALUE!	3,637 (92.4%)	5,967 (89.6%)	0.10
Lab result number- Potassium mean (only 1-7 included)	294	667		17	48		N/A	N/A		311	715	
...mean (sd)	4.33 (0.42)	4.36 (0.38)	-0.07	4.36 (0.54)	4.28 (0.39)	0.17	N/A	N/A	#VALUE!	4.33 (0.43)	4.35 (0.38)	-0.05
...Missing; n (%)	1,178 (80.0%)	2,116 (76.0%)	0.10	2,447 (99.3%)	3,826 (98.8%)	0.05	N/A	N/A	#VALUE!	3,625 (92.1%)	5,942 (89.3%)	0.10
Comorbidity Scores												
Combined comorbidity score, 365 days Copy												
...mean (sd)	3.18 (2.27)	3.34 (2.24)	-0.07	2.50 (2.14)	2.91 (2.13)	-0.19	3.69 (2.64)	3.77 (2.52)	-0.03	3.28 (2.45)	3.32 (2.30)	-0.02

Appendix B

Non-Frailty; n (%)	607 (41.2%)	1,297 (46.6%)	-0.11	986 (40.0%)	1,622 (41.9%)	-0.04	219 (4.4%)	103 (3.0%)	0.07	1,812 (20.3%)	3,022 (30.0%)	-0.22
Frailty Score (mean): Empirical Version 365 days, v2 ...mean (sd)	0.17 (0.06)	0.17 (0.06)	0.00	0.16 (0.05)	0.15 (0.05)	0.20	0.10 (0.08)	0.09 (0.07)	0.13	0.13 (0.07)	0.14 (0.06)	-0.15
Healthcare Utilization												
Any hospitalization; n (%)	1,342 (91.2%)	2,517 (90.4%)	0.03	2,456 (99.7%)	3,872 (99.9%)	-0.04	4,571 (91.7%)	2,940 (86.3%)	0.17	8,369 (93.8%)	9,329 (92.7%)	0.04
Any hospitalization within prior 30 days; n (%)	1,218 (82.7%)	2,064 (74.2%)	0.21	2,325 (94.4%)	3,266 (84.3%)	0.33	3,605 (72.3%)	2,224 (65.3%)	0.15	7148 (80.1%)	7554 (75.1%)	0.12
Any hospitalization during prior 31-180 days; n (%)	210 (14.3%)	596 (21.4%)	-0.19	279 (11.3%)	830 (21.4%)	-0.28	1,509 (30.3%)	1,094 (32.1%)	-0.04	1998 (22.4%)	2520 (25.0%)	-0.06
Internal medicine/family medicine visits; n (%)	1,258 (85.5%)	2,349 (84.4%)	0.03	1,907 (77.4%)	3,135 (80.9%)	-0.09	4,700 (94.3%)	3,253 (95.5%)	-0.05	7865 (88.2%)	8737 (86.8%)	0.04
Internal medicine/family medicine visits (30 days prior) v2; n (%)	1,116 (75.8%)	1,989 (71.5%)	0.10	1,366 (55.4%)	2,291 (59.1%)	-0.07	4,141 (83.1%)	2,772 (81.4%)	0.04	6623 (74.3%)	7052 (70.1%)	0.09
Internal medicine/family medicine visits (31 to 180 days prior) v2; n (%)	789 (53.6%)	1,532 (55.0%)	-0.03	1,473 (59.8%)	2,428 (62.7%)	-0.06	3,375 (67.7%)	2,384 (70.0%)	-0.05	5637 (63.2%)	6344 (63.0%)	0.00
Cardiologist visit; n (%)	1,070 (72.7%)	2,090 (75.1%)	-0.05	635 (25.8%)	1,120 (28.9%)	-0.07	3,481 (69.9%)	2,461 (72.3%)	-0.05	5186 (58.1%)	5671 (56.4%)	0.03
Number of Cardiologist visits (30 days prior); n (%)	938 (63.7%)	1,782 (64.0%)	-0.01	430 (17.5%)	779 (20.1%)	-0.07	2,604 (52.3%)	1,815 (53.3%)	-0.02	3972 (44.5%)	4376 (43.5%)	0.02
Number of Cardiologist visits (31 to 180 days prior); n (%)	283 (19.2%)	629 (22.6%)	-0.08	286 (11.6%)	527 (13.6%)	-0.06	1,509 (30.3%)	1,143 (33.6%)	-0.07	2078 (23.3%)	2299 (22.8%)	0.01
Electrocardiogram v2; n (%)	1,212 (82.3%)	2,366 (85.0%)	-0.07	1,173 (47.6%)	1,921 (49.6%)	-0.04	4,197 (84.2%)	2,949 (86.6%)	-0.07	6582 (73.8%)	7236 (71.9%)	0.04
Use of glucose test strips; n (%)	12 (0.8%)	29 (1.0%)	-0.02	28 (1.1%)	41 (1.1%)	0.00	79 (1.6%)	49 (1.4%)	0.02	119 (1.3%)	119 (1.2%)	0.01
Dialysis; n (%)	0 (0.0%)	** (0.0%)	#DIV/0!	** (0.1%)	** (0.0%)	0.04	** (0.1%)	** (0.1%)	0.00	#VALUE!	#VALUE!	#VALUE!
number of different/distinct medication prescriptions ...mean (sd)	7.51 (5.02)	7.40 (5.43)	0.02	7.83 (4.96)	7.62 (5.35)	0.04	9.24 (6.13)	9.03 (6.18)	0.03	8.56 (5.65)	8.04 (5.67)	0.00
Number of Hospitalizations ...mean (sd)	1.06 (0.59)	1.04 (0.59)	0.03	1.15 (0.49)	1.15 (0.46)	0.00	1.26 (0.90)	1.19 (0.91)	0.08	1.20 (0.76)	1.13 (0.68)	0.00
Number of hospital days ...mean (sd)	4.88 (4.21)	3.69 (3.93)	0.29	5.81 (5.06)	4.29 (4.36)	0.32	5.63 (6.19)	4.42 (5.91)	0.20	5.56 (5.60)	4.17 (4.84)	0.00
Number of Emergency Department (ED) visits v3 ...mean (sd)	1.67 (2.14)	1.71 (2.26)	-0.02	3.11 (4.52)	3.36 (5.17)	-0.05	2.65 (5.20)	2.69 (4.62)	-0.01	2.62 (4.64)	2.68 (4.35)	0.00
Number of Office visits ...mean (sd)	4.43 (4.31)	4.96 (4.44)	-0.12	4.45 (4.21)	5.00 (4.89)	-0.12	9.79 (12.11)	11.14 (13.34)	-0.11	7.43 (9.48)	7.07 (8.65)	0.00
Number of internal medicine/family medicine visits ...mean (sd)	8.44 (11.38)	8.11 (12.98)	0.03	5.17 (8.34)	5.69 (9.30)	-0.06	11.97 (12.82)	10.87 (11.70)	0.09	9.51 (11.51)	8.11 (11.23)	0.00
Number of Cardiologist visits ...mean (sd)	2.25 (3.08)	2.58 (3.92)	-0.09	0.63 (1.78)	0.78 (2.35)	-0.07	2.57 (4.11)	2.71 (4.05)	-0.03	1.98 (3.45)	1.93 (3.45)	0.00
Number electrocardiograms received v2 ...mean (sd)	1.88 (1.87)	2.01 (1.96)	-0.07	0.85 (1.27)	0.91 (1.37)	-0.05	2.23 (2.51)	2.36 (2.62)	-0.05	1.79 (2.13)	1.70 (2.03)	0.00
Number of HbA1c tests ordered ...mean (sd)	0.24 (0.56)	0.27 (0.59)	-0.05	0.20 (0.49)	0.22 (0.53)	-0.04	0.29 (0.63)	0.29 (0.62)	0.00	0.26 (0.58)	0.26 (0.58)	0.00
Number of glucose tests ordered ...mean (sd)	0.10 (0.52)	0.17 (0.82)	-0.10	0.11 (0.91)	0.11 (0.52)	0.00	0.16 (0.58)	0.17 (0.72)	-0.02	0.14 (0.68)	0.15 (0.68)	0.00
Number of lipid tests ordered ...mean (sd)	0.35 (0.62)	0.37 (0.64)	-0.03	0.35 (0.72)	0.36 (0.90)	-0.01	0.34 (0.65)	0.40 (0.65)	-0.09	0.34 (0.67)	0.38 (0.75)	0.00
Total N distinct ICD9/ICD10 diagnoses at the 3rd digit level Copy ...mean (sd)	10.10 (11.60)	10.98 (12.08)	-0.07	8.83 (10.24)	10.70 (10.19)	-0.18	15.68 (15.31)	15.80 (15.08)	-0.01	12.87 (13.50)	12.50 (12.54)	0.00
For PS												
Hemorrhagic stroke+Other cerebrovascular disease+Cerebrovascular procedure (for PS); n (%)	37 (2.5%)	** (0.7%)	17 (0.6%)	20 (0.8%)	23 (0.6%)	0.02	78 (1.6%)	54 (1.6%)	0.00	#VALUE!	94 (0.9%)	#VALUE!
immobilization; n (%)		73 (2.6%)	#DIV/0!	52 (2.1%)	75 (1.9%)	#DIV/0!	2.01 (1.68)	1.45 (1.21)		52 (2.1%)	75 (1.9%)	0.21
Occurrence of creatinine tests ordered (for PS); n (%)	82 (5.6%)	194 (7.0%)	-0.06	147 (6.0%)	199 (5.1%)	0.04	430 (8.6%)	286 (8.4%)	0.01	659 (7.4%)	679 (6.7%)	0.03
Occurrence of BUN tests ordered (for PS); n (%)	33 (2.2%)	81 (2.9%)	-0.04	76 (3.1%)	103 (2.7%)	0.02	225 (4.5%)	151 (4.4%)	0.00	334 (3.7%)	335 (3.3%)	0.02
Occurrence of chronic renal insufficiency w/o CKD (for PS) v2; n (%)	18 (1.2%)	13 (0.5%)	0.08	23 (0.9%)	16 (0.4%)	0.06	102 (2.0%)	32 (0.9%)	0.09	143 (1.6%)	61 (0.6%)	0.10
Chronic kidney disease Stage 1-2 (for PS); n (%)	27 (1.8%)	28 (1.0%)	0.07	18 (0.7%)	29 (0.7%)	0.00	0	0	#VALUE!	#VALUE!	#VALUE!	#VALUE!
Chronic kidney disease Stage 3-6 (for PS); n (%)	48 (3.3%)	90 (3.2%)	0.01	56 (2.3%)	75 (1.9%)	0.03	249 (5.0%)	143 (4.2%)	0.04	353 (4.0%)	308 (3.1%)	0.05
Acute kidney injury; n (%)	86 (5.8%)	204 (7.3%)	#DIV/0!	159 (6.5%)	264 (6.8%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!	159 (6.5%)	264 (6.8%)	0.37
Bladder stones+Kidney stones (for PS); n (%)	58 (3.9%)	111 (4.0%)	-0.01	69 (2.8%)	118 (3.0%)	-0.01	177 (3.6%)	117 (3.4%)	0.01	304 (3.4%)	346 (3.4%)	0.00
Alcohol abuse or dependence+Drug abuse or dependence (for PS); n (%)	93 (6.3%)	210 (7.5%)	-0.05	77 (3.1%)	126 (3.3%)	-0.01	387 (7.8%)	279 (8.2%)	-0.01	557 (6.2%)	615 (6.1%)	0.00
Other atherosclerosis+Cardiac conduction disorders+Other CVD (for PS) v2 Copy; n (%)	459 (31.2%)	916 (32.9%)	-0.04	670 (27.2%)	1,136 (29.3%)	-0.05	1,423 (28.6%)	1,010 (29.7%)	-0.02	2552 (28.6%)	3062 (30.4%)	-0.04

Appendix B

Previous cardiac procedure (CABG or PTCA or Stent) + History of CABG or PTCA (for PS) v3; n (%)	44 (3.0%)	67 (2.4%)	0.04	24 (1.0%)	41 (1.1%)	-0.01	236 (4.7%)	166 (4.9%)	-0.01	304 (3.4%)	274 (2.7%)	0.04
Diabetes with complication; n (%)	61 (4.1%)	193 (6.9%)	#DIV/0!	96 (3.9%)	139 (3.6%)	#DIV/0!	240 (4.8%)	165 (4.8%)	#DIV/0!	96 (3.9%)	139 (3.6%)	0.28
Delirium + Psychosis (for PS); n (%)	56 (3.8%)	123 (4.4%)	-0.03	58 (2.4%)	88 (2.3%)	0.01	681 (13.7%)	456 (13.4%)	0.01	795 (8.9%)	667 (6.6%)	0.09
Any use of Meglitinides (for PS); n (%)	0 (0.0%)	** (0.1%)	-0.04	** (0.1%)	** (0.0%)	0.04	** (0.0%)	** (0.0%)	#DIV/0!	#VALUE!	#VALUE!	#VALUE!
Any use of AGIs (for PS); n (%)	** (0.1%)	** (0.0%)	0.04	** (0.0%)	** (0.0%)	#DIV/0!	** (0.0%)	0 (0.0%)	#DIV/0!	#VALUE!	#VALUE!	#VALUE!
CKD stage 3-6 + dialysis (for PS); n (%)	48 (3.3%)	93 (3.3%)	0.00	58 (2.4%)	77 (2.0%)	0.03	251 (5.0%)	147 (4.3%)	0.03	357 (4.0%)	317 (3.2%)	0.04
Use of thiazide- United; n (%)	80 (5.4%)	111 (4.0%)	0.07	144 (5.8%)	218 (5.6%)	0.01	218 (4.4%)	132 (3.9%)	0.03	442 (5.0%)	461 (4.6%)	0.02
Use of beta blockers; n (%)	204 (13.9%)	361 (13.9%)	0.03	391 (15.9%)	629 (16.2%)	-0.01	933 (18.7%)	556 (16.3%)	0.06	1528 (17.1%)	1546 (15.4%)	0.05
Use of calcium channel blockers; n (%)	151 (10.3%)	283 (10.2%)	0.00	280 (11.4%)	463 (12.0%)	-0.02	507 (10.2%)	305 (9.0%)	0.04	938 (10.5%)	1051 (10.4%)	0.00
All anti diabetic medications except Insulin; n (%)	146 (9.9%)	299 (10.7%)	-0.03	259 (10.5%)	426 (11.0%)	-0.02	620 (12.4%)	405 (11.9%)	0.02	1025 (11.5%)	1130 (11.2%)	0.01
DM Medications - Insulin Copy; n (%)	48 (3.3%)	111 (4.0%)	-0.04	112 (4.5%)	147 (3.8%)	0.04	247 (5.0%)	149 (4.4%)	0.03	407 (4.6%)	407 (4.0%)	0.03
Use of Low Intensity Statins; n (%)	169 (11.5%)	283 (10.2%)	0.04	245 (9.9%)	375 (9.7%)	0.01	788 (15.8%)	546 (16.0%)	-0.01	1202 (13.5%)	1204 (12.0%)	0.04
Use of High Intensity Statins; n (%)	127 (8.6%)	281 (10.1%)	-0.05	216 (8.8%)	380 (9.8%)	-0.03	562 (11.3%)	417 (12.2%)	-0.03	905 (10.1%)	1078 (10.7%)	-0.02
Malignant hypertension; n (%)	** (0.6%)	** (0.1%)	0.08	317 (12.9%)	101 (2.6%)	0.39	517 (10.4%)	93 (2.7%)	0.32	#VALUE!	#VALUE!	#VALUE!
Cardiovascular stress test; n (%)	** (0.7%)	12 (0.4%)	0.04	12 (0.5%)	26 (0.7%)	-0.03	73 (1.5%)	60 (1.8%)	-0.02	#VALUE!	98 (1.0%)	#VALUE!
Echocardiogram; n (%)	909 (61.8%)	1,927 (69.2%)	-0.16	1,573 (63.8%)	2,714 (70.1%)	-0.13	2,941 (59.0%)	2,092 (61.4%)	-0.05	5423 (60.8%)	6733 (66.9%)	-0.13
Number of BNP tests												
...mean (sd)	0.14 (0.44)	0.19 (0.52)	-0.10	0.13 (0.44)	0.17 (0.48)	-0.09	0.20 (0.56)	0.23 (0.56)	-0.05	0.17 (0.51)	0.20 (0.52)	-0.06
Number of Cardiac biomarkers tests (troponin, CK-MBs, Myoglobin, CPK)												
...mean (sd)	0.45 (1.21)	0.61 (1.57)	-0.11	0.42 (1.08)	0.50 (1.30)	-0.07	0.41 (0.85)	0.49 (1.00)	-0.09	0.42 (0.98)	0.53 (1.29)	0.00
Number of Ambulatory Blood pressure monitoring tests												
...mean (sd)	0.00 (0.00)	0.00 (0.03)	0.00	0.00 (0.03)	0.00 (0.02)	0.00	0.00 (0.00)	0.00 (0.00)	#DIV/0!	0.00 (0.02)	0.00 (0.02)	0.00
N of days on antihypertensive medications during baseline							0	0				
...mean (sd)	37.98 (65.20)	35.77 (64.02)	0.03	43.81 (70.14)	45.02 (70.00)	-0.02	41.02 (66.36)	38.28 (65.03)	0.04	41.29 (67.24)	40.18 (66.72)	0.00
N of days in database anytime prior							0	0				
...mean (sd)	1,695.95 (1,337.57)	1,675.11 (1,387.51)	0.02	2,110.22 (1,479.65)	2,106.29 (1,554.62)	0.00	650.58 (464.01)	703.17 (394.05)	-0.12	1226.36 (1010.09)	1512.13 (1231.02)	0.00
Mean Copay for per prescription cost (charges in U.S. \$) (180-1 day prior)							0	0				
...mean (sd)	22.40 (42.74)	20.39 (46.66)	0.04	11.68 (20.56)	11.08 (17.18)	0.03	110.93 (145.27)	119.78 (325.16)	-0.04	68.90 (110.50)	50.45 (191.05)	0.00
...Missing; n (%)	215 (14.6%)	305 (11.0%)	0.11	296 (12.0%)	380 (9.8%)	0.07	595 (11.9%)	349 (10.2%)	0.05	1106 (12.4%)	1034 (10.3%)	0.07
Colonoscopy; n (%)	45 (3.1%)	102 (3.7%)	-0.03	109 (4.4%)	148 (3.8%)	0.03	131 (2.6%)	105 (3.1%)	-0.03	285 (3.2%)	355 (3.5%)	-0.02
Fecal occult blood (FOB) test; n (%)	44 (3.0%)	53 (1.9%)	0.07	81 (3.3%)	117 (3.0%)	0.02	93 (1.9%)	83 (2.4%)	-0.03	218 (2.4%)	253 (2.5%)	-0.01
Flu vaccine; n (%)	180 (12.2%)	385 (13.8%)	-0.05	243 (9.9%)	376 (9.7%)	0.01	1,351 (27.1%)	881 (25.9%)	0.03	1774 (19.9%)	1642 (16.3%)	0.09
Mammogram; n (%)	139 (9.4%)	279 (10.0%)	-0.02	228 (9.3%)	382 (9.9%)	-0.02	437 (8.8%)	313 (9.2%)	-0.01	804 (9.0%)	974 (9.7%)	-0.02
Pap smear; n (%)	81 (5.5%)	152 (5.5%)	0.00	165 (6.7%)	307 (7.9%)	-0.05	164 (3.3%)	120 (3.5%)	-0.01	410 (4.6%)	579 (5.8%)	-0.05
Pneumonia vaccine; n (%)	254 (17.3%)	595 (21.4%)	-0.10	250 (10.1%)	504 (13.0%)	-0.09	1,373 (27.6%)	1,063 (31.2%)	-0.08	1877 (21.0%)	2162 (21.5%)	-0.01
PSA test or Prostate exam for DRE; n (%)	117 (7.9%)	283 (10.2%)	-0.08	225 (9.1%)	381 (9.8%)	-0.02	379 (7.6%)	313 (9.2%)	-0.06	721 (8.1%)	977 (9.7%)	-0.06
Bone mineral density; n (%)	28 (1.9%)	66 (2.4%)	-0.03	29 (1.2%)	55 (1.4%)	-0.02	133 (2.7%)	136 (4.0%)	-0.07	190 (2.1%)	257 (2.6%)	-0.03
Use of CNS stimulants; n (%)	15 (1.0%)	43 (1.5%)	-0.05	19 (0.8%)	67 (1.7%)	-0.08	40 (0.8%)	28 (0.8%)	0.00	74 (0.8%)	138 (1.4%)	-0.06
Use of estrogens, progestins, androgens; n (%)	151 (10.3%)	309 (11.1%)	-0.03	284 (11.5%)	637 (16.4%)	-0.14	220 (4.4%)	183 (5.4%)	-0.05	655 (7.3%)	1129 (11.2%)	-0.13
Use of Angiogenesis inhibitors; n (%)	** (0.1%)	** (0.0%)	0.04	** (0.0%)	** (0.1%)	-0.04	** (0.1%)	** (0.1%)	0.00	#VALUE!	#VALUE!	#VALUE!
Use of Oral Immunosuppressants; n (%)	** (0.1%)	** (0.2%)	-0.03	13 (0.5%)	** (0.3%)	0.03	12 (0.2%)	** (0.2%)	0.00	#VALUE!	#VALUE!	#VALUE!
Use of fondaparinux or Bivalirudin; n (%)	** (0.2%)	** (0.1%)	0.03	13 (0.5%)	** (0.1%)	0.07	** (0.2%)	** (0.1%)	0.03	#VALUE!	#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 ON CED; n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	** (0.0%)	** (0.1%)	-0.04	** (0.0%)	** (0.1%)	-0.04	#VALUE!	#VALUE!	#VALUE!
Use of Ticagrelor; n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	** (0.0%)	** (0.1%)	-0.04	** (0.0%)	** (0.3%)	-0.08	#VALUE!	#VALUE!	#VALUE!
Number of D-dimer tests												
...mean (sd)	0.18 (0.45)	0.20 (0.47)	-0.04	0.16 (0.42)	0.19 (0.48)	-0.07	0.18 (0.44)	0.22 (0.50)	-0.08	0.17 (0.44)	0.20 (0.48)	0.00
Numbe of CRP, high-sensitivity CRP tests												
...mean (sd)	0.09 (0.43)	0.12 (0.59)	-0.06	0.09 (0.39)	0.11 (0.56)	-0.04	0.12 (0.54)	0.15 (0.58)	-0.05	0.11 (0.49)	0.13 (0.58)	0.00
Number of PT or aPTT tests												
...mean (sd)	1.08 (2.54)	0.67 (1.47)	0.20	0.97 (2.49)	0.63 (1.48)	0.17	1.27 (2.98)	0.42 (0.90)	0.39	1.16 (2.78)	0.57 (1.31)	0.00
Number of Bleeding time tests												
...mean (sd)	0.00 (0.00)	0.00 (0.00)	#DIV/0!	0.00 (0.02)	0.00 (0.00)	0.00	0.00 (0.00)	0.00 (0.00)	#DIV/0!	0.00 (0.01)	0.00 (0.00)	0.00
HAS-BLED Score (ICD-9 and ICD-10), 180 days												
...mean (sd)	2.01 (0.69)	1.99 (0.71)	0.03	1.88 (0.70)	1.88 (0.68)	0.00	2.34 (0.79)	2.36 (0.77)	-0.03	2.16 (0.75)	2.07 (0.72)	0.00
N of Generic name drugs												
...mean (sd)	13.81 (14.14)	12.17 (14.72)	0.11	11.84 (10.98)	10.94 (11.84)	0.08	18.87 (18.89)	17.63 (18.34)	0.07	16.09 (16.30)	13.54 (15.09)	0.00
N of Brand name drugs												
...mean (sd)	1.91 (3.43)	3.26 (4.17)	-0.35	2.10 (3.31)	3.10 (3.40)	-0.30	3.01 (5.24)	4.06 (5.03)	-0.20	2.58 (4.51)	3.47 (4.22)	0.00
Use of clopidogrel ; n (%)	12 (0.8%)	** (0.3%)	0.07	18 (0.7%)	16 (0.4%)	0.04	175 (3.5%)	113 (3.3%)	0.01	205 (2.3%)	#VALUE!	#VALUE!
Systemic embolism; n (%)	28 (1.9%)	47 (1.7%)	0.02	52 (2.1%)	73 (1.9%)	0.01	76 (1.5%)	58 (1.7%)	-0.02	156 (1.7%)	178 (1.8%)	-0.01
DVT; n (%)	861 (58.5%)	1,392 (50.0%)	0.17	1,610 (65.3%)	1,981 (51.1%)	0.29	2,794 (56.1%)	1,519 (44.6%)	0.23	5265 (59.0%)	4892 (48.6%)	0.21
Post-thrombotic syndrome; n (%)	0 (0.0%)	** (0.1%)	#DIV/0!	** (0.1%)	** (0.2%)	#DIV/0!	131 (2.6%)	41 (1.2%)	#DIV/0!	** (0.1%)	** (0.2%)	0.04
PE; n (%)	1,472 (100.0%)	2,783 (100.0%)	#DIV/0!	2,457 (99.7%)	3,874 (100.0%)	-0.08	4,964 (99.6%)	3,400 (99.8%)	-0.04	8893 (99.7%)	10057 (99.9%)	-0.04
Coagulation defects; n (%)	28 (1.9%)	42 (1.5%)	#DIV/0!	83 (3.4%)	99 (2.6%)	#DIV/0!	0	0	#DIV/0!	83 (3.4%)	99 (2.6%)	0.27
Diabetes: 1 inpatient or 2 outpatient claims within 183 days; n (%)	217 (14.7%)	446 (16.0%)	-0.04	383 (15.5%)	574 (14.8%)	0.02	1,134 (22.8%)	694 (20.4%)	0.06	1734 (19.4%)	1714 (17.0%)	0.06

Appendix B

Intracranial or retroperitoneal hemorrhage: 1 inpatient or 2 outpatient claims within 183 days; n (%)												
	** (0.2%)	** (0.2%)	0.00	** (0.1%)	** (0.1%)	0.00	17 (0.3%)	** (0.2%)	0.02	#VALUE!	#VALUE!	#VALUE!
Peptic Ulcer Disease; n (%)	372 (25.3%)	669 (24.0%)	0.03	442 (17.9%)	777 (20.1%)	-0.06	1,545 (31.0%)	1,080 (31.7%)	-0.02	2359 (26.4%)	2526 (25.1%)	0.03
Upper GI bleed; n (%)	** (0.2%)	** (0.1%)	0.03	** (0.1%)	** (0.1%)	0.00	** (0.1%)	** (0.3%)	-0.04	#VALUE!	#VALUE!	#VALUE!
Lower/ unspecified GI bleed; n (%)	17 (1.2%)	32 (1.1%)	0.01	38 (1.5%)	38 (1.0%)	0.05	59 (1.2%)	36 (1.1%)	0.01	114 (1.3%)	106 (1.1%)	0.02
Urogenital bleed; n (%)	41 (2.8%)	77 (2.8%)	0.00	75 (3.0%)	115 (3.0%)	0.00	137 (2.7%)	92 (2.7%)	0.00	253 (2.8%)	284 (2.8%)	0.00
Other bleeds; n (%)	49 (3.3%)	103 (3.7%)	-0.02	96 (3.9%)	144 (3.7%)	0.01	196 (3.9%)	114 (3.3%)	0.03	341 (3.8%)	361 (3.6%)	0.01
Prior cancer; n (%)	194 (13.2%)	447 (16.1%)	-0.08	279 (11.3%)	511 (13.2%)	-0.06	901 (18.1%)	751 (22.0%)	-0.10	1374 (15.4%)	1709 (17.0%)	-0.04
Antibiotics; n (%)	633 (43.0%)	1,313 (47.2%)	#DIV/0!	1,127 (45.7%)	1,866 (48.2%)	#DIV/0!	899 (18.0%)	523 (15.4%)	#DIV/0!	1,127 (45.7%)	1,866 (48.2%)	1.30
Aspirin; n (%)	** (0.6%)	15 (0.5%)	0.01	24 (1.0%)	50 (1.3%)	-0.03	** (0.1%)	** (0.2%)	-0.03	#VALUE!	#VALUE!	#VALUE!
Aspirin/dipyridamole; n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	** (0.0%)	#DIV/0!	** (0.0%)	** (0.1%)	-0.04	#VALUE!	#VALUE!	#VALUE!
Other antiplatelet agents; n (%)	** (0.1%)	** (0.1%)	0.00	** (0.1%)	** (0.1%)	0.00	13 (0.3%)	** (0.2%)	0.02	#VALUE!	#VALUE!	#VALUE!
PGP inhibitors; n (%)	290 (19.7%)	590 (21.2%)	-0.04	512 (20.8%)	842 (21.7%)	-0.02	1,127 (22.6%)	834 (24.5%)	-0.04	1929 (21.6%)	2266 (22.5%)	-0.02
Other gastroprotective agents; n (%)	14 (1.0%)	38 (1.4%)	-0.04	22 (0.9%)	51 (1.3%)	-0.04	94 (1.9%)	57 (1.7%)	0.02	130 (1.5%)	146 (1.5%)	0.00
Number of lipid tests ordered												
...mean (sd)	0.35 (0.62)	0.37 (0.64)	-0.03	0.35 (0.72)	0.36 (0.90)	-0.01	0.36 (0.72)	0.42 (0.70)	-0.08	0.36 (0.70)	0.38 (0.77)	0.00
Proton pump inhibitor; n (%)	265 (18.0%)	493 (17.7%)	0.01	416 (16.9%)	666 (17.2%)	-0.01	1,416 (28.4%)	947 (27.8%)	0.01	2097 (23.5%)	2106 (20.9%)	0.06
H2 receptor antagonist; n (%)	48 (3.3%)	74 (2.7%)	0.04	91 (3.7%)	127 (3.3%)	0.02	348 (7.0%)	249 (7.3%)	-0.01	487 (5.5%)	450 (4.5%)	0.05
Vitamin K therapy; n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	** (0.0%)	** (0.0%)	#DIV/0!	** (0.0%)	0 (0.0%)	#DIV/0!	#VALUE!	#VALUE!	#VALUE!
Number of INR (prothrombin) tests ordered												
...mean (sd)	0.84 (2.15)	0.35 (0.80)	0.30	0.76 (2.07)	0.39 (0.86)	0.23	1.24 (2.96)	0.40 (0.86)	0.39	1.04 (2.62)	0.38 (0.84)	0.00
Treating prescriber - Cardiologist; n (%)	950 (64.5%)	1,803 (64.8%)	-0.01	1,503 (61.0%)	2,341 (60.4%)	0.01	2,604 (52.3%)	1,815 (53.3%)	-0.02	5057 (56.7%)	5959 (59.2%)	-0.05
Treating prescriber - Primary Care Physician; n (%)	1,278 (86.8%)	2,280 (81.9%)	0.14	1,112 (45.1%)	1,672 (43.2%)	0.04	1,906 (38.3%)	1,293 (38.0%)	0.01	4296 (48.2%)	5245 (52.1%)	-0.08
Treating prescriber - Other; n (%)	1,449 (98.4%)	2,693 (96.8%)	0.10	2,303 (93.5%)	3,562 (91.9%)	0.06	4,710 (94.5%)	3,212 (94.3%)	0.01	8462 (94.9%)	9467 (94.1%)	0.04
Alpha blockers; n (%)	73 (5.0%)	146 (5.2%)	-0.01	95 (3.9%)	155 (4.0%)	-0.01	373 (7.5%)	278 (8.2%)	-0.03	541 (6.1%)	579 (5.8%)	0.01
CHA2DS2 VASc score, 180 days, V												
...mean (sd)	1.73 (1.38)	1.29 (1.12)	0.35	1.73 (1.43)	1.08 (1.06)	0.52	2.01 (1.68)	1.45 (1.21)	0.38	1.89 (1.57)	1.26 (1.13)	0.00
Use of Prasugrel; n (%)	0 (0.0%)	** (0.1%)	-0.04	0 (0.0%)	** (0.1%)	-0.04	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	#VALUE!	#VALUE!
Use of Loop Diuretics+other diuretics+other hypertension drugs; n (%)	154 (10.5%)	275 (9.9%)	0.02	241 (9.8%)	344 (8.9%)	0.03	899 (18.0%)	523 (15.4%)	0.07	1294 (14.5%)	1142 (11.3%)	0.10
Commercial vs Medicare Advantage- Business Type Code - CORRECT ONE - OPTUM												
...Commercial; n (%)	0,857 (58.2%)	1657 (59.5%)	-0.03	0,177 (7.2%)	224 (5.8%)	0.06	-	-	#VALUE!	#VALUE!	1881 (28.3%)	#VALUE!
...Medicare Advantage; n (%)	0,615 (41.8%)	1126 (40.5%)	0.03	2,287 (92.8%)	3650 (94.2%)	-0.06	-	-	#VALUE!	#VALUE!	4776 (71.7%)	#VALUE!
Commercial vs Medicare Advantage- Business Type Code												
...COM = COMMERCIAL; n (%)	857 (58.2%)	1,657 (59.5%)	-0.03	-	-	-	-	-	#VALUE!	857 (58.2%)	1,657 (59.5%)	-0.03
...MCR = MEDICARE; n (%)	615 (41.8%)	1,126 (40.5%)	0.03	-	-	-	-	-	#VALUE!	615 (41.8%)	1,126 (40.5%)	0.03
...MCD = MEDICAID; n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	-	-	-	-	-	#VALUE!	0 (0.0%)	0 (0.0%)	#DIV/0!
...NONE = NO BUSINESS LINE CODE (added in 2015); n (%)												
...UNK = UNKNOWN (added in 2015); n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	-	-	-	-	-	#VALUE!	0 (0.0%)	0 (0.0%)	#DIV/0!
...UNK = UNKNOWN (added in 2015); n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	-	-	-	-	-	#VALUE!	0 (0.0%)	0 (0.0%)	#DIV/0!
Commercial vs Medicare Advantage- Data Type												
...1 - Fee For Service; n (%)	-	-		2,058 (83.5%)	3,291 (85.0%)	-0.04	-	-		2,058 (83.5%)	3,291 (85.0%)	-0.04
...2 - Encounter; n (%)	-	-		229 (9.3%)	359 (9.3%)	0.00	-	-		229 (9.3%)	359 (9.3%)	0.00
...3 - Medicare; n (%)	-	-		157 (6.4%)	204 (5.3%)	0.05	-	-		157 (6.4%)	204 (5.3%)	0.05
...4 - Medicare Encounter; n (%)	-	-		20 (0.8%)	20 (0.5%)	0.04	-	-		20 (0.8%)	20 (0.5%)	0.04
Metropolitan Statistical Area - Urban (any MSA) vs Rural (non-MSA)												
...Urban; n (%)	-	-		1,819 (73.8%)	2,639 (68.1%)	0.13	-	-		1,819 (73.8%)	2,639 (68.1%)	0.13
...Rural; n (%)	-	-		197 (8.0%)	483 (12.5%)	-0.15	-	-		197 (8.0%)	483 (12.5%)	-0.15
...Unknown/Missing; n (%)	-	-		448 (18.2%)	752 (19.4%)	-0.03	-	-		448 (18.2%)	752 (19.4%)	-0.03

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	Exposure - Apixaban	St. Diff.	Reference - Warfarin	Exposure - Apixaban	St. Diff.	Reference - Warfarin	Exposure - Apixaban	St. Diff.	Reference - Warfarin	Exposure - Apixaban	St. Diff.
Number of patients	490	490		1,381	1,381		1,699	1,699		3,570	3,570	
Age												
...mean (sd)	57.18 (14.30)	57.47 (14.12)	-0.02	51.78 (12.29)	51.77 (12.07)	0.00	62.91 (14.58)	62.87 (14.01)	0.00	57.82 (13.70)	57.83 (13.31)	0.00
Age categories without zero category												
...18 - 54; n (%)	201 (41.0%)	184 (37.6%)	0.07	726 (52.6%)	748 (54.2%)	-0.03	449 (26.4%)	453 (26.7%)	-0.01	1376 (38.5%)	1385 (38.8%)	-0.01
...55 - 64; n (%)	167 (34.1%)	170 (34.7%)	-0.01	568 (41.1%)	547 (39.6%)	0.03	494 (29.1%)	475 (28.0%)	0.02	1,229 (34.4%)	1,192 (33.4%)	0.02
...65 - 74; n (%)	54 (11.0%)	87 (17.8%)	-0.19	53 (3.8%)	48 (3.5%)	0.02	383 (22.5%)	427 (25.1%)	-0.06	490 (13.7%)	562 (15.7%)	-0.06
...≥ 75; n (%)	68 (13.9%)	49 (10.0%)	0.12	34 (2.5%)	38 (2.8%)	-0.02	373 (22.0%)	344 (20.2%)	0.04	475 (13.3%)	431 (12.1%)	0.04
Gender without zero category- United												
...Males; n (%)	240 (49.0%)	229 (46.7%)	0.05	727 (52.6%)	709 (51.3%)	0.03	786 (46.3%)	781 (46.0%)	0.01	1,753 (49.1%)	1,719 (48.2%)	0.02
...Females; n (%)	250 (51.0%)	261 (53.3%)	-0.05	654 (47.4%)	672 (48.7%)	-0.03	913 (53.7%)	918 (54.0%)	-0.01	1,817 (50.9%)	1,851 (51.8%)	-0.02
Race												
...White; n (%)							1,373 (80.8%)	1,381 (81.3%)		1,373 (80.8%)	1,381 (81.3%)	0.00
...Black; n (%)							247 (14.5%)	240 (14.1%)		247 (14.5%)	240 (14.1%)	0.00
...Asian; n (%)							** (0.5%)	** (0.4%)		** (0.5%)	** (0.4%)	0.00
...Hispanic; n (%)							34 (2.0%)	33 (1.9%)		34 (2.0%)	33 (1.9%)	0.00
...North American Native; n (%)							** (0.4%)	** (0.6%)		** (0.4%)	** (0.6%)	0.00
...Other/Unknown; n (%)							29 (1.7%)	28 (1.6%)		29 (1.7%)	28 (1.6%)	0.00
Region without zero category- United v3 (lumping missing&other category												
...Northeast; n (%)	59 (12.0%)	66 (13.5%)	-0.04	246 (17.8%)	232 (16.8%)	0.03	345 (20.3%)	339 (20.0%)	0.01	650 (18.2%)	637 (17.8%)	0.01
...South; n (%)	191 (39.0%)	187 (38.2%)	0.02	387 (28.0%)	397 (28.7%)	-0.02	609 (35.8%)	608 (35.8%)	0.00	1,187 (33.2%)	1,192 (33.4%)	0.00
...Midwest; n (%)	137 (28.0%)	136 (27.8%)	0.00	527 (38.2%)	526 (38.1%)	0.00	442 (26.0%)	468 (27.5%)	-0.03	1,106 (31.0%)	1,130 (31.7%)	-0.02
...West; n (%)	103 (21.0%)	101 (20.6%)	0.01	218 (15.8%)	223 (16.1%)	-0.01	303 (17.8%)	284 (16.7%)	0.03	624 (17.5%)	608 (17.0%)	0.01
...Unknown+missing; n (%)	N/A	N/A	#VALUE!	** (0.2%)	** (0.2%)	0.00	N/A	N/A	#VALUE!	** (0.2%)	** (0.2%)	0.00
CV Covariates												
Ischemic heart disease; n (%)	90 (18.4%)	93 (19.0%)	-0.02	186 (13.5%)	158 (11.4%)	0.06	373 (22.0%)	375 (22.1%)	0.00	649 (18.2%)	626 (17.5%)	0.02
Acute MI; n (%)	23 (4.7%)	25 (5.1%)	-0.02	64 (4.6%)	59 (4.3%)	0.01	81 (4.8%)	84 (4.9%)	0.00	168 (4.7%)	168 (4.7%)	0.00
ACS/unstable angina; n (%)	18 (3.7%)	17 (3.5%)	0.01	44 (3.2%)	35 (2.5%)	0.04	74 (4.4%)	69 (4.1%)	0.01	136 (3.8%)	121 (3.4%)	0.02
Old MI; n (%)	18 (3.7%)	13 (2.7%)	0.06	16 (1.2%)	12 (0.9%)	0.03	89 (5.2%)	97 (5.7%)	-0.02	123 (3.4%)	122 (3.4%)	0.00
Stable angina; n (%)	** (1.4%)	** (1.0%)	0.04	19 (1.4%)	16 (1.2%)	0.02	42 (2.5%)	43 (2.5%)	0.00	#VALUE!	#VALUE!	#VALUE!
Coronary atherosclerosis and other forms of chronic ischemic heart disease; n (%)	62 (12.7%)	58 (11.8%)	0.03	104 (7.5%)	90 (6.5%)	0.04	266 (15.7%)	271 (16.0%)	-0.01	432 (12.1%)	419 (11.7%)	0.01
Other atherosclerosis with ICD10 v2 Copy; n (%)	** (0.4%)	** (0.6%)	-0.03	** (0.4%)	** (0.3%)	0.02	12 (0.7%)	** (0.6%)	0.01	#VALUE!	#VALUE!	#VALUE!
Previous cardiac procedure (CABG or PTCA or Stent) v4; n (%)	** (0.4%)	0 (0.0%)	0.09	** (0.3%)	** (0.7%)	-0.06	** (0.6%)	** (0.4%)	0.03	#VALUE!	#VALUE!	#VALUE!
History of CABG or PTCA; n (%)	20 (4.1%)	14 (2.9%)	0.07	** (0.8%)	** (0.4%)	0.05	87 (5.1%)	96 (5.7%)	-0.03	#VALUE!	#VALUE!	#VALUE!
Any stroke; n (%)	** (1.6%)	** (1.0%)	0.05	13 (0.9%)	** (0.8%)	0.01	58 (3.4%)	58 (3.4%)	0.00	#VALUE!	#VALUE!	#VALUE!
Ischemic stroke (w and w/o mention of cerebral infarction); n (%)	** (1.6%)	** (1.0%)	0.05	13 (0.9%)	** (0.8%)	0.01	54 (3.2%)	56 (3.3%)	-0.01	#VALUE!	#VALUE!	#VALUE!
Hemorrhagic stroke; n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!	** (0.2%)	** (0.1%)	0.03	#VALUE!	#VALUE!	#VALUE!
TIa; n (%)	** (0.4%)	** (0.4%)	0.00	** (0.2%)	** (0.2%)	0.00	** (0.6%)	13 (0.8%)	-0.02	#VALUE!	#VALUE!	#VALUE!
Other cerebrovascular disease; n (%)	** (1.4%)	** (1.2%)	0.02	** (0.8%)	** (0.8%)	0.00	28 (1.6%)	30 (1.8%)	-0.02	#VALUE!	#VALUE!	#VALUE!
Cerebrovascular procedure; n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!	** (0.1%)	0 (0.0%)	0.04	#VALUE!	0 (0.0%)	#VALUE!
Heart failure (CHF); n (%)	52 (10.6%)	53 (10.8%)	-0.01	114 (8.3%)	115 (8.3%)	0.00	285 (16.8%)	304 (17.9%)	-0.03	451 (12.6%)	472 (13.2%)	-0.02
Peripheral Vascular Disease (PVD) or PVD Surgery v2; n (%)	16 (3.3%)	15 (3.1%)	0.01	31 (2.2%)	32 (2.3%)	-0.01	116 (6.8%)	111 (6.5%)	0.01	163 (4.6%)	158 (4.4%)	0.01
Atrial fibrillation; n (%)	36 (7.3%)	36 (7.3%)	0.00	90 (6.5%)	84 (6.1%)	0.02	178 (10.5%)	180 (10.6%)	0.00	304 (8.5%)	300 (8.4%)	0.00
Other cardiac dysrhythmia; n (%)	90 (18.4%)	90 (18.4%)	0.00	241 (17.5%)	234 (16.9%)	0.02	365 (21.5%)	379 (22.3%)	-0.02	696 (19.5%)	703 (19.7%)	-0.01
Cardiac conduction disorders; n (%)	28 (5.7%)	28 (5.7%)	0.00	87 (6.3%)	68 (4.9%)	0.06	126 (7.4%)	127 (7.5%)	0.00	241 (6.8%)	223 (6.2%)	0.02
Other CVD; n (%)	137 (28.0%)	132 (26.9%)	0.02	332 (24.0%)	359 (26.0%)	-0.05	420 (24.7%)	450 (26.5%)	-0.04	889 (24.9%)	941 (26.4%)	-0.03
Diabetes-related complications												
Occurrence of Diabetic Neuropathy v2 Copy; n (%)	18 (3.7%)	24 (4.9%)	-0.06	26 (1.9%)	25 (1.8%)	0.01	100 (5.9%)	99 (5.8%)	0.00	144 (4.0%)	148 (4.1%)	-0.01
Occurrence of diabetic nephropathy V3 with ICD10 Copy; n (%)	13 (2.7%)	** (1.2%)	0.11	18 (1.3%)	14 (1.0%)	0.03	47 (2.8%)	31 (1.8%)	0.07	78 (2.2%)	#VALUE!	#VALUE!
Hypoglycemia v2; n (%)	** (0.6%)	** (0.2%)	0.06	** (0.1%)	** (0.1%)	0.03	51 (3.0%)	44 (2.6%)	0.02	#VALUE!	#VALUE!	#VALUE!
Hyperglycemia; n (%)	53 (10.8%)	41 (8.4%)	0.08	76 (5.5%)	80 (5.8%)	-0.01	151 (8.9%)	158 (9.3%)	-0.01	280 (7.8%)	279 (7.8%)	0.00
Diabetic ketoacidosis; n (%)	** (0.6%)	** (0.4%)	0.03	** (0.1%)	** (0.7%)	-0.10	** (0.4%)	** (0.4%)	0.00	#VALUE!	#VALUE!	#VALUE!
Hypertension: 1 inpatient or 2 outpatient claims within 365 days; n (%)	207 (42.2%)	210 (42.9%)	-0.01	553 (40.0%)	564 (40.8%)	-0.02	775 (45.6%)	782 (46.0%)	-0.01	1,535 (43.0%)	1,556 (43.6%)	-0.01
Hyperlipidemia v2; n (%)	172 (35.1%)	171 (34.9%)	0.00	419 (30.3%)	405 (29.3%)	0.02	709 (41.7%)	710 (41.8%)	0.00	1,300 (36.4%)	1,286 (36.0%)	0.01
Edema; n (%)	92 (18.8%)	74 (15.1%)	0.10	194 (14.0%)	188 (13.6%)	0.01	279 (16.4%)	281 (16.5%)	0.00	565 (15.8%)	543 (15.2%)	0.02
Renal Dysfunction (non-diabetic) v2; n (%)	76 (15.5%)	80 (16.3%)	-0.02	188 (13.6%)	179 (13.0%)	0.02	297 (17.5%)	334 (19.7%)	-0.06	561 (15.7%)	593 (16.6%)	-0.02
Occurrence of acute renal disease v2; n (%)	36 (7.3%)	43 (8.8%)	-0.06	97 (7.0%)	98 (7.1%)	0.00	166 (9.8%)	183 (10.8%)	-0.03	299 (8.4%)	324 (9.1%)	-0.02
Occurrence of chronic renal insufficiency; n (%)	27 (5.5%)	25 (5.1%)	0.02	44 (3.2%)	32 (2.3%)	0.06	109 (6.4%)	128 (7.5%)	-0.04	180 (5.0%)	185 (5.2%)	-0.01

Appendix B

Chronic kidney disease v2; n (%)	24 (4.9%)	23 (4.7%)	0.01	41 (3.0%)	29 (2.1%)	0.06	105 (6.2%)	124 (7.3%)	-0.04	170 (4.8%)	176 (4.9%)	0.00
CKD Stage 3-4; n (%)	16 (3.3%)	15 (3.1%)	0.01	34 (2.5%)	23 (1.7%)	0.06	79 (4.6%)	92 (5.4%)	-0.04	129 (3.6%)	130 (3.6%)	0.00
Occurrence of hypertensive nephropathy; n (%)	15 (3.1%)	17 (3.5%)	-0.02	30 (2.2%)	21 (1.5%)	0.05	63 (3.7%)	73 (4.3%)	-0.03	108 (3.0%)	111 (3.1%)	-0.01
Occurrence of miscellaneous renal insufficiency v2; n (%)	31 (6.3%)	34 (6.9%)	-0.02	88 (6.4%)	77 (5.6%)	0.03	109 (6.4%)	117 (6.9%)	-0.02	228 (6.4%)	228 (6.4%)	0.00
Other Covariates												
Liver disease; n (%)	** (0.4%)	0 (0.0%)	0.09	0 (0.0%)	0 (0.0%)	#DIV/0!	** (0.4%)	** (0.3%)	0.02	#VALUE!	#VALUE!	#VALUE!
Osteoarthritis; n (%)	104 (21.2%)	112 (22.9%)	-0.04	226 (16.4%)	233 (16.9%)	-0.01	436 (25.7%)	414 (24.4%)	0.03	766 (21.5%)	759 (21.3%)	0.00
Other arthritis, arthropathies and musculoskeletal pain; n (%)	282 (57.6%)	277 (56.5%)	0.02	771 (55.8%)	760 (55.0%)	0.02	997 (58.7%)	996 (58.6%)	0.00	2050 (57.4%)	2033 (56.9%)	0.01
Dorsopathies; n (%)	154 (31.4%)	165 (33.7%)	-0.05	368 (26.6%)	358 (25.9%)	0.02	589 (34.7%)	579 (34.1%)	0.01	1111 (31.1%)	1102 (30.9%)	0.00
Fractures; n (%)	26 (5.3%)	28 (5.7%)	-0.02	40 (2.9%)	47 (3.4%)	-0.03	123 (7.2%)	135 (7.9%)	-0.03	189 (5.3%)	210 (5.9%)	-0.03
Falls v2; n (%)	33 (6.7%)	38 (7.8%)	-0.04	29 (2.1%)	26 (1.9%)	0.01	88 (5.2%)	89 (5.2%)	0.00	150 (4.2%)	153 (4.3%)	0.00
Osteoporosis; n (%)	19 (3.9%)	23 (4.7%)	-0.04	31 (2.2%)	28 (2.0%)	0.01	147 (8.7%)	146 (8.6%)	0.00	197 (5.5%)	197 (5.5%)	0.00
Depression; n (%)	100 (20.4%)	96 (19.6%)	0.02	188 (13.6%)	196 (14.2%)	-0.02	479 (28.2%)	471 (27.7%)	0.01	767 (21.5%)	763 (21.4%)	0.00
Anxiety; n (%)	113 (23.1%)	116 (23.7%)	-0.01	236 (17.1%)	250 (18.1%)	-0.03	483 (28.4%)	481 (28.3%)	0.00	832 (23.3%)	847 (23.7%)	-0.01
Sleep_Disorder; n (%)	21 (4.3%)	25 (5.1%)	-0.04	64 (4.6%)	66 (4.8%)	-0.01	83 (4.9%)	80 (4.7%)	0.01	168 (4.7%)	171 (4.8%)	0.00
Dementia; n (%)	26 (5.3%)	29 (5.9%)	-0.03	27 (2.0%)	33 (2.4%)	-0.03	207 (12.2%)	218 (12.8%)	-0.02	260 (7.3%)	280 (7.8%)	-0.02
Delirium; n (%)	16 (3.3%)	16 (3.3%)	0.00	21 (1.5%)	23 (1.7%)	-0.02	137 (8.1%)	136 (8.0%)	0.00	174 (4.9%)	175 (4.9%)	0.00
Psychosis; n (%)	** (1.8%)	12 (2.4%)	-0.04	15 (1.1%)	13 (0.9%)	0.02	154 (9.1%)	160 (9.4%)	-0.01	#VALUE!	185 (5.2%)	#VALUE!
Obesity; n (%)	188 (38.4%)	193 (39.4%)	-0.02	502 (36.4%)	507 (36.7%)	-0.01	472 (27.8%)	483 (28.4%)	-0.01	1162 (32.5%)	1183 (33.1%)	-0.01
Overweight; n (%)	23 (4.7%)	27 (5.5%)	-0.04	49 (3.5%)	57 (4.1%)	-0.03	70 (4.1%)	63 (3.7%)	0.02	142 (4.0%)	147 (4.1%)	-0.01
Smoking; n (%)	192 (39.2%)	196 (40.0%)	-0.02	255 (18.5%)	250 (18.1%)	0.01	829 (48.8%)	826 (48.6%)	0.00	1276 (35.7%)	1272 (35.6%)	0.00
Alcohol abuse or dependence; n (%)	** (2.0%)	** (1.6%)	0.03	18 (1.3%)	16 (1.2%)	0.01	39 (2.3%)	38 (2.2%)	0.01	#VALUE!	#VALUE!	#VALUE!
Drug abuse or dependence; n (%)	26 (5.3%)	29 (5.9%)	-0.03	29 (2.1%)	32 (2.5%)	-0.03	131 (7.7%)	118 (6.9%)	0.03	186 (5.2%)	182 (5.1%)	0.00
COPD; n (%)	92 (18.8%)	97 (19.8%)	-0.03	122 (8.8%)	129 (9.3%)	-0.02	482 (28.4%)	481 (28.3%)	0.00	696 (19.5%)	707 (19.8%)	-0.01
Asthma; n (%)	68 (13.9%)	63 (12.9%)	0.03	160 (11.6%)	163 (11.8%)	-0.01	251 (14.8%)	263 (15.5%)	-0.02	479 (13.4%)	489 (13.7%)	-0.01
Obstructive sleep apnea; n (%)	90 (18.4%)	95 (19.4%)	-0.03	215 (15.6%)	212 (15.4%)	0.01	255 (15.0%)	258 (15.2%)	-0.01	560 (15.7%)	565 (15.8%)	0.00
Pneumonia; n (%)	89 (18.2%)	87 (17.8%)	0.01	217 (15.7%)	229 (16.6%)	-0.02	417 (24.5%)	403 (23.7%)	0.02	723 (20.3%)	719 (20.1%)	0.00
Other Medications												
Use of ACE inhibitors; n (%)	75 (15.3%)	70 (14.3%)	0.03	220 (15.9%)	222 (16.1%)	-0.01	266 (15.7%)	261 (15.4%)	0.01	561 (15.7%)	553 (15.5%)	0.01
Use of ARBs; n (%)	34 (6.9%)	42 (8.6%)	-0.06	124 (9.0%)	132 (9.6%)	-0.02	84 (4.9%)	79 (4.6%)	0.01	242 (6.8%)	253 (7.1%)	-0.01
Use of Loop Diuretics - United; n (%)	47 (9.6%)	49 (10.0%)	-0.01	94 (6.8%)	94 (6.8%)	0.00	236 (13.9%)	243 (14.3%)	-0.01	377 (10.6%)	386 (10.8%)	-0.01
Use of other diuretics-United; n (%)	18 (3.7%)	13 (2.7%)	0.06	30 (2.2%)	22 (1.6%)	0.04	47 (2.8%)	53 (3.1%)	-0.02	95 (2.7%)	88 (2.5%)	0.01
Use of nitrates-United; n (%)	** (1.6%)	** (1.2%)	0.03	20 (1.4%)	19 (1.4%)	0.00	65 (3.8%)	63 (3.7%)	0.01	#VALUE!	#VALUE!	#VALUE!
Use of other hypertension drugs; n (%)	14 (2.9%)	16 (3.3%)	-0.02	37 (2.7%)	41 (3.0%)	-0.02	85 (5.0%)	92 (5.4%)	-0.02	136 (3.8%)	149 (4.2%)	-0.02
Use of Anti-arrhythmics; n (%)	** (1.4%)	** (1.8%)	-0.03	18 (1.3%)	21 (1.5%)	-0.02	24 (1.4%)	31 (1.8%)	-0.03	#VALUE!	#VALUE!	#VALUE!
Use of COPD/asthma meds- United; n (%)	91 (18.6%)	87 (17.8%)	0.02	203 (14.7%)	255 (18.5%)	-0.10	398 (23.4%)	389 (22.9%)	0.01	692 (19.4%)	731 (20.5%)	-0.03
Use of statins; n (%)	111 (22.7%)	111 (22.7%)	0.00	261 (18.9%)	259 (18.8%)	0.00	468 (27.5%)	468 (27.5%)	0.00	840 (23.5%)	838 (23.5%)	0.00
Use of other lipid-lowering drugs; n (%)	20 (4.1%)	18 (3.7%)	0.02	52 (3.8%)	48 (3.5%)	0.02	77 (4.5%)	78 (4.6%)	0.00	149 (4.2%)	144 (4.0%)	0.01
Use of antiplatelet agents; n (%)	** (1.6%)	** (2.0%)	-0.03	26 (1.9%)	31 (2.2%)	-0.02	95 (5.6%)	81 (4.8%)	0.04	#VALUE!	#VALUE!	#VALUE!
Use of heparin and other low-molecular weight heparins; n (%)	95 (19.4%)	101 (20.6%)	-0.03	1 (0.1%)	0 (0.0%)	0.04	156 (9.2%)	153 (9.0%)	0.01	252 (7.1%)	254 (7.1%)	0.00
Use of NSAIDs; n (%)	47 (9.6%)	55 (11.2%)	-0.05	205 (14.8%)	209 (15.1%)	-0.01	203 (11.9%)	193 (11.4%)	0.02	455 (12.7%)	457 (12.8%)	0.00
Use of opioids- United; n (%)	199 (40.6%)	193 (39.4%)	0.02	631 (45.7%)	622 (45.0%)	0.01	740 (43.6%)	718 (42.3%)	0.03	1570 (44.0%)	1533 (42.9%)	0.02
Use of antidepressants; n (%)	137 (28.0%)	135 (27.6%)	0.01	322 (23.3%)	338 (24.5%)	-0.03	683 (40.2%)	671 (39.5%)	0.01	1142 (32.0%)	1144 (32.0%)	0.00
Use of antipsychotics; n (%)	27 (5.5%)	32 (6.5%)	-0.04	58 (4.2%)	57 (4.1%)	0.01	285 (16.8%)	287 (16.9%)	0.00	370 (10.4%)	376 (10.5%)	0.00
Labs												
Lab values- HbA1c (%) v3; n (%)	52 (10.6%)	49 (10.0%)	0.02	** (0.2%)	21 (1.5%)	-0.14	N/A	N/A	#VALUE!	#VALUE!	070 (3.7%)	#VALUE!
Lab values- HbA1c (%) (within 3 months) v3; n (%)	28 (5.7%)	29 (5.9%)	-0.01	** (0.1%)	12 (0.9%)	-0.11	N/A	N/A	#VALUE!	#VALUE!	041 (2.2%)	#VALUE!
Lab values- HbA1c (%) (within 6 months) v3; n (%)	52 (10.6%)	49 (10.0%)	0.02	** (0.2%)	21 (1.5%)	-0.14	N/A	N/A	#VALUE!	#VALUE!	070 (3.7%)	#VALUE!
Lab values- BNP; n (%)	** (1.0%)	** (2.0%)	-0.08	0 (0.0%)	** (0.2%)	-0.06	N/A	N/A	#VALUE!	#VALUE!	#VALUE!	#VALUE!
Lab values- BNP (within 3 months); n (%)	** (1.0%)	** (2.0%)	-0.08	0 (0.0%)	** (0.2%)	-0.06	N/A	N/A	#VALUE!	#VALUE!	#VALUE!	#VALUE!
Lab values- BNP (within 6 months); n (%)	** (1.0%)	** (2.0%)	-0.08	0 (0.0%)	** (0.2%)	-0.06	N/A	N/A	#VALUE!	#VALUE!	#VALUE!	#VALUE!
Lab values- BUN (mg/dl); n (%)	107 (21.8%)	107 (21.8%)	0.00	** (0.8%)	21 (1.5%)	-0.07	N/A	N/A	#VALUE!	#VALUE!	128 (6.8%)	#VALUE!
Lab values- BUN (mg/dl) (within 3 months); n (%)	72 (14.7%)	80 (16.3%)	-0.04	** (0.4%)	12 (0.9%)	-0.06	N/A	N/A	#VALUE!	#VALUE!	092 (4.9%)	#VALUE!
Lab values- BUN (mg/dl) (within 6 months); n (%)	107 (21.8%)	107 (21.8%)	0.00	** (0.8%)	21 (1.5%)	-0.07	N/A	N/A	#VALUE!	#VALUE!	128 (6.8%)	#VALUE!
Lab values- Creatinine (mg/dl) v2; n (%)	109 (22.2%)	115 (23.5%)	-0.03	** (0.8%)	23 (1.7%)	-0.08	N/A	N/A	#VALUE!	#VALUE!	138 (7.4%)	#VALUE!
Lab values- Creatinine (mg/dl) (within 3 months) v2; n (%)	73 (14.9%)	87 (17.8%)	-0.08	** (0.4%)	13 (0.9%)	-0.06	N/A	N/A	#VALUE!	#VALUE!	100 (5.3%)	#VALUE!
Lab values- Creatinine (mg/dl) (within 6 months) v2; n (%)	109 (22.2%)	115 (23.5%)	-0.03	** (0.8%)	23 (1.7%)	-0.08	N/A	N/A	#VALUE!	#VALUE!	138 (7.4%)	#VALUE!
Lab values- HDL level (mg/dl); n (%)	58 (11.8%)	66 (13.5%)	-0.05	** (0.4%)	20 (1.4%)	-0.11	N/A	N/A	#VALUE!	#VALUE!	086 (4.6%)	#VALUE!
Lab values- HDL level (mg/dl) (within 3 months); n (%)	34 (6.9%)	42 (8.6%)	-0.06	** (0.1%)	** (0.8%)	-0.10	N/A	N/A	#VALUE!	#VALUE!	#VALUE!	#VALUE!
Lab values- HDL level (mg/dl) (within 6 months); n (%)	58 (11.8%)	66 (13.5%)	-0.05	** (0.4%)	20 (1.4%)	-0.11	N/A	N/A	#VALUE!	#VALUE!	086 (4.6%)	#VALUE!
Lab values- LDL level (mg/dl) v2; n (%)	59 (12.0%)	69 (14.1%)	-0.06	** (0.4%)	19 (1.4%)	-0.11	N/A	N/A	#VALUE!	#VALUE!	088 (4.7%)	#VALUE!

Appendix B

Lab values- LDL level (mg/dl) (within 3 months) v2; n (%)	34 (6.9%)	43 (8.8%)	-0.07	** (0.2%)	** (0.8%)	-0.09	N/A	N/A	#VALUE!	#VALUE!	#VALUE!	#VALUE!
Lab values- LDL level (mg/dl) (within 6 months) v2; n (%)	59 (12.0%)	69 (14.1%)	-0.06	** (0.4%)	19 (1.4%)	-0.11	N/A	N/A	#VALUE!	#VALUE!	088 (4.7%)	#VALUE!
Lab values- NT-proBNP; n (%)	** (0.8%)	0 (0.0%)	0.13	0 (0.0%)	0 (0.0%)	#DIV/0!	N/A	N/A	#VALUE!	#VALUE!	0 (0.0%)	#VALUE!
Lab values- NT-proBNP (within 3 months); n (%)	** (0.8%)	0 (0.0%)	0.13	0 (0.0%)	0 (0.0%)	#DIV/0!	N/A	N/A	#VALUE!	#VALUE!	0 (0.0%)	-
Lab values- NT-proBNP (within 6 months); n (%)	** (0.8%)	0 (0.0%)	0.13	0 (0.0%)	0 (0.0%)	#DIV/0!	N/A	N/A	#VALUE!	#VALUE!	0 (0.0%)	-
Lab values- Total cholesterol (mg/dl) v2; n (%)	60 (12.2%)	69 (14.1%)	-0.06	** (0.3%)	20 (1.4%)	-0.12	N/A	N/A	#VALUE!	#VALUE!	089 (4.8%)	#VALUE!
Lab values- Total cholesterol (mg/dl) (within 3 months) v2; n (%)	35 (7.1%)	43 (8.8%)	-0.06	** (0.1%)	** (0.8%)	-0.10	N/A	N/A	#VALUE!	#VALUE!	#VALUE!	#VALUE!
Lab values- Total cholesterol (mg/dl) (within 6 months) v2; n (%)	60 (12.2%)	69 (14.1%)	-0.06	** (0.3%)	20 (1.4%)	-0.12	N/A	N/A	#VALUE!	#VALUE!	089 (4.8%)	#VALUE!
Lab values- Triglyceride level (mg/dl); n (%)	60 (12.2%)	68 (13.9%)	-0.05	** (0.4%)	19 (1.4%)	-0.11	N/A	N/A	#VALUE!	#VALUE!	087 (4.6%)	#VALUE!
Lab values- Triglyceride level (mg/dl) (within 3 months); n (%)	35 (7.1%)	43 (8.8%)	-0.06	** (0.1%)	** (0.8%)	-0.10	N/A	N/A	#VALUE!	#VALUE!	#VALUE!	#VALUE!
Lab values- Triglyceride level (mg/dl) (within 6 months); n (%)	60 (12.2%)	68 (13.9%)	-0.05	** (0.4%)	19 (1.4%)	-0.11	N/A	N/A	#VALUE!	#VALUE!	087 (4.6%)	#VALUE!
Lab result number- HbA1c (%) mean (only 2 to 20 included) v4	52	49		3	21		N/A	N/A		55	70	
...mean (sd)	6.43 (1.98)	6.63 (1.68)	-0.11	7.47 (1.98)	6.61 (1.26)	0.52	N/A	N/A	#VALUE!	6.49 (2.00)	6.62 (1.58)	-0.07
...Missing; n (%)	438 (89.4%)	441 (90.0%)	-0.02	1,378 (99.8%)	1,360 (98.5%)	0.14	N/A	N/A	#VALUE!	1,816 (97.1%)	1,801 (96.3%)	0.04
Lab result number- BNP mean v2	5	10		-	3		N/A	N/A		5	13	
...mean (sd)	82.32 (68.33)	593.05 (1,341.63)	-0.54	- (-)	1,474.33 (2,513.81)	#VALUE!	N/A	N/A	#VALUE!	#VALUE!	796.42 (1698.18)	#VALUE!
...Missing; n (%)	485 (99.0%)	480 (98.0%)	0.08	1,381 (100.0%)	1,378 (99.8%)	0.06	N/A	N/A	#VALUE!	1,866 (99.7%)	1,858 (99.3%)	0.06
Lab result number- BUN (mg/dl) mean v2	107	107		11	21		N/A	N/A		118	128	
...mean (sd)	14.59 (4.94)	14.77 (5.11)	-0.04	18,197.88 (44,223.54)	14.28 (4.67)	0.58	N/A	N/A	#VALUE!	1709.64 (13040.81)	14.69 (5.06)	0.18
...Missing; n (%)	383 (78.2%)	383 (78.2%)	0.00	1,370 (99.2%)	1,360 (98.5%)	0.07	N/A	N/A	#VALUE!	1,753 (93.7%)	1,743 (93.2%)	0.02
Lab result number- Creatinine (mg/dl) mean (only 0.1 to 15 included) v3	109	115		9	23		N/A	N/A		118	138	
...mean (sd)	0.89 (0.22)	0.90 (0.23)	-0.04	1.02 (0.21)	0.94 (0.18)	0.41	N/A	N/A	#VALUE!	0.90 (0.22)	0.91 (0.22)	-0.05
...Missing; n (%)	381 (77.8%)	375 (76.5%)	0.03	1,372 (99.3%)	1,358 (98.3%)	0.09	N/A	N/A	#VALUE!	1,753 (93.7%)	1,733 (92.6%)	0.04
Lab result number- HDL level (mg/dl) mean (only <=5000 included) v2	58	66		4	20		N/A	N/A		62	86	
...mean (sd)	53.28 (16.01)	51.19 (15.56)	0.13	43.75 (16.07)	45.90 (14.63)	-0.14	N/A	N/A	#VALUE!	52.67 (16.15)	49.96 (15.45)	0.17
...Missing; n (%)	432 (88.2%)	424 (86.5%)	0.05	1,377 (99.7%)	1,361 (98.6%)	0.12	N/A	N/A	#VALUE!	1,809 (96.7%)	1,785 (95.4%)	0.07
Lab result number- LDL level (mg/dl) mean (only <=5000 included) v2	58	68		4	17		N/A	N/A		62	85	
...mean (sd)	113.22 (39.81)	110.23 (37.87)	0.08	80.50 (59.31)	88.47 (23.32)	-0.18	N/A	N/A	#VALUE!	111.11 (41.35)	105.88 (35.75)	0.14
...Missing; n (%)	432 (88.2%)	422 (86.1%)	0.06	1,377 (99.7%)	1,364 (98.8%)	0.10	N/A	N/A	#VALUE!	1,809 (96.7%)	1,786 (95.5%)	0.06
Lab result number- Total cholesterol (mg/dl) mean (only <=5000 included) v2	60	69		3	20		N/A	N/A		63	89	
...mean (sd)	193.95 (42.54)	190.48 (38.93)	0.09	186.67 (41.79)	161.78 (32.05)	0.67	N/A	N/A	#VALUE!	193.60 (42.87)	184.03 (37.75)	0.24
...Missing; n (%)	430 (87.8%)	421 (85.9%)	0.06	1,378 (99.8%)	1,361 (98.6%)	0.14	N/A	N/A	#VALUE!	1,808 (96.6%)	1,782 (95.2%)	0.07
Lab result number- Triglyceride level (mg/dl) mean (only <=5000 included) v2	60	68		4	19		N/A	N/A		64	87	
...mean (sd)	139.10 (84.71)	141.70 (80.32)	-0.03	248.00 (206.07)	124.68 (70.13)	0.80	N/A	N/A	#VALUE!	145.91 (95.02)	137.98 (78.74)	0.09
...Missing; n (%)	430 (87.8%)	422 (86.1%)	0.05	1,377 (99.7%)	1,362 (98.6%)	0.12	N/A	N/A	#VALUE!	1,807 (96.6%)	1,784 (95.4%)	0.06
Lab result number- Hemoglobin mean (only >0 included)	83	97		6	17		N/A	N/A		89	114	
...mean (sd)	13.73 (1.94)	13.73 (1.83)	0.00	40,008.30 (62,283.25)	14.48 (1.45)	0.91	N/A	N/A	#VALUE!	2709.99 (15017.83)	13.84 (1.79)	0.25
...Missing; n (%)	407 (83.1%)	393 (80.2%)	0.07	1,375 (99.6%)	1,364 (98.8%)	0.09	N/A	N/A	#VALUE!	1,782 (95.2%)	1,757 (93.9%)	0.06
Lab result number- Serum sodium mean (only >90 and <190 included)	103	102		9	22		N/A	N/A		112	124	
...mean (sd)	140.36 (2.80)	140.11 (2.59)	0.09	137.64 (4.57)	140.09 (1.89)	-0.70	N/A	N/A	#VALUE!	140.14 (2.98)	140.11 (2.49)	0.01
...Missing; n (%)	387 (79.0%)	388 (79.2%)	0.00	1,372 (99.3%)	1,359 (98.4%)	0.08	N/A	N/A	#VALUE!	1,759 (94.0%)	1,747 (93.4%)	0.02
Lab result number- Albumin mean (only >0 and <=10 included)	95	100		8	16		N/A	N/A		103	116	
...mean (sd)	4.08 (0.41)	4.08 (0.40)	0.00	4.00 (0.32)	4.16 (0.48)	-0.39	N/A	N/A	#VALUE!	4.07 (0.41)	4.09 (0.41)	-0.05
...Missing; n (%)	395 (80.6%)	390 (79.6%)	0.03	1,373 (99.4%)	1,365 (98.8%)	0.06	N/A	N/A	#VALUE!	1,768 (94.5%)	1,755 (93.8%)	0.03
Lab result number- Glucose (fasting or random) mean (only 10-1000 included)	103	103		9	23		N/A	N/A		112	126	
...mean (sd)	112.05 (46.57)	108.13 (37.41)	0.09	166.42 (108.75)	131.56 (58.94)	0.40	N/A	N/A	#VALUE!	116.42 (53.83)	112.41 (42.21)	0.08
...Missing; n (%)	387 (79.0%)	387 (79.0%)	0.00	1,372 (99.3%)	1,358 (98.3%)	0.09	N/A	N/A	#VALUE!	1,759 (94.0%)	1,745 (93.3%)	0.03
Lab result number- Potassium mean (only 1-7 included)	107	112		9	20		N/A	N/A		116	132	
...mean (sd)	4.34 (0.42)	4.34 (0.40)	0.00	4.37 (0.55)	4.37 (0.40)	0.00	N/A	N/A	#VALUE!	4.34 (0.43)	4.34 (0.40)	0.00
...Missing; n (%)	383 (78.2%)	378 (77.1%)	0.03	1,372 (99.3%)	1,361 (98.6%)	0.07	N/A	N/A	#VALUE!	1,755 (93.8%)	1,739 (92.9%)	0.04
Comorbidity Scores												
CCI (180 days)- ICD9 and ICD10 v2												
...mean (sd)	3.51 (2.21)	3.71 (2.52)	-0.08	2.89 (2.11)	2.83 (2.17)	0.03	3.97 (2.69)	4.05 (2.67)	-0.03	3.49 (2.42)	3.53 (2.47)	-0.02

Appendix B

Non-Frailty; n (%)	206 (42.0%)	210 (42.9%)	-0.02	581 (42.1%)	583 (42.2%)	0.00	57 (3.4%)	47 (2.8%)	0.03	844 (23.6%)	840 (23.5%)	0.00
Frailty Score (mean): Empirical Version												
365 days, v2												
...mean (sd)	0.18 (0.06)	0.18 (0.06)	0.00	0.15 (0.05)	0.15 (0.05)	0.00	0.10 (0.07)	0.10 (0.08)	0.00	0.13 (0.06)	0.13 (0.07)	0.00
Healthcare Utilization												
Any hospitalization; n (%)	438 (89.4%)	453 (92.4%)	-0.10	1,379 (99.9%)	1,380 (99.9%)	0.00	1,564 (92.1%)	1,555 (91.5%)	0.02	3,381 (94.7%)	3,388 (94.9%)	-0.01
Any hospitalization within prior 30 days; n (%)	374 (76.3%)	364 (74.3%)	0.05	1,287 (93.2%)	1,302 (94.3%)	-0.05	1,204 (70.9%)	1,229 (72.3%)	-0.03	2865 (80.3%)	2895 (81.1%)	-0.02
Any hospitalization during prior 31-180 days; n (%)	101 (20.6%)	121 (24.7%)	-0.10	185 (13.4%)	166 (12.0%)	0.04	565 (33.3%)	546 (32.1%)	0.03	851 (23.8%)	833 (23.3%)	0.01
Internal medicine/family medicine visits; n (%)	427 (87.1%)	427 (87.1%)	0.00	1,079 (78.1%)	1,090 (78.9%)	-0.02	1,606 (94.5%)	1,626 (95.7%)	-0.06	3112 (87.2%)	3143 (88.0%)	-0.02
Internal medicine/family medicine visits (30 days prior) v2; n (%)	361 (73.7%)	360 (73.5%)	0.00	753 (54.5%)	821 (59.4%)	-0.10	1,399 (82.3%)	1,402 (82.5%)	-0.01	2513 (70.4%)	2583 (72.4%)	-0.04
Internal medicine/family medicine visits (31 to 180 days prior) v2; n (%)	294 (60.0%)	294 (60.0%)	0.00	855 (61.9%)	817 (59.2%)	0.06	1,184 (69.7%)	1,140 (67.1%)	0.06	2333 (65.4%)	2251 (63.1%)	0.05
Cardiologist visit; n (%)	352 (71.8%)	365 (74.5%)	-0.06	393 (28.5%)	375 (27.2%)	0.03	1,203 (70.8%)	1,213 (71.4%)	-0.01	1948 (54.6%)	1953 (54.7%)	0.00
Number of Cardiologist visits (30 days prior); n (%)	297 (60.6%)	308 (62.9%)	-0.05	271 (19.6%)	270 (19.6%)	0.00	880 (51.8%)	902 (53.1%)	-0.03	1448 (40.6%)	1480 (41.5%)	-0.02
Number of Cardiologist visits (31 to 180 days prior); n (%)	111 (22.7%)	123 (25.1%)	-0.06	173 (12.5%)	165 (11.9%)	0.02	558 (32.8%)	563 (33.1%)	-0.01	842 (23.6%)	851 (23.8%)	0.00
Electrocardiogram v2; n (%)	401 (81.8%)	415 (84.7%)	-0.08	694 (50.3%)	691 (50.0%)	0.01	1,449 (85.3%)	1,442 (84.9%)	0.01	2544 (71.3%)	2548 (71.4%)	0.00
Use of glucose test strips; n (%)	** (1.4%)	** (1.4%)	-0.02	19 (1.4%)	** (0.8%)	0.06	31 (1.8%)	29 (1.7%)	0.01	#VALUE!	#VALUE!	#VALUE!
Dialysis; n (%)	0 (0.0%)	** (0.2%)	-0.06	0 (0.0%)	** (0.1%)	-0.04	** (0.1%)	** (0.1%)	0.00	#VALUE!	#VALUE!	#VALUE!
number of different/distinct medication prescriptions												
...mean (sd)	7.88 (5.51)	8.00 (5.83)	-0.02	7.89 (4.81)	8.01 (5.76)	-0.02	9.33 (6.22)	9.31 (6.22)	0.00	8.57 (5.62)	8.63 (5.99)	-0.01
Number of Hospitalizations												
...mean (sd)	1.11 (0.72)	1.08 (0.56)	0.05	1.17 (0.48)	1.16 (0.49)	0.02	1.30 (0.93)	1.29 (0.93)	0.01	1.22 (0.76)	1.21 (0.74)	0.01
Number of hospital days												
...mean (sd)	5.44 (4.46)	5.11 (7.06)	0.06	5.43 (4.09)	5.28 (6.21)	0.03	5.85 (5.04)	5.73 (7.43)	0.02	5.63 (4.61)	5.47 (6.93)	0.03
Number of Emergency Department (ED) visits v3												
...mean (sd)	1.79 (2.37)	1.82 (2.21)	-0.01	3.20 (5.17)	3.17 (4.44)	0.01	2.70 (7.14)	2.73 (4.23)	-0.01	2.77 (5.95)	2.78 (4.10)	0.00
Number of Office visits												
...mean (sd)	5.01 (4.71)	5.03 (4.44)	0.00	4.72 (4.41)	4.77 (5.34)	-0.01	10.37 (13.98)	10.07 (11.65)	0.02	7.45 (10.18)	7.33 (8.85)	0.01
Number of internal medicine/family medicine visits												
...mean (sd)	10.16 (13.90)	9.39 (12.98)	0.06	5.30 (7.34)	5.51 (8.85)	-0.03	12.46 (13.83)	11.04 (12.11)	0.11	9.37 (11.76)	8.67 (11.10)	0.06
Number of Cardiologist visits												
...mean (sd)	2.58 (3.80)	2.62 (3.94)	-0.01	0.71 (1.95)	0.70 (1.90)	0.01	2.81 (4.52)	2.89 (4.25)	-0.02	1.97 (3.63)	2.01 (3.48)	-0.01
Number electrocardiograms received v2												
...mean (sd)	1.98 (2.00)	2.10 (2.02)	-0.06	0.90 (1.31)	0.92 (1.37)	-0.01	2.31 (2.51)	2.35 (2.54)	-0.02	1.72 (2.05)	1.76 (2.09)	-0.02
Number of HbA1c tests ordered												
...mean (sd)	0.28 (0.63)	0.29 (0.64)	-0.02	0.22 (0.51)	0.22 (0.55)	0.00	0.29 (0.62)	0.29 (0.60)	0.00	0.26 (0.58)	0.26 (0.59)	0.00
Number of glucose tests ordered												
...mean (sd)	0.14 (0.62)	0.17 (0.73)	-0.04	0.13 (1.17)	0.13 (0.60)	0.00	0.15 (0.60)	0.17 (0.60)	-0.03	0.14 (0.87)	0.15 (0.62)	-0.01
Number of lipid tests ordered												
...mean (sd)	0.37 (0.62)	0.39 (0.74)	-0.03	0.38 (0.72)	0.36 (0.66)	0.03	0.36 (0.65)	0.37 (0.64)	-0.02	0.37 (0.67)	0.37 (0.66)	0.00
Total N distinct ICD9/ICD10 diagnoses at the 3rd digit level Copy												
...mean (sd)	12.13 (12.97)	12.28 (12.70)	-0.01	10.37 (10.13)	10.29 (10.87)	0.01	17.46 (15.46)	17.28 (15.89)	0.01	13.99 (13.29)	13.89 (13.71)	0.01
For PS												
Hemorrhagic stroke+Other cerebrovascular disease+Cerebrovascular procedure (for PS); n (%)	** (1.4%)	** (1.2%)	0.02	11 (0.8%)	11 (0.8%)	0.00	31 (1.8%)	31 (1.8%)	0.00	#VALUE!	#VALUE!	#VALUE!
Major trauma potentially causing prolou; 19 (3.9%)	16 (3.3%)		#DIV/0!	31 (2.2%)	33 (2.4%)	#DIV/0!	92 (5.4%)	92 (5.4%)	#DIV/0!	31 (2.2%)	33 (2.4%)	-0.01
Occurrence of creatinine tests ordered (for PS); n (%)	30 (6.1%)	30 (6.1%)	0.00	80 (5.8%)	72 (5.2%)	0.03	129 (7.6%)	151 (8.9%)	-0.05	239 (6.7%)	253 (7.1%)	-0.02
Occurrence of BUN tests ordered (for PS); n (%)	13 (2.7%)	15 (3.1%)	-0.02	36 (2.6%)	42 (3.0%)	-0.02	63 (3.7%)	81 (4.8%)	-0.05	112 (3.1%)	138 (3.9%)	-0.04
Occurrence of chronic renal insufficiency w/o CKD (for PS) v2; n (%)	** (1.0%)	** (0.6%)	0.04	** (0.5%)	** (0.5%)	0.00	18 (1.1%)	26 (1.5%)	-0.04	#VALUE!	#VALUE!	#VALUE!
Chronic kidney disease Stage 1-2 (for PS); n (%)	** (1.4%)	** (1.6%)	-0.02	** (0.7%)	** (0.4%)	0.04	28 (1.6%)	27 (1.6%)	0.00	#VALUE!	#VALUE!	#VALUE!
Chronic kidney disease Stage 3-6 (for PS); n (%)	16 (3.3%)	15 (3.1%)	0.01	34 (2.5%)	23 (1.7%)	0.06	79 (4.6%)	92 (5.4%)	-0.04	129 (3.6%)	130 (3.6%)	0.00
Acute kidney injury; n (%)	38 (7.8%)	43 (8.8%)	#DIV/0!	99 (7.2%)	98 (7.1%)	#DIV/0!	168 (9.9%)	184 (10.8%)	#DIV/0!	99 (7.2%)	98 (7.1%)	0.00
Bladder stones+Kidney stones (for PS); n (%)	21 (4.3%)	19 (3.9%)	0.02	39 (2.8%)	49 (3.5%)	-0.04	62 (3.6%)	64 (3.8%)	-0.01	122 (3.4%)	132 (3.7%)	-0.02
Alcohol abuse or dependence+Drug abuse or dependence (for PS); n (%)	33 (6.7%)	36 (7.3%)	-0.02	46 (3.3%)	49 (3.5%)	-0.01	156 (9.2%)	145 (8.5%)	0.02	235 (6.6%)	230 (6.4%)	0.01
Other atherosclerosis+Cardiac conduction disorders+Other CVD (for PS) v2 Copy; n (%)	155 (31.6%)	149 (30.4%)	0.03	394 (28.5%)	402 (29.1%)	-0.01	500 (29.4%)	539 (31.7%)	-0.05	1049 (29.4%)	1090 (30.5%)	-0.02

Appendix B

Previous cardiac procedure (CABG or PTCA or Stent) + History of CABG or PTCA (for PS) v3; n (%)	22 (4.5%)	14 (2.9%)	0.08	14 (1.0%)	13 (0.9%)	0.01	91 (5.4%)	96 (5.7%)	-0.01	127 (3.6%)	123 (3.4%)	0.01
Diabetes with complication; n (%)	35 (7.1%)	32 (6.5%)	#DIV/0!	53 (3.8%)	50 (3.6%)	#DIV/0!	156 (9.2%)	167 (9.8%)	#DIV/0!	53 (3.8%)	50 (3.6%)	0.01
Delirium + Psychosis (for PS); n (%)	23 (4.7%)	26 (5.3%)	-0.03	30 (2.2%)	33 (2.4%)	-0.01	263 (15.5%)	262 (15.4%)	0.00	316 (8.9%)	321 (9.0%)	0.00
Any use of Meglitinides (for PS); n (%)	0 (0.0%)	** (0.2%)	-0.06	** (0.1%)	** (0.1%)	0.00	0 (0.0%)	0 (0.0%)	#DIV/0!	#VALUE!	#VALUE!	#VALUE!
Any use of AGIs (for PS); n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	** (0.1%)	0 (0.0%)	0.04	0 (0.0%)	0 (0.0%)	#DIV/0!	#VALUE!	0 (0.0%)	#VALUE!
CKD stage 3-6 + dialysis (for PS); n (%)	16 (3.3%)	17 (3.5%)	-0.01	34 (2.5%)	25 (1.8%)	0.05	80 (4.7%)	94 (5.5%)	-0.04	130 (3.6%)	136 (3.8%)	-0.01
Use of thiazide; n (%)	22 (4.5%)	23 (4.7%)	-0.01	79 (5.7%)	88 (6.4%)	-0.03	79 (4.6%)	82 (4.8%)	-0.01	180 (5.0%)	193 (5.4%)	-0.02
Use of beta blockers; n (%)	75 (15.3%)	66 (13.5%)	0.05	231 (16.7%)	218 (15.8%)	0.02	331 (19.5%)	328 (19.3%)	0.01	637 (17.8%)	612 (17.1%)	0.02
Use of calcium channel blockers; n (%)	55 (11.2%)	56 (11.4%)	-0.01	170 (12.3%)	169 (12.2%)	0.00	194 (11.4%)	179 (10.5%)	0.03	419 (11.7%)	404 (11.3%)	0.01
All antidiabetic medications except Insul	57 (11.6%)	62 (12.7%)	-0.03	149 (10.8%)	158 (11.4%)	-0.02	207 (12.2%)	219 (12.9%)	-0.02	413 (11.6%)	439 (12.3%)	-0.02
DM Medications - Insulin Copy; n (%)	23 (4.7%)	27 (5.5%)	-0.04	59 (4.3%)	49 (3.5%)	0.04	80 (4.7%)	91 (5.4%)	-0.03	162 (4.5%)	167 (4.7%)	-0.01
Use of Low Intensity Statins; n (%)	61 (12.4%)	63 (12.9%)	-0.02	136 (9.8%)	132 (9.6%)	0.01	283 (16.7%)	277 (16.3%)	0.01	480 (13.4%)	472 (13.2%)	0.01
Use of High Intensity Statins; n (%)	51 (10.4%)	51 (10.4%)	0.00	127 (9.2%)	132 (9.6%)	-0.01	195 (11.5%)	204 (12.0%)	-0.02	373 (10.4%)	387 (10.8%)	-0.01
Malignant hypertension; n (%)	** (0.2%)	** (0.2%)	0.00	76 (5.5%)	85 (6.2%)	-0.03	82 (4.8%)	73 (4.3%)	0.02	#VALUE!	#VALUE!	#VALUE!
Cardiovascular stress test; n (%)	** (1.0%)	** (0.4%)	0.07	** (0.6%)	** (0.7%)	-0.01	21 (1.2%)	26 (1.5%)	-0.03	#VALUE!	#VALUE!	#VALUE!
Echocardiogram; n (%)	298 (60.8%)	349 (71.2%)	-0.22	910 (65.9%)	960 (69.5%)	-0.08	1,040 (61.2%)	1,058 (62.3%)	-0.02	2248 (63.0%)	2367 (66.3%)	-0.07
Number of BNP tests												
...mean (sd)	0.17 (0.51)	0.22 (0.59)	-0.09	0.15 (0.47)	0.17 (0.49)	-0.04	0.17 (0.51)	0.22 (0.53)	-0.10	0.16 (0.49)	0.20 (0.52)	0.00
Number of Cardiac biomarkers tests (troponin, CK-MBs, Myoglobin, CPK)												
...mean (sd)	0.46 (1.22)	0.73 (1.68)	-0.18	0.44 (1.13)	0.54 (1.46)	-0.08	0.39 (0.80)	0.46 (0.96)	-0.08	0.42 (1.00)	0.53 (1.28)	0.00
Number of Ambulatory Blood pressure monitoring tests												
...mean (sd)	0.00 (0.00)	0.00 (0.06)	0.00	0.00 (0.04)	0.00 (0.03)	0.00	0.00 (0.00)	0.00 (0.00)	#DIV/0!	0.00 (0.02)	0.00 (0.03)	0.00
N of days on antihypertensive medications during baseline												
...mean (sd)	41.64 (66.76)	40.37 (67.11)	0.02	45.23 (70.39)	45.62 (70.62)	-0.01	41.49 (66.16)	43.81 (67.50)	-0.03	42.96 (67.91)	44.04 (68.67)	0.00
N of days in database anytime prior												
...mean (sd)	1,631.36 (1,356.14)	1,568.20 (1,247.77)	0.05	2,203.52 (1,550.45)	2,092.63 (1,508.64)	0.07	720.02 (502.47)	681.78 (392.54)	0.08	1418.98 (1141.20)	1349.21 (1080.43)	0.00
Mean Copay for per prescription cost (charges in U.S. \$) (180-1 day prior)												
...mean (sd)	22.31 (49.02)	22.88 (47.07)	-0.01	11.22 (16.38)	10.92 (16.98)	0.02	111.13 (120.49)	117.56 (187.51)	-0.04	60.29 (85.70)	63.31 (130.97)	0.00
...Missing; n (%)	57 (11.6%)	59 (12.0%)	-0.01	156 (11.3%)	155 (11.2%)	0.00	182 (10.7%)	179 (10.5%)	0.01	395 (11.1%)	393 (11.0%)	0.00
Colonoscopy; n (%)	17 (3.5%)	20 (4.1%)	-0.03	55 (4.0%)	50 (3.6%)	0.02	47 (2.8%)	47 (2.8%)	0.00	119 (3.3%)	117 (3.3%)	0.00
Fecal occult blood (FOB) test; n (%)	14 (2.9%)	14 (2.9%)	0.00	47 (3.4%)	45 (3.3%)	0.01	33 (1.9%)	43 (2.5%)	-0.04	94 (2.6%)	102 (2.9%)	-0.02
Flu vaccine; n (%)	62 (12.7%)	57 (11.6%)	0.03	142 (10.3%)	144 (10.4%)	0.00	440 (25.9%)	432 (25.4%)	0.01	644 (18.0%)	633 (17.7%)	0.01
Mammogram; n (%)	43 (8.8%)	49 (10.0%)	-0.04	138 (10.0%)	152 (11.0%)	-0.03	152 (8.9%)	138 (8.1%)	0.03	333 (9.3%)	339 (9.5%)	-0.01
Pap smear; n (%)	26 (5.3%)	23 (4.7%)	0.03	98 (7.1%)	106 (7.7%)	-0.02	48 (2.8%)	54 (3.2%)	-0.02	172 (4.8%)	183 (5.1%)	-0.01
Pneumonia vaccine; n (%)	94 (19.2%)	85 (17.3%)	0.05	179 (13.0%)	178 (12.9%)	0.00	506 (29.8%)	501 (29.5%)	0.01	779 (21.8%)	764 (21.4%)	0.01
PSA test or Prostate exam for DRE; n (%)	42 (8.6%)	39 (8.0%)	-0.02	132 (9.6%)	132 (9.6%)	0.00	134 (7.9%)	122 (7.2%)	0.03	308 (8.6%)	293 (8.2%)	0.01
Bone mineral density; n (%)	** (1.8%)	15 (3.1%)	-0.08	20 (1.4%)	21 (1.5%)	-0.01	39 (2.3%)	42 (2.5%)	-0.01	#VALUE!	78 (2.2%)	#VALUE!
Use of CNS stimulants; n (%)	** (1.6%)	** (1.8%)	-0.02	** (0.5%)	26 (1.9%)	-0.13	** (0.6%)	** (0.6%)	0.00	#VALUE!	#VALUE!	#VALUE!
Use of estrogens, progestins, androgens; r	48 (9.8%)	42 (8.6%)	0.04	175 (12.7%)	176 (12.7%)	0.00	62 (3.6%)	65 (3.8%)	-0.01	285 (8.0%)	283 (7.9%)	0.00
Use of Angiogenesis inhibitors; n (%)	0 (0.0%)	** (0.2%)	-0.06	** (0.1%)	** (0.1%)	0.00	** (0.1%)	** (0.2%)	-0.03	#VALUE!	#VALUE!	#VALUE!
Use of Oral Immunosuppressants; n (%)	** (0.2%)	** (0.2%)	0.00	** (0.4%)	** (0.2%)	0.04	** (0.2%)	** (0.2%)	0.00	#VALUE!	#VALUE!	#VALUE!
Use of fondaparinux or Bivalirudin; n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	** (0.1%)	** (0.1%)	0.00	** (0.2%)	** (0.1%)	0.03	#VALUE!	#VALUE!	#VALUE!
Use of other direct thrombin inhibitors (l	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 (0.0%)	0.04	0 (0.0%)	** (0.1%)	-0.04	#VALUE!	#VALUE!	#VALUE!
Use of Ticagrelor; n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	** (0.1%)	** (0.1%)	0.00	0 (0.0%)	** (0.2%)	-0.06	#VALUE!	#VALUE!	#VALUE!
Number of D-dimer tests												
...mean (sd)	0.19 (0.44)	0.19 (0.45)	0.00	0.17 (0.44)	0.18 (0.45)	-0.02	0.19 (0.45)	0.18 (0.43)	0.02	0.18 (0.44)	0.18 (0.44)	0.00
Numbe of CRP, high-sensitivity CRP tests												
...mean (sd)	0.13 (0.58)	0.14 (0.77)	-0.01	0.10 (0.45)	0.09 (0.49)	0.02	0.13 (0.59)	0.13 (0.57)	0.00	0.12 (0.54)	0.12 (0.57)	0.00
Number of PT or aPTT tests												
...mean (sd)	1.03 (2.16)	1.03 (2.17)	0.00	0.85 (2.00)	0.81 (1.96)	0.02	0.53 (1.12)	0.52 (1.10)	0.01	0.72 (1.67)	0.70 (1.65)	0.00
Number of Bleeding time tests												
...mean (sd)	0.00 (0.00)	0.00 (0.00)	#DIV/0!	0.00 (0.00)	0.00 (0.00)	#DIV/0!	0.00 (0.00)	0.00 (0.00)	#DIV/0!	0.00 (0.00)	0.00 (0.00)	#DIV/0!
HAS-BLED Score (ICD-9 and ICD-10), 180 days												
...mean (sd)	2.06 (0.69)	2.07 (0.63)	-0.02	1.90 (0.70)	1.90 (0.68)	0.00	2.38 (0.81)	2.39 (0.78)	-0.01	2.15 (0.75)	2.16 (0.72)	0.00
N of Generic name drugs												
...mean (sd)	14.39 (14.69)	14.42 (16.73)	0.00	11.78 (10.46)	12.02 (13.21)	-0.02	19.11 (18.82)	19.05 (19.03)	0.00	15.63 (15.51)	15.70 (16.68)	0.00
N of Brand name drugs												
...mean (sd)	2.59 (4.40)	2.63 (2.88)	-0.01	2.47 (3.76)	2.53 (2.57)	-0.02	3.47 (5.81)	3.51 (3.78)	-0.01	2.96 (4.92)	3.01 (3.24)	0.00
Use of clopidogrel ; n (%)	** (0.6%)	** (0.8%)	-0.02	** (0.5%)	** (0.5%)	0.00	68 (4.0%)	62 (3.6%)	0.02	#VALUE!	#VALUE!	#VALUE!
Systemic embolism; n (%)	** (1.8%)	12 (2.4%)	-0.04	26 (1.9%)	28 (2.0%)	-0.01	29 (1.7%)	29 (1.7%)	0.00	#VALUE!	69 (1.9%)	#VALUE!
DVT; n (%)	257 (52.4%)	248 (50.6%)	0.04	757 (54.8%)	739 (53.5%)	0.03	824 (48.5%)	849 (50.0%)	-0.03	1838 (51.5%)	1836 (51.4%)	0.00
Post-thrombotic syndrome; n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	** (0.1%)	** (0.1%)	#DIV/0!	** (0.2%)	** (0.1%)	#DIV/0!	** (0.1%)	** (0.1%)	0.00
PE; n (%)	490 (100.0%)	490 (100.0%)	#DIV/0!	1,381 (100.0%)	1,381 (100.0%)	#DIV/0!	1,692 (99.6%)	1,695 (99.8%)	-0.04	3563 (99.8%)	3566 (99.9%)	-0.03
Coagulation defects; n (%)	** (1.6%)	** (2.2%)	#DIV/0!	35 (2.5%)	40 (2.9%)	#DIV/0!	28 (1.6%)	32 (1.9%)		35 (2.5%)	40 (2.9%)	-0.02
Diabetes: 1 inpatient or 2 outpatient clai	86 (17.6%)	90 (18.4%)	-0.02	212 (15.4%)	210 (15.2%)	0.01	371 (21.8%)	407 (24.0%)	-0.05	669 (18.7%)	707 (19.8%)	-0.03

Appendix B

Intracranial or retroperitoneal hemorrh	** (0.4%)	** (0.4%)	0.00	** (0.1%)	** (0.1%)	0.00	** (0.3%)	** (0.2%)	0.02	#VALUE!	#VALUE!	#VALUE!
Peptic Ulcer Disease; n (%)	134 (27.3%)	140 (28.6%)	-0.03	257 (18.6%)	268 (19.4%)	-0.02	534 (31.4%)	545 (32.1%)	-0.02	925 (25.9%)	953 (26.7%)	-0.02
Upper GI bleed; n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	** (0.1%)	** (0.1%)	0.00	** (0.2%)	** (0.1%)	0.03	#VALUE!	#VALUE!	#VALUE!
Lower/ unspecified GI bleed; n (%)	** (1.6%)	** (1.4%)	0.02	22 (1.6%)	20 (1.4%)	0.02	19 (1.1%)	20 (1.2%)	-0.01	#VALUE!	#VALUE!	#VALUE!
Urogenital bleed; n (%)	** (1.8%)	12 (2.4%)	-0.04	48 (3.5%)	41 (3.0%)	0.03	37 (2.2%)	48 (2.8%)	-0.04	#VALUE!	101 (2.8%)	#VALUE!
Other bleeds; n (%)	18 (3.7%)	18 (3.7%)	0.00	55 (4.0%)	53 (3.8%)	0.01	70 (4.1%)	63 (3.7%)	0.02	143 (4.0%)	134 (3.8%)	0.01
Prior cancer; n (%)	78 (15.9%)	79 (16.1%)	-0.01	174 (12.6%)	176 (12.7%)	0.00	349 (20.5%)	334 (19.7%)	0.02	601 (16.8%)	589 (16.5%)	0.01
Antibiotics; n (%)	234 (47.8%)	235 (48.0%)	#DIV/0!	664 (48.1%)	671 (48.6%)	#DIV/0!	857 (50.4%)	853 (50.2%)	#DIV/0!	664 (48.1%)	671 (48.6%)	-0.01
Aspirin; n (%)	** (0.4%)	** (0.6%)	-0.03	14 (1.0%)	19 (1.4%)	-0.04	** (0.2%)	** (0.1%)	0.03	#VALUE!	#VALUE!	#VALUE!
Aspirin/dipyridamole; n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!	** (0.1%)	** (0.1%)	0.00	#VALUE!	#VALUE!	#VALUE!
Other antiplatelet agents; n (%)	** (0.2%)	0 (0.0%)	0.06	** (0.1%)	** (0.1%)	0.00	** (0.4%)	** (0.3%)	0.02	#VALUE!	#VALUE!	#VALUE!
PGP inhibitors; n (%)	103 (21.0%)	92 (18.8%)	0.06	306 (22.2%)	316 (22.9%)	-0.02	410 (24.1%)	404 (23.8%)	0.01	819 (22.9%)	812 (22.7%)	0.00
Other gastroprotective agents; n (%)	** (1.0%)	** (0.6%)	0.04	14 (1.0%)	13 (0.9%)	0.01	35 (2.1%)	26 (1.5%)	0.05	#VALUE!	#VALUE!	#VALUE!
Number of lipid tests ordered												
...mean (sd)	0.37 (0.62)	0.39 (0.74)	-0.03	0.38 (0.72)	0.36 (0.66)	0.03	0.37 (0.69)	0.38 (0.68)	-0.01	0.37 (0.69)	0.37 (0.68)	0.00
Proton pump inhibitor; n (%)	94 (19.2%)	105 (21.4%)	-0.05	232 (16.8%)	225 (16.3%)	0.01	494 (29.1%)	490 (28.8%)	0.01	820 (23.0%)	820 (23.0%)	0.00
H2 receptor antagonist; n (%)	15 (3.1%)	21 (4.3%)	-0.06	47 (3.4%)	49 (3.5%)	-0.01	128 (7.5%)	139 (8.2%)	-0.03	190 (5.3%)	209 (5.9%)	-0.03
Vitamin K therapy; 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!
Number of INR (prothrombin) tests ordered												
...mean (sd)	0.80 (1.89)	0.53 (1.24)	0.17	0.68 (1.73)	0.50 (1.11)	0.12	0.51 (1.10)	0.49 (1.06)	0.02	0.62 (1.49)	0.50 (1.11)	0.00
Treating prescriber - Cardiologist; n (%)	299 (61.0%)	313 (63.9%)	-0.06	871 (63.1%)	868 (62.9%)	0.00	880 (51.8%)	902 (53.1%)	-0.03	2050 (57.4%)	2083 (58.3%)	-0.02
Treating prescriber - Primary Care Physici	415 (84.7%)	407 (83.1%)	0.04	600 (43.4%)	636 (46.1%)	-0.05	642 (37.8%)	637 (37.5%)	0.01	1657 (46.4%)	1680 (47.1%)	-0.01
Treating prescriber - Other; n (%)	474 (96.7%)	476 (97.1%)	-0.02	1,287 (93.2%)	1,288 (93.3%)	0.00	1,613 (94.9%)	1,617 (95.2%)	-0.01	3374 (94.5%)	3381 (94.7%)	-0.01
Alpha blockers; n (%)	30 (6.1%)	21 (4.3%)	0.08	54 (3.9%)	56 (4.1%)	-0.01	123 (7.2%)	125 (7.4%)	-0.01	207 (5.8%)	202 (5.7%)	0.00
CHA2DS2 VASc score, 180 days, V												
...mean (sd)	1.49 (1.21)	1.52 (1.17)	-0.03	1.24 (1.16)	1.25 (1.21)	-0.01	1.55 (1.37)	1.56 (1.36)	-0.01	1.42 (1.27)	1.43 (1.28)	0.00
Use of Prasugrel; 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 Loop Diuretics+other diuretics+otl	66 (13.5%)	66 (13.5%)	0.00	138 (10.0%)	139 (10.1%)	0.00	312 (18.4%)	334 (19.7%)	-0.03	516 (14.5%)	539 (15.1%)	-0.02
Commercial vs Medicare Advantage- Business Type Code - CORRECT ONE - OPTUM							0	0				
...Commercial; n (%)	260 (53.1%)	249 (50.8%)	0.05	#VALUE!	#VALUE!	#VALUE!	-	-	#VALUE!	#VALUE!	#VALUE!	#VALUE!
...Medicare Advantage; n (%)	0,230 (46.9%)	241 (49.2%)	-0.05	1287 (93.2%)	1285 (93.0%)	0.01	-	-	#VALUE!	#VALUE!	1,526 (81.6%)	#VALUE!
Commercial vs Medicare Advantage- Business Type Code												
...COM = COMMERCIAL; n (%)	260 (53.1%)	249 (50.8%)	0.05	-	-	#VALUE!	-	-	#VALUE!	260 (53.1%)	249 (50.8%)	0.05
...MCR = MEDICARE; n (%)	230 (46.9%)	241 (49.2%)	-0.05	-	-	#VALUE!	-	-	#VALUE!	230 (46.9%)	241 (49.2%)	-0.05
...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	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	-	-		0	0		-	-				
...1 - Fee For Service; n (%)	-	-		1,156 (83.7%)	1,158 (83.9%)		-	-		1,156 (83.7%)	1,158 (83.9%)	0.00
...2 - Encounter; n (%)	-	-		131 (9.5%)	127 (9.2%)		-	-		131 (9.5%)	127 (9.2%)	0.00
...3 - Medicare; n (%)	-	-		85 (6.2%)	86 (6.2%)		-	-		85 (6.2%)	86 (6.2%)	0.00
...4 - Medicare Encounter; n (%)	-	-		** (0.7%)	** (0.7%)		-	-		** (0.7%)	** (0.7%)	0.00
Metropolitan Statistical Area - Urban (any MSA) vs Rural (non-MSA)										0	0	0.00
...Urban; n (%)	-	-		998 (72.3%)	993 (71.9%)		-	-		998 (72.3%)	993 (71.9%)	0.00
...Rural; n (%)	-	-		151 (10.9%)	153 (11.1%)		-	-		151 (10.9%)	153 (11.1%)	0.00
...Unknown/Missing; n (%)	-	-		232 (16.8%)	235 (17.0%)		-	-		232 (16.8%)	235 (17.0%)	0.00