# Replication of the RECORD1 Anticoagulant 

 Trial in Healthcare Claims DataNCT00329628

July 9, 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 <br> Rivaroxaban versus Enoxaparin for Thromboprophylaxis after Hip Arthroplasty (RECORD1)

1.2 Intended aim(s)

To compare the risk of any deep vein thrombosis, nonfatal pulmonary embolism, or death in patients who underwent elective total hip arthroplasty for rivaroxaban versus standard therapy of enoxaparin.

### 1.3 Primary endpoint for replication

The primary outcome of the study was the composite of any deep-vein thrombosis, nonfatal pulmonary embolism, or death from any cause
1.4 Required power for primary endpoint and noninferiority margin (if applicable)

With an assumed outcome rate of $8 \%$ and non-inferiority absolute margin of $3.5 \%$, it was determined that 1,562 patients per study group would be needed to achieve $95 \%$ power to conclude noninferiority of rivaroxaban over standard therapy at one-sided alpha level of 0.025 .
1.5 Secondary endpoint for replication (assay sensitivity) and RCT finding

Major bleeding; $0.3 \%$ risk in rivaroxaban group and $0.1 \%$ risk in enoxaparin group, with an absolute increase in risk of $0.2 \%$ ( $95 \% \mathrm{Cl}-0.1-0.5$ )

### 1.6 Trial estimate

$0.8 \%$ risk of primary outcome in rivaroxaban group and $3.8 \%$ risk in enoxaparin group, with a risk reduction of 2.5 percentage points with $95 \% \mathrm{Cl} 1.5$ to 3.6 (Eriksson et al., 2008)

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

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

## 3. Data Source(s)

Optum, MarketScan, Medicare

## 4. Study Design Diagram

The study design diagram visualizes key aspects of the longitudinal study design for expedited review.
Figure 1
Design Diagram - RECORD1 TRIAL REPLICATION




Covariate Assessment Wincow
. $\underset{\substack{\text { Follow Up Window } \\ \text { Days }[1, \text { censor }]}}{\text {. }}$



- Start of additional exposure arthroplasty


## 5. Cohort Identification

### 5.1 Cohort Summary

This study will involve a new user, parallel group, propensity score-matched, retrospective cohort study design comparing rivaroxaban to enoxaparin users. The patients will be required to have continuous enrollment during a baseline period of 180 days before initiation of rivaroxaban or enoxaparin (index date). We will restrict the analyses to patients who underwent a total hip arthroplasty.

### 5.2 Important steps for cohort formation

New use of rivaroxaban, exposure, and enoxaparin, 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 rivaroxaban in the U.S. for treatment of deep vein thrombosis in patients undergoing knee or hip replacement surgery on July 1, 2011

- For Medicare: July 1, 2011 - December 31, 2017 (end of available data)
- For Marketscan: July 1, 2011 - December 31, 2018 (end of available data)
- For Optum: July 1, 2011 - March 31, 2020 (end of available data)
5.2.2 Specify inclusion/exclusion criteria for cohort entry and define the index date.

Inclusion and exclusion criteria were adapted from the trial as closely as possible. Definitions for all inclusion/exclusion are provided in Appendix A and are summarized in the flowcharts below.
5.3 Flowchart of the study cohort assembly

|  | Optum |  | Truven |  | Medicare |
| :--- | :--- | :--- | :--- | :--- | :--- |
|  | Less <br> Excluded <br> Patients | Remaining <br> Patients | Less <br> Excluded <br> Patients | Remaining <br> Patients | Less <br> Excluded <br> Patients |
| Remaining |  |  |  |  |  |
| Patients patients |  | $78,779,380$ |  | $200,203,908$ |  |


| Did not meet cohort entry criteria | -78,637,516 | 141,864 | 199,749,129 | 454,779 | -6,288,763 | 598,145 |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Excluded due to insufficient enrollment | -19,354 | 122,510 | -43,798 | 410,981 | -155,681 | 442,464 |
| Excluded due to prior use of referent | -1,842 | 120,668 | -55,562 | 355,419 | -47,539 | 394,925 |
| Excluded due to prior use of exposure | -18,320 | 102,348 | -19,645 | 335,774 | -60,851 | 334,074 |
| Excluded because patient qualified in >1 exposure category | -14 | 102,334 | -81 | 335,693 | -197 | 333,877 |
| Excluded based on Age | 0 | 102,334 | 0 | 335,693 | -136 | 333,741 |
| Excluded based on Gender | 0 | 102,334 | 0 | 335,693 | 0 | 333,741 |
| Excluded based on Use of other NOACs (dabigatran, apixaban, edoxaban) | -905 | 101,429 | -2297 | 333,396 | -7597 | 326,144 |
| Excluded based on Inclusion \# 1-Age >= 18 | -232 | 101,197 | -1,747 | 331,649 | -4 | 326,140 |
| Excluded based on Inclusion \# 2 - total hip arthroplasty | -89,074 | 12,123 | -288,401 | 43,248 | -275,562 | 50,578 |
| Excluded based on Exclusion \#1- bilateral hip replacement | -18 | 12,105 | -195 | 43,053 | -168 | 50,410 |
| Excluded based on Exclusion \#2-Pregnancy | -2 | 12,103 | -8 | 43,045 | -5 | 50,405 |
| Excluded based on Exclusion \#3 - Active Bleeding or High Risk of Bleeding (inpatient) | -59 | 12,044 | -262 | 42,783 | -2840 | 47,565 |
| Excluded based on Exclusion \#5 - Conditions Preventing Bilateral Venography | -618 | 11,426 | -1,544 | 41,239 | -4,198 | 43,367 |
| Excluded based on Exclusion \#6-Substantial Liver Disease | -246 | 11,180 | -668 | 40,571 | -1,036 | 42,331 |
| Excluded based on Exclusion \#7-Severe Renal Impairment | -29 | 11,151 | -123 | 40,448 | -245 | 42,086 |
| Excluded based on Exclusion \#8 - Concomitant Use of Protease Inhibitors for HIV Treatment | -2 | 11,149 | -33 | 40,415 | -37 | 42,049 |
| Excluded based on Use of warfarin | -126 | 11,023 | -1383 | 39,032 | -2889 | 39,160 |
| Final cohort |  | 11,023 |  | 39,032 |  | 39,160 |

## 6. Variables

### 6.1 Exposure-related variables:

## Study drug:

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

Comparator:
New initiators of enoxaparin, defined by no use of rivaroxaban or enoxaparin 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: any deep vein thrombosis, non-fatal pulmonary embolism, or death from any cause

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 rivaroxaban to apixaban would be a censoring event) or warfarin;
- 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
- The occurrence of a bilateral hip arthroplasty

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 36 days.

## 7. Initial Feasibility Analysis

## Aetion report name:

Optum- https://bwh-dope.aetion.com/projects/details/1633/rwrs/70926

Marketscan- https://bwh-dope.aetion.com/projects/details/1634/rwrs/70927
Medicare- https://bwh-dope.aetion.com/projects/details/1635/rwrs/70928

## Date conducted: 06/03/21

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

- Report patient characteristics by treatment group

|  | Optum |  |  | Truven |  |  | Medicare |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Variable | Referent enoxaparin 30 or 40 mg | Exposure rivaroxaban 10 mg | Difference | Referentenoxaparin 40 mg | Exposurerivaroxaban 10 mg | Difference | Referentenoxaparin 40 mg | Exposurerivaroxaban 10 mg | Difference |
| Number of patients | 139 | 10,884 | - (-, -) | 19,921 | 19,111 | - (-, -) | 3,318 | 35,842 | - (-, -) |
| Age |  |  |  |  |  |  |  |  |  |
| ...mean (sd) | $\begin{aligned} & \hline 59.07 \\ & (10.34) \\ & \hline \end{aligned}$ | $\begin{aligned} & 63.88 \\ & (10.73) \end{aligned}$ | $\begin{aligned} & -4.81(-6.55, \\ & -3.06) \end{aligned}$ | $\begin{aligned} & 60.11 \\ & (10.24) \end{aligned}$ | $\begin{aligned} & 60.51 \\ & (10.11) \end{aligned}$ | $\begin{aligned} & -0.41(-0.61, \\ & -0.21) \\ & \hline \end{aligned}$ | 71.28 (9.09) | 70.86 (8.57) | $\begin{aligned} & 0.43(0.10, \\ & 0.75) \end{aligned}$ |
| ...median [IQR] | $\begin{aligned} & 60.00 \\ & {[53.00,} \\ & 64.00] \end{aligned}$ | $\begin{aligned} & 64.00 \\ & {[57.00,} \\ & 71.00] \end{aligned}$ | - (-, -) | $\begin{aligned} & 60.00 \\ & {[54.00,} \\ & 65.00] \end{aligned}$ | $\begin{aligned} & 60.00 \\ & {[55.00,} \\ & 66.00] \end{aligned}$ | - (-, -) | $\begin{aligned} & 72.00 \\ & {[67.00,} \\ & 77.00] \end{aligned}$ | $\begin{aligned} & 71.00 \\ & {[67.00,} \\ & 76.00] \end{aligned}$ | - (-, -) |
| Gender without unknown |  |  |  |  |  |  |  |  |  |
| ...Male; n (\%) | 56 (40.3\%) | $\begin{aligned} & 4,760 \\ & (43.7 \%) \end{aligned}$ | $\begin{aligned} & -3.4 \% ~(- \\ & 12.0 \% \text {, } \\ & 5.1 \%) \end{aligned}$ | $\begin{aligned} & 9,459 \\ & (47.5 \%) \end{aligned}$ | $\begin{aligned} & 9,129 \\ & (47.8 \%) \end{aligned}$ | $\begin{aligned} & -0.3 \% ~(- \\ & 1.3 \%, 0.7 \%) \end{aligned}$ | $\begin{aligned} & 1,332 \\ & (40.1 \%) \end{aligned}$ | $\begin{aligned} & 13,078 \\ & (36.5 \%) \end{aligned}$ | $\begin{aligned} & 3.7 \% ~(1.9 \%, \\ & 5.4 \%) \end{aligned}$ |
| ...Female; n (\%) | 83 (59.7\%) | $\begin{aligned} & 6,124 \\ & (56.3 \%) \end{aligned}$ | $\begin{aligned} & 3.4 \% ~(- \\ & 5.1 \%, \\ & 12.0 \%) \end{aligned}$ | $\begin{aligned} & 10,462 \\ & (52.5 \%) \end{aligned}$ | $\begin{aligned} & 9,982 \\ & (52.2 \%) \end{aligned}$ | $\begin{aligned} & 0.3 \% ~(- \\ & 0.7 \%, 1.3 \%) \end{aligned}$ | $\begin{aligned} & 1,986 \\ & (59.9 \%) \end{aligned}$ | $\begin{aligned} & 22,764 \\ & (63.5 \%) \end{aligned}$ | -3.7\% (5.4\%, 1.9\%) |
| CCI Combined Comorbidity Score (183 days) with ICD10 |  |  |  |  |  |  |  |  |  |
| ...mean (sd) | 1.74 (1.63) | 1.82 (1.58) | $\begin{aligned} & -0.08(-0.36, \\ & 0.19) \end{aligned}$ | 1.49 (1.42) | 1.46 (1.36) | $\begin{aligned} & 0.03(-0.00, \\ & 0.05) \end{aligned}$ | 4.82 (3.05) | 4.06 (2.75) | $\begin{aligned} & 0.76(0.65, \\ & 0.86) \end{aligned}$ |


| ...median [IQR] | $\begin{aligned} & 1.00[0.00, \\ & 3.00] \end{aligned}$ | $\begin{aligned} & 1.00[1.00, \\ & 3.00] \end{aligned}$ | - (-, -) | $\begin{aligned} & 1.00[1.00, \\ & 2.00] \end{aligned}$ | $\begin{aligned} & 1.00[1.00, \\ & 2.00] \end{aligned}$ | - (-, -) | $\begin{aligned} & 4.00 \text { [2.00, } \\ & 6.00] \end{aligned}$ | $\begin{aligned} & 4.00 \text { [2.00, } \\ & 6.00] \end{aligned}$ | - (-, -) |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |

- Report summary parameters of study population

| FEASIBILITY- FOR STUDY OUTCOME |  |  |  |
| :--- | :--- | :--- | :--- |
|  | Optum | Truven | Medicare |
| Variable | Value | Value | Value |
| Number of patients in full cohort | 11,023 | 39,032 | 39,160 |
| Number of patients dropped as incomplete cases | 0 | 0 | 0 |
| Number of patients that did not begin follow-up | 3 | 41 | 26 |
| Number of patients in analytic cohort | 11,020 | 38,991 | 39,134 |
| Number of events | 8 | 35 | 112 |
| Number of person-years | 747.15 | $2,814.10$ | $3,148.61$ |
| Number of patients in group: Referent - enoxaparin 40 mg | 139 | 19,902 | 3,306 |
| Number of patients in group: Exposure - rivaroxaban 10 mg | 10,881 | 19,089 | 35,828 |
| Risk per 1,000 patients | 0.73 | 0.9 | 2.86 |
| Rate per 1,000 person-years | 10.71 | 12.44 | 35.57 |

- Report median follow-up time by treatment group

| MEDIAN FOLLOW-UP TIME FOR STUDY OUTCOME |  |  |  |
| :--- | :--- | :--- | :--- |
| Median Follow-Up Time (Days) [IQR] |  |  |  |
|  | Optum | Truven | Medicare |
| Patient Group | Median Follow-Up <br> Time (Days) [IQR] | Median Follow-Up <br> Time (Days) [IQR] | Median Follow-Up <br> Time (Days) [IQR] |
|  | $28[15,38]$ | $23[18,36]$ | $29[20,38]$ |


| Referent | $11[10,13]$ | $20[18,28]$ | $20[16,27]$ |
| :--- | :--- | :--- | :--- |
| Exposure | $28[15,38]$ | $35[22,38]$ | $32[22,38]$ |

- Report reasons for censoring in the overall study population

| CENSORING REASONS FOR STUDY OUTCOME |  |  |  |
| :--- | :--- | :--- | :--- |
|  | Optum | Truven | Medicare |
| Overall |  |  |  |
| Outcome | $8(0.1 \%)$ | $35(0.1 \%)$ | $112(0.3 \%)$ |
| Death | $0(0.0 \%)$ | $0(0.0 \%)$ | $0(0.0 \%)$ |
| Start of an additional exposure | $0(0.0 \%)$ | $72(0.2 \%)$ | $124(0.3 \%)$ |
| End of index exposure | 8,398 | 37,568 | 36,891 |
| $(96.3 \%)$ |  |  |  |
| Specified date reached | $21(0.2 \%)$ | $142(0.4 \%)$ | $391(1.0 \%)$ |
| End of patient data | $0(0.0 \%)$ | $0(0.0 \%)$ | $0(0.0 \%)$ |
| End of patient enrollment | $212(1.9 \%)$ | $928(2.4 \%)$ | $108(0.3 \%)$ |
| Censoring - Switch to other NOAC + nursing home + bilateral hip arthroplasty <br> Occurred | 2,381 | $246(0.6 \%)$ | $1,508(3.9 \%)$ |

- Report overall risk of the primary outcome.

|  | Optum | Marketscan | Medicare | Pooled |
| :--- | :--- | :--- | :--- | :--- |
| Risk per 1,000 patients | 0.73 | 0.9 | 2.86 | 1.74 |

## 8. Initial Power Assessment

## Aetion report name:

Optum- https://bwh-dope.aetion.com/projects/details/1633/rwrs/71036
Marketscan- https://bwh-dope.aetion.com/projects/details/1634/rwrs/71035
Medicare- https://bwh-dope.aetion.com/projects/details/1635/rwrs/71034

## Date conducted: 06/04/21

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

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

| Reviewed by PI: |  | Date reviewed: |  |
| :--- | :--- | :--- | :--- |
| Reviewed by FDA: |  | Date reviewed: |  |
| Reasons for stopping <br> analysis (if required): |  |  |  |

## 9. Balance Assessment

## Aetion report name:

Optum: https://bwh-dope.aetion.com/projects/details/1633/rwrs/70922
Marketscan: https://bwh-dope.aetion.com/projects/details/1634/rwrs/70924
Medicare: https://bwh-dope.aetion.com/projects/details/1635/rwrs/70925
Date conducted: 06/03/21
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- Please refer to Appendix B.

- Report reasons for censoring by treatment group.

|  | Overall | Referent | Exposure |
| :--- | :---: | :---: | :---: |
| Dummy outcome | $0(0 \%)$ | $0(0 \%)$ | $0(0 \%)$ |
| Death | $10(0.03 \%)$ | $5(0.03 \%)$ | $5(0.03 \%)$ |
| Start of an additional exposure | $127(0.36 \%)$ | $101(0.58 \%)$ | $26(0.15 \%)$ |
| End of index exposure | $33,215(95.24 \%)$ | $16,577(95.06 \%)$ | $16,638(95.41 \%)$ |
| Specified date reached | $192(0.55 \%)$ | $83(0.48 \%)$ | $109(0.63 \%)$ |
| End of patient enrollment | $712(2.04 \%)$ | $281(1.61 \%)$ | $431(2.47 \%)$ |
| Censoring - Switch to other NOAC + nursing home <br> bilateral hip arthroplasty Occurred | $620(1.78 \%)$ | $391(2.24 \%)$ | $229(1.31 \%)$ |

- Report follow-up time by treatment group.

| Median Follow-Up Time (Days) [IQR] |  |  |  |
| :--- | :--- | :--- | :--- |
| Patient Group | Optum | Marketscan | Medicare |
| Overall Patient Population | $15[10,32]$ | $24[18,36]$ | $22[18,36]$ |
| Referent | $11[10,15]$ | $20[18,28]$ | $20[16,28]$ |
| Exposure | $31[18,38]$ | $35[22,38]$ | $31[22,38]$ |

## 10. Final Power Assessment

Date conducted: 06/03/21

- 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.

Note: Although the pooled power calculation from the emulation is below the $95 \%$ power threshold under similar assumptions as the trial, we saw the trial was overpowered for noninferiority, given the actual size of the effect. Given the trial finding of a $70 \%$ lower risk, we expect to have enough power in this trial emulation.

| O Pooled |  |
| :--- | ---: |
| Non-inferiority Analysis |  |
| Number of patients matched | 34,876 |
| Reference | 17,438 |
| Exposed | 17,438 |
| Risk per 1000 patients | 1.74 |
| Assumed HR from RCT | 1 |
| Alpha (2-sided) | 0.05 |
| Non-inferiority margin | 1.95 |
|  |  |
| Number of events expected | 60.68424 |
| Power | 0.739314806 |

- Optum

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

| Non-inferiority Analysis |  |
| :--- | ---: |
| Number of patients matched | 214 |
| Reference | 107 |
| Exposed | 107 |
| Risk per 1000 patients | 0.73 |
| Assumed HR from RCT | 1 |
| Alpha (2-sided) | 0.05 |
| Non-inferiority margin | 1.95 |
|  | 0.15622 |
| Number of events expected | 0.03377588 |
| Power |  |

- MarketScan

| Non-inferiority Analysis |  |
| :--- | ---: |
| Number of patients matched | 28,132 |
| Reference | 14,066 |
| Exposed | 14,066 |
| Risk per 1000 patients | 0.90 |
| Assumed HR from RCT | 1 |
| Alpha (2-sided) | 0.05 |
| Non-inferiority margin | 1.95 |
|  | 25.3188 |
| Number of events expected | 0.389823503 |
| Power |  |

- Medicare

| Non-inferiority Analysis |  |
| :--- | ---: |
| Number of patients matched | 6,530 |
| Reference | 3,265 |
| Exposed | 3,265 |
| Risk per 1000 patients | 2.86 |
| Assumed HR from RCT | 1 |
| Alpha (2-sided) | 0.05 |
| Non-inferiority margin | 1.95 |
|  | 18.6758 |
| Number of events expected | 0.302600852 |
| Power |  |

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

| Reviewed by PI: |  | Date reviewed: |  |
| :--- | :--- | :--- | :--- |
| Reviewed by FDA: |  | Date reviewed: |  |
| Reasons for stopping <br> analysis (if required): |  |  |  |

## 11. Study Confidence and Concerns

Deadline for voting on study confidence and listing concerns:
Date votes and concerns are summarized:

- If final feasibility and power analyses are reviewed and approved, proceed to the remaining protocol steps.
- All study team and advisory board members that review this protocol should at this stage provide their level of confidence for the success of the RWD study in the Google Form. This form also provides space for reviewers to list any concerns that they feel may
contribute to a failure to replicate the findings of the RCT, including differences in study populations, poor measurement of study variables, or residual confounding. All responses will be kept confidential and individual-level results will only be shared with the individual respondent.
- After the deadline for voting has passed, provide the distribution of responses and summarize all concerns here.


## 12. Register study protocol on clinicalTrials.gov

Date conducted:

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


## 13. Comparative Analyses

## Aetion 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 |  |  |  |  |  |  |  |
| $\ldots$ |  |  |  |  |  |  |  |

### 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 |  |  |  |
| $\ldots$ |  |  |  |

### 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 |  |  |  |  |  |
| $\ldots$ |  |  |  |  |  |

HR, Hazard Ratio; CI, Confidence Interval.
14.5 Table 5: Results from secondary analyses;

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

## 15. References

Eriksson B, Borris L, Friedman R, et al. Rivaroxaban versus Enoxaparin for Thromboprophylaxis after Hip Arthroplasty. N Engl J Med. 2008; 358:2765-75

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

## Appendix A

Trial Name (with web

| links) | RECORD1 |
| :---: | :---: |
| Trial Name (with pdf |  |
| links) | RECORD1 |
| NCT | NCT00329628 |
| Therapeutic Area | Cardiology/Vascular Diseases |
| Study Batch | NOACs |
| Brand Name | Xarelto |
| Generic Name | Rivaroxaban |
| Sponsor | Bayer |
| Year | 2008 |

Composite endpoint of total VTE i.e.: Any DVT (proximal
Measurable Endpoint and/or distal), Non fatal PE, Death of all causes [ Time Frame: Treatment period : up to day 36+/-6 ]

## Exposure Rivaroxaban

Comparator Enoxaparin

Population $\quad$| Patients of legal |
| :--- |
| hip replacement |

## Trial Finding $\quad H R=1$

No. of Patients $\quad 4,591(2,266$ in exposed arm)
Non-inferiority
Margin

Power
$H R=1.95$
0.95 . If these assumptions were
correct, 1562 patients per study group would be sufficient to show noninferiority with a power of
$95 \%$ and a one-sided type I error rate of $2.5 \%$. It was assumed that $25 \%$ of patients would not have valid venograms, resulting in a target sample size of 4200 patients.

## Appendix A

## Title <br> PE DVT outcome

ICD-9 Dx inpatient primary position
PE
415.1
415.11
415.19

DVT
451.1
451.11
451.19
451.2
451.81
451.9

453
453.1
453.2
453.4
453.40
453.41
453.42
453.5
453.50
453.51
453.52
453.8
453.82
453.83
453.84
453.85
453.86
453.87

PULMONARY EMBOLISM AND INFARCTION
IATROGENIC PULMONARY EMBOLISM AND INFARCTION
OTHER PULMONARY EMBOLISM AND INFARCTION

PHLEBITIS AND THROMBOPHLEBITIS OF DEEP VEINS OF LOWER EXTREMITIES
PHLEBITIS AND THROMBOPHLEBITIS OF FEMORAL VEIN (DEEP) (SUPERFICIAL)
PHLEBITIS AND THROMBOPHLEBITIS OF OTHER
PHLEBITIS AND THROMBOPHLEBITIS OF LOWER EXTREMITIES UNSPECIFIED
PHLEBITIS AND THROMBOPHLEBITIS OF ILIAC VEIN
PHLEBITIS AND THROMBOPHLEBITIS OF UNSPECIFIED SITE
BUDD-CHIARI SYNDROME
THROMBOPHLEBITIS MIGRANS
EMBOLISM AND THROMBOSIS OF INFERIOR VENA CAVA
ACUTE VENOUS EMBOLISM AND THROMBOSIS OF DEEP VESSELS OF LOWER EXTREMITY
ACUTE VENOUS EMBOLISM AND THROMBOSIS OF UNSPECIFIED DEEP VESSELS OF LOWER EXTREMITY
ACUTE VENOUS EMBOLISM AND THROMBOSIS OF DEEP VESSELS OF PROXIMAL LOWER EXTREMITY
ACUTE VENOUS EMBOLISM AND THROMBOSIS OF DEEP VESSELS OF DISTAL LOWER EXTREMITY
CHRONIC VENOUS EMBOLISM AND THROMBOSIS OF DEEP VESSELS OF LOWER EXTREMITY
CHRONIC VENOUS EMBOLISM AND THROMBOSIS OF UNSPECIFIED DEEP VESSELS OF LOWER EXTREMITY
CHRONIC VENOUS EMBOLISM AND THROMBOSIS OF DEEP VESSELS OF PROXIMAL LOWER EXTREMITY
CHRONIC VENOUS EMBOLISM AND THROMBOSIS OF DEEP VESSELS OF DISTAL LOWER EXTREMITY
ACUTE VENOUS EMBOLISM AND THROMBOSIS OF OTHER SPECIFIED VEINS
ACUTE VENOUS EMBOLISM AND THROMBOSIS OF DEEP VEINS OF UPPER EXTREMITY
ACUTE VENOUS EMBOLISM AND THROMBOSIS OF UPPER EXTREMITY UNSPECIFIED
ACUTE VENOUS EMBOLISM AND THROMBOSIS OF AXILLARY VEINS
ACUTE VENOUS EMBOLISM AND THROMBOSIS OF SUBCLAVIAN VEINS
ACUTE VENOUS EMBOLISM AND THROMBOSIS OF INTERNAL JUGULAR VEINS
ACUTE VENOUS EMBOLISM AND THROMBOSIS OF OTHER THORACIC VEINS

## Appendix A

453.89
453.9

## ICD-10 Dx inpatient primary position

## PE

126.0
126.01
126.02
126.09
126.9
126.99

DVT
180.1
180.10
180.11
180.12
180.13
180.2
180.20
180.201
180.202
180.203
180.209
180.21
180.211
180.212
180.213
180.219
180.22
180.221
180.222
180.223
180.229

Pulmonary embolism with acute cor pulmonale
Septic pulmonary embolism with acute cor pulmonale
Saddle embolus of pulmonary artery with acute cor pulmonale
Other pulmonary embolism with acute cor pulmonale
Pulmonary embolism without acute cor pulmonale
Other pulmonary embolism without acute cor pulmonale

Phlebitis and thrombophlebitis of femoral vein
Phlebitis and thrombophlebitis of unspecified femoral vein
Phlebitis and thrombophlebitis of right femoral vein
Phlebitis and thrombophlebitis of left femoral vein
Phlebitis and thrombophlebitis of femoral vein, bilateral
Phlebitis and thrombophlebitis of other and unspecified deep vessels of lower extremities
Phlebitis and thrombophlebitis of unspecified deep vessels of lower extremities
Phlebitis and thrombophlebitis of unspecified deep vessels of right lower extremity
Phlebitis and thrombophlebitis of unspecified deep vessels of left lower extremity
Phlebitis and thrombophlebitis of unspecified deep vessels of lower extremities, bilateral
Phlebitis and thrombophlebitis of unspecified deep vessels of unspecified lower extremity
Phlebitis and thrombophlebitis of iliac vein
Phlebitis and thrombophlebitis of right iliac vein
Phlebitis and thrombophlebitis of left iliac vein
Phlebitis and thrombophlebitis of iliac vein, bilateral
Phlebitis and thrombophlebitis of unspecified iliac vein
Phlebitis and thrombophlebitis of popliteal vein
Phlebitis and thrombophlebitis of right popliteal vein
Phlebitis and thrombophlebitis of left popliteal vein
Phlebitis and thrombophlebitis of popliteal vein, bilateral
Phlebitis and thrombophlebitis of unspecified popliteal vein

## Appendix A

180.23
180.231
180.232
180.233
180.239
180.29
180.291
180.292
180.293
180.299
180.3
180.9
182.0
182.1

I80.3
182.4
182.40
182.401
182.402
182.403
182.409
182.41
182.411
182.412
182.413
182.419
182.42
182.421
182.422
182.423
182.429
182.43
182.431
182.432

Phlebitis and thrombophlebitis of tibial vein
Phlebitis and thrombophlebitis of right tibial vein
Phlebitis and thrombophlebitis of left tibial vein
Phlebitis and thrombophlebitis of tibial vein, bilateral
Phlebitis and thrombophlebitis of unspecified tibial vein
Phlebitis and thrombophlebitis of other deep vessels of lower extremities
Phlebitis and thrombophlebitis of other deep vessels of right lower extremity
Phlebitis and thrombophlebitis of other deep vessels of left lower extremity
Phlebitis and thrombophlebitis of other deep vessels of lower extremity, bilateral
Phlebitis and thrombophlebitis of other deep vessels of unspecified lower extremity
Phlebitis and thrombophlebitis of lower extremities, unspecified
Phlebitis and thrombophlebitis of unspecified site
Budd-Chiari syndrome
Thrombophlebitis migrans
Phlebitis and thrombophlebitis of lower extremities, unspecified
Acute embolism and thrombosis of deep veins of lower extremity
Acute embolism and thrombosis of unspecified deep veins of lower extremity Acute embolism and thrombosis of unspecified deep veins of right lower extremity Acute embolism and thrombosis of unspecified deep veins of left lower extremity Acute embolism and thrombosis of unspecified deep veins of lower extremity, bilateral
Acute embolism and thrombosis of unspecified deep veins of unspecified lower extremity
Acute embolism and thrombosis of femoral vein
Acute embolism and thrombosis of right femoral vein
Acute embolism and thrombosis of left femoral vein
Acute embolism and thrombosis of femoral vein, bilateral
Acute embolism and thrombosis of unspecified femoral vein
Acute embolism and thrombosis of iliac vein
Acute embolism and thrombosis of right iliac vein
Acute embolism and thrombosis of left iliac vein
Acute embolism and thrombosis of iliac vein, bilateral
Acute embolism and thrombosis of unspecified iliac vein
Acute embolism and thrombosis of popliteal vein
Acute embolism and thrombosis of right popliteal vein
Acute embolism and thrombosis of left popliteal vein

## Appendix A

182.433
182.439
182.44
182.441
182.442
182.443
182.449
182.49
182.491
182.492
182.493
182.499
182.4 Y
182.4Y1
182.4Y2
182.4Y3
182.4Y9
$182.4 Z$
$182.4 Z 1$
$182.4 Z 2$
182.4Z3
182.4Z9
182.5
182.50
182.501
182.502
182.503
182.509
182.51
182.511
182.512
182.513
182.519
182.52

Acute embolism and thrombosis of popliteal vein, bilateral
Acute embolism and thrombosis of unspecified popliteal vein
Acute embolism and thrombosis of tibial vein
Acute embolism and thrombosis of right tibial vein
Acute embolism and thrombosis of left tibial vein
Acute embolism and thrombosis of tibial vein, bilateral
Acute embolism and thrombosis of unspecified tibial vein
Acute embolism and thrombosis of other specified deep vein of lower extremity
Acute embolism and thrombosis of other specified deep vein of right lower extremity
Acute embolism and thrombosis of other specified deep vein of left lower extremity
Acute embolism and thrombosis of other specified deep vein of lower extremity, bilateral
Acute embolism and thrombosis of other specified deep vein of unspecified lower extremity
Acute embolism and thrombosis of unspecified deep veins of proximal lower extremity
Acute embolism and thrombosis of unspecified deep veins of right proximal lower extremity
Acute embolism and thrombosis of unspecified deep veins of left proximal lower extremity
Acute embolism and thrombosis of unspecified deep veins of proximal lower extremity, bilateral
Acute embolism and thrombosis of unspecified deep veins of unspecified proximal lower extremity
Acute embolism and thrombosis of unspecified deep veins of distal lower extremity
Acute embolism and thrombosis of unspecified deep veins of right distal lower extremity
Acute embolism and thrombosis of unspecified deep veins of left distal lower extremity
Acute embolism and thrombosis of unspecified deep veins of distal lower extremity, bilateral
Acute embolism and thrombosis of unspecified deep veins of unspecified distal lower extremity
Chronic embolism and thrombosis of deep veins of lower extremity
Chronic embolism and thrombosis of unspecified deep veins of lower extremity
Chronic embolism and thrombosis of unspecified deep veins of right lower extremity
Chronic embolism and thrombosis of unspecified deep veins of left lower extremity
Chronic embolism and thrombosis of unspecified deep veins of lower extremity, bilateral
Chronic embolism and thrombosis of unspecified deep veins of unspecified lower extremity
Chronic embolism and thrombosis of femoral vein
Chronic embolism and thrombosis of right femoral vein
Chronic embolism and thrombosis of left femoral vein
Chronic embolism and thrombosis of femoral vein, bilateral
Chronic embolism and thrombosis of unspecified femoral vein
Chronic embolism and thrombosis of iliac vein

## Appendix A

182.521
182.522
182.523
182.529
182.53
182.531
182.532
182.533
182.539
182.54
182.541
182.542
182.543
182.549
182.59
182.591
182.592
182.593
182.599
182.5Y
182.5Y1
182.5Y2
182.5Y3
182.5Y9
$182.5 Z$
182.571
182.572
182.523
182.579
182.6
182.60
182.601
182.602
182.603

Chronic embolism and thrombosis of right iliac vein
Chronic embolism and thrombosis of left iliac vein
Chronic embolism and thrombosis of iliac vein, bilateral
Chronic embolism and thrombosis of unspecified iliac vein
Chronic embolism and thrombosis of popliteal vein
Chronic embolism and thrombosis of right popliteal vein
Chronic embolism and thrombosis of left popliteal vein
Chronic embolism and thrombosis of popliteal vein, bilateral
Chronic embolism and thrombosis of unspecified popliteal vein
Chronic embolism and thrombosis of tibial vein
Chronic embolism and thrombosis of right tibial vein
Chronic embolism and thrombosis of left tibial vein
Chronic embolism and thrombosis of tibial vein, bilateral
Chronic embolism and thrombosis of unspecified tibial vein
Chronic embolism and thrombosis of other specified deep vein of lower extremity
Chronic embolism and thrombosis of other specified deep vein of right lower extremity
Chronic embolism and thrombosis of other specified deep vein of left lower extremity
Chronic embolism and thrombosis of other specified deep vein of lower extremity, bilateral
Chronic embolism and thrombosis of other specified deep vein of unspecified lower extremity
Chronic embolism and thrombosis of unspecified deep veins of proximal lower extremity
Chronic embolism and thrombosis of unspecified deep veins of right proximal lower extremity
Chronic embolism and thrombosis of unspecified deep veins of left proximal lower extremity
Chronic embolism and thrombosis of unspecified deep veins of proximal lower extremity, bilateral
Chronic embolism and thrombosis of unspecified deep veins of unspecified proximal lower extremity
Chronic embolism and thrombosis of unspecified deep veins of distal lower extremity
Chronic embolism and thrombosis of unspecified deep veins of right distal lower extremity
Chronic embolism and thrombosis of unspecified deep veins of left distal lower extremity
Chronic embolism and thrombosis of unspecified deep veins of distal lower extremity, bilateral
Chronic embolism and thrombosis of unspecified deep veins of unspecified distal lower extremity
Acute embolism and thrombosis of veins of upper extremity
Acute embolism and thrombosis of unspecified veins of upper extremity
Acute embolism and thrombosis of unspecified veins of right upper extremity
Acute embolism and thrombosis of unspecified veins of left upper extremity
Acute embolism and thrombosis of unspecified veins of upper extremity, bilateral

## Appendix A

182.609
182.62
182.621
182.622
182.623
182.629
182.890
182.90
182.A1
182.A11
182.A12
182.A13
182.A19
182.B1
182.B11

I82.B12
182.B13
182.B19
182.C1

I82.C11
182.C12
182.C13
182.C19

Acute embolism and thrombosis of unspecified veins of unspecified upper extremity
Acute embolism and thrombosis of deep veins of upper extremity
Acute embolism and thrombosis of deep veins of right upper extremity
Acute embolism and thrombosis of deep veins of left upper extremity
Acute embolism and thrombosis of deep veins of upper extremity, bilateral
Acute embolism and thrombosis of deep veins of unspecified upper extremity
Acute embolism and thrombosis of other specified veins
Acute embolism and thrombosis of unspecified vein
Acute embolism and thrombosis of axillary vein
Acute embolism and thrombosis of right axillary vein
Acute embolism and thrombosis of left axillary vein
Acute embolism and thrombosis of axillary vein, bilateral
Acute embolism and thrombosis of unspecified axillary vein
Acute embolism and thrombosis of subclavian vein
Acute embolism and thrombosis of right subclavian vein
Acute embolism and thrombosis of left subclavian vein
Acute embolism and thrombosis of subclavian vein, bilateral
Acute embolism and thrombosis of unspecified subclavian vein
Acute embolism and thrombosis of internal jugular vein
Acute embolism and thrombosis of right internal jugular vein
Acute embolism and thrombosis of left internal jugular vein
Acute embolism and thrombosis of internal jugular vein, bilateral
Acute embolism and thrombosis of unspecified internal jugular vein

## Appendix A

Title
Major Ble

ICD-9 Dx
423
430
431
432
432.1
432.9
459
531
531
531.01
531.2
531.2
531.21
531.4
531.4
531.41
531.6
531.6
531.61
532
532
532.01
532.2
532.2
532.21
532.4
532.4
532.41

1 inpatient or 2 outpatient diagnosis

## inpatient any position

(ICD9) SUBARACHNOID HEMORRHAGE
(ICD9) INTRACEREBRAL HEMORRHAGE
(ICD9) NONTRAUMATIC EXTRADURAL HEMORRHAGE
(ICD9) SUBDURAL HEMORRHAGE
(ICD9) UNSPECIFIED INTRACRANIAL HEMORRHAGE
(ICD9) HEMORRHAGE UNSPECIFIED
(ICD9) ACUTE GASTRIC ULCER WITH HEMORRHAGE
(ICD9) ACUTE GASTRIC ULCER WITH HEMORRHAGE WITHOUT OBSTRUCTION
(ICD9) ACUTE GASTRIC ULCER WITH HEMORRHAGE WITH OBSTRUCTION
(ICD9) ACUTE GASTRIC ULCER WITH HEMORRHAGE AND PERFORATION
(ICD9) ACUTE GASTRIC ULCER WITH HEMORRHAGE AND PERFORATION WITHOUT OBSTRUCTION
(ICD9) ACUTE GASTRIC ULCER WITH HEMORRHAGE AND PERFORATION WITH OBSTRUCTION
(ICD9) CHRONIC OR UNSPECIFIED GASTRIC ULCER WITH HEMORRHAGE
(ICD9) CHRONIC OR UNSPECIFIED GASTRIC ULCER WITH HEMORRHAGE WITHOUT OBSTRUCTION
(ICD9) CHRONIC OR UNSPECIFIED GASTRIC ULCER WITH HEMORRHAGE WITH OBSTRUCTION
(ICD9) CHRONIC OR UNSPECIFIED GASTRIC ULCER WITH HEMORRHAGE AND PERFORATION
(ICD9) CHRONIC OR UNSPECIFIED GASTRIC ULCER WITH HEMORRHAGE AND PERFORATION WITHOUT OBSTRUCTION
(ICD9) CHRONIC OR UNSPECIFIED GASTRIC ULCER WITH HEMORRHAGE AND PERFORATION WITH OBSTRUCTION (ICD9) ACUTE DUODENAL ULCER WITH HEMORRHAGE
(ICD9) ACUTE DUODENAL ULCER WITH HEMORRHAGE WITHOUT OBSTRUCTION
(ICD9) ACUTE DUODENAL ULCER WITH HEMORRHAGE WITH OBSTRUCTION
(ICD9) ACUTE DUODENAL ULCER WITH HEMORRHAGE AND PERFORATION
(ICD9) ACUTE DUODENAL ULCER WITH HEMORRHAGE AND PERFORATION WITHOUT OBSTRUCTION
(ICD9) ACUTE DUODENAL ULCER WITH HEMORRHAGE AND PERFORATION WITH OBSTRUCTION
(ICD9) CHRONIC OR UNSPECIFIED DUODENAL ULCER WITH HEMORRHAGE
(ICD9) CHRONIC OR UNSPECIFIED DUODENAL ULCER WITH HEMORRHAGE WITHOUT OBSTRUCTION
(ICD9) CHRONIC OR UNSPECIFIED DUODENAL ULCER WITH HEMORRHAGE WITH OBSTRUCTION

## Appendix A

532.6
532.6
532.61

533
533
533.01
533.2
533.2
533.21
533.4
533.4
533.41
533.6
533.6
533.61

534
534
534.01
534.2
534.2
534.21
534.4
534.4
534.41
534.6
(ICD9) CHRONIC OR UNSPECIFIED DUODENAL ULCER WITH HEMORRHAGE AND PERFORATION
(ICD9) CHRONIC OR UNSPECIFIED DUODENAL ULCER WITH HEMORRHAGE AND PERFORATION WITHOUT OBSTRUCTION
(ICD9) CHRONIC OR UNSPECIFIED DUODENAL ULCER WITH HEMORRHAGE AND PERFORATION WITH OBSTRUCTION
(ICD9) ACUTE PEPTIC ULCER OF UNSPECIFIED SITE WITH HEMORRHAGE
(ICD9) ACUTE PEPTIC ULCER OF UNSPECIFIED SITE WITH HEMORRHAGE WITHOUT OBSTRUCTION
(ICD9) ACUTE PEPTIC ULCER OF UNSPECIFIED SITE WITH HEMORRHAGE WITH OBSTRUCTION
(ICD9) ACUTE PEPTIC ULCER OF UNSPECIFIED SITE WITH HEMORRHAGE AND PERFORATION
(ICD9) ACUTE PEPTIC ULCER OF UNSPECIFIED SITE WITH HEMORRHAGE AND PERFORATION WITHOUT OBSTRUCTION
(ICD9) ACUTE PEPTIC ULCER OF UNSPECIFIED SITE WITH HEMORRHAGE AND PERFORATION WITH OBSTRUCTION (ICD9) CHRONIC OR UNSPECIFIED PEPTIC ULCER OF UNSPECIFIED SITE WITH HEMORRHAGE
(ICD9) CHRONIC OR UNSPECIFIED PEPTIC ULCER OF UNSPECIFIED SITE WITH HEMORRHAGE WITHOUT OBSTRUCTION
(ICD9) CHRONIC OR UNSPECIFIED PEPTIC ULCER OF UNSPECIFIED SITE WITH HEMORRHAGE WITH OBSTRUCTION
(ICD9) CHRONIC OR UNSPECIFIED PEPTIC ULCER OF UNSPECIFIED SITE WITH HEMORRHAGE AND PERFORATION (ICD9) CHRONIC OR UNSPECIFIED PEPTIC ULCER OF UNSPECIFIED SITE WITH HEMORRHAGE AND PERFORATION WITHOUT OBSTRUCTION
(ICD9) CHRONIC OR UNSPECIFIED PEPTIC ULCER OF UNSPECIFIED SITE WITH HEMORRHAGE AND PERFORATION WITH OBSTRUCTION
(ICD9) ACUTE GASTROJEJUNAL ULCER WITH HEMORRHAGE
(ICD9) ACUTE GASTROJEJUNAL ULCER WITH HEMORRHAGE WITHOUT OBSTRUCTION
(ICD9) ACUTE GASTROJEJUNAL ULCER WITH HEMORRHAGE WITH OBSTRUCTION
(ICD9) ACUTE GASTROJEJUNAL ULCER WITH HEMORRHAGE AND PERFORATION
(ICD9) ACUTE GASTROJEJUNAL ULCER WITH HEMORRHAGE AND PERFORATION WITHOUT OBSTRUCTION
(ICD9) ACUTE GASTROJEJUNAL ULCER WITH HEMORRHAGE AND PERFORATION WITH OBSTRUCTION
(ICD9) CHRONIC OR UNSPECIFIED GASTROJEJUNAL ULCER WITH HEMORRHAGE
(ICD9) CHRONIC OR UNSPECIFIED GASTROJEJUNAL ULCER WITH HEMORRHAGE WITHOUT OBSTRUCTION
(ICD9) CHRONIC OR UNSPECIFIED GASTROJEJUNAL ULCER WITH HEMORRHAGE WITH OBSTRUCTION
(ICD9) CHRONIC OR UNSPECIFIED GASTROJEJUNAL ULCER WITH HEMORRHAGE AND PERFORATION

## Appendix A

534.6
534.61
562.02
562.03
562.12
562.13
568.81
569.3
569.83
569.85
569.86

578
578.1
578.9
719.1
719.1
719.11
719.12
719.13
719.14
719.15
719.16
719.17
719.18
719.19
784.7
784.8
599.7
599.7
599.71
599.72
786.3
(ICD9) CHRONIC OR UNSPECIFIED GASTROJEJUNAL ULCER WITH HEMORRHAGE AND PERFORATION WITHOUT OBSTRUCTION
(ICD9) CHRONIC OR UNSPECIFIED GASTROJEJUNAL ULCER WITH HEMORRHAGE AND PERFORATION WITH OBSTRUCTION
(ICD9) DIVERTICULOSIS OF SMALL INTESTINE WITH HEMORRHAGE
(ICD9) DIVERTICULITIS OF SMALL INTESTINE WITH HEMORRHAGE
(ICD9) DIVERTICULOSIS OF COLON WITH HEMORRHAGE
(ICD9) DIVERTICULITIS OF COLON WITH HEMORRHAGE
(ICD9) HEMOPERITONEUM (NONTRAUMATIC)
(ICD9) HEMORRHAGE OF RECTUM AND ANUS
(ICD9) PERFORATION OF INTESTINE
(ICD9) ANGIODYSPLASIA OF INTESTINE WITH HEMORRHAGE
(ICD9) DIEULAFOY LESION (HEMORRHAGIC) OF INTESTINE
(ICD9) HEMATEMESIS
(ICD9) BLOOD IN STOOL
(ICD9) HEMORRHAGE OF GASTROINTESTINAL TRACT UNSPECIFIED
(ICD9) HEMARTHROSIS
(ICD9) HEMARTHROSIS SITE UNSPECIFIED
(ICD9) HERARTHROSIS INVOLVING SHOULDER REGION
(ICD9) HEMARTHORSIS INVOLVING UPPER ARM
(ICD9) HEMARTHROSIS INVOLVING FOREARM
(ICD9) HEMARTHROSIS INVOLVING HAND
(ICD9) HEMARTHROSIS INVOLVING PELVIC REGION AND THIGH
(ICD9) HEMARTHROSIS INVOLVING LOWER LEG
(ICD9) HEMARTHROSIS INVOLVING ANKLE AND FOOT
(ICD9) HEMARTHROSIS INVOLVING OTHER SPECIFIED SITES
(ICD9) HEMARTHROSIS INVOLVING MULTIPLE SITES
(ICD9) EPISTAXIS
(ICD9) HEMORRHAGE FROM THROAT
(ICD9) HEMATURIA
(ICD9) HEMATURIA UNSPECIFIED
(ICD9) GROSS HEMATURIA
(ICD9) MICROSCOPIC HEMATURIA
(ICD9) HEMOPTYSIS

## Appendix A

## 786.3

786.31
786.39

## ICD-10 Dx inpatient any position

## I31.2

160.00
160.01
160.02
160.10
160.11
160.12
160.2
160.30
160.31
160.32
160.4
160.50
160.51
160.52
160.6
160.7
160.8
160.9
161.0
161.1
161.2
161.3
161.4
161.5
161.6
161.8
161.9
162.00
(ICD9) HEMOPTYSIS UNSPECIFIED
(ICD9) ACUTE IDIOPATHIC PULMONARY HEMORRHAGE IN INFANTS
(ICD9) OTHER HEMOPTYSIS
(ICD10) Hemopericardium, not elsewhere classified
(ICD10) Nontraumatic subarachnoid hemorrhage from unspecified carotid siphon and bifurcation
(ICD10) Nontraumatic subarachnoid hemorrhage from right carotid siphon and bifurcation
(ICD10) Nontraumatic subarachnoid hemorrhage from left carotid siphon and bifurcation
(ICD10) Nontraumatic subarachnoid hemorrhage from unspecified middle cerebral artery
(ICD10) Nontraumatic subarachnoid hemorrhage from right middle cerebral artery
(ICD10) Nontraumatic subarachnoid hemorrhage from left middle cerebral artery
(ICD10) Nontraumatic subarachnoid hemorrhage from anterior communicating artery
(ICD10) Nontraumatic subarachnoid hemorrhage from unspecified posterior communicating artery
(ICD10) Nontraumatic subarachnoid hemorrhage from right posterior communicating artery
(ICD10) Nontraumatic subarachnoid hemorrhage from left posterior communicating artery
(ICD10) Nontraumatic subarachnoid hemorrhage from basilar artery
(ICD10) Nontraumatic subarachnoid hemorrhage from unspecified vertebral artery
(ICD10) Nontraumatic subarachnoid hemorrhage from right vertebral artery
(ICD10) Nontraumatic subarachnoid hemorrhage from left vertebral artery
(ICD10) Nontraumatic subarachnoid hemorrhage from other intracranial arteries
(ICD10) Nontraumatic subarachnoid hemorrhage from unspecified intracranial artery
(ICD10) Other nontraumatic subarachnoid hemorrhage
(ICD10) Nontraumatic subarachnoid hemorrhage, unspecified
(ICD10) Nontraumatic intracerebral hemorrhage in hemisphere, subcortical
(ICD10) Nontraumatic intracerebral hemorrhage in hemisphere, cortical
(ICD10) Nontraumatic intracerebral hemorrhage in hemisphere, unspecified
(ICD10) Nontraumatic intracerebral hemorrhage in brain stem
(ICD10) Nontraumatic intracerebral hemorrhage in cerebellum
(ICD10) Nontraumatic intracerebral hemorrhage, intraventricular
(ICD10) Nontraumatic intracerebral hemorrhage, multiple localized
(ICD10) Other nontraumatic intracerebral hemorrhage
(ICD10) Nontraumatic intracerebral hemorrhage, unspecified
(ICD10) Nontraumatic subdural hemorrhage, unspecified

## Appendix A

(ICD10) Nontraumatic acute subdural hemorrhage
(ICD10) Nontraumatic subacute subdural hemorrhage
(ICD10) Nontraumatic chronic subdural hemorrhage
(ICD10) Nontraumatic extradural hemorrhage
(ICD10) Nontraumatic intracranial hemorrhage, unspecified
(ICD10) Acute gastric ulcer with hemorrhage
(ICD10) Acute gastric ulcer with both hemorrhage and perforation
(ICD10) Chronic or unspecified gastric ulcer with hemorrhage
(ICD10) Chronic or unspecified gastric ulcer with both hemorrhage and perforation
(ICD10) Acute duodenal ulcer with hemorrhage
(ICD10) Acute duodenal ulcer with both hemorrhage and perforation
(ICD10) Chronic or unspecified duodenal ulcer with hemorrhage
(ICD10) Chronic or unspecified duodenal ulcer with both hemorrhage and perforation
(ICD10) Acute peptic ulcer, site unspecified, with hemorrhage
(ICD10) Acute peptic ulcer, site unspecified, with both hemorrhage and perforation
(ICD10) Chronic or unspecified peptic ulcer, site unspecified, with hemorrhage
(ICD10) Chronic or unspecified peptic ulcer, site unspecified, with both hemorrhage and perforation
(ICD10) Acute gastrojejunal ulcer with hemorrhage
(ICD10) Acute gastrojejunal ulcer with both hemorrhage and perforation
(ICD10) Chronic or unspecified gastrojejunal ulcer with hemorrhage
(ICD10) Chronic or unspecified gastrojejunal ulcer with both hemorrhage and perforation
(ICD10) Angiodysplasia of colon with hemorrhage
(ICD10) Unspecified intestinal obstruction
(ICD10) Diverticulitis of small intestine with perforation and abscess with bleeding
(ICD10) Diverticulosis of small intestine without perforation or abscess with bleeding
(ICD10) Diverticulitis of small intestine without perforation or abscess with bleeding
(ICD10) Diverticulitis of large intestine with perforation and abscess with bleeding
(ICD10) Diverticulosis of large intestine without perforation or abscess with bleeding
(ICD10) Diverticulitis of large intestine without perforation or abscess with bleeding
(ICD10) Diverticulitis of both small and large intestine with perforation and abscess with bleeding
(ICD10) Diverticulosis of both small and large intestine without perforation or abscess with bleeding
(ICD10) Diverticulitis of both small and large intestine without perforation or abscess with bleeding
(ICD10) Diverticulitis of intestine, part unspecified, with perforation and abscess with bleeding
(ICD10) Diverticulosis of intestine, part unspecified, without perforation or abscess with bleeding

## Appendix A

K57.93
K62.5
K63.1
K63.81
K66.1
K92.0
K92.1
K92.2
M25.00
M25.011
M25.012
M25.019
M25.021
M25.022
M25.029
M25.031
M25.032
M25.039
M25.041
M25.042
M25.049
M25.051
M25.052
M25.059
M25.061
M25.062
M25.069
M25.071
M25.072
M25.073
M25.074
M25.075
M25.076
M25.08
(ICD10) Diverticulitis of intestine, part unspecified, without perforation or abscess with bleeding
(ICD10) Hemorrhage of anus and rectum
(ICD10) Perforation of intestine (nontraumatic)
(ICD10) Dieulafoy lesion of intestine
(ICD10) Hemoperitoneum
(ICD10) Hematemesis
(ICD10) Melena
(ICD10) Gastrointestinal hemorrhage, unspecified
(ICD10) Hemarthrosis, unspecified joint
(ICD10) Hemarthrosis, right shoulder
(ICD10) Hemarthrosis, left shoulder
(ICD10) Hemarthrosis, unspecified shoulder
(ICD10) Hemarthrosis, right elbow
(ICD10) Hemarthrosis, left elbow
(ICD10) Hemarthrosis, unspecified elbow
(ICD10) Hemarthrosis, right wrist
(ICD10) Hemarthrosis, left wrist
(ICD10) Hemarthrosis, unspecified wrist
(ICD10) Hemarthrosis, right hand
(ICD10) Hemarthrosis, left hand
(ICD10) Hemarthrosis, unspecified hand
(ICD10) Hemarthrosis, right hip
(ICD10) Hemarthrosis, left hip
(ICD10) Hemarthrosis, unspecified hip
(ICD10) Hemarthrosis, right knee
(ICD10) Hemarthrosis, left knee
(ICD10) Hemarthrosis, unspecified knee
(ICD10) Hemarthrosis, right ankle
(ICD10) Hemarthrosis, left ankle
(ICD10) Hemarthrosis, unspecified ankle
(ICD10) Hemarthrosis, right foot
(ICD10) Hemarthrosis, left foot
(ICD10) Hemarthrosis, unspecified foot
(ICD10) Hemarthrosis, other specified site

## Appendix A

| R58 | (ICD10) Hemorrhage, not elsewhere classified |
| :--- | :--- |
| R04 | (ICD10) Hemorrhage from respiratory passages |
| R04.0 | (ICD10) Epistaxis |
| R04.1 | (ICD10) Hemorrhage from throat |
| R04.2 | (ICD10) Hemoptysis |
| R04.8 | (ICD10) Hemorrhage from other sites in respiratory passages |
| R04.81 | (ICD10) Acute idiopathic pulmonary hemorrhage in infants |
| R04.89 | (ICD10) Hemorrhage from other sites in respiratory passages |
| R04.9 | (ICD10) Hemorrhage from respiratory passages, unspecified |
| R31 | (ICD10) Hematuria |
| R31.0 | (ICD10) Gross hematuria |
| R31.1 | (ICD10) Benign essential microscopic hematuria |
| R31.2 | (ICD10) Other microscopic hematuria |
| R31.21 | (ICD10) Asymptomatic microscopic hematuria |
| R31.29 | (ICD10) Other microscopic hematuria |
| R31.9 | (ICD10) Hematuria, unspecified |
| Px inpatient any position | (ICD9) ENDOSCOPIC CONTROL OF GASTRIC OR DUODENAL BLEEDING |
| 44.43 | (ICD10) Control Bleeding in Gastrointestinal Tract, Via Natural or Artificial Opening Endoscopic |
| 0W3P8ZZ | (HCPCS) Esophagogastroduodenoscopy, flexible, transoral; with control of bleeding, any method / Upper |
| 43255 | gastrointestinal endoscopy including esophagus, stomach, and either the duodenum and/or jejunum as |
|  | appropriate; with control of bleeding, any method |

## Appendix A

## Title <br> Pregnancy

ICD-9 Dx inpatient any position

| 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 perneum 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 |

ICD-9 Px inpatient any position
72.0

Low forceps operation
Low forceps operation with episiotomy

## Appendix A

| 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 |
| 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 |
|  |  |

## Appendix A

73.9

73.92
73.93
73.94
73.99
74.0
74.1
74.2
74.3
74.4
74.9
74.91
74.99
75.4
75.5
75.6
75.7
75.9

Other operations assisting delivery
External version assisting delivery
Replacement of prolapsed umbilical cord
Incision of cervix to assist delivery
Pubiotomy to assist delivery
Other operations assisting delivery
Classical cesarean section
Low cervical cesarean section
Extraperitoneal cesarean section
Removal of extratubal ectopic pregnancy
Cesarean section of other specified type
Cesarean section of unspecified type
Hysterotomy to terminate pregnancy
Other cesarean section of unspecified type
Manual removal of retained placenta
Repair of current obstetric laceration of uterus
Repair of other current obstetric laceration
Manual exploration of uterine cavity, postpartum
Other obstetric operations

## Appendix B



## Appendix B

| Unmatched |  |  |  |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | Optum |  |  | Marketscan |  |  | Medicare |  |  | Referent-enoxaparin | Exposure- rivaroxaban | POOLED |
|  | Referent - enoxaparin | Exposure-rivaroxaban |  | Referent - enoxaparin | Exposure - rivaroxaban |  | Referent- enoxaparin | rivaroxaban 10 |  |  |  |  |
| Variable | 30 or 40 mg | 10 mg | St. Diff. | 30 or 40 mg | 10 mg | St. Diff. | 30 or 40 mg | mg | St. Diff. | 30 or 40 mg | 10 mg | St. Diff. |
| Number of patients | 139 | 10,884 |  | 19,921 | 19,111 |  | 3,318 | 35,842 |  | 23,378 | 65,837 |  |
| Age |  |  |  |  |  |  |  |  |  |  |  |  |
| ...mean (sd) | 59.07 (10.34) | 63.88 (10.73) | -0.46 | 60.11 (10.24) | 60.51 (10.11) | -0.04 | 71.28 (9.09) | 70.86 (8.57) | 0.05 | 61.69 (10.09) | 66.70 (9.42) | -0.51 |
| Age categories without zero category |  |  |  |  |  |  |  |  |  |  |  |  |
| ...18-54; n (\%) | 38 (27.3\%) | 2,010 (18.5\%) | 0.21 | 5,174 (26.0\%) | 4,754 (24.9\%) | 0.03 | 189 (5.7\%) | 1,749 (4.9\%) | 0.04 | 5,401 (23.1\%) | 8513 (12.9\%) | 0.27 |
| ...55-64; n (\%) | 70 (50.4\%) | 3,480 (32.0\%) | 0.38 | 9,296 (46.7\%) | 9,049 (47.3\%) | -0.01 | 260 (7.8\%) | 2,506 (7.0\%) | 0.03 | 9,626 (41.2\%) | 15,035 (22.8\%) | 0.40 |
| ...65-74; n (\%) | 21 (15.1\%) | 3,580 (32.9\%) | -0.43 | 3,699 (18.6\%) | 3,423 (17.9\%) | 0.02 | 1,698 (51.2\%) | 20,246 (56.5\%) | -0.11 | 5,418 (23.2\%) | 27,249 (41.4\%) | -0.40 |
| ...7= $75 ; \mathrm{n}$ (\%) | **(7.2\%) | 1,814 (16.7\%) | -0.30 | 1,752 (8.8\%) | 1,885 (9.9\%) | -0.04 | 1,171 (35.3\%) | 11,341 (31.6\%) | 0.08 | \#Value! | 15,040 (22.8\%) | \#VaLue! |
| Gender without zero category-United |  |  |  |  |  |  |  |  |  |  |  |  |
| ...Males; n (\%) | 56 (40.3\%) | 4,760 (43.7\%) | -0.07 | 9,459 (47.5\%) | 9,129 (47.8\%) | -0.01 | 1,332 (40.1\%) | 13,078 (36.5\%) | 0.07 | 10,847 (46.4\%) | 26,967 (41.0\%) | 0.11 |
| ...Females; n (\%) | 83 (59.7\%) | 6,124 (56.3\%) | 0.07 | 10,462 (52.5\%) | 9,982 (52.2\%) | 0.01 | 1,986 (59.9\%) | 22,764 (63.5\%) | -0.07 | 12,531 (53.6\%) | 38,870 (59.0\%) | -0.11 |
| Race |  |  |  |  |  |  |  |  |  |  |  |  |
| ...White; n (\%) | - | - |  | - | - |  | 3,042 (91.7\%) | 32,865 (91.7\%) | 0.00 | 3,042 (91.7\%) | 32,865 (91.7\%) | 0.00 |
| ...Black; n (\%) | - | - |  | - | - |  | 204 (6.1\%) | 1,944 (5.4\%) | 0.03 | 204 (6.1\%) | 1,944 (5.4\%) | 0.03 |
| ...Asian; n (\%) | - | - |  | - |  |  | 7 (0.2\%) | 125 (0.3\%) | -0.02 | 7 (0.2\%) | 125 (0.3\%) | -0.02 |
| .... Hispanic; n (\%) | - | - |  | - | - |  | 14 (0.4\%) | 194 (0.5\%) | -0.01 | 14 (0.4\%) | 194 (0.5\%) | -0.01 |
| ...North American Native; n (\%) | - | - |  | - | - |  | 13 (0.4\%) | 127 (0.4\%) | 0.00 | 13 (0.4\%) | 127 (0.4\%) | 0.00 |
| Other/Unknown; n (\%) Region without zero category- United v3 | - | - |  | - | - |  | 38 (1.1\%) | 587 (1.6\%) | -0.04 | 38 (1.1\%) | 587 (1.6\%) | -0.04 |
| (lumping missing\&other category with West) |  |  |  |  |  |  |  |  |  |  |  |  |
| ...Northeast; n (\%) | 15 (10.8\%) | 764 (7.0\%) | 0.13 | 3,721 (18.7\%) | 2,807 (14.7\%) | 0.11 | 595 (17.9\%) | 4,860 (13.6\%) | 0.12 | 4331 (18.5\%) | 8,431 (12.8\%) | 0.16 |
| ...South; n (\%) | 41 (29.5\%) | 4,477 (41.1\%) | -0.24 | 4,974 (25.0\%) | 6,048 (31.6\%) | -0.15 | 1,288 (38.8\%) | 14,004 (39.1\%) | -0.01 | 6,303 (27.0\%) | 24,529 (37.3\%) | -0.22 |
| ...Midwest; n (\%) | 57 (41.0\%) | 3,329 (30.6\%) | 0.22 | 7,167 (36.0\%) | 7,407 (38.8\%) | -0.06 | 845 (25.5\%) | 11,225 (31.3\%) | -0.13 | 8,069 (34.5\%) | 21,961 (33.4\%) | 0.02 |
| ...West; n (\%) | 26 (18.7\%) | 2,314(21.3\%) | -0.07 | 3,856 (19.4\%) | 2,607 (13.6\%) | 0.16 | 588 (17.7\%) | 5,729 (16.0\%) | 0.05 | 4,470 (19.1\%) | 10,650 (16.2\%) | 0.08 |
| ...Unknown+missing; n (\%) | N/A | N/A | \#value! | 203 (1.0\%) | 242 (1.3\%) | -0.03 | N/A | N/A | \#value! | 203 (1.0\%) | 242 (1.3\%) | -0.03 |
| Metropolitan Statistical Area - Urban (any MSA) |  |  |  |  |  |  |  |  |  |  |  |  |
| vs Rural (non-MSA) |  |  |  |  |  |  |  |  |  | 0 | 0 | 0.00 |
| ...Urban; n (\%) | - |  |  | 15,704 (78.8\%) | 14,277 (74.7\%) | 0.10 | - | - |  | 15,704 (78.8\%) | 14,277 (74.7\%) | 0.10 |
| ...Rural; n (\%) | - | - |  | 522 (2.6\%) | 573 (3.0\%) | -0.02 | - | - |  | 522 (2.6\%) | 573 (3.0\%) | -0.02 |
| ...Unknown/Missing; n (\%) | - | - |  | 3,695 (18.5\%) | 4,261 (22.3\%) | -0.09 | - | - |  | 3,695 (18.5\%) | 4,261 (22.3\%) | -0.09 |
| Commercial vs Medicare Advantage- Data Type |  |  |  |  |  |  |  |  |  |  |  |  |
| ...1- Fee For Service; n (\%) | - | - |  | 12,420 (62.3\%) | 12,513 (65.5\%) | -0.07 | - | - |  | 12,420 (62.3\%) | 12,513 (65.5\%) | -0.07 |
| ... 2 - Encounter; n (\%) | - |  |  | 2,035 (10.2\%) | 1,222 (6.4\%) | 0.14 |  |  |  | 2,035 (10.2\%) | 1,222 (6.4\%) | 0.14 |
| ... 3 - Medicare; n (\%) | - | - |  | 4,495 (22.6\%) | 4,772 (25.0\%) | -0.06 |  | - |  | 4,495 (22.6\%) | 4,772 (25.0\%) | -0.06 |
| ...4-Medicare Encounter; n (\%) | - | - |  | 971 (4.9\%) | 604 (3.2\%) | 0.09 | - | - |  | 971 (4.9\%) | 604 (3.2\%) | 0.09 |
| cv Covariates |  |  |  |  |  |  |  |  |  |  |  |  |
| Ischemic heart disease; n (\%) | 15 (10.8\%) | 1,346 (12.4\%) | -0.05 | 2,150 (10.8\%) | 2,063 (10.8\%) | 0.00 | 815 (24.6\%) | 6,934 (19.3\%) | 0.13 | 2,980 (12.7\%) | 10,343 (15.7\%) | -0.09 |
| Acute MI; n (\%) | 0 (0.0\%) | 43 (0.4\%) | -0.09 | 90 (0.5\%) | 77 (0.4\%) | 0.01 | 21 (0.6\%) | 198 (0.6\%) | 0.00 | 111 (0.5\%) | 318 (0.5\%) | 0.00 |
| ACS/unstable angina; n (\%) | **(0.7\%) | 53 (0.5\%) | 0.03 | 88 (0.4\%) | 68 (0.4\%) | 0.00 | 25 (0.8\%) | 194 (0.5\%) | 0.04 | \#VaLue! | 315 (0.5\%) | \#Value! |
| Old M1; n (\%) | **(2.2\%) | 328 (3.0\%) | -0.05 | 354 (1.8\%) | 338 (1.8\%) | 0.00 | 198 (6.0\%) | 1,556 (4.3\%) | 0.08 | \#VALUE! | 2222 (3.4\%) | \#VALUE! |
| Stable angina; n (\%) | 0 (0.0\%) | 160 (1.5\%) | -0.17 | 227 (1.1\%) | 204 (1.1\%) | 0.00 | 71 (2.1\%) | 608 (1.7\%) | 0.03 | 298 (1.3\%) | 972 (1.5\%) | -0.02 |
| Coronary atherosclerosis and other forms of |  |  |  |  |  |  |  |  |  |  |  |  |
| chronic ischemic heart disease; n (\%) | 15 (10.8\%) | 1,222 (11.2\%) | -0.01 | 1,938 (9.7\%) | 1,858 (9.7\%) | 0.00 | 756 (22.8\%) | 6,427 (17.9\%) | 0.12 | 2709 (11.6\%) | 9,507 (14.4\%) | -0.08 |
| Other atherosclerosis with ICD10 v2 Copy; n (\%) | 0 (0.0\%) | 62 (0.6\%) | -0.11 | 124 (0.6\%) | 120 (0.6\%) | 0.00 | 31 (0.9\%) | 361 (1.0\%) | -0.01 | 155 (0.7\%) | 543 (0.8\%) | -0.01 |
| Previous cardiac procedure (CABG or PTCA or |  |  |  |  |  |  |  |  |  |  |  |  |
| Stent) v4; n (\%) | 0 (0.0\%) | 10 (0.1\%) | -0.04 | 14 (0.1\%) | 9 (0.0\%) | 0.04 | 7 (0.2\%) | 57 (0.2\%) | 0.00 | 21 (0.1\%) | 76 (0.1\%) | 0.00 |
| History of CABG or PTCA; n (\%) | **(2.2\%) | 441 (4.1\%) | -0.11 | 397 (2.0\%) | 400 (2.1\%) | -0.01 | 329 (9.9\%) | 2,757 (7.7\%) | 0.08 | \#VaLue! | 3,598 (5.5\%) | \#VaLue! |
| Any stroke; n (\%) | **(3.6\%) | 326 (3.0\%) | 0.03 | 452 (2.3\%) | 445 (2.3\%) | 0.00 | 152 (4.6\%) | 1,560 (4.4\%) | 0.01 | \#VaLuE! | 2,331 (3.5\%) | \#Value! |
| Ischemic stroke (w and w/o mention of cerebral |  |  |  |  |  |  |  |  |  |  |  |  |
| infarction); n (\%) | **(3.6\%) | 324 (3.0\%) | 0.03 | 447 (2.2\%) | 442 (2.3\%) | -0.01 | 152 (4.6\%) | 1,558 (4.3\%) | 0.01 | \#Value! | 2,324 (3.5\%) | \#Value! |
| Hemorrhagic stroke; n (\%) | 0 (0.0\%) | ${ }^{* *}(0.0 \%)$ | \#DIV/0! | 5 (0.0\%) | 4 (0.0\%) | \#DIV/0! | 0 (0.0\%) | 3 (0.0\%) | \#DIV/0! | 005 (0.0\%) | \#Value! | \#VaLue! |
| TA; n (\%) | **(0.7\%) | 88 (0.8\%) | -0.01 | 124 (0.6\%) | 122 (0.6\%) | 0.00 | 36 (1.1\%) | 300 (0.8\%) | 0.03 | \#VaLUE! | 510 (0.8\%) | \#VaLue! |
| Other cerebrovascular disease; n (\%) | ** (0.7\%) | 89 (0.8\%) | -0.01 | 103 (0.5\%) | 90 (0.5\%) | 0.00 | 29 (0.9\%) | 321 (0.9\%) | 0.00 | \#VALUE! | 500 (0.8\%) | \#VaLue! |
| Cerebrovascular procedure; n (\%) | 0 (0.0\%) | **(0.0\%) | \#DIV/0! | 7 (0.0\%) | 4 (0.0\%) | \#Div/0! | 2 (0.1\%) | 32 (0.1\%) | 0.00 | 009 (0.0\%) | \#Value! | \#Value! |
| Heart failure (CHF); n (\%) | **(1.4\%) | 107 (1.0\%) | 0.04 | 109 (0.5\%) | 114 (0.6\%) | -0.01 | 103 (3.1\%) | 567 (1.6\%) | 0.10 | \#VALUE! | 788 (1.2\%) | \#VaLuE! |
| Peripheral Vascular Disease (PVD) or PVD Surgery |  |  |  |  |  |  |  |  |  |  |  |  |
| v2; $n$ (\%) | **(4.3\%) | 403 (3.7\%) | 0.03 | 441 (2.2\%) | 462 (2.4\%) | -0.01 | 209 (6.3\%) | 1,746 (4.9\%) | 0.06 | \#Value! | 2,611 (4.0\%) | \#value! |
| Atrial fibrillation; n (\%) | **(1.4\%) | 437 (4.0\%) | -0.16 | 560 (2.8\%) | 579 (3.0\%) | -0.01 | 682 (20.6\%) | 2,083 (5.8\%) | 0.45 | \#VALUE! | 3,099 (4.7\%) | \#VALUE! |
| Other cardiac dyshythmia; n (\%) | 21 (15.1\%) | 1,304 (12.0\%) | 0.09 | 1,906 (9.6\%) | 1,869 (9.8\%) | -0.01 | 812 (24.5\%) | 4,816 (13.4\%) | 0.29 | 2,739 (11.7\%) | 7,989 (12.1\%) | -0.01 |
| Cardiac conduction disorders; n (\%) | **(2.9\%) | 488 (4.5\%) | -0.08 | 654 (3.3\%) | 608 (3.2\%) | 0.01 | 251 (7.6\%) | 1,982 (5.5\%) | 0.08 | \#VaLuE! | 3078 (4.7\%) | \#VALuE! |
| Other CVD; n (\%) | 13 (9.4\%) | 1,015 (9.3\%) | 0.00 | 1,551 (7.8\%) | 1,443 (7.6\%) | 0.01 | 560 (16.9\%) | 4,172 (11.6\%) | 0.15 | 2,124 (9.1\%) | 6,630 (10.1\%) | -0.03 |

## Appendix B

Diabetes-related complications

| Occurrence of Diabetic Neuropathy v2 Copy; n (\%) | **(1.4\%) | 299 (2.7\%) | -0.09 | 331 (1.7\%) | 301 (1.6\%) | 0.01 | 109 (3.3\%) | 991 (2.8\%) | 0.03 | \#Value! | 1591 (2.4\%) | \#Value! |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Occurrence of diabetic nephropathy V3 with |  |  |  |  |  |  |  |  |  |  |  |  |
| ICD10 Copy; n (\%) | ** (0.7\%) | 204 (1.9\%) | -0.11 | 184 (0.9\%) | 123 (0.6\%) | 0.03 | 53 (1.6\%) | 404 (1.1\%) | 0.04 | \#value! | 731 (1.1\%) | \#Value! |
| Hypoglycemia v2; n (\%) | 0 (0.0\%) | 49 (0.5\%) | -0.10 | 126 (0.6\%) | 91 (0.5\%) | 0.01 | 49 (1.5\%) | 398 (1.1\%) | 0.04 | 175 (0.7\%) | 538 (0.8\%) | -0.01 |
| Hyperglycemia; n (\%) | 12 (8.6\%) | 727 (6.7\%) | 0.07 | 846 (4.2\%) | 763 (4.0\%) | 0.01 | 283 (8.5\%) | 2,584 (7.2\%) | 0.05 | 1141 (4.9\%) | 4074 (6.2\%) | -0.06 |
| Diabetic ketoacidosis; n (\%) | 0 (0.0\%) | ** (0.1\%) | -0.04 | 15 (0.1\%) | 8 (0.0\%) | 0.04 | 2 (0.1\%) | 24 (0.1\%) | 0.00 | 017 (0.1\%) | \#Value! | value! |
| Hypertension: 1 inpatient or 2 outpatient claims |  |  |  |  |  |  |  |  |  |  |  |  |
| within 365 days; n (\%) | 80 (57.6\%) | 7,019 (64.5\%) | -0.14 | 11,425 (57.4\%) | 11,326 (59.3\%) | -0.04 | 2,697 (81.3\%) | 27,636 (77.1\%) | 0.10 | 14,202 (60.7\%) | 45,981 (69.8\%) | -0.19 |
| Hyperlipidemia v2; n (\%) | 65 (46.8\%) | 6,037 (55.5\%) | -0.17 | 8,975 (45.1\%) | 8,800 (46.0\%) | -0.02 | 2,020 (60.9\%) | 22,035 (61.5\%) | -0.01 | 11,060 (47.3\%) | 36,872 (56.0\%) | -0.17 |
| Edema; n (\%) | **(5.0\%) | 514 (4.7\%) | 0.01 | 567 (2.8\%) | 558 (2.9\%) | -0.01 | 200 (6.0\%) | 1,340 (3.7\%) | 0.11 | \#VALUE! | 2412 (3.7\%) | \#VaLUE! |
| Renal Dysfunction (non-diabetic) v2; n (\%) | 14 (10.1\%) | 1,218 (11.2\%) | -0.04 | 1,436 (7.2\%) | 1,210 (6.3\%) | 0.04 | 545 (16.4\%) | 3,863 (10.8\%) | 0.16 | 1,995 (8.5\%) | 6,291 (9.6\%) | 0.04 |
| Occurrence of acute renal disease v2; n (\%) | ** (3.6\%) | 246 (2.3\%) | 0.08 | 374 (1.9\%) | 299 (1.6\%) | 0.02 | 154 (4.6\%) | 927 (2.6\%) | 0.11 | \#Value! | 1472 (2.2\%) | \#Value! |
| Occurrence of chronic renal insufficiency; n (\%) | **(5.0\%) | 764 (7.0\%) | -0.08 | 811 (4.1\%) | 609 (3.2\%) | 0.05 | 367 (11.1\%) | 2,446 (6.8\%) | 0.15 | \#Value! | 3,819 (5.8\%) | \#value! |
| Chronic kidney disease vz; n (\%) | **(4.3\%) | 736 (6.8\%) | -0.11 | 781 (3.9\%) | 582 (3.0\%) | 0.05 | 358 (10.8\%) | 2,335 (6.5\%) | 0.15 | \#VALUE! | 3,653 (5.5\%) | \#VALUE! |
| CKD Stage 3-4; n (\%) | **(3.6\%) | 459 (4.2\%) | -0.03 | 461 (2.3\%) | 299 (1.6\%) | 0.05 | 230 (6.9\%) | 1,317 (3.7\%) | 0.14 | \#Value! | 2,075 (3.2\%) | \#VaLue! |
| Occurrence of hypertensive nephropathy; n (\%) | **(5.0\%) | 491 (4.5\%) | 0.02 | 496 (2.5\%) | 351 (1.8\%) | 0.05 | 282 (8.5\%) | 1,779 (5.0\%) | 0.14 | \#Value! | 2,621 (4.0\%) | \#value! |
| Occurrence of miscellaneous renal insufficiency |  |  |  |  |  |  |  |  |  |  |  |  |
| v2; n (\%) | ** (4.3\%) | 457 (4.2\%) | 0.00 | 493 (2.5\%) | 468 (2.4\%) | 0.01 | 155 (4.7\%) | 1,371 (3.8\%) | 0.04 | \#Value! | 2,296 (3.5\%) | \#Value! |
| Other Covariates |  |  |  |  |  |  |  |  |  |  |  |  |
| Liver disease; n (\%) | ** (0.7\%) | 187 (1.7\%) | -0.09 | 252 (1.3\%) | 228 (1.2\%) | 0.01 | 64 (1.9\%) | 518 (1.4\%) | 0.04 | \#Value! | 933 (1.4\%) | \#value! |
| Osteoarthritis; n (\%) | 134 (96.4\%) | 10,669 (98.0\%) | -0.10 | 19,329 (97.0\%) | 18,746 (98.1\%) | -0.07 | 3,172 (95.6\%) | 34,972 (97.6\%) | -0.11 | 22635 (96.8\%) | 64387 (97.8\%) | -0.06 |
| Other arthritis, arthropathies and musculoskeletal |  |  |  |  |  |  |  |  |  |  |  |  |
| pain; n (\%) | 130 (93.5\%) | 9,890 (90.9\%) | 0.10 | 17,212 (86.4\%) | 16,823 (88.0\%) | -0.05 | 2,941 (88.6\%) | 31,128 (86.8\%) | 0.05 | 20283 (86.8\%) | 57841 (87.9\%) | -0.03 |
| Dorsopathies; n (\%) | 60 (43.2\%) | 4,652 (42.7\%) | 0.01 | 7,491 (37.6\%) | 7,564 (39.6\%) | -0.04 | 1,500 (45.2\%) | 15,155 (42.3\%) | 0.06 | 9051 (38.7\%) | 27371 (41.6\%) | -0.06 |
| Fractures; n (\%) | 13 (9.4\%) | 831 (7.6\%) | 0.06 | 1,625 (8.2\%) | 1,248 (6.5\%) | 0.07 | 496 (14.9\%) | 3,348 (9.3\%) | 0.17 | 2134 (9.1\%) | 5427 (8.2\%) | 0.03 |
| Falls v2; n (\%) | **(4.3\%) | 554 (5.1\%) | -0.04 | 416 (2.1\%) | 306 (1.6\%) | 0.04 | 90 (2.7\%) | 563 (1.6\%) | 0.08 | \#Value! | 1423 (2.2\%) | \#Value! |
| Osteoporosis; n (\%) | ** (6.5\%) | 1,064 (9.8\%) | -0.12 | 1,222 (6.1\%) | 1,201 (6.3\%) | -0.01 | 488 (14.7\%) | 4,845 (13.5\%) | 0.03 | \#VALUE! | 7110 (10.8\%) | \#VALUE! |
| Depression; n (\%) | 35 (25.2\%) | 1,873 (17.2\%) | 0.20 | 2,694 (13.5\%) | 2,426 (12.7\%) | 0.02 | 616 (18.6\%) | 6,160 (17.2\%) | 0.04 | 3345 (14.3\%) | 10459 (15.9\%) | -0.04 |
| Anxiety; n (\%) | 32 (23.0\%) | 1,808 (16.6\%) | 0.16 | 2,198 (11.0\%) | 2,180 (11.4\%) | -0.01 | 605 (18.2\%) | 5,418 (15.1\%) | 0.08 | 2835 (12.1\%) | 9406 (14.3\%) | -0.07 |
| Sleep_Disorder; n (\%) | ** (7.2\%) | 1,206 (11.1\%) | -0.14 | 2,331 (11.7\%) | 2,254 (11.8\%) | 0.00 | 292 (8.8\%) | 3,878 (10.8\%) | -0.07 | \#VaLuE! | 7338 (11.1\%) | \#Value! |
| Dementia; n (\%) | **(1.4\%) | 159 (1.5\%) | -0.01 | 165 (0.8\%) | 162 (0.8\%) | 0.00 | 106 (3.2\%) | 866 (2.4\%) | 0.05 | \#VALUE! | 1187 (1.8\%) | \#Value! |
| Delirium; n (\%) | ** (0.7\%) | 112 (1.0\%) | -0.03 | 142 (0.7\%) | 125 (0.7\%) | 0.00 | 75 (2.3\%) | 501 (1.4\%) | 0.07 | \#Value! | 738 (1.1\%) | \#value! |
| Psychosis; n (\%) | 0 (0.0\%) | 62 (0.6\%) | -0.11 | 80 (0.4\%) | 76 (0.4\%) | 0.00 | 50 (1.5\%) | 482 (1.3\%) | 0.02 | 130 (0.6\%) | 620 (0.9\%) | -0.03 |
| Obesity; n (\%) | 50 (36.0\%) | 2,913 (26.8\%) | 0.20 | 4,426 (22.2\%) | 4,230 (22.1\%) | 0.00 | 811 (24.4\%) | 7,621 (21.3\%) | 0.07 | 5287 (22.6\%) | 14764 (22.4\%) | 0.00 |
| Overweight; n (\%) | **(5.8\%) | 646 (5.9\%) | 0.00 | 576 (2.9\%) | 579 (3.0\%) | -0.01 | 184 (5.5\%) | 1,628 (4.5\%) | 0.05 | \#VaLuE! | 2853 (4.3\%) | \#Value! |
| Smoking; n (\%) | 50 (36.0\%) | 3,407 (31.3\%) | 0.10 | 3,476 (17.4\%) | 3,375 (17.7\%) | -0.01 | 1,265 (38.1\%) | 12,192 (34.0\%) | 0.09 | 4791 (20.5\%) | 18974 (28.8\%) | -0.19 |
| Alcohol abuse or dependence; n (\%) | ** (6.5\%) | 278 (2.6\%) | 0.19 | 387 (1.9\%) | 324 (1.7\%) | 0.02 | 52 (1.6\%) | 351 (1.0\%) | 0.05 | \#VALUE! | 953 (1.4\%) | \#VALUE! |
| Drug abuse or dependence; n (\%) | **(5.0\%) | 271 (2.5\%) | 0.13 | 325 (1.6\%) | 254 (1.3\%) | 0.03 | 112 (3.4\%) | 430 (1.2\%) | 0.15 | \#VALUE! | 955 (1.5\%) | \#VALUE! |
| COPD; n (\%) | 16 (11.5\%) | 1,084 (10.0\%) | 0.05 | 1,213 (6.1\%) | 1,262 (6.6\%) | -0.02 | 491 (14.8\%) | 4,398 (12.3\%) | 0.07 | 1720 (7.4\%) | 6744 (10.2\%) | -0.10 |
| Asthma; n (\%) | 20 (14.4\%) | 1,136 (10.4\%) | 0.12 | 1,653 (8.3\%) | 1,537 (8.0\%) | 0.01 | 418 (12.6\%) | 3,756 (10.5\%) | 0.07 | 2091 (8.9\%) | 6429 (9.8\%) | -0.03 |
| Obstructive sleep apnea; n (\%) | 19 (13.7\%) | 1,275 (11.7\%) | 0.06 | 2,004 (10.1\%) | 2,001 (10.5\%) | -0.01 | 401 (12.1\%) | 3,279 (9.1\%) | 0.10 | 2424 (10.4\%) | 6555 (10.0\%) | 0.01 |
| Pneumonia; n (\%) | **(1.4\%) | 191 (1.8\%) | -0.03 | 268 (1.3\%) | 252 (1.3\%) | 0.00 | 109 (3.3\%) | 690 (1.9\%) | 0.09 | \#VALUE! | 1133 (1.7\%) | \#VALUE! |
| Other Medications |  |  |  |  |  |  |  |  |  |  |  |  |
| Use of ACE inhibitors; n (\%) | 32 (23.0\%) | 2,596 (23.9\%) | -0.02 | 4,387 (22.0\%) | 4,419 (23.1\%) | -0.03 | 929 (28.0\%) | 10,210 (28.5\%) | -0.01 | 5348 (22.9\%) | 17225 (26.2\%) | -0.08 |
| Use of ARBS; n (\%) | 20 (14.4\%) | 1,781 (16.4\%) | -0.06 | 3,111 (15.6\%) | 3,105 (16.2\%) | -0.02 | 665 (20.0\%) | 6,843 (19.1\%) | 0.02 | 3796 (16.2\%) | 11729 (17.8\%) | -0.04 |
| Use of Loop Diuretics - United; n (\%) | **(3.6\%) | 425 (3.9\%) | -0.02 | 710 (3.6\%) | 686 (3.6\%) | 0.00 | 352 (10.6\%) | 2,466 (6.9\%) | 0.13 | \#Value! | 3577 (5.4\%) | \#Value! |
| Use of other diuretics-United; n (\%) | **(1.4\%) | 113 (1.0\%) | 0.04 | 216 (1.1\%) | 192 (1.0\%) | 0.01 | 89 (2.7\%) | 536 (1.5\%) | 0.08 | \#VALUE! | 841 (1.3\%) | \#Value! |
| Use of nitrates-United; n (\%) | ** (0.7\%) | 157 (1.4\%) | -0.07 | 292 (1.5\%) | 227 (1.2\%) | 0.03 | 120 (3.6\%) | 970 (2.7\%) | 0.05 | \#VALUE! | 1354 (2.1\%) | \#VALUE! |
| Use of other hypertension drugs; n (\%) | ** (0.7\%) | 344 (3.2\%) | -0.18 | 571 (2.9\%) | 486 (2.5\%) | 0.02 | 186 (5.6\%) | 1,624 (4.5\%) | 0.05 | \#Value! | 2454 (3.7\%) | \#Value! |
| Use of Anti-arrhythmics; n (\%) | 0 (0.0\%) | 69 (0.6\%) | -0.11 | 131 (0.7\%) | 121 (0.6\%) | 0.01 | 142 (4.3\%) | 400 (1.1\%) | 0.20 | 273 (1.2\%) | 590 (0.9\%) | 0.03 |
| Use of COPD/asthma meds-United; n (\%) | 15 (10.8\%) | 1,446 (13.3\%) | -0.08 | 2,740 (13.8\%) | 2,573 (13.5\%) | 0.01 | 651 (19.6\%) | 5,973 (16.7\%) | 0.08 | 3406 (14.6\%) | 9992 (15.2\%) | -0.02 |
| Use of statins; n (\%) | 33 (23.7\%) | 3,971 (36.5\%) | -0.28 | 6,536 (32.8\%) | 6,413 (33.6\%) | -0.02 | 1,512 (45.6\%) | 16,255 (45.4\%) | 0.00 | 8081 (34.6\%) | 26639 (40.5\%) | -0.12 |
| Use of other lipid-lowering drugs; n (\%) | **(4.3\%) | 545 (5.0\%) | -0.03 | 1,161 (5.8\%) | 1,168 (6.1\%) | -0.01 | 232 (7.0\%) | 2,427 (6.8\%) | 0.01 | \#Value! | 4140 (6.3\%) | \#Value! |
| Use of antiplatelet agents; n (\%) | 15 (10.8\%) | 489 (4.5\%) | 0.24 | 1,348 (6.8\%) | 864 (4.5\%) | 0.10 | 247 (7.4\%) | 2,223 (6.2\%) | 0.05 | 1610 (6.9\%) | 3576 (5.4\%) | 0.06 |
| Use of heparin and other low-molecular weight |  |  |  |  |  |  |  |  |  |  |  |  |
| heparins ; n (\%) | 0 (0.0\%) | ** (0.0\%) | \#DIV/0! | 2 (0.0\%) | 2 (0.0\%) | \#DIV/0! | 21 (0.6\%) | 35 (0.1\%) | 0.08 | 23 (0.1\%) | \#VaLUE! | \#Value! |
| Use of NSAIDs; n (\%) | 58 (41.7\%) | 4,197 (38.6\%) | 0.06 | 8,013 (40.2\%) | 7,707 (40.3\%) | 0.00 | 1,135 (34.2\%) | 13,126 (36.6\%) | -0.05 | 9206 (39.4\%) | 25030 (38.0\%) | 0.03 |
| Use of opioids-United; n (\%) | 81 (58.3\%) | 9,462 (86.9\%) | -0.68 | 17,760 (89.2\%) | 16,956 (88.7\%) | 0.02 | 2,874 (86.6\%) | 30,567 (85.3\%) | 0.04 | 20715 (88.6\%) | 56985 (86.6\%) | 0.06 |
| Use of antidepressants; n (\%) | 42 (30.2\%) | 2,756 (25.3\%) | 0.11 | 4,750 (23.8\%) | 4,608 (24.1\%) | -0.01 | 1,035 (31.2\%) | 9,939 (27.7\%) | 0.08 | 5827 (24.9\%) | 17303 (26.3\%) | -0.03 |
| Use of antipsychotics; n (\%) | **(1.4\%) | 186 (1.7\%) | -0.0 | 333 (1.7\%) | 311 (1.6\%) | 0.01 | 135 (4.1\%) | 1,030 (2.9\%) | 0.07 | \#VaLUE! | 1527 (2.3\%) | \#VALUE! |
| Labs |  |  |  |  |  |  |  |  |  | 20,060 | 29,995 |  |
| Lab values- HbA1c (\%) v3; n (\%) | 12 (8.6\%) | 1,307 (12.0\%) | -0.11 | 250 (1.3\%) | 151 (0.8\%) | 0.05 | N/A | N/A | \#Value! | 262 (1.3\%) | 1,458 (4.9\%) | -0.21 |

## Appendix B



| **(5.8\%) | 859 (7.9\%) | -0.08 | 169 (0.8\%) | 96 (0.5\%) | 0.04 | N/A | N/A | \#Value! | \#Value! | 955 (3.2\%) | \#Value! |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| 12 (8.6\%) | 1,307 (12.0\%) | -0.11 | 250 (1.3\%) | 151 (0.8\%) | 0.05 | N/A | N/A | \#value! | 262 (1.3\%) | 1,458 (4.9\%) | -0.21 |
| 0 (0.0\%) | 20 (0.2\%) | -0.06 | 2 (0.0\%) | 3 (0.0\%) | \#DIV/0! | N/A | N/A | \#Value! | 002 (0.0\%) | 023 (0.1\%) | -0.04 |
| 0 (0.0\%) | **(0.1\%) | -0.04 | 2 (0.0\%) | $1(0.0 \%)$ | \#DIV/0! | N/A | N/A | \#value! | 002 (0.0\%) | \#Value! | \#VaLuE! |
| 0 (0.0\%) | 20 (0.2\%) | -0.06 | 2 (0.0\%) | 3 (0.0\%) | \#DIV/0! | N/A | N/A | \#value! | 002 (0.0\%) | 023 (0.1\%) | -0.04 |
| 28 (20.1\%) | 3,470 (31.9\%) | -0.27 | 234 (1.2\%) | 214 (1.1\%) | 0.01 | N/A | N/A | \#VaLue! | 262 (1.3\%) | 3,684 (12.3\%) | -0.45 |
| 21 (15.1\%) | 2,788 (25.6\%) | -0.26 | 190 (1.0\%) | 165 (0.9\%) | 0.01 | N/A | N/A | \#Value! | 211 (1.1\%) | 2,953 (9.8\%) | -0.39 |
| 28 (20.1\%) | 3,470 (31.9\%) | -0.27 | 234 (1.2\%) | 214 (1.1\%) | 0.01 | N/A | N/A | \#Value! | 262 (1.3\%) | 3,684 (12.3\%) | -0.45 |
| 30 (21.6\%) | 3,543 (32.6\%) | -0.25 | 241 (1.2\%) | 222 (1.2\%) | 0.00 | N/A | N/A | \#VaLue! | 271 (1.4\%) | 3,765 (12.6\%) | -0.45 |
| 22 (15.8\%) | 2,851 (26.2\%) | -0.26 | 197 (1.0\%) | 171 (0.9\%) | 0.01 | N/A | N/A | \#Value! | 219 (1.1\%) | 3,022 (10.1\%) | -0.40 |
| 30 (21.6\%) | 3,543 (32.6\%) | -0.25 | 241 (1.2\%) | 222 (1.2\%) | 0.00 | N/A | N/A | \#Value! | 271 (1.4\%) | 3,765 (12.6\%) | -0.45 |
| 23 (16.5\%) | 2,029 (18.6\%) | -0.06 | 217 (1.1\%) | 162 (0.8\%) | 0.03 | N/A | N/A | \#Value! | 240 (1.2\%) | 2,191 (7.3\%) | -0.31 |
| 17 (12.2\%) | 1,178 (10.8\%) | 0.04 | 118 (0.6\%) | 93 (0.5\%) | 0.01 | N/A | N/A | \#VaLue! | 135 (0.7\%) | 1,271 (4.2\%) | -0.23 |
| 23 (16.5\%) | 2,029 (18.6\%) | -0.06 | 217 (1.1\%) | 162 (0.8\%) | 0.03 | N/A | N/A | \#Value! | 240 (1.2\%) | 2,191 (7.3\%) | -0.31 |
| 22 (15.8\%) | 2,073 (19.0\%) | -0.08 | 237 (1.2\%) | 161 (0.8\%) | 0.04 | N/A | N/A | \#Value! | 259 (1.3\%) | 2,234 (7.4\%) | -0.30 |
| 16 (11.5\%) | 1,204 (11.1\%) | 0.01 | 131 (0.7\%) | 93 (0.5\%) | 0.03 | N/A | N/A | \#Value! | 147 (0.7\%) | 1,297 (4.3\%) | -0.23 |
| 22 (15.8\%) | 2,073 (19.0\%) | -0.08 | 237 (1.2\%) | 161 (0.8\%) | 0.04 | N/A | N/A | \#VaLue! | 259 (1.3\%) | 2,234 (7.4\%) | -0.30 |
| 0 (0.0\%) | ** (0.1\%) | -0.04 | 0 (0.0\%) | 0 (0.0\%) | \#DIV/0! | N/A | N/A | \#Value! | 00 (0.0\%) | \#VaLUE! | \#VALUE! |
| 0 (0.0\%) | **(0.0\%) | \#DIV/0! | 0 (0.0\%) | 0 (0.0\%) | \#DIV/0! | N/A | N/A | \#Value! | 00 (0.0\%) | \#Value! |  |
| 0 (0.0\%) | ** (0.1\%) | -0.04 | 0 (0.0\%) | 0 (0.0\%) | \#DIV/0! | N/A | N/A | \#Value! | 00 (0.0\%) | \#Value! |  |
| 23 (16.5\%) | 2,070 (19.0\%) | -0.07 | 215 (1.1\%) | 162 (0.8\%) | 0.03 | N/A | N/A | \#Value! | 238 (1.2\%) | 2,232 (7.4\%) | -0.31 |
| 17 (12.2\%) | 1,207 (11.1\%) | 0.03 | 116 (0.6\%) | 93 (0.5\%) | 0.01 | N/A | N/A | \#VaLue! | 133 (0.7\%) | 1,300 (4.3\%) | -0.23 |
| 23 (16.5\%) | 2,070 (19.0\%) | -0.07 | 215 (1.1\%) | 162 (0.8\%) | 0.03 | N/A | N/A | \#VaLue! | 238 (1.2\%) | 2,232 (7.4\%) | -0.31 |
| 23 (16.5\%) | 2,052 (18.9\%) | -0.06 | 211 (1.1\%) | 156 (0.8\%) | 0.03 | N/A | N/A | \#Value! | 234 (1.2\%) | 2,208 (7.4\%) | -0.31 |
| 17 (12.2\%) | 1,198 (11.0\%) | 0.04 | 114 (0.6\%) | 88 (0.5\%) | 0.01 | N/A | N/A | \#Value! | 131 (0.7\%) | 1,286 (4.3\%) | -0.23 |
| 23 (16.5\%) | 2,052 (18.9\%) | -0.06 | 211 (1.1\%) | 156 (0.8\%) | ${ }^{0.03}$ | N/A | N/A | \#VaLUE! | 234 (1.2\%) | 2,208 (7.4\%) | -0.31 |
| 12 | 1,304 |  | 194 | 140 |  | N/A | N/A |  | 206 | 1,444 |  |
| 5.72 (0.62) | 6.12 (0.96) | -0.49 | 6.79 (1.45) | 6.49 (1.20) | 0.23 | N/A | N/A | \#Value! | 6.73 (1.42) | 6.16 (0.99) | 0.47 |
| 127 (91.4\%) | 9,580 (88.0\%) | 0.11 | 19,727 (99.0\%) | 18,971 (99.3\%) | -0.03 | N/A | N/A | \#Value! | 19,854 (99.0\%) | 28,551 (95.2\%) | 0.23 |
| - | 20 |  | 2 | 3 |  | N/A | N/A |  | 2 | 23 |  |
| -(-) | 49.77 (32.33) | \#VaLue! | 102.50 (89.80) | 38.03 (27.78) | 0.97 | N/A | N/A | \#Value! | \#VaLuE! | 48.24 (32.71) | \#VaLue! |
| 139 (100.0\%) | 10,864 (99.8\%) | 0.06 | 19,919 (100.0\%) | 19,108 (100.0\%) | \#Div/0! | N/A | N/A | \#Value! | 20,058 (100.0\%) | 29,972 (99.9\%) | 0.04 |
| 28 | 3,470 |  | 234 | 214 |  | N/A | N/A |  | 262 | 3,684 |  |
| 14.89 (5.35) | 16.95 (5.50) | -0.38 | 16.87 (6.16) | 17.62 (7.31) | -0.11 | N/A | N/A | \#Value! | 16.66 (6.09) | 16.99 (5.62) | -0.06 |
| 111 (79.9\%) | 7,414 (68.1\%) | 0.27 | 19,687 (98.8\%) | 18,897 (98.9\%) | $-0.01$ | N/A | N/A | \#Value! | 19,798 (98.7\%) | 26,311 (87.7\%) | 0.45 |
| 30 | 3,523 |  | 232 | 209 |  | N/A | N/A |  | 262 | 3,732 |  |
| 0.80 (0.18) | 0.90 (0.23) | -0.48 | 0.91 (0.25) | 0.94 (0.27) | -0.12 | N/A | N/A | \#Value! | 0.90 (0.24) | 0.90 (0.23) | 0.00 |
| 109 (78.4\%) | 7,361 (67.6\%) | 0.25 | 19,689 (98.8\%) | 18,902 (98.9\%) | $-0.01$ | N/A | N/A | \#Value! | 19,798 (98.7\%) | 26,263 (87.6\%) | 0.45 |
| 23 | 2,029 |  | 217 | 162 |  | N/A | N/A |  | 240 | 2,191 |  |
| 55.54 (14.15) | 56.38 (17.14) | -0.05 | 50.15 (18.06) | 51.63 (19.80) | -0.08 | N/A | N/A | \#Value! | 50.67 (17.77) | 56.03 (17.35) | -0.31 |
| 116 (83.5\%) | 8,855 (81.4\%) | 0.06 | 19,704 (98.9\%) | 18,949 (99.2\%) | $-0.03$ | N/A | N/A | \#Value! | 19,820 (98.8\%) | 27,804 (92.7\%) | 0.31 |
|  | 2,058 |  | 217 | 152 |  | N/A | N/A |  | 239 | 2,210 |  |
| 110.18 (29.39) | 101.97 (36.21) | 0.25 | 94.81 (43.44) | 94.78 (40.78) | 0.00 | N/A | N/A | \#Value! | 96.22 (42.47) | 101.48 (36.55) | -0.13 |

## Appendix B


117 (84.2\%)

| N/A | N/A | \#value! | 19,821 (98.8\%) | 27,785 (92.6\%) | 0.31 |
| :---: | :---: | :---: | :---: | :---: | :---: |
| N/A | N/A |  | 238 | 2,232 |  |
| N/A | N/A | \#Value! | 176.30 (51.58) | 185.73 (42.66) | -0.20 |
| N/A | N/A | \#Value! | 19,822 (98.8\%) | 27,763 (92.6\%) | 1 |
| N/A | N/A |  | 234 | 2,208 |  |
| N/A | N/A | \#Value! | 145.35 (87.60) | 136.69 (105.40) | 0.09 |
| N/A | N/A | \#VALUE! | 19,826 (98.8\%) | 27,787 (92.6\%) | 0.31 |
| N/A | N/A |  | 221 | 3,278 |  |
| N/A | N/A | \#VaLue! | 13.28 (2.53) | 13.73 (1.65) | -0.21 |
| N/A | N/A | \#Value! | 19,839 (98.9\%) | 26,717 (89.1\%) | 0.42 |
| N/A | N/A |  | 245 | 3,623 |  |
| N/A | N/A | \#VaLue! | 139.84 (2.36) | 140.08 (2.66) | -0.10 |
| N/A | N/A | \#Value! | 19,815 (98.8\%) | 26,372 (87.9\%) | 0.45 |
| N/A | N/A |  | 205 | 3,151 |  |
| N/A | N/A | \#Value! | 4.23 (0.60) | 4.29 (0.36) | -0.12 |
| N/A | N/A | \#VaLue! | 19,855 (99.0\%) | 26,844 (89.5\%) | 0.42 |
| N/A | N/A |  | 251 | 3,579 |  |
| N/A | N/A | \#VaLuE! | 117.09 (38.05) | 102.66 (28.00) | 0.43 |
| N/A | N/A | \#Value! | 19,809 (98.7\%) | 26,416 (88.1\%) | 0.44 |
| N/A | N/A |  | 255 | 3,736 |  |
| N/A | N/A | \#Value! | 4.36 (0.37) | 4.37 (0.39) | -0.03 |
| N/A | N/A | \#Value! | 19,805 (98.7\%) | 26,259 (87.5\%) | 0.45 |
| 1.72 (2.27) | 0.97 (1.79) | 0.37 | 0.73 (1.64) | 0.83 (1.70) | -0.06 |
| 88 (2.7\%) | 778 (2.2\%) | 0.03 | 9,773 (41.8\%) | 16,105 (24.5\%) | 0.37 |
| 0.19 (0.06) | 0.18 (0.05) | 0.18 | 0.16 (0.04) | 0.17 (0.05) | -0.22 |
| 3,318 (100.0\%) | 35,840 (100.0\%) | \#DIV/0! | 23,377 (100.0\%) | 65,833 (100.0\%) | \#DIV/0! |
| 3,306 (99.6\%) | 35,537 (99.1\%) | 0.06 | 23352 (99.9\%) | 65454 (99.4\%) | 0.08 |
| 342 (10.3\%) | 2,410 (6.7\%) | 0.13 | \#value! | 3614 (5.5\%) | \#Value! |
| 3,041 (91.7\%) | 33,013 (92.1\%) | -0.01 | 19130 (81.8\%) | 58324 (88.6\%) | -0.19 |
| 2,641 (79.6\%) | 28,843 (80.5\%) | -0.02 | 14915 (63.8\%) | 48722 (74.0\%) | -0.22 |
| 2,466 (74.3\%) | 26,111 (72.9\%) | 0.03 | 15826 (67.7\%) | 46732 (71.0\%) | -0.07 |
| 2,027 (61.1\%) | 18,680 (52.1\%) | 0.18 | 8849 (37.9\%) | 30177 (45.8\%) | -0.16 |
| 1,425 (42.9\%) | 13,200 (36.8\%) | 0.12 | 6508 (27.8\%) | 21713 (33.0\%) | -0.11 |
| 1,185 (35.7\%) | 9,490 (26.5\%) | 0.20 | 3932 (16.8\%) | 14246 (21.6\%) | -0.12 |
| 2,883 (86.9\%) | 31,257 (87.2\%) | -0.01 | 17933 (76.7\%) | 55295 (84.0\%) | -0.18 |
| 23 (0.7\%) | 222 (0.6\%) | 0.01 | 135 (0.6\%) | 366 (0.6\%) | 0.00 |
| 1 (0.0\%) | 4 (0.0\%) | \#Div/0! | $2(0.0 \%)$ | \#value! | \#Value! |
| 10.47 (4.98) | 9.29 (4.51) | 0.25 | 8.86 (4.60) | 8.97 (4.51) | 0.00 |
| 1.22 (0.58) | 1.14 (0.42) | 0.16 | 1.08 (0.35) | 1.11 (0.36) | 0.00 |
| 4.99 (4.62) | 4.87 (4.37) | 0.03 | 3.75 (2.71) | 4.28 (3.73) | 0.00 |
| 0.76 (2.00) | 0.46 (1.44) | 0.17 | 0.26 (1.37) | 0.34 (1.24) | 0.00 |
| 16.89 (13.03) | 15.60 (11.79) | 0.10 | 8.00 (6.25) | 11.44 (9.10) | 0.00 |

## Appendix B

| Number of internal medicine/family medicine visits |  |  |  |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| ...mean (sd) | 4.01 (6.39) | 7.87 (10.96) | -0.43 | 5.92 (8.06) | 6.47 (8.68) | -0.07 | 9.46 (10.07) | 8.96 (9.05) | 0.05 | 6.41 (8.37) | 8.06 (9.29) | 0.00 |
| Number of Cardiologist visits |  |  |  |  |  |  |  |  |  |  |  |  |
| ...mean (sd) | 1.64 (3.03) | 1.28 (2.64) | 0.13 | 0.93 (2.16) | $0.99(2.35)$ | -0.03 | 2.52 (4.15) | 1.95 (3.70) | 0.14 | 1.16 (2.54) | 1.56 (3.20) | 0.00 |
| Number electrocardiograms received v2 |  |  |  |  |  |  |  |  |  |  |  |  |
| ...mean (sd) | 1.55 (1.37) | 1.35 (1.15) | 0.16 | 1.15 (1.01) | 1.21 (0.98) | -0.06 | 1.82 (1.56) | 1.60 (1.25) | 0.16 | 1.25 (1.11) | 1.45 (1.16) | 0.00 |
| Number of HbAlc tests ordered |  |  |  |  |  |  |  |  |  |  |  |  |
| ...mean (sd) | 0.46 (0.65) | 0.36 (0.67) | 0.15 | 0.26 (0.59) | 0.24 (0.57) | 0.03 | 0.41 (0.75) | 0.37 (0.68) | 0.06 | 0.28 (0.62) | 0.33 (0.65) | 0.00 |
| Number of glucose tests ordered |  |  |  |  |  |  |  |  |  |  |  |  |
| ...mean (sd) | 0.12 (0.35) | 0.09 (0.51) | 0.07 | 0.13 (0.49) | 0.07 (0.36) | 0.14 | 0.11 (0.48) | 0.09 (0.42) | 0.04 | 0.13 (0.49) | 0.08 (0.42) | 0.00 |
| Number of lipid tests ordered |  |  |  |  |  |  |  |  |  |  |  |  |
| ...mean (sd) | 0.49 (0.81) | 0.56 (0.73) | -0.09 | 0.48 (0.85) | 0.46 (0.78) | 0.02 | 0.57 (0.69) | 0.60 (0.70) | -0.04 | 0.49 (0.83) | 0.55 (0.73) | 0.00 |
| Total N distinct ICD9/ICD10 diagnoses at the 3rd digit level Copy |  |  |  |  |  |  |  |  |  |  |  |  |
| $\ldots$...mean (sd) | 11.04 (11.16) | 7.32 (9.40) | 0.36 | 3.53 (6.42) | 3.58 (6.21) | -0.01 | 12.49 (12.95) | 8.02 (10.00) | 0.39 | 4.85 (7.72) | 6.62 (8.96) | 0.00 |
| For PS |  |  |  |  |  |  |  |  |  |  |  |  |
| Hemorrhagic stroke+Other cerebrovascular |  |  |  |  |  |  |  |  |  |  |  |  |
| disease+Cerebrovascular procedure (for PS); n (\%) | ** (0.7\%) | 94 (0.9\%) | -0.02 | 112 (0.6\%) | 98 (0.5\%) | 0.01 | 31 (0.9\%) | 349 (1.0\%) | -0.01 | \#VaLuE! | 541 (0.8\%) | \#Value! |
| Major trauma potentially causing prolonged | **(2.2\%) | 319 (2.9\%) | $-0.04$ | 557 (2.8\%) | 411 (2.2\%) | 0.04 | 2.45 (1.23) | 2.63 (1.25) | \#Num! | 557 (2.8\%) | 411 (2.2\%) | 0.24 |
| Occurrence of creatinine tests ordered (for PS); n (\%) | 22 (15.8\%) | 614 (5.6\%) | 0.33 | 2,077 (10.4\%) | 929 (4.9\%) | 0.21 | 382 (11.5\%) | 2,755 (7.7\%) | 0.13 | 2481 (10.6\%) | 4298 (6.5\%) | 0.15 |
|  |  |  |  |  |  |  |  |  |  |  |  |  |
| Occurrence of BUN tests ordered (for PS); n (\%) | 13 (9.4\%) | 308 (2.8\%) | 0.28 | 1,508 (7.6\%) | 575 (3.0\%) | 0.21 | 206 (6.2\%) | 1,547 (4.3\%) | 0.09 | 1727 (7.4\%) | 2430 (3.7\%) | 0.16 |
| Occurrence of chronic renal insufficiency w/o CKD |  |  |  |  |  |  |  |  |  |  |  |  |
| (for PS) v2; n (\%) | **(1.4\%) | 308 (2.8\%) | -0.10 | 346 (1.7\%) | 295 (1.5\%) | 0.02 | 161 (4.9\%) | 1,221 (3.4\%) | 0.08 | \#VaLuE! | 1824 (2.8\%) | \#Value! |
| Chronic kidney disease Stage 1-2 (for PS); n (\%) | 0 (0.0\%) | 165 (1.5\%) | -0.17 | 166 (0.8\%) | 122 (0.6\%) | 0.02 | 0 | 0 | \#Value! | \#Value! | \#value! | \#Value! |
| Chronic kidney disease Stage 3-6 (for PS); n (\%) | ** (3.6\%) | 459 (4.2\%) | -0.03 | 461 (2.3\%) | 299 (1.6\%) | 0.05 | 230 (6.9\%) | 1,317 (3.7\%) | 0.14 | \#Value! | 2075 (3.2\%) | \#Value! |
| Acute kidney injury; n (\%) | ** (3.6\%) | 262 (2.4\%) | 0.07 | 404 (2.0\%) | 333 (1.7\%) | 0.02 | 0 (0.0\%) | ** (0.0\%) | \#Div/0! | 404 (2.0\%) | 333 (1.7\%) | 0.20 |
| Bladder stones+Kidney stones (for PS); n (\%) | ** (3.6\%) | 196 (1.8\%) | 0.11 | 372 (1.9\%) | 319 (1.7\%) | 0.02 | 68 (2.0\%) | 570 (1.6\%) | 0.03 | \#Value! | 1085 (1.6\%) | \#Value! |
| Alcohol abuse or dependence+Drug abuse or |  |  |  |  |  |  |  |  |  |  |  |  |
| dependence (for PS); n (\%) | 15 (10.8\%) | 521 (4.8\%) | 0.23 | 686 (3.4\%) | 544 (2.8\%) | 0.03 | 155 (4.7\%) | 752 (2.1\%) | 0.14 | 856 (3.7\%) | 1817 (2.8\%) | 0.05 |
| Other atherosclerosis Cardiac conduction |  |  |  |  |  |  |  |  |  |  |  |  |
| disorders+Other CVD (for PS) v2 Copy; n (\%) | 15 (10.8\%) | 1,442 (13.2\%) | $-0.07$ | 2,179 (10.9\%) | 2,046 (10.7\%) | 0.01 | 753 (22.7\%) | 5,973 (16.7\%) | 0.15 | 2947 (12.6\%) | 9461 (14.4\%) | -0.05 |
| Previous cardiac procedure (CABG or PTCA or |  |  |  |  |  |  |  |  |  |  |  |  |
| Stent) + History of CABG or PTCA (for PS) v3; n (\%) | **(2.2\%) | 443 (4.1\%) | -0.11 | 402 (2.0\%) | 403 (2.1\%) | -0.01 | 331 (10.0\%) | 2,766 (7.7\%) | 0.08 | \#Value! | 3612 (5.5\%) | \#Value! |
| Diabetes with complication; n (\%) | **(3.6\%) | 599 (5.5\%) | -0.09 | 757 (3.8\%) | 627 (3.3\%) | 0.03 | 185 (5.6\%) | 1,122 (3.1\%) | 0.12 | 757 (3.8\%) | 627 (3.3\%) | 0.28 |
| Delirium + Psychosis (for PS); n (\%) | **(0.7\%) | 161 (1.5\%) | -0.08 | 207 (1.0\%) | 187 (1.0\%) | 0.00 | 114 (3.4\%) | 919 (2.6\%) | 0.05 | \#Value! | 1267 (1.9\%) | \#VALUE! |
| Any use of Meglitinides (for PS); n (\%) | 0 (0.0\%) | ** (0.0\%) | \#DIV/0! | 20 (0.1\%) | 24 (0.1\%) | 0.00 | 3 (0.1\%) | 52 (0.1\%) | 0.00 | 23 (0.1\%) | \#value! | \#value! |
| Any use of AGIs (for PS); n (\%) | **(0.7\%) | ** (0.0\%) | 0.12 | 8 (0.0\%) | 8 (0.0\%) | \#Div/0! | 1 (0.0\%) | 17 (0.0\%) | \#Div/0! | \#Value! | \#value! | \#VaLuE! |
| CKD stage 3-6 + dialysis (for PS); n (\%) | **(3.6\%) | 460 (4.2\%) | $-0.03$ | 462 (2.3\%) | 300 (1.6\%) | 0.05 | 230 (6.9\%) | 1,320 (3.7\%) | 0.14 | \#Value! | 2080 (3.2\%) | \#value! |
| Use of thiazide- United; n (\%) | **(6.5\%) | 1,002 (9.2\%) | -0.10 | 1,805 (9.1\%) | 1,642 (8.6\%) | 0.02 | 406 (12.2\%) | 4,461 (12.4\%) | -0.01 | \#VALUE! | 7105 (10.8\%) | \#Value! |
| Use of beta blockers; n (\%) | 25 (18.0\%) | 2,388 (21.9\%) | -0.10 | 4,065 (20.4\%) | 3,988 (20.9\%) | -0.01 | 1,276 (38.5\%) | 11,174 (31.2\%) | 0.15 | 5366 (23.0\%) | 17550 (26.7\%) | -0.09 |
| Use of calcium channel blockers; n (\%) | 27 (19.4\%) | 1,964 (18.0\%) | 0.04 | 3,202 (16.1\%) | 3,037 (15.9\%) | 0.01 | 855 (25.8\%) | 8,105 (22.6\%) | 0.07 | 4084 (17.5\%) | 13106 (19.9\%) | -0.06 |
| All antidiabetic medications except Insulin; n (\%) | 12 (8.6\%) | 1,221 (11.2\%) | -0.09 | 1,987 (10.0\%) | 1,960 (10.3\%) | -0.01 | 435 (13.1\%) | 4,734 (13.2\%) | 0.00 | 2434 (10.4\%) | 7915 (12.0\%) | -0.05 |
| DM Medications - Insulin Copy; n (\%) | 0 (0.0\%) | 214 (2.0\%) | -0.20 | 431 (2.2\%) | 387 (2.0\%) | 0.01 | 96 (2.9\%) | 680 (1.9\%) | 0.07 | 527 (2.3\%) | 1281 (1.9\%) | 0.03 |
| Use of Low Intensity Statins; n (\%) | 14 (10.1\%) | 2,360 (21.7\%) | $-0.32$ | 3,970 (19.9\%) | 3,853 (20.2\%) | -0.01 | 893 (26.9\%) | 10,561 (29.5\%) | -0.06 | 4877 (20.9\%) | 16774 (25.5\%) | -0.11 |
| Use of High Intensity Statins; n (\%) | 17 (12.2\%) | 1,626 (14.9\%) | $-0.08$ | 2,485 (12.5\%) | 2,476 (13.0\%) | -0.01 | 639 (19.3\%) | 5,766 (16.1\%) | 0.08 | 3141 (13.4\%) | 9868 (15.0\%) | -0.05 |
| Malignant hypertension; n (\%) | ** (0.7\%) | 133 (1.2\%) | -0.05 | 8,674 (43.5\%) | 8,565 (44.8\%) | -0.03 | 228 (6.9\%) | 2,335 (6.5\%) | 0.02 | \#Value! | 11033 (16.8\%) | \#Value! |
| Cardiovascular stress test; n (\%) | 0 (0.0\%) | 15 (0.1\%) | -0.04 | 33 (0.2\%) | 34 (0.2\%) | 0.00 | 20 (0.6\%) | 96 (0.3\%) | 0.04 | 53 (0.2\%) | 145 (0.2\%) | 0.00 |
| Echocardiogram; n (\%) | 17 (12.2\%) | 1,134 (10.4\%) | 0.06 | 2,133 (10.7\%) | 2,072 (10.8\%) | 0.00 | 695 (20.9\%) | 5,364 (15.0\%) | 0.15 | 2845 (12.2\%) | 8570 (13.0\%) | -0.02 |
| Number of BNP tests |  |  |  |  |  |  |  |  |  |  |  |  |
| ...mean (sd) | 0.02 (0.15) | 0.02 (0.14) | 0.00 | 0.01 (0.13) | 0.01 (0.12) | 0.00 | 0.04 (0.23) | 0.03 (0.18) | 0.05 | 0.01 (0.15) | 0.02 (0.16) | -0.06 |
| Number of Cardiac biomarkers tests (tropnin, CK-M | obin, CPK) |  |  |  |  |  |  |  |  |  |  |  |
| ...mean (sd) | 0.12 (0.62) | 0.11 (0.58) | 0.02 | 0.10 (0.66) | 0.09 (0.53) | 0.02 | 0.14 (0.44) | 0.11 (0.37) | 0.07 | 0.11 (0.63) | 0.10 (0.46) | 0.00 |
| Number of Ambulatory Blood pressure monitoring ...mean (sd) | 0.00 (0.00) | 0.00 (0.02) | 0.00 | 0.00 (0.03) | 0.00 (0.05) | 0.00 | 0.00 (0.02) | 0.00 (0.02) | 0.00 | 0.00 (0.03) | 0.00 (0.03) | 0.00 |

## Appendix B

| N of days on antihypertensive medications during ...mean (sd) | line 76.12 (80.99) | 84.53 (81.34) | -0.10 | 78.54 (81.20) | 80.62 (81.24) | -0.03 | 117.86 (75.46) | 108.41 (79.14) | 0.12 | 84.11 (80.41) | 96.40 (80.12) | 0.00 |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| $N$ of days in database anytime prior |  |  |  |  |  |  |  |  |  |  |  |  |
| ...mean (sd) | 1,935.15 (1,404.74) | 1,778.37 (1,325.30) | 0.11 | 1,945.19 (1,314.79) | 2,012.46 (1,354.87) | -0.05 | 851.97 (590.35) | 682.18 (363.83) | 0.35 | 1789.97 (1238.66) | 1249.55 (946.19) | 0.00 |
| Mean Copay for per prescription cost (charges in U.S. $\$$ ) (180-1 day prior) |  |  |  |  |  |  |  |  |  |  |  |  |
| ....mean (sd) | 32.23 (150.62) | 20.77 (23.25) | 0.11 | 15.73 (19.19) | 14.88 (22.80) | 0.04 | 109.51 (85.40) | 105.78 (106.74) | 0.04 | 29.14 (38.51) | 65.34 (80.27) | -0.01 |
| ...Missing; n (\%) | ** (5.0\%) | 394 (3.6\%) | 0.07 | 867 (4.4\%) | 820 (4.3\%) | 0.00 | 42 (1.3\%) | $741(2.1 \%)$ | -0.06 | \#Value! | 1955 (3.0\%) | \#Value! |
| Colonoscopy; n (\%) | **(4.3\%) | 545 (5.0\%) | -0.03 | 959 (4.8\%) | 946 (5.0\%) | -0.01 | 159 (4.8\%) | 1,533 (4.3\%) | 0.02 | \#Value! | 3024 (4.6\%) | \#value! |
| Fecal occult blood (FOB) test; n (\%) | **(2.9\%) | 381 (3.5\%) | -0.03 | 971 (4.9\%) | $781(4.1 \%)$ | 0.04 | 80 (2.4\%) | 1,033 (2.9\%) | -0.03 | \#VALUE! | 2195 (3.3\%) | \#Value! |
| Flu vaccine; n (\%) | 33 (23.7\%) | 1,998 (18.4\%) | 0.13 | 2,607 (13.1\%) | 2,534 (13.3\%) | -0.01 | 1,030 (31.0\%) | 11,550 (32.2\%) | -0.03 | 3670 (15.7\%) | 16082 (24.4\%) | -0.22 |
| Mammogram; n (\%) | 19 (13.7\%) | 1,604 (14.7\%) | -0.03 | 2,647 (13.3\%) | 2,400 (12.6\%) | 0.02 | 480 (14.5\%) | 5,978 (16.7\%) | -0.06 | 3146 (13.5\%) | 9982 (15.2\%) | -0.05 |
| Pap smear; n (\%) | **(3.6\%) | 558 (5.1\%) | -0.07 | 1,371 (6.9\%) | 1,252 (6.6\%) | 0.01 | 123 (3.7\%) | 1,606 (4.5\%) | -0.04 | \#VaLuE! | 3416 (5.2\%) | \#Value! |
| Pneumonia vaccine; n (\%) | 39 (28.1\%) | 1,712 (15.7\%) | 0.30 | 1,233 (6.2\%) | 1,258(6.6\%) | -0.02 | 842 (25.4\%) | 7,109 (19.8\%) | 0.13 | 2114 (9.0\%) | 10079 (15.3\%) | -0.19 |
| PSA test or Prostate exam for DRE; n (\%) | 17 (12.2\%) | 1,370 (12.6\%) | -0.01 | 2,321 (11.7\%) | 2,185 (11.4\%) | 0.01 | 416 (12.5\%) | 4,318 (12.0\%) | 0.02 | 2754 (11.8\%) | 7873 (12.0\%) | -0.01 |
| Bone mineral density; n (\%) | **(2.9\%) | 586 (5.4\%) | -0.13 | 685 (3.4\%) | 706 (3.7\%) | -0.02 | 207 (6.2\%) | 2,353 (6.6\%) | -0.02 | \#Value! | 3645 (5.5\%) | \#Value! |
| Use of CNS Stimulants; n (\%) | **(1.4\%) | 72 (0.7\%) | 0.07 | 162 (0.8\%) | 159 (0.8\%) | 0.00 | 18 (0.5\%) | 118 (0.3\%) | 0.03 | \#VALUE! | 349 (0.5\%) | \#VALUE! |
| Use of estrogens, progestins, androgens; n (\%) | 17 (12.2\%) | 753 (6.9\%) | 0.18 | 1,722 (8.6\%) | 1,629 (8.5\%) | 0.00 | 184 (5.5\%) | 1,981 (5.5\%) | 0.00 | 1923 (8.2\%) | 4363 (6.6\%) | 0.06 |
| Use of Angiogenesis inhibitors; n (\%) | 0 (0.0\%) | ** (0.0\%) | \#DIV/0! | 11 (0.1\%) | 5 (0.0\%) | 0.04 | 3 (0.1\%) | 15 (0.0\%) | 0.04 | 14 (0.1\%) | \#value! | \#Value! |
| Use of Oral Immunosuppressants; n (\%) | 0 (0.0\%) | 11 (0.1\%) | -0.04 | 56 (0.3\%) | 19 (0.1\%) | 0.04 | 4 (0.1\%) | 31 (0.1\%) | 0.00 | 60 (0.3\%) | 61 (0.1\%) | 0.04 |
| Use of fondaparinux or Bivalirudin; n (\%) | 0 (0.0\%) | **(0.1\%) | -0.04 | 21 (0.1\%) | 18 (0.1\%) | 0.00 | 2 (0.1\%) | 18 (0.1\%) | 0.00 | 23 (0.1\%) | \#Value! | \#value! |
| Use of other direct thrombin inhibitors (lepirudin, |  |  |  |  |  |  |  |  |  |  |  |  |
| desirudin, argatroban); n (\%) | 0 (0.0\%) | 0 (0.0\%) | \#DIV/0! | 0 (0.0\%) | 0 (0.0\%) | \#Div/0! | 0 (0.0\%) | 0 (0.0\%) | \#Div/0! | 0 (0.0\%) | 0 (0.0\%) | \#DIV/0! |
| Use of Ticagrelor ON CED; n (\%) | 0 (0.0\%) | **(0.0\%) | \#DIV/0! | 6 (0.0\%) | 2 (0.0\%) | \#DIV/0! | 0 (0.0\%) | 0 (0.0\%) | \#DIV/0! | 6 (0.0\%) | \#VALUE! | \#VALUE! |
| Use of Ticagrelor; n (\%) | 0 (0.0\%) | **(0.1\%) | -0.04 | 8 (0.0\%) | 7 (0.0\%) | \#DIV/0! | 7 (0.2\%) | 26 (0.1\%) | 0.03 | 15 (0.1\%) | \#Value! | \#Value! |
| Number of D-dimer tests |  |  |  |  |  |  |  |  |  |  |  |  |
| ...mean (sd) | 0.02 (0.15) | 0.01 (0.12) | 0.07 | 0.01 (0.10) | 0.01 (0.11) | 0.00 | 0.02 (0.15) | 0.01 (0.13) | 0.07 | 0.01 (0.11) | 0.01 (0.12) | 0.00 |
| Numbe of CRP, high-sensitivity CRP tests |  |  |  |  |  |  |  |  |  |  |  |  |
| ...mean (sd) | 0.27 (0.68) | 0.12 (0.46) | 0.26 | 0.11 (0.47) | 0.09 (0.38) | 0.05 | 0.25 (0.83) | 0.14 (0.51) | 0.16 | 0.13 (0.54) | 0.12 (0.47) | 0.00 |
| Number of PT or aPTTt tests |  |  |  |  |  |  |  |  |  |  |  |  |
| ...mean (sd) | 0.95 (1.16) | 0.87 (1.19) | 0.07 | 0.88 (1.28) | 0.77 (1.22) | 0.09 | 0.78 (1.29) | 0.61 (0.93) | 0.15 | 0.87 (1.28) | 0.70 (1.07) | 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 (0.02) | 0.00 | 0.00 (0.00) | 0.00 (0.02) | 0.00 | 0.00 (0.02) | 0.00 (0.02) | 0.00 |
| HAS-BLED Score (ICD-9 and ICD-10), 180 days |  |  |  |  |  |  |  |  |  |  |  |  |
| ...mean (sd) | 2.90 (1.05) | 3.20 (1.08) | -0.28 | 2.87 (1.05) | 2.91 (1.05) | -0.04 | 3.76 (0.91) | 3.74 (0.95) | 0.02 | 3.00 (1.03) | 3.41 (1.00) | 0.00 |
| $N$ of Generic name drugs |  |  |  |  |  |  |  |  |  |  |  |  |
| ...mean (sd) | 13.86 (12.71) | 15.02 (12.51) | -0.09 | 14.21 (11.01) | 13.44 (10.99) | 0.07 | 20.14 (14.72) | 16.53 (13.12) | 0.26 | 15.05 (11.62) | 15.38 (12.44) | 0.00 |
| N of Brand name drugs |  |  |  |  |  |  |  |  |  |  |  |  |
| ...mean (sd) | 3.01 (4.72) | 3.39 (3.92) | -0.09 | 2.94 (4.13) | 3.82 (4.06) | -0.21 | 3.03 (5.27) | 3.72 (4.36) | -0.14 | 2.95 (4.31) | 3.69 (4.20) | 0.00 |
| Use of clopidogrel; n (\%) | **(2.2\%) | 216 (2.0\%) | 0.01 | 438 (2.2\%) | 406 (2.1\%) | 0.01 | 159 (4.8\%) | 1,355 (3.8\%) | 0.05 | \#Value! | 1977 (3.0\%) | \#Value! |
| Systemic embolism; n (\%) | 0 (0.0\%) | 14 (0.1\%) | -0.04 | $31(0.2 \%)$ | 10 (0.1\%) | 0.03 | 6 (0.2\%) | 47 (0.1\%) | 0.03 | 37 (0.2\%) | 71 (0.1\%) | 0.03 |
| DVT; n (\%) | **(1.4\%) | 224 (2.1\%) | -0.05 | 289 (1.5\%) | 301 (1.6\%) | -0.01 | 189 (5.7\%) | 629 (1.8\%) | 0.21 | \#Value! | 1154 (1.8\%) | \#Value! |
| Post-thrombotic syndrome; n (\%) | 0 (0.0\%) | **(0.0\%) | \#DIV/0! | **(0.0\%) | 0 (0.0\%) | \#Div/0! | 63 (1.9\%) | 718 (2.0\%) | -0.01 | ** (0.0\%) | 0 (0.0\%) | \#DIV/0! |
| PE; n (\%) | 0 (0.0\%) | 60 (0.6\%) | -0.11 | 63 (0.3\%) | 88 (0.5\%) | -0.03 | 64 (1.9\%) | 161 (0.4\%) | 0.14 | 127 (0.5\%) | 309 (0.5\%) | 0.00 |
| Coagulation defects; n (\%) | 0 (0.0\%) | 134 (1.2\%) | -0.16 | 210 (1.1\%) | 274 (1.4\%) | -0.03 |  |  | \#DIV/0! | 210 (1.1\%) | 274 (1.4\%) | 0.15 |
| Diabetes: 1 inpatient or 2 outpatient claims |  |  |  |  |  |  |  |  |  |  |  |  |
| within 183 days ; n (\%) | 16 (11.5\%) | 1,773 (16.3\%) | -0.14 | 2,832 (14.2\%) | 2,714 (14.2\%) | 0.00 | 676 (20.4\%) | 7,074 (19.7\%) | 0.02 | 3524 (15.1\%) | 11561 (17.6\%) | -0.07 |
| Intracranial or retroperitoneal hemorrhage: 1 |  |  |  |  |  |  |  |  |  |  |  |  |
| inpatient or 2 outpatient claims within 183 days; |  |  |  |  |  |  |  |  |  |  |  |  |
| n (\%) | 0 (0.0\%) | **(0.1\%) | -0.04 | 15 (0.1\%) | 14 (0.1\%) | 0.00 | 4 (0.1\%) | 19 (0.1\%) | 0.00 | 19 (0.1\%) | \#value! | \#value! |
| Peptic Ulcer Disease; n (\%) | 46 (33.1\%) | 3,473 (31.9\%) | 0.03 | 4,260 (21.4\%) | 4,176 (21.9\%) | -0.01 | 1,302 (39.2\%) | 12,496 (34.9\%) | 0.09 | 5608 (24.0\%) | 20145 (30.6\%) | -0.15 |
| Upper GI bleed; n (\%) | 0 (0.0\%) | 18 (0.2\%) | -0.06 | 29 (0.1\%) | 16 (0.1\%) | 0.00 | 2 (0.1\%) | 39 (0.1\%) | 0.00 | 31 (0.1\%) | 73 (0.1\%) | 0.00 |
| Lower/ unspecified GI bleed; n (\%) | **(1.4\%) | 161 (1.5\%) | -0.01 | 250 (1.3\%) | 220 (1.2\%) | 0.01 | 8 (0.2\%) | 56 (0.2\%) | 0.00 | \#VaLue! | 437 (0.7\%) | \#Value! |
| Urogenital bleed; n (\%) | **(3.6\%) | 340 (3.1\%) | 0.03 | 466 (2.3\%) | 506 (2.6\%) | -0.02 | 39 (1.2\%) | 559 (1.6\%) | -0.03 | \#Value! | 1405 (2.1\%) | \#Value! |
| Other bleeds; n (\%) | 48 (34.5\%) | 3,015 (27.7\%) | 0.15 | 5,036 (25.3\%) | 4,905 (25.7\%) | -0.01 | 991 (29.9\%) | 11,276 (31.5\%) | -0.03 | 6075 (26.0\%) | 19196 (29.2\%) | -0.07 |
| Prior cancer; n (\%) | 21 (15.1\%) | 1,367 (12.6\%) | 0.07 | 1,410 (7.1\%) | 1,317 (6.9\%) | 0.01 | 589 (17.8\%) | 4,401 (12.3\%) | 0.15 | 2020 (8.6\%) | 7085 (10.8\%) | -0.07 |
| Antibiotics; n (\%) | 53 (38.1\%) | 4,441 (40.8\%) | -0.06 | 8,121 (40.8\%) | 7,772 (40.7\%) | 0.00 | 558 (16.8\%) | 4,161 (11.6\%) | 0.15 | 8,121 (40.8\%) | 7,772 (40.7\%) | 1.17 |
| Aspirin; n (\%) | 12 (8.6\%) | 123 (1.1\%) | 0.35 | 630 (3.2\%) | 194 (1.0\%) | 0.15 | 11 (0.3\%) | 109 (0.3\%) | 0.00 | 653 (2.8\%) | 426 (0.6\%) | 0.17 |
| Aspirin/dipyridamole; n (\%) | 0 (0.0\%) | **(0.0\%) | \#Div/0! | 20 (0.1\%) | 21 (0.1\%) | 0.00 | 4 (0.1\%) | 65 (0.2\%) | -0.03 | 24 (0.1\%) | \#value! | \#Value! |
| Other antiplatelet agents; n (\%) | 0 (0.0\%) | 11 (0.1\%) | -0.04 | 21 (0.1\%) | 15 (0.1\%) | 0.00 | 9 (0.3\%) | 66 (0.2\%) | 0.02 | 30 (0.1\%) | 92 (0.1\%) | 0.00 |
| PGP inhibitors; n (\%) | 19 (13.7\%) | 1,705 (15.7\%) | -0.06 | 3,248 (16.3\%) | 3,118 (16.3\%) | 0.00 | 846 (25.5\%) | 7,135 (19.9\%) | 0.13 | 4113 (17.6\%) | 11958 (18.2\%) | -0.02 |
| Other gastroprotective agents; n (\%) | **(1.4\%) | 125 (1.1\%) | 0.03 | 309 (1.6\%) | 273 (1.4\%) | 0.02 | 69 (2.1\%) | 527 (1.5\%) | 0.05 | \#Value! | 925 (1.4\%) | \#Value! |
| Number of lipid tests ordered |  |  |  |  |  |  |  |  |  |  |  |  |
| ...mean (sd) | 0.49 (0.81) | 0.56 (0.73) | -0.09 | 0.48 (0.85) | 0.46 (0.78) | 0.02 | 0.59 (0.75) | 0.62 (0.77) | -0.04 | 0.50 (0.84) | 0.56 (0.77) | 0.00 |
| Proton pump inhibitor; n (\%) | 31 (22.3\%) | 2,149 (19.7\%) | 0.06 | 3,867 (19.4\%) | 3,740 (19.6\%) | -0.01 | 1,004 (30.3\%) | 9,498 (26.5\%) | 0.08 | 4902 (21.0\%) | 15387 (23.4\%) | -0.06 |
| H2 receptor antagonist; n (\%) | **(2.2\%) | 267 (2.5\%) | -0.02 | 608 (3.1\%) | 513 (2.7\%) | 0.02 | 209 (6.3\%) | 1,737 (4.8\%) | 0.07 | \#Value! | 2517 (3.8\%) | \#value! |
| Vitamin K therapy; n (\%) | 0 (0.0\%) | 0 (0.0\%) | \#DIV/0! | **(0.0\%) | ${ }^{* *}(0.0 \%)$ | \#DIV/0! | 0 (0.0\%) | $1(0.0 \%)$ | \#DIV/0! | \#VALUE! | \#VALUE! | \#VALUE! |
| Number of INR (prothrombin) tests ordered |  |  |  |  |  |  |  |  |  |  |  |  |
| ...mean (sd) | 0.58 (0.66) | 0.49 (0.66) | 0.14 | 0.51 (0.74) | 0.44 (0.68) | 0.10 | 0.64 (1.08) | 0.49 (0.68) | 0.17 | 0.53 (0.80) | 0.48 (0.68) | 0.00 |
| Treating prescriber - Cardiologist; n (\%) | 63 (45.3\%) | 3,504 (32.2\%) | 0.27 | 5,695 (28.6\%) | 5,613 (29.4\%) | -0.02 | 1,425 (42.9\%) | 13,200 (36.8\%) | 0.12 | 7183 (30.7\%) | 22317 (33.9\%) | -0.07 |
| Treating prescriber - Primary Care Physician; n (\%) | 109 (78.4\%) | 8,804 (80.9\%) | -0.06 | 7,125 (35.8\%) | 7,775 (40.7\%) | -0.10 | 1,075 (32.4\%) | 13,283 (37.1\%) | -0.10 | 8309 (35.5\%) | 29862 (45.4\%) | -0.20 |

## Appendix B



| 139 (100.0\%) | 10,881 (100.0\%) | \#DIV/0! | 19,725 (99.0\%) | 18,871 (98.7\%) | 0.03 | 3,318 (100.0\%) | 35,807 (99.9\%) | 0.04 | 23182 (99.2\%) | 65559 (99.6\%) | -0.05 |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| ** (4.3\%) | 693 (6.4\%) | -0.09 | 1,101 (5.5\%) | 1,076 (5.6\%) | 0.00 | 347 (10.5\%) | 3,170 (8.8\%) | 0.06 | \#Value! | 4939 (7.5\%) | \#Value! |
| 1.36 (1.26) | 1.93 (1.35) | -0.44 | 1.70 (1.32) | 1.73 (1.34) | -0.02 | 2.45 (1.23) | 2.63 (1.25) | -0.15 | 1.80 (1.31) | 2.25 (1.29) | 0.00 |
| 0 (0.0\%) | 15 (0.1\%) | -0.04 | 36 (0.2\%) | 33 (0.2\%) | 0.00 | 0 (0.0\%) | ** (0.0\%) | \#Div/0! | 36 (0.2\%) | \#value! | alue! |
| **(5.0\%) | 811 (7.5\%) | -0.10 | 1,363 (6.8\%) | 1,248 (6.5\%) | 0.01 | 558 (16.8\%) | 4,161 (11.6\%) | 0.15 | \#Value! | 6220 (9.4\%) | \#Value! |
| **(2.2\%) | 350 (3.2\%) | -0.06 | 416 (2.1\%) | 388 (2.0\%) | 0.01 | 207 (6.2\%) | 1,679 (4.7\%) | 0.0 | \#Value! | 2417 (3.7\%) | \#Value! |
| **(0.7\%) | 197 (1.8\%) | -0.10 | 296 (1.5\%) | 258 (1.4\%) | 0.01 | 90 (2.7\%) | 769 (2.1\%) | 0.04 | \#Value! | 1224 (1.9\%) | \#VaLuE! |
| **(3.6\%) | 407 (3.7\%) | -0.01 | 561 (2.8\%) | 546 (2.9\%) | -0.01 | 191 (5.8\%) | 1,950 (5.4\%) | 0.02 | \#VaLue! | 2903 (4.4\%) | \#VaLuE! |
| **(1.4\%) | 265 (2.4\%) | -0.07 | 340 (1.7\%) | 361 (1.9\%) | -0.02 | 237 (7.1\%) | 749 (2.1\%) | 0.24 | \#VALUE! | 1375 (2.1\%) | \#VALUE! |
| 53 (38.1\%) | 3,342 (30.7\%) | 0.16 | 5,570 (28.0\%) | 5,435 (28.4\%) | -0.01 | 1,021 (30.8\%) | 11,697 (32.6\%) | -0.04 | 6644 (28.4\%) | 20474 (31.1\%) | -0.06 |

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

## Appendix B

| PS-matched |  |  |  |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | Optum ${ }^{\text {I }}$ | MarketScan |  |  | Medicare] |  |  | Referent-enoxaparin |  | Exposure-rivaroxaban | POOLED |
|  |  |  |  |  |  |  |  |  |  |  |  |
| Variable | - enoxaparin 30 or 40 mg sure - | roxaban 10 mg | St. Diff. | rin 30 or 40 mg s | aroxaban 10 mg | St. Diff. | in 30 or 40 mg | roxaban 10 mg | St. Diff. | 30 or 40 mg |  | 10 mg | St. Diff. |
| Number of patientsAge |  |  |  |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| ...mean (sd) | 60.34 (9.90) | 59.53 (11.06) | 0.08 | 60.19 (10.11) | 60.18 (10.21) | 0.00 | 71.28 (9.08) | 71.03 (9.16) | 0.03 | 62.27 (9.92) | 62.21 (10.03) | 0.01 |
| Age categories without zero category |  |  |  |  |  |  |  |  |  |  |  |  |
| ...18-54; n (\%) | 25 (23.4\%) | 35 (32.7\%) | -0.21 | 3,610 (25.7\%) | 3,677 (26.1\%) | -0.01 | 184 (5.6\%) | 181(5.5\%) | 0.00 | 3819 (21.9\%) | 3893 (22.3\%) | -0.01 |
| ...55-64; n (\%) | 53 (4.5\%) | 35 (32.7\%) | 0.35 | 6,621 (47.1\%) | 6,587 (46.8\%) | 0.01 | 256 (7.8\%) | 258 (7.9\%) | 0.00 | 6,930 (39.7\%) | 6,880 (39.5\%) | 0.00 |
| ...65-74; n (\%) | 19 (17.8\%) | 30 (28.0\%) | -0.24 | 2,601 (18.5\%) | 2,457 (17.5\%) | 0.03 | 1,672 (51.2\%) | 1,741 (53.3\%) | -0.04 | 4292 (24.6\%) | 4228 (24.2\%) | 0.01 |
| ... $=75 ; \mathrm{n}$ (\%) | 10 (9.3\%) | 7 (6.5\%) | 0.10 | 1,234 (8.8\%) | 1,345 (9.6\%) | -0.03 | 1,153 (35.3\%) | 1,085 (33.2\%) | 0.04 | 2397 (13.7\%) | 2,437 (14.0\%) | -0.01 |
| Gender without zero category- |  |  |  |  |  |  |  |  |  |  |  |  |
| United |  |  |  |  |  |  |  |  |  |  |  |  |
| ...Males; n (\%) | 39 (36.4\%) | 48 (44.9\%) | -0.17 | 6,734 (47.9\%) | 6,677 (47.5\%) | 0.01 | 1,303 (39.9\%) | 1,310 (40.1\%) | 0.00 | 8,076 (46.3\%) | 8,035 (46.1\%) | 0.00 |
| ...Females; n (\%) | 68 (63.6\%) | 59 (55.1\%) | 0.17 | 7,332 (52.1\%) | 7,389 (52.5\%) | -0.01 | 1,962 (60.1\%) | 1,955 (59.9\%) | 0.00 | 9,362 (53.7\%) | 9,403 (53.9\%) | 0.00 |
| Race |  |  |  |  |  |  |  |  |  |  |  |  |
| ...White; n (\%) | - | - |  | - | - |  | 2,993 (91.7\%) | 2,990 (91.6\%) | 0.00 | 2,993 (91.7\%) | 2,990 (91.6\%) | 0.00 |
| ...Black; n (\%) | - | - |  | - | - |  | 200 (6.1\%) | 201 (6.2\%) | 0.00 | 200 (6.1\%) | 201 (6.2\%) | 0.00 |
| ...Asian; n (\%) | - | - |  | - | - |  | 7 (0.2\%) | 6 (0.2\%) | 0.00 | 7 (0.2\%) | 6 (0.2\%) | 0.00 |
| .... H ispanic; n (\%) |  | - |  | - | - |  | 14 (0.4\%) | 14 (0.4\%) | 0.00 | 14 (0.4\%) | 14 (0.4\%) | 0.00 |
| ...North American Native; n (\%) | - | - |  | - | - |  | 13 (0.4\%) | 22 (0.7\%) | -0.04 | 13 (0.4\%) | 22 (0.7\%) | -0.04 |
| ...Other/Unknown; n (\%) | - | - |  | - | - |  | 38 (1.2\%) | 32 (1.0\%) | 0.02 | 38 (1.2\%) | 32 (1.0\%) | 0.02 |
| Region without zero category- United |  |  |  |  |  |  |  |  |  |  |  |  |
| v3 (lumping missing\&other category |  |  |  |  |  |  |  |  |  |  |  |  |
| ...Northeast; n (\%) | 10 (9.3\%) | 12 (11.2\%) | -0.06 | 2,293 (16.3\%) | 2,417 (17.2\%) | -0.02 | 582 (17.8\%) | 567 (17.4\%) | 0.01 | 2885 (16.5\%) | 2,996 (17.2\%) | -0.02 |
| ...South; n (\%) | 39 (36.4\%) | 42 (39.3\%) | -0.06 | 4,002 (28.5\%) | 3,829 (27.2\%) | 0.03 | 1,270 (38.9\%) | 1,258 (38.5\%) | 0.01 | 5,311 (30.5\%) | 5,129 (29.4\%) | 0.02 |
| ...Midwest; n (\%) | 37 (34.6\%) | 34 (31.8\%) | 0.06 | 5,476 (38.9\%) | 5,373 (38.2\%) | 0.01 | 832 (25.5\%) | 850 (26.0\%) | -0.01 | 6,345 (36.4\%) | 6,257 (35.9\%) | 0.01 |
| ...West; n (\%) | 21 (19.6\%) | 19 (17.8\%) | 0.05 | 2,129 (15.1\%) | 2,291 (16.3\%) | -0.03 | 581 (17.8\%) | 590 (18.1\%) | -0.01 | 2731 (15.7\%) | 2,900 (16.6\%) | -0.02 |
| ...Unknown+missing; n (\%) | N/A | N/A | \#Value! | 166 (1.2\%) | 156 (1.1\%) | 0.01 | N/A | N/A | \#Value! | 166 (1.2\%) | 156 (1.1\%) | 0.01 |
| Metropolitan Statistical Area - Urban (any MSA) vs Rural (non-MSA) |  |  |  |  |  |  |  |  |  | 0 | 0 | 0.00 |
| ...Urban; n (\%) | - | - |  | 10,777 (76.6\%) | 10,818 (76.9\%) | -0.01 | - | - |  | 10,777 (76.6\%) | 10,818 (76.9\%) | -0.01 |
| ...Rural; n (\%) | - | - |  | 420 (3.0\%) | 411(2.9\%) | 0.01 | - | - |  | 420 (3.0\%) | 411 (2.9\%) | 0.01 |
| ...Unknown/Missing; n (\%) | - | - |  | 2,869 (20.4\%) | 2,837 (20.2\%) | 0.00 | - | - |  | 2,869 (20.4\%) | 2,837 (20.2\%) | 0.00 |
| Commercial vs Medicare Advantage-D |  | - |  |  |  |  | - | - |  |  |  |  |
| ...1-Fee For Service; n (\%) | - | - |  | 9,208 (65.5\%) | 9,122 (64.9\%) | 0.01 | - | - |  | 9,208 (65.5\%) | 9,122 (64.9\%) | 0.01 |
| ...2-Encounter; n (\%) | - | - |  | 1,007 (7.2\%) | 1,074 (7.6\%) | -0.02 | - | - |  | 1,007 (7.2\%) | 1,074 (7.6\%) | -0.02 |
| ... 3 - Medicare; n (\%) | - | - |  | 3,378 (24.0\%) | 3,356 (23.9\%) | 0.00 | - | - |  | 3,378 (24.0\%) | 3,356 (23.9\%) | 0.00 |
| cv covariates |  |  |  |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Ischemic heart disease; n (\%) | 12 (11.2\%) | 17 (15.9\%) | -0.14 | 1,488 (10.6\%) | 1,506 (10.7\%) | 0.00 | 794 (24.3\%) | 776 (23.8\%) | 0.01 | 2294 (13.2\%) | 2299 (13.2\%) | 0.00 |
| Acute MI; n (\%) | 0 (0.0\%) | 0 (0.0\%) | \#Div/0! | 63 (0.4\%) | 57 (0.4\%) | 0.00 | 20 (0.6\%) | 18 (0.6\%) | 0.00 | 83 (0.5\%) | 75 (0.4\%) | 0.01 |
| ACS/unstable angina; n (\%) | 1 (0.9\%) | 1 (0.9\%) | 0.00 | 51 (0.4\%) | 52 (0.4\%) | 0.00 | 24 (0.7\%) | 27 (0.8\%) | -0.01 | 76 (0.4\%) | 80 (0.5\%) | -0.01 |
| Old M1; n (\%) | 3 (2.8\%) | $4(3.7 \%)$ | -0.05 | 247 (1.8\%) | 248 (1.8\%) | 0.00 | 192 (5.9\%) | 168 (5.1\%) | 0.04 | 442 (2.5\%) | 420 (2.4\%) | 0.01 |
| Stable angina; n (\%) | 0 (0.0\%) | 1 (0.9\%) | -0.13 | 155 (1.1\%) | 145 (1.0\%) | 0.01 | 68 (2.1\%) | 72 (2.2\%) | -0.01 | 223 (1.3\%) | 218 (1.3\%) | 0.00 |
| Coronary atherosclerosis and other |  |  |  |  |  |  |  |  |  |  |  |  |
| forms of chronic ischemic heart |  |  |  |  |  |  |  |  |  |  |  |  |
| disease; n (\%) | 12 (11.2\%) | 17 (15.9\%) | -0.14 | 1,340 (9.5\%) | 1,358 (9.7\%) | -0.01 | 735 (22.5\%) | 718 (22.0\%) | 0.01 | 2087 (12.0\%) | 2093 (12.0\%) | 0.00 |
| Other atherosclerosis with CD 10 v 2 |  |  |  |  |  |  |  |  |  |  |  |  |
| Copy; n (\%) | 0 (0.0\%) | 1 (0.9\%) | -0.13 | 92 (0.7\%) | 87 (0.6\%) | 0.01 | 31 (0.9\%) | 36 (1.1\%) | -0.02 | 123 (0.7\%) | 124 (0.7\%) | 0.00 |
| Previous cardiac procedure (CABG or |  |  |  |  |  |  |  |  |  |  |  |  |
| PTCA or Stent) v4; $n$ (\%) | 0 (0.0\%) | 0 (0.0\%) | \#Div/0! | 9 (0.1\%) | 8 (0.1\%) | 0.00 | 7 (0.2\%) | 7 (0.2\%) | 0.00 | 16 (0.1\%) | 15 (0.1\%) | 0.00 |
| History of CABG or PTCA; n (\%) | 3 (2.8\%) | 2 (1.9\%) | 0.06 | 267 (1.9\%) | 269 (1.9\%) | 0.00 | 321 (9.8\%) | 308 (9.4\%) | 0.01 | 591 (3.4\%) | 579 (3.3\%) | 0.01 |
| Any stroke; n (\%) | 4 (3.7\%) | $1(0.9 \%)$ | 0.19 | 306 (2.2\%) | 302 (2.1\%) | 0.01 | 147 (4.5\%) | 145 (4.4\%) | 0.00 | 457 (2.6\%) | 448 (2.6\%) | 0.00 |
| Ischemic stroke (w and w/o mention |  |  |  |  |  |  |  |  |  |  |  |  |
| of cerebral infarction); n (\%) | 4 (3.7\%) | 1 (0.9\%) | 0.19 | 302 (2.1\%) | 299 (2.1\%) | 0.00 | 147 (4.5\%) | 145 (4.4\%) | 0.00 | 453 (2.6\%) | 445 (2.6\%) | 0.00 |
| Hemorrhagic stroke; n (\%) | 0 (0.0\%) | 0 (0.0\%) | \#DIV/0! | 4 (0.0\%) | 4 (0.0\%) | \#DIV/0! | 0 (0.0\%) | 0 (0.0\%) | \#DIV/0! | 4 (0.0\%) | 4 (0.0\%) | \#Div/0! |
| TA; n (\%) | 1 (0.9\%) | 0 (0.0\%) | 0.13 | 88 (0.6\%) | 83 (0.6\%) | 0.00 | 35 (1.1\%) | 40 (1.2\%) | -0.01 | 124 (0.7\%) | 123 (0.7\%) | 0.00 |
| Other cerebrovascular disease; n (\%) | 1 (0.9\%) | 0 (0.0\%) | 0.13 | 70 (0.5\%) | 71 (0.5\%) | 0.00 | 29 (0.9\%) | 33 (1.0\%) | -0.01 | 100 (0.6\%) | 104 (0.6\%) | 0.00 |
| Cerebrovascular procedure; n (\%) | 0 (0.0\%) | 0 (0.0\%) | \#Div/0! | 5 (0.0\%) | 3 (0.0\%) | \#DIV/0! | 2 (0.1\%) | 2 (0.1\%) | 0.00 | 7 (0.0\%) | 5 (0.0\%) | \#Div/0! |
| Peripheral Vascular Disease (PVD) or |  |  |  |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| PVD Surgery V2; n (\%) | 5 (4.7\%) | 4 (3.7\%) | 0.05 | 305 (2.2\%) | 309 (2.2\%) | 0.00 | 200 (6.1\%) | 185 (5.7\%) | 0.02 | 510 (2.9\%) | 498 (2.9\%) | 0.00 |
| Atrial fibrillation; n (\%) | 1 (0.9\%) | 2 (1.9\%) | -0.09 | 402 (2.9\%) | 408 (2.9\%) | 0.00 | 656 (20.1\%) | 664 (20.3\%) | 0.00 | 1059 (6.1\%) | 1,074 (6.2\%) | 0.00 |
| Other cardiac dyshyythmia; n (\%) | 14 (13.1\%) | 18 (16.8\%) | -0.10 | 1,352 (9.6\%) | 1,356 (9.6\%) | 0.00 | 791 (24.2\%) | 813 (24.9\%) | -0.02 | 2157 (12.4\%) | 2,187 (12.5\%) | 0.00 |
| Cardiac conduction disorders; n (\%) | 1 (0.9\%) | 11 (10.3\%) | -0.42 | 465 (3.3\%) | 452 (3.2\%) | 0.01 | 244 (7.5\%) | 241 (7.4\%) | 0.00 | 710 (4.1\%) | 704 (4.0\%) | 0.01 |
| Other CVD; n (\%) | 12 (11.2\%) | 7 (6.5\%) | 0.17 | 1,088 (7.7\%) | 1,073 (7.6\%) | 0.00 | 540 (16.5\%) | 502 (15.4\%) | 0.03 | 1640 (9.4\%) | 1,582 (9.1\%) | 0.01 |

## Appendix B

Diabetes-related complications
Occurrence of Diabetic Neurop

| Copy; n (\%) | 1 (0.9\%) | 6 (5.6\%) | -0.27 | 208 (1.5\%) | 235 (1.7\%) | -0.02 | 106 (3.2\%) | 127 (3.9\%) | -0.04 | 315 (1.8\%) | 368 (2.1\%) | -0.02 |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Occurrence of diabetic nephropathy |  |  |  |  |  |  |  |  |  |  |  |  |
| V3 with ICD10 Copy; n (\%) | 1 (0.9\%) | 2 (1.9\%) | -0.09 | 95 (0.7\%) | 98 (0.7\%) | 0.00 | 50 (1.5\%) | 54 (1.7\%) | -0.02 | 146 (0.8\%) | 154 (0.9\%) | -0.01 |
| Hypogivcemia 2 ; n (\%) | 0 (0.0\%) | 0 (0.0\%) | \#Div/o! | 73 (0.5\%) | 69 (0.5\%) | 0.00 | 48 (1.5\%) | 50 (1.5\%) | 0.00 | 121 (0.7\%) | 119 (0.7\%) | 0.00 |
| Hyperglycemia; n (\%) | 11 (10.3\%) | 2 (1.9\%) | 0.36 | 595 (4.2\%) | 550 (3.9\%) | 0.02 | 279 (8.5\%) | 265 (8.1\%) | 0.01 | 885 (5.1\%) | 817 (4.7\%) | 0.02 |
| Diabetic ketoacidosis; n (\%) | 0 (0.0\%) | 0 (0.0\%) | \#DIV/0! | 11 (0.1\%) | 3 (0.0\%) | 0.04 | 2 (0.1\%) | 3 (0.1\%) | 0.00 | 13 (0.1\%) | 6 (0.0\%) | 0.04 |
| Hypertension: 1 inpatient or 2 outpatient claims within 365 days; $n$ |  |  |  |  |  |  |  |  |  |  |  |  |
| (\%) | 67 (62.6\%) | 67 (62.6\%) | 0.00 | 8,177 (58.1\%) | 8,203 (58.3\%) | 0.00 | 2,648 (81.1\%) | 2,676 (82.0\%) | -0.02 | 10,892 (62.5\%) | 10,946 (62.8\%) | -0.01 |
| Hyperlipidemia v2; n (\%) | 55 (51.4\%) | 48 (44.9\%) | 0.13 | 6,362 (45.2\%) | 6,406 (45.5\%) | -0.01 | 1,981 (60.7\%) | 1,950 (59.7\%) | 0.02 | 8,398 (48.2\%) | 8,404 (48.2\%) | 0.00 |
| Edema; n (\%) | 6 (5.6\%) | 8 (7.5\%) | -0.08 | 403 (2.9\%) | 406 (2.9\%) | 0.00 | 194 (5.9\%) | 186 (5.7\%) | 0.01 | 603 (3.5\%) | 600 (3.4\%) | 0.01 |
| Renal Dysfunction (non-diabetic) v2; n |  |  |  |  |  |  |  |  |  |  |  |  |
| (\%) | 13 (12.1\%) | 9 (8.4\%) | 0.12 | 911 (6.5\%) | 947 (6.7\%) | -0.01 | 530 (16.2\%) | 488 (14.9\%) | 0.04 | 1454 (8.3\%) | 1444 (8.3\%) | 0.00 |
| Occurrence of acute renal disease v2; |  |  |  |  |  |  |  |  |  |  |  |  |
| n (\%) | 4 (3.7\%) | 2 (1.9\%) | 0.11 | 240 (1.7\%) | 245 (1.7\%) | 0.00 | 150 (4.6\%) | 151 (4.6\%) | 0.00 | 394 (2.3\%) | 398 (2.3\%) | 0.00 |
| Occurrence of chronic renal |  |  |  |  |  |  |  |  |  |  |  |  |
| insufficiency; n (\%) | 7 (6.5\%) | 5 (4.7\%) | 0.08 | 482 (3.4\%) | 491 (3.5\%) | -0.01 | 355 (10.9\%) | 342 (10.5\%) | 0.01 | 844 (4.8\%) | 838 (4.8\%) | 0.00 |
| Chronic kidney disease v2; n (\%) | 6 (5.6\%) | 5 (4.7\%) | 0.04 | 461 (3.3\%) | 472 (3.4\%) | -0.01 | 346 (10.6\%) | 329 (10.1\%) | 0.02 | 813 (4.7\%) | 806 (4.6\%) | 0.00 |
| CKD Stage 3-4; n (\%) | 5 (4.7\%) | 3 (2.8\%) | 0.10 | 247 (1.8\%) | 256 (1.8\%) | 0.00 | 222 (6.8\%) | 214 (6.6\%) | 0.01 | 474 (2.7\%) | 473 (2.7\%) | 0.00 |
| Occurrence of hypertensive |  |  |  |  |  |  |  |  |  |  |  |  |
| nephropathy; n (\%) | 7 (6.5\%) | 3 (2.8\%) | 0.18 | 281 (2.0\%) | 288 (2.0\%) | 0.00 | 272 (8.3\%) | 256 (7.8\%) | 0.02 | 560 (3.2\%) | 547 (3.1\%) | 0.01 |
| Occurrence of miscellaneous renal |  |  |  |  |  |  |  |  |  |  |  |  |
| insufficiency v2; n (\%) | 6 (5.6\%) | 7 (6.5\%) | -0.04 | 348 (2.5\%) | 344 (2.4\%) | 0.01 | 152 (4.7\%) | 126 (3.9\%) | 0.04 | 506 (2.9\%) | 477 (2.7\%) | 0.01 |
| Other Covariates |  |  |  |  |  |  |  |  |  |  |  |  |
| Liver disease; n (\%) | 0 (0.0\%) | 1 (0.9\%) | -0.13 | 183 (1.3\%) | 171 (1.2\%) | 0.01 | 63 (1.9\%) | 60 (1.8\%) | 0.01 | 246 (1.4\%) | 232 (1.3\%) | 0.01 |
| Osteoarthritis; n (\%) | 105 (98.1\%) | 105 (98.1\%) | 0.00 | 13,771 (97.9\%) | 13,741 (97.7\%) | 0.01 | 3,127 (95.8\%) | 3,134 (96.0\%) | -0.01 | 17003 (97.5\%) | 16980 (97.4\%) | 0.01 |
| Other arthritis, arthropathies and |  |  |  |  |  |  |  |  |  |  |  |  |
| musculoskeletal pain; n (\%) | 99 (92.5\%) | 96 (89.7\%) | 0.10 | 12,323 (87.6\%) | 12,304 (87.5\%) | 0.00 | 2,889 (88.5\%) | 2,902 (88.9\%) | -0.01 | 15311 (87.8\%) | 15302 (87.8\%) | 0.00 |
| Dorsopathies; n (\%) | 46 (43.0\%) | 45 (42.1\%) | 0.02 | 5,480 (39.0\%) | 5,477 (38.9\%) | 0.00 | 1,465 (44.9\%) | 1,504 (46.1\%) | -0.02 | 6991 (40.1\%) | 7026 (40.3\%) | 0.00 |
| Fractures; n (\%) | 9 (8.4\%) | 6 (5.6\%) | 0.11 | 986 (7.0\%) | 1,027 (7.3\%) | -0.01 | 483 (14.8\%) | 484 (14.8\%) | 0.00 | 1478 (8.5\%) | 1517 (8.7\%) | -0.01 |
| Falls V ; n (\%) | 4 (3.7\%) | 4 (3.7\%) | 0.00 | 247 (1.8\%) | 268 (1.9\%) | -0.01 | 85 (2.6\%) | 104 (3.2\%) | -0.04 | 336 (1.9\%) | 376 (2.2\%) | -0.02 |
| Osteoporosis; n (\%) | 8 (7.5\%) | 7 (6.5\%) | 0.04 | 846 (6.0\%) | 853 (6.1\%) | 0.00 | 483 (14.8\%) | 485 (14.9\%) | 0.00 | 1337 (7.7\%) | 1345 (7.7\%) | 0.00 |
| Depression; n (\%) | 25 (23.4\%) | 31 (29.0\%) | -0.13 | 1,829 (13.0\%) | 1,881 (13.4\%) | -0.01 | 607 (18.6\%) | 624 (19.1\%) | -0.01 | 2461 (14.1\%) | 2536 (14.5\%) | -0.01 |
| Anxiety; n (\%) | 21 (19.6\%) | 26 (24.3\%) | -0.11 | 1,602 (11.4\%) | 1,590 (11.3\%) | 0.00 | 590 (18.1\%) | 603 (18.5\%) | -0.01 | 2213 (12.7\%) | 2219 (12.7\%) | 0.00 |
| Sleep_Disorder; n (\%) | 8 (7.5\%) | 11 (10.3\%) | -0.10 | 1,629 (11.6\%) | 1,685 (12.0\%) | -0.01 | 286 (8.8\%) | 287 (8.8\%) | 0.00 | 1923 (11.0\%) | 1983 (11.4\%) | -0.01 |
| Dementia; n (\%) | 2 (1.9\%) | 1 (0.9\%) | 0.09 | 109 (0.8\%) | 118 (0.8\%) | 0.00 | 102 (3.1\%) | 97 (3.0\%) | 0.01 | 213 (1.2\%) | 216 (1.2\%) | 0.00 |
| Delirium; n (\%) | $1(0.9 \%)$ | $2(1.9 \%)$ | -0.09 | 88 (0.6\%) | 100 (0.7\%) | -0.01 | $71(2.2 \%)$ | 68 (2.1\%) | 0.01 | 160 (0.9\%) | 170 (1.0\%) | -0.01 |
| Psychosis; n (\%) | 0 (0.0\%) | 0 (0.0\%) | \#DIV/0! | 53 (0.4\%) | 51 (0.4\%) | 0.00 | 49 (1.5\%) | $72(2.2 \%)$ | -0.05 | 102 (0.6\%) | 123 (0.7\%) | -0.01 |
| Obesity; n (\%) | 37 (34.6\%) | 42 (39.3\%) | -0.10 | 3,102 (22.1\%) | 3,175 (22.6\%) | -0.01 | 798 (24.4\%) | 823 (25.2\%) | -0.02 | 3937 (22.6\%) | 4040 (23.2\%) | -0.01 |
| Overweight; n (\%) | 7 (6.5\%) | 7 (6.5\%) | 0.00 | 430 (3.1\%) | 436 (3.1\%) | 0.00 | 179 (5.5\%) | 189 (5.8\%) | -0.01 | 616 (3.5\%) | 632 (3.6\%) | -0.01 |
| Smoking; n (\%) | 42 (39.3\%) | 38 (35.5\%) | 0.08 | 2,492 (17.7\%) | 2,423 (17.2\%) | 0.01 | 1,241 (38.0\%) | 1,174 (36.0\%) | 0.04 | 3775 (21.6\%) | 3635 (20.8\%) | 0.02 |
| Alcohol abuse or dependence; n (\%) | 8 (7.5\%) | $3(2.8 \%)$ | 0.21 | 244 (1.7\%) | 271 (1.9\%) | -0.02 | 49 (1.5\%) | 61 (1.9\%) | -0.03 | 301 (1.7\%) | 335 (1.9\%) | -0.02 |
| Drug abuse or dependence; n (\%) | 5 (4.7\%) | 5 (4.7\%) | 0.00 | 205 (1.5\%) | 211 (1.5\%) | 0.00 | 106 (3.2\%) | 95 (2.9\%) | 0.02 | 316 (1.8\%) | 311 (1.8\%) | 0.00 |
| COPD; n (\%) | 12 (11.2\%) | 12 (11.2\%) | 0.00 | 880 (6.3\%) | 890 (6.3\%) | 0.00 | 481 (14.7\%) | 470 (14.4\%) | 0.01 | 1373 (7.9\%) | 1372 (7.9\%) | 0.00 |
| Asthma; n (\%) | 17 (15.9\%) | 16 (15.0\%) | 0.02 | 1,138 (8.1\%) | 1,170 (8.3\%) | -0.01 | 415 (12.7\%) | 426 (13.0\%) | -0.01 | 1570 (9.0\%) | 1612 (9.2\%) | -0.01 |
| Obstructive sleep apnea; n (\%) | 15 (14.0\%) | 11 (10.3\%) | 0.11 | 1,442 (10.3\%) | 1,469 (10.4\%) | 0.00 | 381 (11.7\%) | 389 (11.9\%) | -0.01 | 1838 (10.5\%) | 1869 (10.7\%) | -0.01 |
| Pneumonia; n (\%) | 2 (1.9\%) | 4 (3.7\%) | -0.11 | 177 (1.3\%) | 181 (1.3\%) | 0.00 | 104 (3.2\%) | 106 (3.2\%) | 0.00 | 283 (1.6\%) | 291 (1.7\%) | -0.01 |
| Other Medications |  |  |  |  |  |  |  |  |  |  |  |  |
| Use of ACE inhibitors; n (\%) | 27 (25.2\%) | 23 (21.5\%) | 0.09 | 3,154 (22.4\%) | 3,178 (22.6\%) | 0.00 | 913 (28.0\%) | 952 (29.2\%) | -0.03 | 4094 (23.5\%) | 4153 (23.8\%) | -0.01 |
| Use of ARBS; n (\%) | 17 (15.9\%) | 14 (13.1\%) | 0.08 | 2,240 (15.9\%) | 2,264 (16.1\%) | -0.01 | 653 (20.0\%) | 652 (20.0\%) | 0.00 | 2910 (16.7\%) | 2930 (16.8\%) | 0.00 |
| Use of Loop Diuretics - United; n (\%) | 5 (4.7\%) | 0 (0.0\%) | 0.31 | 494 (3.5\%) | 517 (3.7\%) | -0.01 | 340 (10.4\%) | 344 (10.5\%) | 0.00 | 839 (4.8\%) | 861 (4.9\%) | 0.00 |
| Use of other diuretics-United; n (\%) | 2 (1.9\%) | 0 (0.0\%) | 0.20 | 149 (1.1\%) | 142 (1.0\%) | 0.01 | 87 (2.7\%) | 77 (2.4\%) | 0.02 | 238 (1.4\%) | 219 (1.3\%) | 0.01 |
| Use of nitrates-United; n (\%) | $1(0.9 \%)$ | 1 (0.9\%) | 0.00 | 179 (1.3\%) | 182 (1.3\%) | 0.00 | 113 (3.5\%) | 101 (3.1\%) | 0.02 | 293 (1.7\%) | 284 (1.6\%) | 0.01 |
| Use of other hypertension drugs; n |  |  |  |  |  |  |  |  |  |  |  |  |
| (\%) | 1 (0.9\%) | 1 (0.9\%) | 0.00 | 366 (2.6\%) | 387 (2.8\%) | -0.01 | 179 (5.5\%) | 184 (5.6\%) | 0.00 | 546 (3.1\%) | 572 (3.3\%) | -0.01 |
| Use of Anti-arrhythmics; n (\%) | 0 (0.0\%) | 1 (0.9\%) | -0.13 | 91 (0.6\%) | 89 (0.6\%) | 0.00 | 138 (4.2\%) | 143 (4.4\%) | -0.01 | 229 (1.3\%) | 233 (1.3\%) | 0.00 |
| Use of COPD/asthma meds-United; n |  |  |  |  |  |  |  |  |  |  |  |  |
| (\%) | 12 (11.2\%) | 16 (15.0\%) | -0.11 | 1,984 (14.1\%) | 1,911 (13.6\%) | 0.01 | 640 (19.6\%) | 594 (18.2\%) | 0.04 | 2636 (15.1\%) | 2521 (14.5\%) | 0.02 |
| Use of statins; n (\%) | 29 (27.1\%) | 26 (24.3\%) | 0.06 | 4,598 (32.7\%) | 4,654 (33.1\%) | -0.01 | 1,483 (45.4\%) | 1,448 (44.3\%) | 0.02 | 6110 (35.0\%) | 6128 (35.1\%) | 0.00 |
| Use of other lipid-lowering drugs; n |  |  |  |  |  |  |  |  |  |  |  |  |
| (\%) | 6 (5.6\%) | 5 (4.7\%) | 0.04 | 800 (5.7\%) | 841 (6.0\%) | -0.01 | 228 (7.0\%) | 221 (6.8\%) | 0.01 | 1034 (5.9\%) | 1067 (6.1\%) | -0.01 |
| Use of antiplatelet agents; n (\%) | 6 (5.6\%) | 12 (11.2\%) | -0.20 | 702 (5.0\%) | 658 (4.7\%) | 0.01 | 242 (7.4\%) | 218 (6.7\%) | 0.03 | 950 (5.4\%) | 888 (5.1\%) | 0.01 |
| Use of heparin and other low- |  |  |  |  |  |  |  |  |  |  |  |  |
| molecular weight hepariss; n (\%) | 0 (0.0\%) | 0 (0.0\%) | \#Div/0! | 2 (0.0\%) | 2 (0.0\%) | \#DIV/0! | 18 (0.6\%) | 19 (0.6\%) | 0.00 | 20 (0.1\%) | 21 (0.1\%) | 0.00 |
| Use of NSAIS; n (\%) | 50 (46.7\%) | 49 (45.8\%) | 0.02 | 5,648 (40.2\%) | 5,696 (40.5\%) | -0.01 | 1,122 (34.4\%) | 1,144 (35.0\%) | -0.01 | 6820 (39.1\%) | 6889 (39.5\%) | -0.01 |
| Use of opioids-United; n (\%) | 72 (67.3\%) | 74 (69.2\%) | -0.04 | 12,495 (88.8\%) | 12,506 (88.9\%) | 0.00 | 2,831 (86.7\%) | 2,834 (86.8\%) | 0.00 | 15398 (88.3\%) | 15414 (88.4\%) | 0.00 |
| Use of antidepressants; n (\%) | 33 (30.8\%) | 27 (25.2\%) | 0.12 | 3,339 (23.7\%) | 3,410 (24.2\%) | -0.01 | 1,018 (31.2\%) | 1,029 (31.5\%) | -0.01 | 4390 (25.2\%) | 4466 (25.6\%) | -0.01 |
| Use of antipsychotics; n (\%) | 2 (1.9\%) | 1 (0.9\%) | 0.09 | 214 (1.5\%) | 246 (1.7\%) | -0.02 | 130 (4.0\%) | 146 (4.5\%) | $-0.02$ | 346 (2.0\%) | 393 (2.3\%) | -0.02 |
| Labs |  |  |  |  |  |  |  |  |  | 14,173 | 14,173 |  |
| Lab values- HbA1c (\%) v3; n (\%) | 11 (10.3\%) | 16 (15.0\%) | -0.14 | 136 (1.0\%) | 118 (0.8\%) | 0.02 | N/A | N/A | \#value! | 147 (1.0\%) | 134 (0.9\%) | 0.01 |

## Appendix B

| Lab values- HbA1c (\%) (within 3 months) v3; n (\%) | 7 (6.5\%) | 15 (14.0\%) | -0.25 | 95 (0.7\%) | 72 (0.5\%) | 0.03 | N/A | N/A | \#VALUE! | 102 (0.7\%) | 087 (0.6\%) | 0.01 |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Lab values- - HbAlc (\%) (within 6 |  |  |  |  |  |  |  |  |  |  |  |  |
| months) $\mathbf{3}$; n (\%) | 11 (10.3\%) | 16 (15.0\%) | -0.14 | 136 (1.0\%) | 118 (0.8\%) | 0.02 | N/A | N/A | \#value! | 147 (1.0\%) | 134 (0.9\%) | 0.01 |
| Lab values- BNP; n (\%) | 0 (0.0\%) | 0 (0.0\%) | \#DIV/0! | 2 (0.0\%) | $2(0.0 \%)$ | \#Div/0! | N/A | N/A | \#value! | $2(0.0 \%)$ | 2 (0.0\%) | \#Div/0! |
| Lab values- BNP (within 3 months); n |  |  |  |  |  |  |  |  |  |  |  |  |
| (\%) | 0 (0.0\%) | 0 (0.0\%) | \#Div/0! | 2 (0.0\%) | 1 (0.0\%) | \#DIV/0! | N/A | N/A | \#value! | 02 (0.0\%) | 01 (0.0\%) | \#Div/o! |
| Lab values- BNP (within 6 months); n |  |  |  |  |  |  |  |  |  |  |  |  |
| (\%) | 0 (0.0\%) | 0 (0.0\%) | \#Div/0! | 2 (0.0\%) | 2 (0.0\%) | \#DIV/0! | N/A | N/A | \#Value! | 2 (0.0\%) | 2 (0.0\%) | \#Div/o! |
| Lab values- BUN (mg/dl); n (\%) | 25 (23.4\%) | 40 (37.4\%) | -0.31 | 166 (1.2\%) | 161 (1.1\%) | 0.01 | N/A | N/A | \#value! | 191 (1.3\%) | 201 (1.4\%) | -0.01 |
| Lab values- BUN (mg/d) (within 3 |  |  |  |  |  |  |  |  |  |  |  |  |
| months); n (\%) | 18 (16.8\%) | 34 (31.8\%) | -0.36 | 139 (1.0\%) | 121 (0.9\%) | 0.01 | N/A | N/A | \#value! | 157 (1.1\%) | 155 (1.1\%) | 0.00 |
| Lab values- BUN (mg/di) (within 6 |  |  |  |  |  |  |  |  |  |  |  |  |
| months); n (\%) | 25 (23.4\%) | 40 (37.4\%) | -0.31 | 166 (1.2\%) | 161 (1.1\%) | 0.01 | N/A | N/A | \#value! | 191 (1.3\%) | 201 (1.4\%) | -0.01 |
| Lab values-Creatinine (mg/d) v2; n |  |  |  |  |  |  |  |  |  |  |  |  |
| (\%) | 27 (25.2\%) | 41 (38.3\%) | -0.28 | 171 (1.2\%) | 167 (1.2\%) | 0.00 | N/A | N/A | \#value! | 198 (1.4\%) | 208 (1.5\%) | -0.01 |
| Lab values- Creatinine (mg/dl) (within |  |  |  |  |  |  |  |  |  |  |  |  |
| 3 months) v2; ${ }^{\text {(\%) }}$ | 19 (17.8\%) | 35 (32.7\%) | -0.35 | 144 (1.0\%) | 125 (0.9\%) | 0.01 | N/A | N/A | \#value! | 163 (1.2\%) | 160 (1.1\%) | 0.01 |
| Lab values-Creatinine ( $\mathrm{mg} / \mathrm{dl}$ ) (within |  |  |  |  |  |  |  |  |  |  |  |  |
| 6 months) v2; n (\%) | 27 (25.2\%) | 41 (38.3\%) | -0.28 | 171 (1.2\%) | 167 (1.2\%) | 0.00 | N/A | N/A | \#VALUE! | 198 (1.4\%) | 208 (1.5\%) | -0.01 |
| Lab values- HDL level (mg/dl); n (\%) | 21 (19.6\%) | 22 (20.6\%) | -0.02 | 125 (0.9\%) | 126 (0.9\%) | 0.00 | N/A | N/A | \#value! | 146 (1.0\%) | 148 (1.0\%) | 0.00 |
| Lab values-HDL level ( $\mathrm{mg} / \mathrm{dll}$ ) (within |  |  |  |  |  |  |  |  |  |  |  |  |
| 3 months); n (\%) | 15 (14.0\%) | 16 (15.0\%) | -0.03 | 72 (0.5\%) | 70 (0.5\%) | 0.00 | N/A | N/A | \#value! | 087 (0.6\%) | 086 (0.6\%) | 0.00 |
| Lab values- HDL level (mg/dl) (within |  |  |  |  |  |  |  |  |  |  |  |  |
| 6 months); n (\%) | 21 (19.6\%) | 22 (20.6\%) | -0.02 | 125 (0.9\%) | 126 (0.9\%) | 0.00 | N/A | N/A | \#Value! | 146 (1.0\%) | 148 (1.0\%) | 0.00 |
| Lab values-LDL level (mg/dl) v2; n (\%) | 20 (18.7\%) | 22 (20.6\%) | -0.05 | 131 (0.9\%) | 125 (0.9\%) | 0.00 | N/A | N/A | \#value! | 151 (1.1\%) | 147 (1.0\%) | 0.01 |
| Lab values- LDL level (mg/d) ( (ithin 3 |  |  |  |  |  |  |  |  |  |  |  |  |
| months) V2; n (\%) | 14 (13.1\%) | 16 (15.0\%) | -0.05 | 77 (0.5\%) | 69 (0.5\%) | 0.00 | N/A | N/A | \#value! | 091 (0.6\%) | 085 (0.6\%) | 0.00 |
| Lab values- LDL level (mg/d) ( (ithin 6 |  |  |  |  |  |  |  |  |  |  |  |  |
| months) v2; n (\%) | 20 (18.7\%) | 22 (20.6\%) | -0.05 | 131 (0.9\%) | 125 (0.9\%) | 0.00 | N/A | N/A | \#value! | 151 (1.1\%) | 147 (1.0\%) | 0.01 |
| Lab values- NT-proBNP; n (\%) | 0 (0.0\%) | 0 (0.0\%) | \#DIV/0! | 0 (0.0\%) | 0 (0.0\%) | \#DIV/0! | N/A | N/A | \#VALUE! | 00 (0.0\%) | 0 (0.0\%) | \#Div/o! |
| Lab values-NT-proBNP (within 3 |  |  |  |  |  |  |  |  |  |  |  |  |
| months); n (\%) | 0 (0.0\%) | 0 (0.0\%) | \#Div/0! | 0 (0.0\%) | 0 (0.0\%) | \#DIV/0! | N/A | N/A | \#value! | 00 (0.0\%) | 0 (0.0\%) | \#Div/0! |
| Lab values- NT-proBNP (within 6 |  |  |  |  |  |  |  |  |  |  |  |  |
| months); n (\%) | 0 (0.0\%) | 0 (0.0\%) | \#Div/0! | 0 (0.0\%) | 0 (0.0\%) | \#DIV/0! | N/A | N/A | \#value! | 00 (0.0\%) | 0 (0.0\%) | \#DIV/0! |
| Lab values- Total cholesterol (mg/dl) |  |  |  |  |  |  |  |  |  |  |  |  |
| v2; n (\%) | 21 (19.6\%) | 22 (20.6\%) | -0.02 | 126 (0.9\%) | 126 (0.9\%) | 0.00 | N/A | N/A | \#value! | 147 (1.0\%) | 148 (1.0\%) | 0.00 |
| Lab values- Total cholesterol (mg/dl) |  |  |  |  |  |  |  |  |  |  |  |  |
| (within 3 months) v2; $n$ (\%) | 15 (14.0\%) | 16 (15.0\%) | -0.03 | 72 (0.5\%) | 70 (0.5\%) | 0.00 | N/A | N/A | \#value! | 087 (0.6\%) | 086 (0.6\%) | 0.00 |
| Lab values- Total cholesterol (mg/d) |  |  |  |  |  |  |  |  |  |  |  |  |
| (within 6 months) v2; $n$ (\%) | 21 (19.6\%) | 22 (20.6\%) | -0.02 | 126 (0.9\%) | 126 (0.9\%) | 0.00 | N/A | N/A | \#value! | 147 (1.0\%) | 148 (1.0\%) | 0.00 |
| Lab values- Triglyceride level ( $\mathrm{mg} / \mathrm{d}$ ) ; |  |  |  |  |  |  |  |  |  |  |  |  |
| n (\%) | 21 (19.6\%) | 22 (20.6\%) | -0.02 | 125 (0.9\%) | 122 (0.9\%) | 0.00 | N/A | N/A | \#Value! | 146 (1.0\%) | 144 (1.0\%) | 0.00 |
| Lab values- Triglyceride level (mg/d) |  |  |  |  |  |  |  |  |  |  |  |  |
| (within 3 months); n (\%) | 15 (14.0\%) | 16 (15.0\%) | -0.03 | 71 (0.5\%) | 66 (0.5\%) | 0.00 | N/A | N/A | \#VaLuE! | 086 (0.6\%) | 082 (0.6\%) | 0.00 |
| Lab values- Triglyceride level (mg/d) |  |  |  |  |  |  |  |  |  |  |  |  |
| (within 6 months); n (\%) | 21 (19.6\%) | 22 (20.6\%) | -0.02 | 125 (0.9\%) | 122 (0.9\%) | 0.00 | N/A | N/A | \#VaLuE! | 146 (1.0\%) | 144 (1.0\%) | 0.00 |
| Lab result number- HbA1c (\%) mean |  |  |  |  |  |  |  |  |  |  |  |  |
| (only 2 to 20 included) v4 | 11 | 16 |  | 115 | 109 |  | N/A | N/A |  | 126 | 125 |  |
| ...mean (sd) | 5.69 (0.65) | 5.72 (0.61) | -0.05 | 6.86 (1.63) | 6.46 (1.29) | 0.27 | N/A | N/A | \#Value! | 6.76 (1.58) | 6.37 (1.23) | 0.28 |
| ...Missing; n (\%) | 96 (89.7\%) | 91 (85.0\%) | 0.14 | 13,951 (99.2\%) | 13,957 (99.2\%) | 0.00 | N/A | N/A | \#VALUE! | 14,047 (99.1\%) | 14,048 (99.1\%) | 0.00 |
| Lab result number- BNP mean v2 | - | - |  | 2 | 2 |  | N/A | N/A |  | 2 | 2 |  |
| ...mean (sd) | -(-) | -(-) | \#Value! | 102.50 (89.80) | 35.55 (38.82) | 0.97 | N/A | N/A | \#value! | \#VALUE! | \#VALUE! | \#VaLuE! |
| ...Missing; n (\%) | 107 (100.0\%) | 107 (100.0\%) | \#DIV/0! | 14,064 (100.0\%) | 14,064 (100.0\%) | \#DIV/0! | N/A | N/A | \#VaLuE! | 14,171 (100.0\%) | 14,171 (100.0\%) | \#DIV/0! |
| Lab result number-BUN (mg/di) mean |  |  |  |  |  |  |  |  |  |  |  |  |
| $v 2$ | 25 | 40 |  | 166 | 161 |  | N/A | N/A |  | 191 | 201 |  |
| ...mean (sd) | 14.94 (5.61) | 16.13 (4.47) | -0.23 | 16.91 (5.75) | 17.73 (7.38) | -0.12 | N/A | N/A | \#VaLuE! | 16.65 (5.75) | 17.41 (6.92) | -0.12 |
| ...Missing; n (\%) | 82 (76.6\%) | 67 (62.6\%) | 0.31 | 13,900 (98.8\%) | 13,905 (98.9\%) | -0.01 | N/A | N/A | \#VaLuE! | 13,982 (98.7\%) | 13,972 (98.6\%) | 0.01 |
| Lab result number- Creatinine (mg/dl) |  |  |  |  |  |  |  |  |  |  |  |  |
| mean (only 0.1 to 15 included) v3 | 27 | 41 |  | 164 | 158 |  | N/A | N/A |  | 191 | 199 |  |
| ...mean (sd) | 0.79 (0.18) | 0.90 (0.25) | -0.50 | 0.90 (0.23) | 0.95 (0.25) | -0.21 | N/A | N/A | \#VALUE! | 0.88 (0.22) | 0.94 (0.25) | -0.25 |
| ...Missing; n (\%) | 80 (74.8\%) | 66 (61.7\%) | 0.28 | 13,902 (98.8\%) | 13,908 (98.9\%) | -0.01 | N/A | N/A | \#VALUE! | 13,982 (98.7\%) | 13,974 (98.6\%) | 0.01 |
| Lab result number-HDL level (mg/dl) |  |  |  |  |  |  |  |  |  |  |  |  |
| mean (only $=55000$ included) v2 | 21 | 22 |  | 125 | 126 |  | N/A | N/A |  | 146 | 148 |  |
| ...mean (sd) | 56.98 (13.95) | 60.50 (21.22) | -0.20 | 49.39 (17.42) | 51.96 (20.30) | -0.14 | N/A | N/A | \#VALUE! | 50.48 (17.04) | 53.23 (20.51) | -0.15 |
| ...Missing; n (\%) | 86 (80.4\%) | 85 (79.4\%) | 0.02 | 13,941 (99.1\%) | 13,940 (99.1\%) | 0.00 | N/A | N/A | \#VALUE! | 14,027 (99.0\%) | 14,025 (99.0\%) | 0.00 |
| Lab result number-LDL level ( $\mathrm{mg} / \mathrm{dl}$ ) |  |  |  |  |  |  |  |  |  |  |  |  |
| mean (only $=55000$ included) v2 | 20 | 22 |  | 125 | 119 |  | N/A | N/A |  | 145 | 141 |  |
| ...mean (sd) | 110.05 (30.80) | 110.57 (33.47) | -0.02 | 95.17 (41.62) | 95.19 (40.07) | 0.00 | N/A | N/A | \#VALUE! | 97.22 (40.49) | 97.59 (39.29) | -0.01 |

## Appendix B



| 87 (81.3\%) | 85 (79.4\%) | 0.05 | 13,941 (99.1\%) | 13,947 (99.2\%) | -0.01 |
| :---: | :---: | :---: | :---: | :---: | :---: |
| 21 | 22 |  | 126 | 126 |  |
| 194.67 (33.54) | 190.14 (40.99) | 0.12 | 173.55 (50.72) | 178.39 (50.25) | -0.10 |
| 86 (80.4\%) | 85 (79.4\%) | 0.02 | 13,940 (99.1\%) | 13,940 (99.1\%) | 0.00 |
| 21 | 22 |  | 125 | 122 |  |
| 133.29 (57.02) | 97.52 (48.21) | 0.68 | 147.76 (90.74) | 154.99 (99.96) | -0.08 |
| 86 (80.4\%) | 85 (79.4\%) | 0.02 | 13,941 (99.1\%) | 13,944 (99.1\%) | 0.00 |
| 27 | 36 |  | 134 | 132 |  |
| 14.11 (1.18) | 13.80 (1.77) | 0.21 | 13.30 (2.58) | 12.99 (2.98) | 0.11 |
| 80 (74.8\%) | 71 (66.4\%) | 0.19 | 13,932 (99.0\%) | 13,934 (99.1\%) | -0.01 |
| 27 | 41 |  | 153 | 146 |  |
| 140.69 (2.32) | 140.84 (2.63) | -0.06 | 139.67 (2.23) | 139.69 (2.13) | -0.01 |
| 80 (74.8\%) | 66 (61.7\%) | 0.28 | 13,913 (98.9\%) | 13,920 (99.0\%) | -0.01 |
| 26 | 36 |  | 119 | 126 |  |
| 4.24 (0.39) | 4.31 (0.27) | -0.21 | 4.23 (0.63) | 4.23 (0.82) | 0.00 |
| 81 (75.7\%) | 71 (66.4\%) | 0.21 | 13,947 (99.2\%) | 13,940 (99.1\%) | 0.01 |
| 27 | 40 |  | 153 | 137 |  |
| 102.14 (31.99) | 97.65 (21.67) | 0.16 | 122.92 (42.46) | 116.13 (35.05) | 0.17 |
| 80 (74.8\%) | 67 (62.6\%) | 0.27 | 13,913 (98.9\%) | 13,929 (99.0\%) | -0.01 |
| 27 | 41 |  | 160 | 149 |  |
| 4.36 (0.33) | 4.30 (0.46) | 0.15 | 4.35 (0.38) | 4.36 (0.43) | -0.02 |
| 80 (74.8\%) | 66 (61.7\%) | 0.28 | 13,906 (98.9\%) | 13,917 (98.9\%) | 0.00 |
| 1.12 (2.02) | 1.40 (1.95) | -0.14 | 0.51 (1.45) | 0.52 (1.50) | -0.01 |
| 63 (58.9\%) | 59 (55.1\%) | 0.08 | 6,861 (48.8\%) | 6,990 (49.7\%) | -0.02 |
| 0.17 (0.05) | 0.17 (0.05) | 0.00 | 0.16 (0.04) | 0.16 (0.04) | 0.00 |
| 106 (99.1\%) | 107 (100.0\%) | -0.13 | 14,066 (100.0\%) | 14,066 (100.0\%) | \#Div/0! |
| 105 (98.1\%) | 107 (100.0\%) | -0.20 | 14,055 (99.9\%) | 14,047 (99.9\%) | 0.00 |
| 8 (7.5\%) | 7 (6.5\%) | 0.04 | 486 (3.5\%) | 507 (3.6\%) | -0.01 |
| 83 (77.6\%) | 82 (76.6\%) | 0.02 | 11,722 (83.3\%) | 11,926 (84.8\%) | -0.04 |
| 72 (67.3\%) | 59 (55.1\%) | 0.25 | 9,021 (64.1\%) | 8,971 (63.8\%) | 0.01 |
| 51 (47.7\%) | 71 (66.4\%) | -0.38 | 9,702 (69.0\%) | 10,038 (71.4\%) | -0.05 |
| 54 (50.5\%) | 61 (57.0\%) | -0.13 | 4,970 (35.3\%) | 4,982 (35.4\%) | 0.00 |
| 45 (42.1\%) | 49 (45.8\%) | -0.07 | 3,723 (26.5\%) | 3,655 (26.0\%) | 0.01 |
| 17 (15.9\%) | 27 (25.2\%) | -0.23 | 2,001 (14.2\%) | 2,015 (14.3\%) | 0.00 |
| 85 (79.4\%) | 97 (90.7\%) | -0.32 | 10,886 (77.4\%) | 10,967 (78.0\%) | -0.01 |
| 0 (0.0\%) | 1 (0.9\%) | -0.13 | 54 (0.4\%) | 87 (0.6\%) | -0.03 |
| 0 (0.0\%) | 0 (0.0\%) | \#DIV/0! | 1 (0.0\%) | 1 (0.0\%) | \#DIV/0! |
| 8.14 (5.20) | 7.94 (4.36) | 0.04 | 8.46 (4.46) | 8.59 (4.56) | -0.03 |
| 1.11 (0.37) | 1.09 (0.35) | 0.06 | 1.06 (0.28) | 1.06 (0.27) | 0.00 |
| 2.44 (2.66) | 2.59 (1.99) | -0.06 | 3.51 (2.21) | 3.54 (2.43) | -0.01 |
| 0.48 (1.22) | 0.42 (1.17) | 0.05 | 0.13 (1.01) | 0.13 (1.01) | 0.00 |
| 7.42 (5.03) | 7.62 (5.67) | -0.04 | 6.41 (3.99) | 6.50 (4.12) | -0.02 |


| N/A | N/A | \#Value! | 14,028 (99.0\%) | 14,032 (99.0\%) | 0.00 |
| :---: | :---: | :---: | :---: | :---: | :---: |
| N/A | N/A |  | 147 | 148 |  |
| N/A | N/A | \#Value! | 176.57 (48.88) | 180.14 (49.19) | -0.07 |
| N/A | N/A | \#Value! | 14,026 (99.0\%) | 14,025 (99.0\%) | 0.00 |
| N/A | N/A |  | 146 | 144 |  |
| N/A | N/A | \#value! | 145.68 (87.15) | 146.21 (90.82) | -0.01 |
| N/A | N/A | \#Value! | 14,027 (99.0\%) | 14,029 (99.0\%) | 0.00 |
| N/A | N/A |  | 161 | 168 |  |
| N/A | N/A | \#Value! | 13.44 (2.42) | 13.16 (2.78) | 0.11 |
| N/A | N/A | \#Value! | 14,012 (98.9\%) | 14,005 (98.8\%) | 0.01 |
| N/A | N/A |  | 180 | 187 |  |
| N/A | N/A | \#Value! | 139.82 (2.25) | 139.94 (2.25) | -0.05 |
| N/A | N/A | \#VALUE! | 13,993 (98.7\%) | 13,986 (98.7\%) | 0.00 |
| N/A | N/A |  | 145 | 162 |  |
| N/A | N/A | \#Value! | 4.23 (0.60) | 4.25 (0.74) | -0.03 |
| N/A | N/A | \#VALUE! | 14,028 (99.0\%) | 14,011 (98.9\%) | 0.01 |
| N/A | N/A |  | 180 | 177 |  |
| N/A | N/A | \#Value! | 119.80 (41.21) | 111.95 (32.64) | 0.21 |
| N/A | N/A | \#VALUE! | 13,993 (98.7\%) | 13,996 (98.8\%) | -0.01 |
| N/A | N/A |  | 187 | 190 |  |
| N/A | N/A | \#Value! | 4.35 (0.37) | 4.35 (0.44) | 0.00 |
| N/A | N/A | \#Value! | 13,986 (98.7\%) | 13,983 (98.7\%) | 0.00 |
| 1.70 (2.24) | 1.67 (2.23) | 0.01 | 0.74 (1.63) | 0.74 (1.66) | 0.00 |
| 86 (2.6\%) | 52 (1.6\%) | 0.07 | 7010 (40.2\%) | 7101 (40.7\%) | -0.01 |
| 0.19 (0.06) | 0.19 (0.06) | 0.00 | 0.17 (0.04) | 0.17 (0.04) | 0.00 |
| 3,265 (100.0\%) | 3,265 (100.0\%) | \#Div/0! | 17,437 (100.0\%) | 17,438 (100.0\%) | \#DIV/0! |
| 3,253 (99.6\%) | 3,234 (99.1\%) | 0.06 | 17413 (99.9\%) | 17388 (99.7\%) | 0.04 |
| 324 (9.9\%) | 349 (10.7\%) | -0.03 | 818 (4.7\%) | 863 (4.9\%) | -0.01 |
| 2,991 (91.6\%) | 2,995 (91.7\%) | 0.00 | 14796 (84.8\%) | 15003 (86.0\%) | -0.03 |
| 2,593 (79.4\%) | 2,591 (79.4\%) | 0.00 | 11686 (67.0\%) | 11621 (66.6\%) | 0.01 |
| 2,423 (74.2\%) | 2,452 (75.1\%) | ${ }^{-0.02}$ | 12176 (69.8\%) | 12561 (72.0\%) | -0.05 |
| 1,988 (60.9\%) | 1,977 (60.6\%) | 0.01 | 7012 (40.2\%) | 7020 (40.3\%) | 0.00 |
| 1,396 (42.8\%) | 1,355 (41.5\%) | 0.03 | 5164 (29.6\%) | 5059 (29.0\%) | 0.01 |
| 1,155 (35.4\%) | 1,204 (36.9\%) | -0.03 | 3173 (18.2\%) | 3246 (18.6\%) | -0.01 |
| 2,831 (86.7\%) | 2,861 (87.6\%) | -0.03 | 13802 (79.1\%) | 13925 (79.9\%) | -0.02 |
| 23 (0.7\%) | 26 (0.8\%) | -0.01 | 77 (0.4\%) | 114 (0.7\%) | -0.04 |
| 1 (0.0\%) | 0 (0.0\%) | \#DiV/0! | 2 (0.0\%) | 1 (0.0\%) | \#DIV/0! |
| 10.42 (4.93) | 10.53 (4.98) | -0.02 | 8.83 (4.56) | 8.95 (4.64) | -0.03 |
| 1.20 (0.54) | 1.21 (0.54) | -0.02 | 1.09 (0.34) | 1.09 (0.34) | 0.00 |
| 4.96 (4.57) | 4.93 (4.38) | 0.01 | 3.77 (2.81) | 3.79 (2.89) | -0.01 |
| 0.74 (1.94) | 0.81 (2.53) | -0.03 | 0.25 (1.24) | 0.26 (1.42) | -0.01 |
| 16.83 (12.94) | 16.94 (12.61) | -0.01 | 8.37 (6.66) | 8.46 (6.61) | -0.01 |

## Appendix B

| Number of internal medicine/family medicine visits |  |  |  |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| ...mean (sd) | 4.64 (7.05) | 7.58 (16.00) | -0.24 | 6.16 (8.17) | 6.37 (8.70) | -0.02 | 9.34 (9.94) | 9.35 (9.72) | 0.00 | 6.75 (8.52) | 6.94 (8.96) | -0.02 |
| Number of Cardiologist visits |  |  |  |  |  |  |  |  |  |  |  |  |
| ...mean (sd) | 1.65 (3.01) | 1.95 (3.07) | -0.10 | 0.97 (2.21) | 0.97 (2.27) | 0.00 | 2.49 (4.14) | 2.59 (4.60) | -0.02 | 1.26 (2.68) | 1.28 (2.86) | -0.01 |
| Number electrocardiograms received |  |  |  |  |  |  |  |  |  |  |  |  |
| v2 |  |  |  |  |  |  |  |  |  |  |  |  |
| ...mean (sd) | 1.49 (1.25) | 1.62 (1.07) | -0.11 | 1.19 (1.01) | 1.19 (0.98) | 0.00 | 1.80 (1.54) | 1.82 (1.52) | -0.01 | 1.31 (1.13) | 1.31 (1.10) | 0.00 |
| Number of HbA1c tests ordered |  |  |  |  |  |  |  |  |  |  |  |  |
| ...mean (sd) | 0.41 (0.61) | 0.49 (0.79) | -0.11 | 0.24 (0.57) | 0.25 (0.58) | -0.02 | 0.40 (0.73) | 0.41 (0.72) | -0.01 | 0.27 (0.60) | 0.28 (0.61) | -0.02 |
| Number of glucose tests ordered |  |  |  |  |  |  |  |  |  |  |  |  |
| ...mean (sd) | 0.10 (0.33) | 0.18 (1.20) | -0.09 | 0.08 (0.36) | 0.08 (0.40) | 0.00 | 0.11 (0.48) | 0.11 (0.47) | 0.00 | 0.09 (0.39) | 0.09 (0.42) | 0.00 |
| Number of lipid tests ordered |  |  |  |  |  |  |  |  |  |  |  |  |
| ...mean (sd) | 0.55 (0.87) | 0.49 (0.65) | 0.08 | 0.46 (0.81) | 0.47 (0.81) | -0.01 | 0.57 (0.69) | 0.57 (0.71) | 0.00 | 0.48 (0.79) | 0.49 (0.79) | -0.01 |
| Total N distinct ICD9/ICD10 diagnoses at the 3 rd digit level Copy |  |  |  |  |  |  |  |  |  |  |  |  |
| ...mean (sd) | 11.04 (11.14) | 9.78 (10.49) | 0.12 | 3.63 (6.39) | 3.62 (6.31) | 0.00 | 12.35 (12.72) | 12.26 (12.44) | 0.01 | 5.31 (8.00) | 5.28 (7.86) | 0.00 |
| For PS |  |  |  |  |  |  |  |  |  |  |  |  |
| Hemorrhagic stroke+Other cerebrovascular |  |  |  |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |
| disease+Cerebrovascular procedure |  |  |  |  |  |  |  |  |  |  |  |  |
| (for PS); n (\%) | 1 (0.9\%) | 0 (0.0\%) | 0.13 | 76 (0.5\%) | 78 (0.6\%) | -0.01 | 31 (0.9\%) | 35 (1.1\%) | -0.02 | 108 (0.6\%) | 113 (0.6\%) | 0.00 |
| Major trauma potentially causing prolc | **(2.8\%) | **(1.9\%) | \#Div/0! | 316 (2.2\%) | 336 (2.4\%) | \#DIV/0! | 180 (5.5\%) | 174 (5.3\%) | \#Div/0! | 316 (2.2\%) | 336 (2.4\%) | -0.01 |
| Occurrence of creatinine tests |  |  |  |  |  |  |  |  |  |  |  |  |
| ordered (for PS); n (\%) | 14 (13.1\%) | 4 (3.7\%) | 0.34 | 1,125 (8.0\%) | 693 (4.9\%) | 0.13 | 374 (11.5\%) | 264 (8.1\%) | 0.11 | 1513 (8.7\%) | 961 (5.5\%) | 0.12 |
| Occurrence of BUN tests ordered (for |  |  |  |  |  |  |  |  |  |  |  |  |
| PS); n (\%) | 8 (7.5\%) | 3 (2.8\%) | 0.21 | 775 (5.5\%) | 437 (3.1\%) | 0.12 | 203 (6.2\%) | 164 (5.0\%) | 0.05 | 986 (5.7\%) | 604 (3.5\%) | 0.11 |
| Occurrence of chronic renal |  |  |  |  |  |  |  |  |  |  |  |  |
| insufficiency w/o CKD (for PS) v2; n |  |  |  |  |  |  |  |  |  |  |  |  |
| (\%) | 2 (1.9\%) | 1 (0.9\%) | 0.09 | 225 (1.6\%) | 224 (1.6\%) | 0.00 | 156 (4.8\%) | 161 (4.9\%) | 0.00 | 383 (2.2\%) | 386 (2.2\%) | 0.00 |
| Chronic kidney disease Stage 1-2 (for |  |  |  |  |  |  |  |  |  |  |  |  |
| PS); n (\%) | 0 (0.0\%) | 2 (1.9\%) | -0.20 | 106 (0.8\%) | 101 (0.7\%) | 0.01 | 47 (1.4\%) | 47 (1.4\%) | 0.00 | 153 (0.9\%) | 150 (0.9\%) | 0.00 |
| Chronic kidney disease Stage $3-6$ (for |  |  |  |  |  |  |  |  |  |  |  |  |
| PS); n (\%) | 5 (4.7\%) | 3 (2.8\%) | 0.10 | 247 (1.8\%) | 256 (1.8\%) | 0.00 | 222 (6.8\%) | 214 (6.6\%) | 0.01 | 474 (2.7\%) | 473 (2.7\%) | 0.00 |
| Acute kidney injury; n (\%) | **(3.7\%) | **(1.9\%) | \#Div/0! | 261 (1.9\%) | 270 (1.9\%) | \#DIV/0! | 158 (4.8\%) | 160 (4.9\%) | \#Div/0! | 261 (1.9\%) | 270 (1.9\%) | 0.00 |
| Bladder stones+kidney stones (for |  |  |  |  |  |  |  |  |  |  |  |  |
| PS); n (\%) | 4 (3.7\%) | 2 (1.9\%) | 0.11 | 266 (1.9\%) | 223 (1.6\%) | 0.02 | 66 (2.0\%) | 70 (2.1\%) | -0.01 | 336 (1.9\%) | 295 (1.7\%) | 0.02 |
| Alcohol abuse or dependence+Drug |  |  |  |  |  |  |  |  |  |  |  |  |
| abuse or dependence (for PS); n (\%) | 12 (11.2\%) | 8 (7.5\%) | 0.13 | 435 (3.1\%) | 450 (3.2\%) | $-0.01$ | 147 (4.5\%) | 151 (4.6\%) | 0.00 | 594 (3.4\%) | 609 (3.5\%) | -0.01 |
| Other atherosclerosis + Cardiac |  |  |  |  |  |  |  |  |  |  |  |  |
| conduction disorders+Other CVD (for |  |  |  |  |  |  |  |  |  |  |  |  |
| PS) v2 Copy; n (\%) | 12 (11.2\%) | 17 (15.9\%) | -0.14 | 1,530 (10.9\%) | 1,529 (10.9\%) | 0.00 | 729 (22.3\%) | 699 (21.4\%) | 0.02 | 2271 (13.0\%) | 2245 (12.9\%) | 0.00 |
| Previous cardiac procedure (CABG or |  |  |  |  |  |  |  |  |  |  |  |  |
| PTCA or Stent) + History of CABG or |  |  |  |  |  |  |  |  |  |  |  |  |
| PTCA (for PS) V3; n (\%) | 3 (2.8\%) | 2 (1.9\%) | 0.06 | 271 (1.9\%) | 272 (1.9\%) | 0.00 | 323 (9.9\%) | 308 (9.4\%) | 0.02 | 597 (3.4\%) | 582 (3.3\%) | 0.01 |
| Diabetes with complication; n (\%) | **(3.7\%) | 11 (10.3\%) | \#DIV/0! | 469 (3.3\%) | 484 (3.4\%) | \#DIV/0! | 235 (7.2\%) | 249 (7.6\%) | \#DIV/0! | 469 (3.3\%) | 484 (3.4\%) | -0.01 |
| Delirium + Psychosis (for PS); n (\%) | 1 (0.9\%) | 2 (1.9\%) | -0.09 | 133 (0.9\%) | 139 (1.0\%) | -0.01 | 110 (3.4\%) | 129 (4.0\%) | -0.03 | 244 (1.4\%) | 270 (1.5\%) | -0.01 |
| Any use of Meglitinides (for PS); n (\%) | 0 (0.0\%) | 0 (0.0\%) | \#DIV/0! | 12 (0.1\%) | 20 (0.1\%) | 0.00 | 3 (0.1\%) | 6 (0.2\%) | -0.03 | 15 (0.1\%) | 26 (0.1\%) | 0.00 |
| Any use of AGIs (for PS); n (\%) | 1 (0.9\%) | 0 (0.0\%) | 0.13 | 5 (0.0\%) | 6 (0.0\%) | \#DIV/0! | 1 (0.0\%) | 4 (0.1\%) | -0.04 | 7 (0.0\%) | 10 (0.1\%) | -0.04 |
| CKD stage 3-6 + dialysis (for PS); n (\%) | 5 (4.7\%) | $3(2.8 \%)$ | 0.10 | 248 (1.8\%) | 257 (1.8\%) | 0.00 | 222 (6.8\%) | 214 (6.6\%) | 0.01 | 475 (2.7\%) | 474 (2.7\%) | 0.00 |
| Use of thiazide; n (\%) | 8 (7.5\%) | 5 (4.7\%) | 0.12 | 1,232 (8.8\%) | 1,242 (8.8\%) | 0.00 | 397 (12.2\%) | 397 (12.2\%) | 0.00 | 1637 (9.4\%) | 1644 (9.4\%) | 0.00 |
| Use of beta blockers; n (\%) | 22 (20.6\%) | 18 (16.8\%) | 0.10 | 2,871 (20.4\%) | 2,910 (20.7\%) | -0.01 | 1,249 (38.3\%) | 1,261 (38.6\%) | -0.01 | 4142 (23.8\%) | 4189 (24.0\%) | 0.00 |
| Use of calcium channel blockers; n (20) |  |  |  |  |  |  |  |  |  |  |  |  |
| (\%) | 22 (20.6\%) | 19 (17.8\%) | 0.07 | 2,230 (15.9\%) | 2,250 (16.0\%) | 0.00 | 834 (25.5\%) | 858 (26.3\%) | -0.02 | 3086 (17.7\%) | 3127 (17.9\%) | -0.01 |
| All antidiabetic medications except Ins | 10 (9.3\%) | 10 (9.3\%) | 0.00 | 1,390 (9.9\%) | 1,403 (10.0\%) | 0.00 | 426 (13.0\%) | 428 (13.1\%) | 0.00 | 1826 (10.5\%) | 1841 (10.6\%) | 0.00 |
| DM Medications - Insulin Copy; n (\%) | 0 (0.0\%) | 2 (1.9\%) | -0.20 | 271 (1.9\%) | 289 (2.1\%) | -0.01 | $93(2.8 \%)$ | 100 (3.1\%) | -0.02 | 364 (2.1\%) | 391 (2.2\%) | -0.01 |
| Use of Low Intensity Statins; n (\%) | 14 (13.1\%) | 11 (10.3\%) | 0.09 | 2,738 (19.5\%) | 2,854 (20.3\%) | -0.02 | 874 (26.8\%) | 925 (28.3\%) | -0.03 | 3626 (20.8\%) | 3790 (21.7\%) | -0.02 |
| Use of High Intensity Statins; n (\%) | 13 (12.1\%) | 15 (14.0\%) | -0.06 | 1,802 (12.8\%) | 1,748 (12.4\%) | 0.01 | 629 (19.3\%) | 548 (16.8\%) | 0.07 | 2444 (14.0\%) | 2311 (13.3\%) | 0.02 |
| Malignant hypertension; n (\%) | 1 (0.9\%) | 1 (0.9\%) | 0.00 | 6,163 (43.8\%) | 6,140 (43.7\%) | 0.00 | 222 (6.8\%) | 238 (7.3\%) | -0.02 | 6386 (36.6\%) | 6379 (36.6\%) | 0.00 |
| Cardiovascular stress test; n (\%) | 0 (0.0\%) | 0 (0.0\%) | \#DIV/0! | 23 (0.2\%) | 22 (0.2\%) | 0.00 | 20 (0.6\%) | 10 (0.3\%) | 0.04 | 43 (0.2\%) | 32 (0.2\%) | 0.00 |
| Number of BNP tests |  |  |  |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |
| ...mean (sd) | 0.02 (0.14) | 0.03 (0.17) | -0.06 | 0.01 (0.13) | 0.01 (0.13) | 0.00 | 0.04 (0.23) | 0.04 (0.23) | 0.00 | 0.02 (0.15) | 0.02 (0.15) | 0.00 |
| Number of Cardiac biomarkers tests (tropnin, CK-MBS, Myoglobin, CPK) |  |  |  |  |  |  |  |  |  |  |  |  |
| ...mean (sd) | 0.08 (0.39) | 0.10 (0.43) | -0.05 | 0.10 (0.63) | 0.10 (0.54) | 0.00 | 0.14 (0.43) | 0.14 (0.43) | 0.00 | 0.11 (0.60) | 0.11 (0.52) | 0.00 |
| Number of Ambulatory Blood pressure monitoring tests |  |  |  |  |  |  |  |  |  |  |  |  |
| ...mean (sd) | 0.00 (0.00) | 0.00 (0.00) | \#DIV/0! | 0.00 (0.03) | 0.00 (0.04) | 0.00 | 0.00 (0.02) | 0.00 (0.00) | 0.00 | 0.00 (0.03) | 0.00 (0.04) | 0.00 |

## Appendix B

| $N$ of days on antihypertensive medications during baseline |  |  |  |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| ...mean (sd) | 82.41 (82.13) | 69.62 (79.26) | 0.16 | 79.44 (81.28) | 79.84 (81.30) | 0.00 | 117.64 (75.56) | 116.32 (76.36) | 0.02 | 86.61 (80.25) | 86.61 (80.39) | 0.00 |
| $N$ of days in database anytime prior |  |  |  |  |  |  |  |  |  |  |  |  |
| ...mean (sd) | 1,974.76 (1,364.00) | 1,826.59 (1,479.87) | 0.10 | 1,995.34 (1,338.60) | 1,959.03 (1,335.68) | 0.03 | 851.39 (590.43) | 718.16 (409.59) | 0.26 | 1781.03 (1233.73) | 1725.88 (1218.17) | 0.00 |
| Mean Copay for per prescription cost (charges in U.S. $\$$ ) ( $180-1$ day prior) |  |  |  |  |  |  |  |  |  |  |  |  |
| ...mean (sd) | 20.62 (28.12) | 17.60 (21.97) | 0.12 | 15.14 (17.44) | 15.12 (24.94) | 0.00 | 109.49 (85.68) | 108.86 (92.05) | 0.01 | 32.84 (40.30) | 32.69 (45.73) | 0.00 |
| ...Missing; n (\%) | $3(2.8 \%)$ | 4 (3.7\%) | -0.05 | 615 (4.4\%) | $599(4.3 \%)$ | 0.00 | 41 (1.3\%) | 36 (1.1\%) | 0.02 | 659 (3.8\%) | 639 (3.7\%) | 0.01 |
| Colonoscopy; n (\%) | 6 (5.6\%) | 5 (4.7\%) | 0.04 | 669 (4.8\%) | 696 (4.9\%) | 0.00 | 154 (4.7\%) | 166 (5.1\%) | -0.02 | 829 (4.8\%) | 867 (5.0\%) | -0.01 |
| Fecal occult blood (FOB) test; n (\%) | $4(3.7 \%)$ | 3 (2.8\%) | 0.05 | 597 (4.2\%) | 630 (4.5\%) | -0.01 | 80 (2.5\%) | 78 (2.4\%) | 0.01 | 681 (3.9\%) | 711 (4.1\%) | -0.01 |
| Flu vaccine; n (\%) | 27 (25.2\%) | 18 (16.8\%) | 0.21 | 1,927 (13.7\%) | 1,898 (13.5\%) | 0.01 | 1,023 (31.3\%) | 1,029 (31.5\%) | 0.00 | 2977 (17.1\%) | 2945 (16.9\%) | 0.01 |
| Mammogram; n (\%) | 16 (15.0\%) | 18 (16.8\%) | -0.05 | 1,810 (12.9\%) | 1,825 (13.0\%) | 0.00 | 472 (14.5\%) | 498 (15.3\%) | -0.02 | 2298 (13.2\%) | 2341 (13.4\%) | -0.01 |
| Pap smear; n (\%) | $5(4.7 \%)$ | 7 (6.5\%) | -0.08 | 935 (6.6\%) | 950 (6.8\%) | -0.01 | 122 (3.7\%) | 126 (3.9\%) | -0.01 | 1062 (6.1\%) | 1083 (6.2\%) | 0.00 |
| Pneumonia vaccine; n (\%) | 33 (30.8\%) | 22 (20.6\%) | 0.24 | 922 (6.6\%) | 891 (6.3\%) | 0.01 | 833 (25.5\%) | 805 (24.7\%) | 0.02 | 1788 (10.3\%) | 1718 (9.9\%) | 0.01 |
| PSA test or Prostate exam for DRE; n (9, | 14 (13.1\%) | 12 (11.2\%) | 0.06 | 1,608 (11.4\%) | 1,632 (11.6\%) | -0.01 | 409 (12.5\%) | 408 (12.5\%) | 0.00 | 2031 (11.6\%) | 2052 (11.8\%) | -0.01 |
| Bone mineral density; n (\%) | 4 (3.7\%) | 4 (3.7\%) | 0.00 | 502 (3.6\%) | 484 (3.4\%) | 0.01 | 206 (6.3\%) | 182 (5.6\%) | 0.03 | 712 (4.1\%) | 670 (3.8\%) | 0.02 |
| Use of CNS stimulants; n (\%) | 2 (1.9\%) | 1 (0.9\%) | 0.09 | 95 (0.7\%) | 130 (0.9\%) | -0.02 | 18 (0.6\%) | 19 (0.6\%) | 0.00 | 115 (0.7\%) | 150 (0.9\%) | -0.02 |
| Use of estrogens, progestins, androger | 16 (15.0\%) | 8 (7.5\%) | 0.24 | 1,199 (8.5\%) | 1,245 (8.9\%) | -0.01 | 179 (5.5\%) | 197 (6.0\%) | -0.02 | 1394 (8.0\%) | 1450 (8.3\%) | -0.01 |
| Use of Angiogenesis inhibitors; n (\%) | 0 (0.0\%) | 0 (0.0\%) | \#Div/0! | 8 (0.1\%) | 5 (0.0\%) | 0.04 | 3 (0.1\%) | 0 (0.0\%) | 0.04 | 11 (0.1\%) | 5 (0.0\%) | 0.04 |
| Use of Oral Immunosuppressants; n (\% | 0 (0.0\%) | 0 (0.0\%) | \#DIV/0! | 29 (0.2\%) | 15 (0.1\%) | 0.03 | 4 (0.1\%) | 6 (0.2\%) | -0.03 | 33 (0.2\%) | 21 (0.1\%) | 0.03 |
| Use of fondaparinux or Bivalirudin; n (' | 0 (0.0\%) | 0 (0.0\%) | \#DIV/0! | 16 (0.1\%) | 16 (0.1\%) | 0.00 | 2 (0.1\%) | 11 (0.3\%) | -0.04 | 18 (0.1\%) | 27 (0.2\%) | -0.03 |
| Use of other direct thrombin inhibitors | 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! | 3 (0.0\%) | 2 (0.0\%) | \#DIV/0! | 0 (0.0\%) | 0 (0.0\%) | \#DIV/0! | 3 (0.0\%) | 2 (0.0\%) | \#DIV/0! |
| Use of Ticagrelor; n (\%) | 0 (0.0\%) | 0 (0.0\%) | \#DIV/0! | 5 (0.0\%) | 7 (0.0\%) | \#DIV/0! | 7 (0.2\%) | 4 (0.1\%) | 0.03 | 12 (0.1\%) | 11 (0.1\%) | 0.00 |
| Number of D-dimer tests |  |  |  |  |  |  |  |  |  |  |  |  |
| ...mean (sd) | 0.01 (0.10) | 0.04 (0.23) | -0.17 | 0.01 (0.10) | 0.01 (0.11) | 0.00 | 0.02 (0.15) | 0.02 (0.16) | 0.00 | 0.01 (0.11) | 0.01 (0.12) | 0.00 |
| Numbe of CRP, high-sensitivity CRP tests |  |  |  |  |  |  |  |  |  |  |  |  |
| ...mean (sd) | 0.29 (0.73) | 0.11 (0.50) | 0.29 | 0.10 (0.41) | 0.10 (0.41) | 0.00 | 0.25 (0.80) | 0.26 (0.91) | -0.01 | 0.13 (0.51) | 0.13 (0.54) | 0.00 |
| Number of PT or aPTTT tests |  |  |  |  |  |  |  |  |  |  |  |  |
| ...mean (sd) | 0.93 (1.18) | 1.03 (1.34) | -0.08 | 0.81 (1.23) | 0.82 (1.24) | -0.01 | 0.77 (1.27) | 0.75 (1.08) | 0.02 | 0.80 (1.24) | 0.81 (1.21) | 0.00 |
| Number of Bleeding time tests |  |  |  |  |  |  |  |  |  |  |  |  |
| ...mean (sd) | 0.00 (0.00) | 0.00 (0.00) | \#DIV/0! | 0.00 (0.01) | 0.00 (0.01) | 0.00 | 0.00 (0.00) | 0.00 (0.03) | 0.00 | 0.00 (0.01) | 0.00 (0.02) | 0.00 |
| HAS-BLED Score (ICD-9 and ICD-10), 180 days |  |  |  |  |  |  |  |  |  |  |  |  |
| ...mean (sd) | 3.03 (1.05) | 2.98 (1.11) | 0.05 | 2.88 (1.05) | 2.89 (1.05) | -0.01 | 3.76 (0.91) | 3.76 (0.93) | 0.00 | 3.05 (1.03) | 3.05 (1.03) | 0.00 |
| $N$ of Generic name drugs |  |  |  |  |  |  |  |  |  |  |  |  |
| ...mean (sd) | 15.08 (13.34) | 13.54 (11.69) | 0.12 | 13.67 (10.34) | 13.93 (11.31) | -0.02 | 19.98 (14.50) | 20.37 (16.10) | -0.03 | 14.86 (11.26) | 15.13 (12.35) | 0.00 |
| $N$ of Brand name drugs |  |  |  |  |  |  |  |  |  |  |  |  |
| ...mean (dd) | 3.48 (5.01) | 3.21 (3.94) | 0.06 | 3.17 (4.44) | 3.43 (3.63) | -0.06 | 3.03 (5.29) | 3.27 (3.97) | -0.05 | 3.15 (4.61) | 3.40 (3.70) | 0.00 |
| Use of clopidogrel; n (\%) | $3(2.8 \%)$ | 2 (1.9\%) | 0.06 | 292 (2.1\%) | 304 (2.2\%) | -0.01 | 156 (4.8\%) | 156 (4.8\%) | 0.00 | 451 (2.6\%) | 462 (2.6\%) | 0.00 |
| Systemic embolism; n (\%) | 0 (0.0\%) | 0 (0.0\%) | \#DIV/0! | 11 (0.1\%) | 10 (0.1\%) | 0.00 | 6 (0.2\%) | 7 (0.2\%) | 0.00 | 17 (0.1\%) | 17 (0.1\%) | 0.00 |
| DVT; n (\%) | 2 (1.9\%) | 1 (0.9\%) | 0.09 | 210 (1.5\%) | 204 (1.5\%) | 0.00 | 170 (5.2\%) | 191 (5.8\%) | -0.03 | 382 (2.2\%) | 396 (2.3\%) | -0.01 |
| Post-thrombotic syndrome; n (\%) | 0 (0.0\%) | 0 (0.0\%) | \#DIV/0! | ** (0.0\%) | 0 (0.0\%) | \#DIV/0! | ** (0.0\%) | **(0.1\%) | \#DIV/0! | ** (0.0\%) | 0 (0.0\%) | \#Div/o! |
| PE; n (\%) | 0 0 $0.0 \%$ ) | 1 (0.9\%) | -0.13 | 52 (0.4\%) | 51 (0.4\%) | 0.00 | 58 (1.8\%) | 63 (1.9\%) | -0.01 | 110 (0.6\%) | 115 (0.7\%) | -0.01 |
| Coagulation defects; n (\%) | 0 (0.0\%) | 0 (0.0\%) | \#DIV/0! | 172 (1.2\%) | 168 (1.2\%) | \#DIV/0! | 61 (1.9\%) | 57 (1.7\%) |  | 172 (1.2\%) | 168 (1.2\%) | 0.00 |
| Diabetes: 1 inpatient or 2 outpatient cl | 14 (13.1\%) | 21 (19.6\%) | -0.18 | 1,941 (13.8\%) | 1,944 (13.8\%) | 0.00 | 663 (20.3\%) | 664 (20.3\%) | 0.00 | 2618 (15.0\%) | 2629 (15.1\%) | 0.00 |
| Intracranial or retroperitoneal hemorr | 0 (0.0\%) | 0 (0.0\%) | \#DIV/0! | 9 (0.1\%) | 11 (0.1\%) | 0.00 | 4 (0.1\%) | 1 (0.0\%) | 0.04 | 13 (0.1\%) | 12 (0.1\%) | 0.00 |
| Peptic Ulcer Disease; n (\%) | 35 (32.7\%) | 42 (39.3\%) | -0.14 | 3,059 (21.7\%) | 3,058 (21.7\%) | 0.00 | 1,278 (39.1\%) | 1,271 (38.9\%) | 0.00 | 4372 (25.1\%) | 4371 (25.1\%) | 0.00 |
| Upper GI bleed; n (\%) | 0 (0.0\%) | 0 (0.0\%) | \#DIV/0! | 17 (0.1\%) | 15 (0.1\%) | 0.00 | $2(0.1 \%)$ | 7 (0.2\%) | -0.03 | 19 (0.1\%) | 22 (0.1\%) | 0.00 |
| Lower/ unspecified G1 bleed; n (\%) | 1 (0.9\%) | 2 (1.9\%) | -0.09 | 173 (1.2\%) | 170 (1.2\%) | 0.00 | 8 (0.2\%) | $9(0.3 \%)$ | -0.02 | 182 (1.0\%) | 181 (1.0\%) | 0.00 |
| Urogenital bleed; n (\%) | $5(4.7 \%)$ | 5 (4.7\%) | 0.00 | 339 (2.4\%) | 358 (2.5\%) | -0.01 | 39 (1.2\%) | 44 (1.3\%) | -0.01 | 383 (2.2\%) | 407 (2.3\%) | -0.01 |
| Other bleeds; n (\%) | 34 (31.8\%) | 34 (31.8\%) | 0.00 | 3,581 (25.5\%) | 3,558 (25.3\%) | 0.00 | 972 (29.8\%) | 945 (28.9\%) | 0.02 | 4587 (26.3\%) | 4537 (26.0\%) | 0.01 |
| Prior cancer; n (\%) | 15 (14.0\%) | 17 (15.9\%) | -0.05 | 978 (7.0\%) | 1,013 (7.2\%) | -0.01 | 578 (17.7\%) | 560 (17.2\%) | 0.01 | 1571 (9.0\%) | 1590 (9.1\%) | 0.00 |
| Antibiotics; n (\%) | 43 (40.2\%) | 44 (41.1\%) | \#DIV/0! | 5,663 (40.3\%) | 5,720 (40.7\%) | \#Div/0! | 1,684 (51.6\%) | 1,704 (52.2\%) | \#DIV/0! | 5,663 (40.3\%) | 5,720 (40.7\%) | -0.01 |
| Aspirin; n (\%) | $3(2.8 \%)$ | 9 (8.4\%) | -0.25 | 187 (1.3\%) | 185 (1.3\%) | 0.00 | 11 (0.3\%) | $9(0.3 \%)$ | 0.00 | 201 (1.2\%) | 203 (1.2\%) | 0.00 |
| Aspirin/dipyridamole; n (\%) | 0 (0.0\%) | 0 (0.0\%) | \#DIV/0! | 13 (0.1\%) | 14 (0.1\%) | 0.00 | 4 (0.1\%) | 5 (0.2\%) | -0.03 | 17 (0.1\%) | 19 (0.1\%) | 0.00 |
| Other antiplatelet agents; n (\%) | 0 0 $0.0 \%$ ) | 0 (0.0\%) | \#DIV/0! | 16 (0.1\%) | 11 (0.1\%) | 0.00 | 8 (0.2\%) | 6 (0.2\%) | 0.00 | 24 (0.1\%) | 17 (0.1\%) | 0.00 |
| PGP inhibitors; n (\%) | 17 (15.9\%) | 16 (15.0\%) | 0.02 | 2,289 (16.3\%) | 2,339 (16.6\%) | -0.01 | 825 (25.3\%) | 818 (25.1\%) | 0.00 | 3131 (18.0\%) | 3173 (18.2\%) | -0.01 |
| Other gastroprotective agents; n (\%) | 2 (1.9\%) | 3 (2.8\%) | -0.06 | 190 (1.4\%) | 201 (1.4\%) | 0.00 | 68 (2.1\%) | 68 (2.1\%) | 0.00 | 260 (1.5\%) | 272 (1.6\%) | -0.01 |
| Number of lipid tests ordered |  |  |  |  |  |  |  |  |  |  |  |  |
| ...mean (sd) | 0.55 (0.87) | 0.49 (0.65) | 0.08 | 0.46 (0.81) | 0.47 (0.81) | -0.01 | 0.60 (0.75) | 0.60 (0.76) | 0.00 | 0.49 (0.80) | 0.49 (0.80) | 0.00 |
| Proton pump inhibitor; n (\%) | 25 (23.4\%) | 28 (26.2\%) | -0.06 | 2,726 (19.4\%) | 2,771 (19.7\%) | -0.01 | 983 (30.1\%) | 996 (30.5\%) | -0.01 | 3734 (21.4\%) | 3795 (21.8\%) | -0.01 |
| H2 receptor antagonist; $n(\%)$ | ** (1.9\%) | ** (0.9\%) | 0.09 | 378 (2.7\%) | 404 (2.9\%) | -0.01 | 203 (6.2\%) | 203 (6.2\%) | 0.00 | \#value! | \#value! | \#Value! |
| Vitamin K therapy; n (\%) | 0 (0.0\%) | 0 (0.0\%) | \#DIV/0! | **(0.0\%) | **(0.0\%) | \#Div/0! | 0 (0.0\%) | 1 (0.0\%) | \#DIV/0! | \#value! | \#value! | \#VALUE! |
| Number of $\operatorname{INR}$ (prothrombin) tests ordered |  |  |  |  |  |  |  |  |  |  |  |  |
| ...mean (sd) | 0.56 (0.66) | 0.64 (0.85) | -0.11 | 0.47 (0.71) | 0.46 (0.70) | 0.01 | 0.63 (1.06) | 0.61 (0.82) | 0.02 | 0.50 (0.79) | 0.49 (0.72) | 0.00 |
| Treating prescriber - Cardiologist; n (\% | 46 (43.0\%) | 50 (46.7\%) | -0.07 | 4,111 (29.2\%) | 4,078 (29.0\%) | 0.00 | 1,396 (42.8\%) | 1,355 (41.5\%) | 0.03 | 5553 (31.8\%) | 5483 (31.4\%) | 0.01 |
| Treating prescriber - Primary Care Phy: | 88 (82.2\%) | 75 (70.1\%) | 0.29 | 5,479 (39.0\%) | 5,380 (38.2\%) | 0.02 | 1,061 (32.5\%) | 1,039 (31.8\%) | 0.01 | 6628 (38.0\%) | 6494 (37.2\%) | 0.02 |

## Appendix B


\(\left.$$
\begin{array}{rrr}107(100.0 \%) \\
{ }^{* *}(2.8 \%)\end{array}
$$ \quad \begin{array}{rrr}107(100.0 \%) <br>

{ }^{* *}(4.7 \%)\end{array}\right)\)| \#DIV/0! |
| ---: |
| 1.0 .10 |

| $13,904(998.8 \%)$ | $13,911(98.9 \%)$ | -0.01 |
| ---: | ---: | ---: |
| $763(5.4 \%)$ | $775(5.5 \%)$ | 0.00 |
| $1.68(1.31)$ | $1.69(1.33)$ | -0.01 |
| $23(0.2 \%)$ | $28(0.2 \%)$ | 0.00 |
| $924(6.6 \%)$ | $958(6.8 \%)$ | -0.01 |
| $291(2.1 \%)$ | $288(2.0 \%)$ | 0.01 |
| $196(.14 \%)$ | $185(1.3 \%)$ | 0.01 |
| $384(2.7 \%)$ | $368(2.6 \%)$ | 0.01 |
| $251(1.8 \%)$ | $239(1.7 \%)$ | 0.01 |
|  |  |  |
| $3,971(28.2 \%)$ | $3,956(28.1 \%)$ | 0.00 |


| $3,263(99.9 \%)$ |  |
| ---: | ---: |
| $344(10.5 \%)$ | 0.04 |
| $2.44(1.28)$ | 0.00 |
| $0(0.0 \%)$ | 0.01 |
| \#DIV/0! |  |
| $525(16.1 \%)$ | 0.01 |
| $180(5.5 \%)$ | 0.03 |
| $97(3.0 \%)$ | -0.02 |
| $183(5.6 \%)$ | 0.00 |
| $232(7.1 \%)$ | -0.02 |
|  |  |
| $985(30.2 \%)$ | 0.01 |

17276 (99.1\%)

\#VALUE! | 17281 (99.1\%) |
| ---: | ---: | ---: |
| \#VALUE! |$\quad$| \#VALUE! |
| ---: |
| $1.82(1.30)$ |
| $23(0.1 \%)$ |

