

Once-Yearly Zoledronic Acid for Treatment of Postmenopausal Osteoporosis
(HORIZON - Pivotal Fracture Trial, PFT)

DUPLICATE HORIZON-PFT

February 11, 2021

NCT00049829

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

Once-Yearly Zoledronic Acid for Treatment of Postmenopausal Osteoporosis ([HORIZON - Pivotal Fracture Trial, PFT](#))

1.2 Intended aim(s)

To assess the effects of 15-minutes annual infusions of zoledronic acid (5mg) on hip fracture risk in postmenopausal women with osteoporosis during a 3-year period.

1.3 Primary endpoint for replication

Co-primary endpoints were incidence of hip fracture and incidence of vertebral fracture. We focus on the risk of hip fracture for replication.

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

Assuming a 3-year fracture rate of 1.8% in the placebo group, it was determined that with 7,400 patients the log-rank test had a power of 90% (with a two-sided alpha of 0.05) to detect a 50% reduction in hip fractures.

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

Non-vertebral fracture

1.6 Trial estimate

Hazard Ratio, HR = 0.59 (95% CI, 0.42 to 0.83) comparing zoledronic-acid group vs. placebo group during a 3-year period (Black et al., 2007).

Note. The follow-up period of the RWE replication is set at 18months. In the trial, the HR comparing zoledronic-acid group vs. placebo group during an 18-month period is estimated to be ~ 0.745. The HR at 18 months is defined as the ratio between the cumulative incidences of hip fracture events in the zoledronic-acid and placebo groups ($HR = \frac{CI_{ZA}}{CI_{placebo}}$) measured after 18 months of follow-up. The estimates of the cumulative incidences of hip fracture events have been extracted by the Kaplan-Meier curves reported in the trial using a dedicated software (Graph Grabber 2.0.2, Quintessa Ltd).

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2. Person responsible for implementation of replication in Aetion

Elvira D'Andrea, MD, 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.

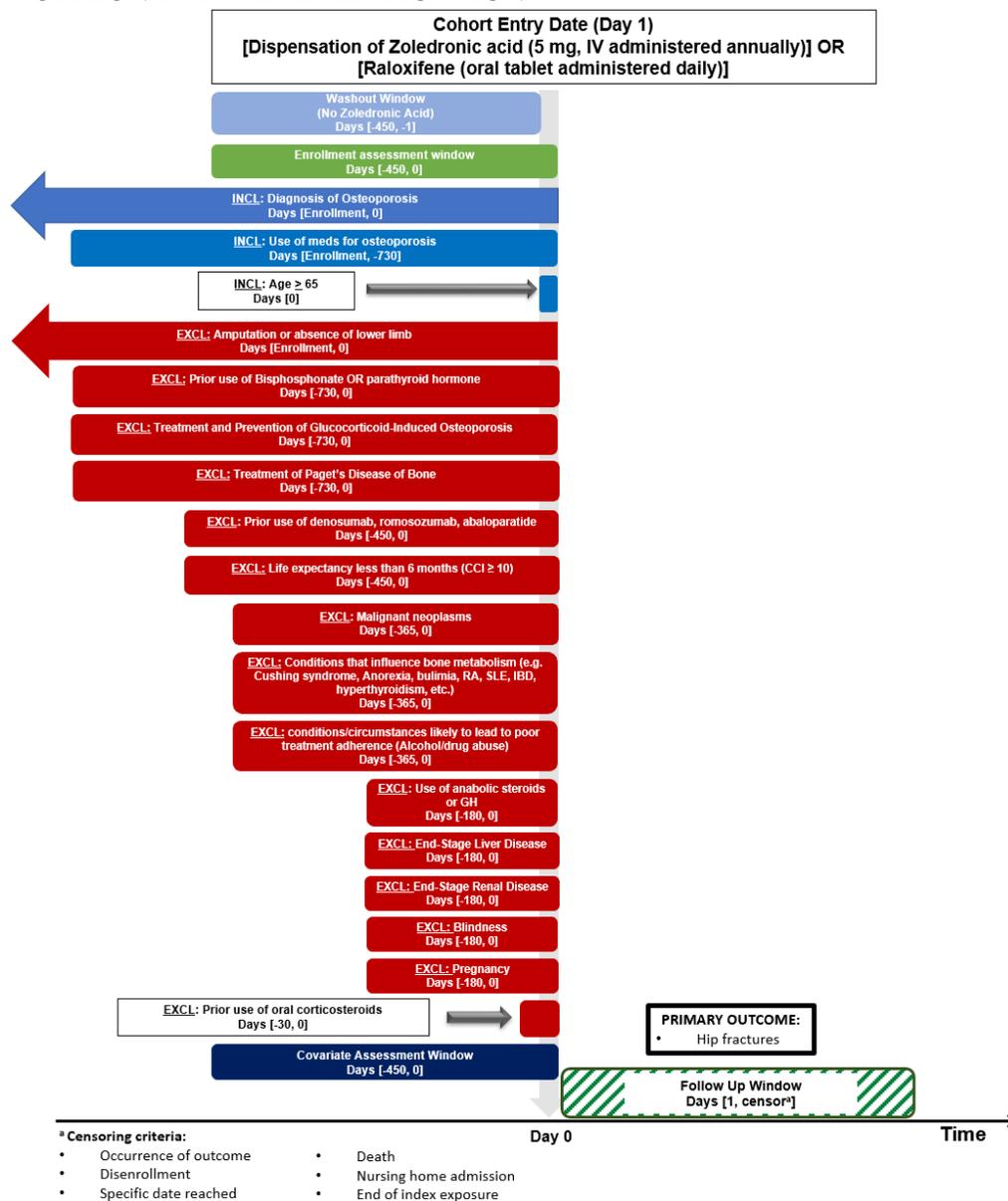
3. Data Source(s)

Optum CDM, IBM® MarketScan®

4. Study Design Diagram

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

Figure 1. Design Diagram – HORIZON-PFT TRIAL REPLICATION



5. Cohort Identification

5.1 Cohort Summary

This study will involve a new user, parallel group, propensity score-matched, retrospective cohort study design comparing 15-minute annual infusions of zoledronic acid (5mg) to raloxifene (as a proxy for placebo). Raloxifene was selected as the placebo proxy because raloxifene was the most common concomitant osteoporosis medication used in the trial in both study arms. In addition, prior evidence indicates no effect of raloxifene on the primary outcome of hip fracture (Ettinger et al., 1999, Ensrud et al., 2008). The patients will be required to have continuous enrollment during a baseline period of 450 days (15 months) before initiation of zoledronic acid or comparator. We will restrict the analyses to women, older than 65, with osteoporosis.

5.2 Important steps for cohort formation

New use of zoledronic acid (exposure) is defined as no use of the exposure drug in the 450 days prior to index date. New users of zoledronic acid will be allowed to receive concomitant therapy with raloxifene before and/or during the study period, similar to the trial. We use the long look-back period of 450 days to define new use because zoledronic acid is given as a yearly infusion; thus, identifying whether a patient has current zoledronic acid exposure requires at least 365 days of look back. We extended this lookback to 450 days (approximately 15 months) to allow for patients who have a short gap between infusions. To keep the amount of lookback available in the 2 treatment groups equal, New use of raloxifene (comparator, proxy to placebo) was also defined as no use of either exposure or comparator drugs in the 450 days prior to index date.

5.2.1 Eligible cohort entry dates

Zoledronic acid indication for treatment of postmenopausal women with osteoporosis was approved by FDA on Aug 20, 2007.

- IBM® MarketScan®: Aug 21, 2007 – December 31, 2018 (end of available data)
- Optum CDM: Aug 21, 2007 – Mar 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

For zoledronic acid vs. raloxifene

	Optum CDM		IBM® MarketScan®	
	Excluded Patients	Remaining Patients	Excluded Patients	Remaining Patients
All patients		77,673,639		200,203,908

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Did not meet cohort entry criteria	-77,476,067	197,572	-	489,107
Excluded due to insufficient enrollment	-52,317	145,255	199,714,801	324,865
Excluded due to prior use of referent	-81,791	63,464	-164,242	139,407
Excluded due to prior use of exposure	-9,268	54,196	-185,458	110,254
Excluded because patient qualified in >1 exposure category	-1	54,195	-29,153	110,253
Excluded based on Inclusion #1 - Age, range 65-89 years	-1	54,195	-1	110,253
Excluded based on Inclusion #1 - Age, range 65-89 years	-17,914	36,281	-58,739	51,514
Excluded based on Inclusion #2 - Gender, female [Excluded if Male or Unknown]	-6,080	30,201	-6,857	44,657
Excluded based on Inclusion #3 - Osteoporosis	-3,624	26,577	-3,936	40,721
Excluded based on Exclusion #1 - Oral bisphosphonate use	-6,854	19,723	-10,259	30,462
Excluded based on Exclusion #2.1 - PTH or PTH analogue use	-305	19,418	-814	29,648
Excluded based on Exclusion #2.2 - Anabolic-androgenic steroids (AAS) and growth hormones (GH)	-10	19,408	-32	29,616
Excluded based on Exclusion #2.3 - Glucocorticoids use	-1,352	18,056	-1,697	27,919
Excluded based on Exclusion #3 - CCI (180 days) >=10	-196	17,860	-154	27,765
Excluded based on Exclusion #4 - Malignant neoplasm, excluding non-melanoma skin cancer	-2,461	15,399	-4,141	23,624
Excluded based on Exclusion #5 - Disorders that influence bone metabolism	-1,426	13,973	-2,235	21,389
Excluded based on Exclusion #6 - Glucocorticoid-Induced Osteoporosis	-4	13,969	-5	21,384
Excluded based on Exclusion #7 - Paget's Disease	-43	13,926	-65	21,319
Excluded based on Exclusion #8 - Alcohol abuse or Drug addiction or Non-compliance	-141	13,785	-137	21,182
Excluded based on Exclusion #9 - Pregnancy	-1	13,784	-3	21,179
Excluded based on Exclusion #10 - Lower extremity amputation	-18	13,766	-37	21,142
Excluded based on Exclusion #11 - Denosumab use	-53	13,713	-35	21,107
Excluded based on Exclusion #12 - Zoledronic Acid use (for raloxifene users)	-223	13,490	-313	20,794
Excluded based on Exclusion criteria #13 - End-stage renal disease	-5	13,485	-12	20,782
Excluded based on Exclusion criteria #14 - End-stage liver disease	-33	13,452	-66	20,716
Excluded based on Exclusion criteria #15 - Blindness or low vision	-32	13,420	-25	20,691
Excluded based on Exclusion criteria #16 - Abaloparatide	-0	13,420	-0	20,691
Excluded based on Exclusion criteria #17 - Romosozumab	-0	13,420	-0	20,691
Final cohort	--	13,420	--	20,691

6. Variables

6.1 Exposure-related variables:

Study drug:

The study exposure of interest is new initiation of zoledronic acid 5 mg, IV administered annually. New initiation will be defined by no use of zoledronic acid in the prior 15 months (450 days) before treatment initiation (washout period).

Comparator agents:

Primary analysis:

- New initiators of raloxifene, oral tablet administered daily. New initiation will be defined by no use of raloxifene and zoledronic acid in the prior 15 months (450 days) before treatment initiation (washout period).

Secondary analysis:

- Non-user comparator (risk-set sampled cohort).

6.2 Preliminary Covariates:

- Age
- 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**). Gender is not included since the study is already restricted to female subjects.

6.3 Outcome variables and study follow-up:

6.3.1 Outcome variables

Effectiveness outcome variables of interest (definitions provided in **Appendix A**):

- **Primary outcome:** Hip fracture

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- Secondary outcome:
 - Non-vertebral fracture

6.3.2 Study follow-up

Intention-to-treat (ITT) analysis will be conducted with treatment defined as the index drug on day of cohort entry. Because the exposure (zoledronic acid) is administered annually, patients receiving the exposure are automatically covered with medication for at least 12 months. In addition, the comparator (raloxifene) is intended to proxy for placebo, so nonadherence to the comparator does not result in meaningful exposure misclassification. Therefore, the **ITT analysis with a follow-up of 18 months (540 days) will be the primary analysis.**

The follow-up will start the day after drug initiation (i.e., cohort entry date), as described in the HORIZON-PFT, and will continue until the earliest date of the following events:

- The first occurrence of the outcome of interest,
- 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.

7. Initial Feasibility Analysis

Action report name:

For zoledronic acid vs. raloxifene

Optum CDM- <https://bwh-dope.action.com/projects/details/1406/results/60058/result/0>

IBM® MarketScan®- <https://bwh-dope.action.com/projects/details/1407/results/60060/result/0>

Date conducted: 10/17/2020

Complete Aetion feasibility analysis using age 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

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- For zoledronic acid vs. raloxifene

Variable	Optum CDM			IBM® MarketScan®		
	Raloxifene - Comparator	Zoledronic Acid - Exposure	Difference	Raloxifene - Reference	Zoledronic acid - Exposure	Difference
Number of patients	6,815	6,605	-	6,694	13,997	-
Age						
...mean (sd)	73.41 (5.90)	74.02 (5.52)	-0.62 (-0.81, -0.42)	73.81 (7.06)	75.61 (7.14)	-1.80 (-2.01, -1.60)
...median [IQR]	73.00 [68.00, 78.00]	75.00 [69.00, 79.00]	-	72.00 [68.00, 79.00]	75.00 [70.00, 81.00]	-
Combined Comorbidity Score - CCI (180 days)						
...mean (sd)	1.38 (1.52)	1.49 (1.56)	-0.11 (-0.16, -0.06)	0.96 (1.20)	1.22 (1.35)	-0.27 (-0.30, -0.23)
...median [IQR]	1.00 [0.00, 2.00]	1.00 [0.00, 2.00]	-	1.00 [0.00, 1.00]	1.00 [0.00, 2.00]	-

- Report summary parameters of study population **FEASIBILITY- FOR STUDY OUTCOME**
 - For zoledronic acid vs. raloxifene

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	Optum CDM	IBM® MarketScan®
Number of patients in full cohort	13,420	20,691
Number of patients dropped as incomplete cases	0	0
Number of patients that did not begin follow-up	0	0
Number of patients in analytic cohort	13,420	20,691
Number of events	146	208
Number of person-years	16,243	24,519
Number of patients in group: Raloxifene - Comparator	6,815	6,694
Number of patients in group: Zoledronic Acid - Exposure	6,605	13,997
Risk per 1,000 patients	10.88	10.05
Rate per 1,000 person-years	-	-

- Report median follow-up time by treatment group
 - For zoledronic acid vs. raloxifene

Median Follow-Up Time (Days) [IQR] – ITT analysis		
Patient Group	Optum CDM	IBM® MarketScan®
Overall Patient Population	540 [375, 540]	540 [340, 540]
Referent - Raloxifene	540 [363, 540]	540 [363, 540]
Exposure - ZA	540 [383, 540]	540 [329, 540]

- Report reasons for censoring in the overall study population
 - For zoledronic acid vs. raloxifene

Reasons	Optum CDM	IBM® MarketScan®
Overall	10750	17260
Outcome	146 (1.1%)	208 (1.0%)
Death	0 (0.0%)	62 (0.3%)
Maximum follow-up time	8,891 (66.3%)	13,112 (63.4%)
End of patient data	0 (0.0%)	0 (0.0%)
End of patient enrollment	2,589 (19.3%)	5,969 (28.8%)
Nursing home Occurred	838 (6.2%)	630 (3.0%)

- Report overall risk of the primary outcome.

	Optum CDM	IBM® MarketScan®	Pooled
Risk per 1,000 patients	10.9	10.1	10.4

8. Initial Power Assessment

Action report name:

For zoledronic acid vs. raloxifene

Optum CDM- <https://bwh-dope.action.com/projects/details/1406/results/60059/result/0>

IBM® MarketScan®- <https://bwh-dope.action.com/projects/details/1407/results/60061/result/0>

Date conducted: 10/17/2020

In order to complete the initial power analysis, the dummy outcome of a 90-day gap in database enrollment will be used. This outcome is used to ensure that no information on the comparative risks of the outcomes of interest are available at this stage. Complete a 1:1 PS-matched comparative analysis using this outcome. PS should include only 2 covariates: age and combined comorbidity index. Power calculations are based on the formulas from Chow et al. (2008).

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- 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.

- Pooled

Superiority Analysis	
Number of patients matched	25,518
Reference	12,759
Exposed	12,759
Risk per 1,000 patients	10.40
Desired HR from RCT	0.59
Alpha (2-sided)	0.05
Number of events expected	265.3872
Power	0.990300973

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○ Optum CDM

Superiority Analysis	
Number of patients matched	12,130
Reference	6,065
Exposed	6,065
Risk per 1,000 patients	10.90
Desired HR from RCT	0.59
Alpha (2-sided)	0.05
Number of events expected	132.217
Power	0.858487133

○ IBM® MarketScan®

Superiority Analysis	
Number of patients matched	13,388
Reference	6,694
Exposed	6,694
Risk per 1,000 patients	10.10
Desired HR from RCT	0.59
Alpha (2-sided)	0.05
Number of events expected	135.2188
Power	0.86602361

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

Reviewed by PI:	Jessica Franklin	Date reviewed:	10/29/20
Reviewed by FDA:	Ken Quinto	Date reviewed:	11/15/20
Reasons for stopping analysis (if required):			

9. Balance Assessment

Action report name:

For zoledronic acid vs. raloxifene

Optum CDM: <https://bwh-dope.aetion.com/projects/details/1406/results/64560/result/0>

IBM® MarketScan®: <https://bwh-dope.aetion.com/projects/details/1407/results/64559/result/0>

Date conducted: 01/19/2021

After review of initial feasibility and power analyses, complete creation of the remaining covariates from Section 6.2. Again, using the dummy outcome of a 90-day gap in database enrollment, complete a 1:1 PS-matched analysis. The PS should include the complete list of covariates.

- Provide plot of PS distributions stratified by treatment group.

Note- Please refer to **Appendix B**.

- Report covariate balance after matching.

Note- For Table 1, please refer to **Appendix B**.

- Report reasons for censoring by treatment group.

	Overall	Referent	Exposure
Dummy outcome	697 (3.87%)	350 (3.88%)	347 (3.85%)
Death	89 (0.49%)	36 (0.40%)	53 (0.59%)
End of index exposure	762 (4.23%)	372 (4.13%)	390 (4.33%)
Maximum follow-up time	11993 (66.52%)	6058 (67.21%)	5935 (65.84%)
End of patient enrollment	4487 (24.89%)	2198 (24.38%)	2289 (25.39%)

- Report follow-up time by treatment group.

Median Follow-Up Time (Days) [IQR] – ITT analysis		
Patient Group	Optum CDM	IBM® MarketScan®
Overall Patient Population	540 [404.5, 540]	540 [365, 540]
Referent - Raloxifene	540 [426, 540]	540 [365, 540]
Exposure - ZA	540 [386, 540]	540 [364.5, 540]

- Report overall risk of the primary outcome.

	Optum CDM	IBM® MarketScan®	Pooled
Risk per 1,000 patients	10.9	10.1	10.4

10. Final Power Assessment

Date conducted: 01/19/2021

- Re-calculate power in the appropriate excel table, using the revised number of matched patients from the PS-match in Section 9. All other parameters in the table should be the same as in Section 8.

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○ Pooled

Superiority Analysis	
Number of patients matched	18,028
Reference	9,014
Exposed	9,014
Risk per 1,000 patients	10.40
Desired HR from RCT	0.59
Alpha (2-sided)	0.05
Number of events expected	187.4912
Power	0.950774073

○ Optum CDM

Superiority Analysis	
Number of patients matched	6,396
Reference	3,198
Exposed	3,198
Risk per 1,000 patients	10.90
Desired HR from RCT	0.59
Alpha (2-sided)	0.05
Number of events expected	69.7164
Power	0.595938014

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- IBM® MarketScan®

Superiority Analysis	
Number of patients matched	11,632
Reference	5,816
Exposed	5,816
Risk per 1,000 patients	10.10
Desired HR from RCT	0.59
Alpha (2-sided)	0.05
Number of events expected	117.4832
Power	0.815816276

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

Reviewed by PI:	Jessica Franklin	Date reviewed:	01/19/21
Reviewed by FDA:	Ken Quinto	Date reviewed:	01/19/21
Reasons for stopping analysis (if required):			

11. Study Confidence and Concerns

Deadline for voting on study confidence and listing concerns:

Date votes and concerns are summarized:

- If final feasibility and power analyses are reviewed and approved, proceed to the remaining protocol steps.
- All study team and advisory board members that review this protocol should at this stage provide their level of confidence for the success of the RWD study in the [Google Form](#). This form also provides space for reviewers to list any concerns that they feel may contribute to a failure to replicate the findings of the RCT, including differences in study populations, poor measurement of study variables, or residual confounding.

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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](https://clinicaltrials.gov)

Date conducted:

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

13. Comparative Analyses

Action report name:

Date conducted:

13.1 For primary analysis:

In the PS-matched cohort from Section 9, to estimate the risk of hip fracture for zoledronic acid users versus raloxifene users during an 18-month period using a Cox regression hazard regression model.

13.2 For sensitivity analyses:

Secondary analyses:

- In the PS-matched cohort from Section 9, to estimate the risk of non-vertebral fracture for zoledronic acid users versus raloxifene users during an 18-month period using a Cox regression hazard regression model.
- To estimate the risk of hip fracture for zoledronic acid versus non-user comparator using a risk-set sampled cohort.

Subgroup analysis: In the PS-matched cohort from Section 9, to estimate the risk of hip fracture stratified by age (women younger or older than 75 years). The estimates are compared with the results from a post-hoc analysis of the Horizon-PFT on women older than or equal to 75 (Boonen et al.).

14. Requested Results

14.1 Table 1: Baseline characteristics before and after adjustment

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

14.2 Table 2: Follow-up time

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

14.3 Table 3: Censoring events

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

14.4 Table 4: Results from primary analysis

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

HR, Hazard Ratio; CI, Confidence Interval.

14.5 Table 5: Results from secondary analyses

15. References

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Wright NC, Daigle SG, Melton ME, Delzell ES, Balasubramanian A, Curtis JR. The Design and Validation of a New Algorithm to Identify Incident Fractures in Administrative Claims Data. *J Bone Miner Res.* 2019 Oct;34(10):1798-1807. doi: 10.1002/jbmr.3807.

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Appendix A

#	HORIZON-PFT trial definitions	Implementation in routine care	Please see the following Google Drive for further details or any missing information: https://drive.google.com/drive/folders/1WD618wyyYfFaXzJl_TcuK-VYc6n6h-gV?usp=sharing	
Trial details - clinicaltrials.gov NCT00049829			ICD-10 codes are not listed in this document because of excel cell size limitations and excessive number of ICD-10 codes. Full ICD-10 code lists will be available in the above Google Drive Folder (link above). ICD-9 to ICD-10 code conversions were completed using a SAS macro that implements forward/ backward mapping based on the CMS ICD-9 to ICD-10 mapping: https://www.nber.org/data/icd9-icd10-cm-and-ncs-crosswalk-general-equiv-alence-mapping.html	
EXPOSURE vs. COMPARISON			References/Rationale	Color coding
	<p>Exposure: Zoledronic acid (5 mg) 15-minute intravenous administration every year for 3 years vs. placebo</p> <p>Reference: Placebo</p> <p>Aim: To evaluate the effect of annual infusions of zoledronic acid on fracture risk during a 3-year period in postmenopausal women with osteoporosis</p> <p>All patients received oral daily calcium (1000 to 1500 mg) and vitamin D (400 to 1200 IU).</p> <p>Exposure: new-use of Zoledronic acid (washout 450 days)</p> <p>NDC Generic Name: ZOLEDRONIC ACID ZOLEDRONIC ACID IN MANNITOL & WATER FOR INJECTION ZOLEDRONIC ACID IN MANNITOL AND 0.9% SODIUM CHLORIDE ZOLEDRONIC ACID IN MANNITOL AND WATER FOR INJECTION</p> <p>NDC codes: 143964201, 16729024231, 17478032705, 25021080167, 42023015101, 43598033011, 47335003540, 47335096241, 54288010001, 5511106850755150026605, 67457039054, 68001036625, 78035084, 78038725, 409421501, 409421505, 16714081501, 17478032745, 23155017031, 25021080166, 45963044055, 51991006598, 53150087101, 60505611000, 63323096198, 68001036622, 78043561, 78059061, 409422801, 409422901, 23155018631, 25021082666, 25021082667, 25021082682, 25021083082, 35356035101, 42023016301, 43598033111, 51991006498, 55111068852, 63323096600, 67457061910, 67457079410, 70860021051</p> <p>CPT/HCPCS Procedure Codes: C9115, J3487, J3488, J3489, Q2051, Q4095</p> <p>Reference of primary analysis: Raloxifene (proxy of placebo) Reference of secondary analysis: non-users (proxy of placebo)</p>		Criteria	
PRIMARY OUTCOME			Adequate mapping in claims	
<p>Hip fracture</p> <p>(Dual-energy x-ray absorptiometry of the hip was performed at baseline and at months 6, 12, 24, and 36 for bone loss) - both patients in stratum 1 and stratum 2</p>	<p>Measured 1 day after drug initiation (codes reported in "Hip and femur fractures codes":</p> <p>Hip and femur fracture: <u>Algorithm include the following case-qualifying (CQ):</u> CQ = 1 Inpatient claim with primary diagnosis code AND AND CQ = 2 Inpatient claim with secondary diagnosis code AND AND CQ = 3 Non-inpatient claim with diagnosis code AND HCPCS in (27125, 27130, 27220, 27222, 27226-27228, 27230-27248, 27254, 27267-27269, 27500-27514) OR Non-inpatient claim with diagnosis code AND ICD-9 Procedure Code in (7855, 7905, 7915, 7925, 7935, 7965, 8151, 8152)</p>	<p>Wright NC, Daigle SG, Melton ME, Delzell ES, Balasubramanian A, Curtis JR. The Design and Validation of a New Algorithm to Identify Incident Fractures in Administrative Claims Data. J Bone Miner Res. 2019 Oct;34(10):1798-1807. doi: 10.1002/jbmr.3807. Epub 2019 Aug 5. PMID: 31170317.</p>	Intermediate mapping in claims	
<p>New Vertebral Fractures [only in patients who were not taking any osteoporosis medications at the time of randomization] only patients in stratum 1</p> <p>(Spinal lateral radiographs were obtained at baseline and at 12, 24, and 36 months or early termination for patients in stratum 1 and at baseline and at 36 months or early termination for patients in stratum 2)</p>	<p>Measured 1 day after drug initiation:</p> <p>Vertebral Fractures: <u>Algorithm include the following case-qualifying (CQ):</u> CQ = 1 Inpatient claim with primary diagnosis code AND AND CQ = 2 Non-inpatient claim with diagnosis code AND HCPCS in (22305, 22310, 22315, 22318, 22319, 22325-22328, 22510-22515, 22520-22525, 27200, 27202, 72291, 72292, 76012, 76013, 77082, 77085, 77086, 82360-82363) AND AND CQ = 3 Non-inpatient claim with diagnosis code AND HCPCS in (99024, 99058, 99201-99215, 99241-99245, 99271-99285, 99301-99355, 99366, 99385-99387, 99395-99404, 99429, 99499) [Physician E&M codes] plus, up to 10 days earlier (or on the same day), Outpatient claim with HCPCS in (72010-72159, 72240-72285, 72295) [Spine imaging codes]</p>	<p>Outcome not included in the final analysis</p> <p>Wright NC, Daigle SG, Melton ME, Delzell ES, Balasubramanian A, Curtis JR. The Design and Validation of a New Algorithm to Identify Incident Fractures in Administrative Claims Data. J Bone Miner Res. 2019 Oct;34(10):1798-1807. doi: 10.1002/jbmr.3807. Epub 2019 Aug 5. PMID: 31170317.</p>	Poor mapping or cannot be measured in claims	
INCLUSION CRITERIA			Can't be measured in claims but not important for the analysis	
<p>1</p> <p>Postmenopausal women between the ages of 65 and 89 years</p>	<p>Female, 65-89 years at the time of drug initiation</p>			
<p>2</p> <p>Bone mineral density T score of -2.5 or less at the femoral neck, with or without evidence of existing vertebral fracture, or a T score of -1.5 or less, with radiologic evidence of at least two mild vertebral fractures or one moderate vertebral fracture.</p>	<p>Measured time of enrollment to prior to the day of drug initiation inpatient (any position), outpatient (any position):</p> <p>Osteoporosis diagnosis ICD-9 diagnosis: 733.00, 733.01, 733.02, 733.03, 733.09, 733.13 ICD-10 diagnosis: M81.0, M81.6, M81.8, M80.88*, M80.08*</p> <p>OR</p> <p>Measured time of enrollment to 730 days (2 years) prior to the day of drug initiation: Alendronate, Ibandronate, Risedronate, Pamidronate, Etdronate, Tiludronate</p>		<p>Adequate mapping in claims of criteria extracted from clinicaltrials.gov (ESLD and Svere eye disease), after clinical review with FDA (Abaloparatide, Romosozumab) or from the protocol of Horizon-recurrent (all other criteria in blue): "Colón-Emeric CS, Caminis J, Suh TT, Pieper CF, Janning C, Magaziner J, Adachi J, Rosario-Jansen T, Mesenbrink P, Horowitz ZD, Lyles KW; HORIZON Recurrent Fracture Trial. The HORIZON Recurrent Fracture Trial: design of a clinical trial in the prevention of subsequent fractures after low trauma hip fracture repair. Curr Med Res Opin. 2004 Jun;20(6):903-10. doi: 10.1185/030079904125003683. PMID: 15200749."</p> <p>Protocol of Horizon-pivotal not available - numerous unsuccessful attempts had been made to retrieve it from the authors</p>	

Appendix A

EXCLUSION CRITERIA			
1	Bisphosphonate users such as Aredia® (pamidronate), Didronel® (etidronate), Fosamax® (alendronate), Actonel® (risedronate), Skelid® (tiludronate)	<p>Measured 730 days (2 years) prior to the day of drug initiation:</p> <p><u>Generic names:</u> Alendronate, Ibandronate, Risedronate, Pamidronate, Etidronate, Tiludronate</p>	
2.1	Previous use of: (1) any previous use of parathyroid hormone	<p>Measured 730 days (2 years) prior to the day of drug initiation:</p> <p><u>Generic names:</u> parathyroid hormone , teriparatide, abaloparatide</p> <p><u>Brand names:</u> Natpara® (parathyroid hormone), Forteo®, Bonsity (teriparatide), Tymlos® (abaloparatide)</p>	
2.2	(2) use of anabolic steroids or growth hormone within 6 months before trial entry	<p>Measured 180 days prior to the day of drug initiation:</p> <p>AASs: Generic names: TESTOSTERONE, DIHYDROTESTOSTERONE PROPIONATE, ESTROGENS, ESTERIFIED/METHYLTESTOSTERONE, TESTOSTERONE CYPIONATE, MICRONIZED, TESTOSTERONE CYPIONATE/ESTRADIOL, CYPIONATE, TESTOSTERONE ENANTHATE/ESTRADIOL VALERATE, TESTOSTERONE MICRONIZED, TESTOSTERONE UNDECANOATE, METHYLTESTOSTERONE, MICRONIZED, STANOLONE, OXYMETHOLONE, NANDROLONE PHENPROPIONATE, OXANDROLONE, STANZOLOL, FLUOXYMESTERONE, TESTOSTERONE ENANTHATE, TESTOSTERONE PROPIONATE, NANDROLONE DECANOATE, METHYLTESTOSTERONE, TESTOSTERONE CYPIONATE</p> <p>GHs: Generic names: SOMATROPIN, TESAMORELIN ACETATE Brand names: OMNITROPE, SAIZEN, ZOMACTON, GEREFF, HUMATROPE, NUTROPIN, SEROSTIM, ZORBTIVE, EGRIFTA, MACRILEN, NORDITROPIN FLEXPRO, GENOTROPIN, TEV-TROPIN</p>	
2.3	OR (3) oral or intravenous systemic corticosteroids within 12 months,	<p>Measured 30 days prior to the day of drug initiation:</p> <p>Injectable (IV) or (IM):</p> <p><u>NDC Generic Name:</u> methylprednisolone, hydrocortisone, dexamethasone <u>CPT/HCPCS Procedure Code:</u> J1020, J1030, J1040, J1720, J2920, J2930</p> <p>Oral:</p> <p><u>NDC Generic Name:</u> Cortisone, hydrocortisone, prednisone, prednisolone, methylprednisolone, dexamethasone <u>CPT/HCPCS Procedure Code:</u> J7506, J7509, J7510, J8540</p>	
2.4	OR (4) any previous use of strontium, or sodium fluoride within 6 months before trial entry	CRITERIA NOT APPLIED	Strontium not approved in USA for treatment of osteoporosis. Sodium Fluoride is not used to treat the osteoporosis since 2001/2002 when a RCT and sub meta-analysis showed an increased of risk of fractures in the exp arm
NA	Patients with a serum calcium level of more than 2.75 mmol per liter or less than 2.00 mmol per liter	N/A	
NA	Patients with a calculated creatinine clearance of less than 30.0 ml per minute at either of two baseline visits or urine dipstick results of more than 2+ for protein, without evidence of contamination or bacteriuria.	N/A	
NA	Written informed consent	N/A	
3	Serious disease that may limit life expectancy to less than 6 months (including sever liver and renal diseases)	<p>Measured 180 days prior to the day of drug initiation:</p> <p>CCI >=10 (life expectancy less than the expected duration of the trial)</p>	
4	New diagnosis or active treatment for any nonskin malignancy ≤ 12 months prior to randomization and any metastatic cancer	<p>Measured 365 days prior to the day of drug initiation inpatient (any position), outpatient (any position):</p> <p><u>Malignant neoplasm:</u> ICD-9 diagnosis: 140.xx-208.xx (except 173.xx, non-melanoma skin cancer) ICD-10 diagnosis: C00-C43, C45-C97, D45</p>	

Appendix A

5	<p>Conditions that influence bone metabolism</p>	<p>Measured 365 days prior to the day of drug initiation:</p> <p><u>Anorexia and Bulimia:</u> ICD-9 diagnosis: 307.1, 307.5x, 783.0, 783.2x,783.3,783.6,783.9 ICD-10 diagnosis: F50.xx, R63.x</p> <p><u>Cushing syndrome and disorders of adrenal glands:</u> ICD-9 diagnosis: 255.xx ICD-10 diagnosis: E24.x</p> <p><u>Hyperparathyroidism and hyperthyroidism:</u> ICD-9 diagnosis: 252.x ICD-10 diagnosis: E21.x, E20.x</p> <p>Inflammatory conditions: <u>Rheumatoid arthritis</u> ICD-9 diagnosis: 714.0-714.4 ICD-10 diagnosis: M05.00,M05.05x,M05.15x,M05.25x,M05.35x,M05.45x, M05.55x, M05.65x, M05.75x,M05.85x,M05.60,M08.00,M08.40</p> <p><u>Lupus</u> ICD-9 diagnosis: 710.0 ICD-10 diagnosis: M32.10</p> <p><u>Crohn's disease and other IBD</u> ICD-9 diagnosis: 555.x, 556.x ICD-10 diagnosis: K50.xx, K51.xx</p>	
6	<p>Treatment and Prevention of Glucocorticoid-Induced Osteoporosis</p> <p>NB. The recommended regimen is a 5 mg infusion once a year given intravenously over no less than 15 minutes.</p>	<p>Measured 730 days (2 years) prior to the day of drug initiation:</p> <p>ICD-9 diagnosis: E858.0, 962.0 Poisoning by adrenal cortical steroids, ICD-10 diagnosis: T38.0xx Adverse effect of glucocorticoids and synthetic analogues</p>	
7	<p>Treatment of Paget's Disease of Bone</p> <p>NB. The recommended dose is a 5 mg infusion. The infusion time must not be less than 15 minutes given over a constant infusion rate.</p>	<p>Measured 730 days (2 years) prior to drug initiation:</p> <p>ICD-9 diagnosis: 731.0 Osteitis deformans without mention of bone tumor (Paget's Disease) ICD-10 diagnosis: M88.xxx Osteitis deformans [Paget's disease of bone]</p>	
8	<p>Other conditions/circumstances likely to lead to poor treatment adherence</p>	<p>Measured 365 days prior to drug initiation in any diagnosis position in inpatient or outpatient care setting:</p> <p><u>Alcohol Abuse or Dependence</u> ICD-9 diagnosis: 291.xx, 303.xx, 305.0x, 571.0x, 571.1x, 571.2x, 571.3x, 357.5x, 425.5x, E860.0x (CMS has not released mapping for new ICD10 for this code), V11.3x ICD-10 diagnosis: F10.x, K70.x, G62.1, I42.6, 099.31x</p> <p>OR</p> <p><u>Drug Abuse or Dependence</u> ICD-9 diagnosis: 292.xx, 304.xx, 305.2x-305.9x, 648.3x ICD-10 diagnosis: F11.x, F12.x, F13.x, F14.x, F15.x, F16.x, F17.2x, F18.x, F19.x, F55.2, G62.0, 099.32x</p> <p>OR</p> <p><u>Non-compliance:</u> ICD-9 diagnosis: V45.12, V15.81 ICD-10 diagnosis: Z91.19, Z91.15</p>	
9	<p>Pregnancy (even though it is very unlikely to found cases we add this criteria to make sure all women are postmenopausal)</p>	<p>Measured 180 days prior to and including day of drug initiation in any diagnosis position and inpatient or outpatient care setting</p> <p>Pregnancy (see "Pregnancy codes")</p>	
10	<p>Low fracture risk or unlikely to benefit:</p> <ul style="list-style-type: none"> • Amputee 	<p>Measured time of enrollment to prior to the day of drug initiation inpatient (any position), outpatient (any position):</p> <p>ICD-9 Diagnosis: Acquired absence of lower limb: V49.7x, Traumatic amputation 895.x, 896.x, 897.x ICD-9 Procedure: Amputation Of Lower Limb: 84.1xx, 84.25-84.28 ICD-10 Diagnosis: Acquired absence of lower limb: Z89.4xx, Z89.5xx, Z89.6xx, Traumatic amputation: S78.xxx ICD-10 Procedure: Detachment of lower limb: 0Y6xxx</p>	
11	<p>Zoledronic acid use (to exclude ZA use in the raloxifene group)</p>	<p>Measured 450 (1 year + 90 days) prior to the day of drug initiation: (same as exposure)</p>	
12	<p>Denosumab use</p>	<p>Measured 450 (1 year + 90 days) prior to the day of drug initiation: <u>Generic name:</u> Denosumab</p>	

Appendix A

13	End-Stage Renal Disease	<p>Measured 180 days prior to and including day of drug initiation in any diagnosis position and inpatient or outpatient care setting:</p> <p>2 codes for occurrence of ESRD/dialysis (either inpatient or outpatient), separated by at least 30 days: ICD-9 Diagnosis: 585.6, V45.1, V56.0, V56.8, 585.5 ICD-9 Procedure: 39.95, 54.98 ICD-10 Diagnosis: N18.5, N18.6, Z49.31, Z49.32, Z99.2 ICD-10 Procedure: 3E1M39Z, 5A1D60Z, 5A1D00Z, 3E1M39Z, 5A1D60Z, 5A1D00Z HCPCS/CPT codes: 50360, 50380, 90921, 90925, 90935, 90937, 90940, 90947, 90957, 90959, 90960, 90961, 90962, 90966, 90969, 90989, 99512, G0257, G0318, G0319, G0322, G0326, S9335, S9339, 50365, 90920, 90924, 90945, 90958, 90965, 90970, 90993, 90999, 99559, G0314, G0315, G0316, G0317, G0323, G0327</p> <p>OR</p> <p><u>Kidney transplant:</u> ICD-9 Diagnosis: 996.81, V42.0 ICD-9 Procedure: 55.6, 55.69 ICD-10 Diagnosis: T86.10, T86.13, T86.19, Z48.22, Z94.0, T86.11, T86.12 ICD-10 Procedure: 0TY0020, 0TY0022, 0TY10Z0, 0TY00Z1, 0TY10Z1, 0TY10Z2 HCPCS/CPT Code: 50360, 50365</p>	<p>Paterno, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gliflozin antidiabetic drugs: population based cohort study." <i>BMJ</i> 2018;360:k119 http://dx.doi.org/10.1136/bmj.k119</p> <p>Paterno, Elisabetta et al. "Empagliflozin and the Risk of Heart Failure Hospitalization in Routine Clinical Care: A First Analysis from the Empagliflozin Comparative Effectiveness and Safety (EMPRISE) Study." <i>Circulation</i>. 2019 Apr 8. doi: 10.1161/CIRCULATIONAHA.118.039177</p>
14	End-Stage Liver Disease	<p>Measured 180 days prior to and including day of drug initiation in any diagnosis position and inpatient or outpatient care setting:</p> <p><u>Cirrhosis:</u> ICD-9 Diagnosis: 571.2, 571.5, 571.6 ICD-10 Diagnosis: K70.11, K70.2, K70.3x, K70.4x, K74.x</p> <p><u>Hepatic decompensation:</u> ICD-9 Diagnosis: 456.0, 456.20, 456.1, 456.21, 789.5, 789.59, 572.2, 567.0, 567.2, 567.21, 567.22, 567.29, 567.8, 567.89, 567.9, 572.4 ICD-10 Diagnosis: R18.x, I85.x, K72.x, K65.x, K66.x, K67</p> <p>HCC is already excluded with exclusion criteria 4</p>	
15	Blindness or compromised vision	<p>Measured 180 days prior to and including day of drug initiation in any diagnosis position and inpatient or outpatient care setting:</p> <p>ICD-9 Diagnosis: 369.x ICD-10 Diagnosis: H54.x</p>	
16	Abaloparatide	<p>Measured 450 (1 year + 90 days) prior to the day of drug initiation:</p> <p><u>Generic name:</u> Abaloparatide</p>	
17	Ramosozumab	<p>Measured 450 (1 year + 90 days) prior to the day of drug initiation:</p> <p><u>Generic name:</u> Ramosozumab</p>	

Appendix A

HIP AND FEMUR FRACTURES CODES	
ICD9 Diagnosis codes (excluding rare fractures in young children)	
Fracture of neck of femur	
820 Fracture of neck of femur	
820.0 Closed fracture of intracapsular section	
820.00 Closed fracture of intracapsular section of neck of femur, unspecified	
820.02 Closed fracture of midcervical section of neck of femur	
820.03 Closed fracture of base of neck of femur	
820.09 Other closed transcervical fracture of neck of femur	
820.1 Open fracture of intracapsular section of neck of femur	
820.10 Open fracture of intracapsular section of neck of femur, unspecified	
820.11 Open fracture of epiphysis (separation) (upper) of neck of femur	
820.12 Open fracture of midcervical section of neck of femur	
820.13 Open fracture of base of neck of femur	
820.19 Other open transcervical fracture of neck of femur	
820.2 Closed fracture of trochanteric section	
820.20 Closed fracture of trochanteric section of neck of femur	
820.21 Closed fracture of intertrochanteric section of neck of femur	
820.22 Closed fracture of subtrochanteric section of neck of femur	
820.3 Open fracture of trochanteric section	
820.30 Open fracture of trochanteric section of neck of femur, unspecified	
820.31 Open fracture of intertrochanteric section of neck of femur	
820.32 Open fracture of subtrochanteric section of neck of femur	
820.8 Closed fracture of unspecified part of neck of femur	
820.9 Open fracture of unspecified part of neck of femur	
Fracture of other and unspecified parts of femur	
821 Closed fracture	
821.0 Closed fracture of femur	
821.00 Closed fracture of unspecified part of femur	
821.01 Closed fracture of shaft of femur convert	
821.10 Open fracture of unspecified part of femur	
821.11 Open fracture of shaft of femur convert	
821.20 Closed fracture of lower end of femur, unspecified part	
821.21 Closed fracture of condyle, femoral	
821.23 Closed supracondylar fracture of femur	
821.29 Other closed fracture of lower end of femur	
821.3 Open fracture of lower end of femur	
821.30 Open fracture of lower end of femur, unspecified part	
821.31 Open fracture of condyle, femoral	
821.32 Open fracture of epiphysis. Lower (separation) of femur	
821.33 Open supracondylar fracture of femur	
821.39 Other open fracture of lower end of femur	
HIP AND FEMUR FRACTURES	
ICD10 Diagnosis codes (incident fracture - excluding subsequent encounter and sequela, and rare fractures in young children)	
S72.0 Fracture of head and neck of femur (all)	
S72.00 Fracture of unspecified part of neck of femur	
S72.001 Fracture of unspecified part of neck of right femur	
S72.001A initial encounter for closed fracture	
S72.001B initial encounter for open fracture type I or II	
S72.001C initial encounter for open fracture type IIIA, IIIB, or IIIC	
S72.002 Fracture of unspecified part of neck of left femur	
S72.002A initial encounter for closed fracture	
S72.002B initial encounter for open fracture type I or II	
S72.002C initial encounter for open fracture type IIIA, IIIB, or IIIC	
S72.009 Fracture of unspecified part of neck of unspecified femur	
S72.009A initial encounter for closed fracture	

Appendix A

S72.009B initial encounter for open fracture type I or II
S72.009C initial encounter for open fracture type IIIA, IIIB, or IIIC
S72.01 Unspecified intracapsular fracture of femur
S72.011 Unspecified intracapsular fracture of right femur
S72.011A initial encounter for closed fracture
S72.011B initial encounter for open fracture type I or II
S72.011C initial encounter for open fracture type IIIA, IIIB, or IIIC
S72.012 Unspecified intracapsular fracture of left femur
S72.012A initial encounter for closed fracture
S72.012B initial encounter for open fracture type I or II
S72.012C initial encounter for open fracture type IIIA, IIIB, or IIIC
S72.019 Unspecified intracapsular fracture of unspecified femur
S72.019A initial encounter for closed fracture
S72.019B initial encounter for open fracture type I or II
S72.019C initial encounter for open fracture type IIIA, IIIB, or IIIC
S72.021 Displaced fracture of epiphysis (separation) (upper) of right femur
S72.021A initial encounter for closed fracture
S72.021B initial encounter for open fracture type I or II
S72.021C initial encounter for open fracture type IIIA, IIIB, or IIIC
S72.022 Displaced fracture of epiphysis (separation) (upper) of left femur
S72.022A initial encounter for closed fracture
S72.022B initial encounter for open fracture type I or II
S72.022C initial encounter for open fracture type IIIA, IIIB, or IIIC
S72.023 Displaced fracture of epiphysis (separation) (upper) of unspecified femur
S72.023A initial encounter for closed fracture
S72.023B initial encounter for open fracture type I or II
S72.023C initial encounter for open fracture type IIIA, IIIB, or IIIC
S72.03 Midcervical fracture of femur
S72.031 Displaced midcervical fracture of right femur
S72.031A initial encounter for closed fracture
S72.031B initial encounter for open fracture type I or II
S72.031C initial encounter for open fracture type IIIA, IIIB, or IIIC
S72.032 Displaced midcervical fracture of left femur
S72.032A initial encounter for closed fracture
S72.032B initial encounter for open fracture type I or II
S72.032C initial encounter for open fracture type IIIA, IIIB, or IIIC
S72.033 Displaced midcervical fracture of unspecified femur
S72.033A initial encounter for closed fracture
S72.033B initial encounter for open fracture type I or II
S72.033C initial encounter for open fracture type IIIA, IIIB, or IIIC
S72.034 Nondisplaced midcervical fracture of right femur
S72.034A initial encounter for closed fracture
S72.034B initial encounter for open fracture type I or II
S72.034C initial encounter for open fracture type IIIA, IIIB, or IIIC
S72.035 Nondisplaced midcervical fracture of left femur
S72.035A initial encounter for closed fracture
S72.035B initial encounter for open fracture type I or II
S72.035C initial encounter for open fracture type IIIA, IIIB, or IIIC
S72.036 Nondisplaced midcervical fracture of unspecified femur
S72.036A initial encounter for closed fracture
S72.036B initial encounter for open fracture type I or II
S72.036C initial encounter for open fracture type IIIA, IIIB, or IIIC
S72.04 Fracture of base of neck of femur
S72.041 Displaced fracture of base of neck of right femur
S72.041A initial encounter for closed fracture
S72.041B initial encounter for open fracture type I or II
S72.041C initial encounter for open fracture type IIIA, IIIB, or IIIC
S72.042 Displaced fracture of base of neck of left femur

Appendix A

S72.042A initial encounter for closed fracture
S72.042B initial encounter for open fracture type I or II
S72.042C initial encounter for open fracture type IIIA, IIIB, or IIIC
S72.043 Displaced fracture of base of neck of unspecified femur
S72.043A initial encounter for closed fracture
S72.043B initial encounter for open fracture type I or II
S72.043C initial encounter for open fracture type IIIA, IIIB, or IIIC
S72.044 Nondisplaced fracture of base of neck of right femur
S72.044A initial encounter for closed fracture
S72.044B initial encounter for open fracture type I or II
S72.044C initial encounter for open fracture type IIIA, IIIB, or IIIC
S72.045 Nondisplaced fracture of base of neck of left femur
S72.045A initial encounter for closed fracture
S72.045B initial encounter for open fracture type I or II
S72.045C initial encounter for open fracture type IIIA, IIIB, or IIIC
S72.046 Nondisplaced fracture of base of neck of unspecified femur
S72.046A initial encounter for closed fracture
S72.046B initial encounter for open fracture type I or II
S72.046C initial encounter for open fracture type IIIA, IIIB, or IIIC
S72.05 Unspecified fracture of head of femur
S72.051 Unspecified fracture of head of right femur
S72.051A initial encounter for closed fracture
S72.051B initial encounter for open fracture type I or II
S72.051C initial encounter for open fracture type IIIA, IIIB, or IIIC
S72.052 Unspecified fracture of head of left femur
S72.052A initial encounter for closed fracture
S72.052B initial encounter for open fracture type I or II
S72.052C initial encounter for open fracture type IIIA, IIIB, or IIIC
S72.059 Unspecified fracture of head of unspecified femur
S72.059A initial encounter for closed fracture
S72.059B initial encounter for open fracture type I or II
S72.059C initial encounter for open fracture type IIIA, IIIB, or IIIC
S72.06 Articular fracture of head of femur
S72.061 Displaced articular fracture of head of right femur
S72.061A initial encounter for closed fracture
S72.061B initial encounter for open fracture type I or II
S72.061C initial encounter for open fracture type IIIA, IIIB, or IIIC
S72.062 Displaced articular fracture of head of left femur
S72.062A initial encounter for closed fracture
S72.062B initial encounter for open fracture type I or II
S72.062C initial encounter for open fracture type IIIA, IIIB, or IIIC
S72.063 Displaced articular fracture of head of unspecified femur
S72.063A initial encounter for closed fracture
S72.063B initial encounter for open fracture type I or II
S72.063C initial encounter for open fracture type IIIA, IIIB, or IIIC
S72.064 Nondisplaced articular fracture of head of right femur
S72.064A initial encounter for closed fracture
S72.064B initial encounter for open fracture type I or II
S72.064C initial encounter for open fracture type IIIA, IIIB, or IIIC
S72.065 Nondisplaced articular fracture of head of left femur
S72.065A initial encounter for closed fracture
S72.065B initial encounter for open fracture type I or II
S72.065C initial encounter for open fracture type IIIA, IIIB, or IIIC
S72.066 Nondisplaced articular fracture of head of unspecified femur
S72.066A initial encounter for closed fracture
S72.066B initial encounter for open fracture type I or II
S72.066C initial encounter for open fracture type IIIA, IIIB, or IIIC
S72.09 Other fracture of head and neck of femur

Appendix A

S72.091 Other fracture of head and neck of right femur
 S72.091A initial encounter for closed fracture
 S72.091B initial encounter for open fracture type I or II
 S72.091C initial encounter for open fracture type IIIA, IIIB, or IIIC
 S72.092 Other fracture of head and neck of left femur
 S72.092A initial encounter for closed fracture
 S72.092B initial encounter for open fracture type I or II
 S72.092C initial encounter for open fracture type IIIA, IIIB, or IIIC
 S72.099 Other fracture of head and neck of unspecified femur
 S72.099A initial encounter for closed fracture
 S72.099B initial encounter for open fracture type I or II
 S72.099C initial encounter for open fracture type IIIA, IIIB, or IIIC
 S79.001A initial encounter for closed fracture
 S79.002A initial encounter for closed fracture
 S79.009A initial encounter for closed fracture
 S79.091A initial encounter for closed fracture
 S79.092A initial encounter for closed fracture
 S79.099A initial encounter for closed fracture
 S79.101A initial encounter for closed fracture
 S79.102A initial encounter for closed fracture
 S79.109A initial encounter for closed fracture
 S79.191A initial encounter for closed fracture
 S79.192A initial encounter for closed fracture
 S79.199A initial encounter for closed fracture

Pathologic fracture

ICD9 Diagnosis Codes

733.14 Pathologic fracture of neck of femur
 733.15 Pathologic fracture of other specified part of femur

ICD10 Diagnosis Codes

M80 Osteoporosis with current pathological fracture
 M80.05 Age-related osteoporosis with current pathological fracture, femur
 M80.051 Age-related osteoporosis with current pathological fracture, right femur
 M80.051A initial encounter for fracture
 M80.052 Age-related osteoporosis with current pathological fracture, left femur
 M80.052A initial encounter for fracture
 M80.059 Age-related osteoporosis with current pathological fracture, unspecified femur
 M80.059A initial encounter for fracture
 M80.85 Other osteoporosis with current pathological fracture, femur
 M80.851 Other osteoporosis with current pathological fracture, right femur
 M80.851A initial encounter for fracture
 M80.852 Other osteoporosis with current pathological fracture, left femur
 M80.852A initial encounter for fracture
 M80.859 Other osteoporosis with current pathological fracture, unspecified femur
 M80.859A initial encounter for fracture
 M84.4 Pathological fracture, not elsewhere classified
 M84.45 Pathological fracture, femur and pelvis
 M84.451 Pathological fracture, right femur
 M84.451A initial encounter for fracture
 M84.452 Pathological fracture, left femur
 M84.452A initial encounter for fracture
 M84.453 Pathological fracture, unspecified femur
 M84.453A initial encounter for fracture
 M84.459 Pathological fracture, hip, unspecified
 M84.459A initial encounter for fracture
 M84.6 Pathological fracture in other disease
 M84.651 Pathological fracture in other disease, right femur
 M84.651A initial encounter for fracture

Appendix A

M84.652 Pathological fracture in other disease, left femur
 M84.652A..... initial encounter for fracture
 M84.653 Pathological fracture in other disease, unspecified femur
 M84.653A..... initial encounter for fracture
 M84.659 Pathological fracture in other disease, hip, unspecified
 M84.659A..... initial encounter for fracture
 M84.7 Nontraumatic fracture, not elsewhere classified
 M84.75 Atypical femoral fracture
 M84.750A..... initial encounter for fracture
 M84.751 Incomplete atypical femoral fracture, right leg
 M84.751A..... initial encounter for fracture
 M84.752 Incomplete atypical femoral fracture, left leg
 M84.752A..... initial encounter for fracture
 M84.753 Incomplete atypical femoral fracture, unspecified leg
 M84.753A..... initial encounter for fracture
 M84.754 Complete transverse atypical femoral fracture, right leg
 M84.754A..... initial encounter for fracture
 M84.755 Complete transverse atypical femoral fracture, left leg
 M84.755A..... initial encounter for fracture
 M84.756 Complete transverse atypical femoral fracture, unspecified leg
 M84.756A..... initial encounter for fracture
 M84.757 Complete oblique atypical femoral fracture, right leg
 M84.757A..... initial encounter for fracture
 M84.758 Complete oblique atypical femoral fracture, left leg
 M84.758A..... initial encounter for fracture
 M84.759 Complete oblique atypical femoral fracture, unspecified leg
 M84.759A..... initial encounter for fracture

Fracture Aftercare

ICD9 Diagnosis Codes

V54.13 Aftercare for healing traumatic fracture of hip
 V54.15 Aftercare for healing traumatic fracture of upper leg

Fracture Aftercare

ICD10 Diagnosis Codes

S72.001D Fx unsp part of nk of r femr, subs for clos fx w routn heal
 S72.002D Fx unsp part of nk of l femr, subs for clos fx w routn heal
 S72.009D Fx unsp prt of nk of unsp femr, 7thD
 S72.011D Unsp intracap fx right femur, subs for clos fx w routn heal
 S72.012D Unsp intracap fx left femur, subs for clos fx w routn heal
 S72.019D Unsp intracap fx unsp femur, subs for clos fx w routn heal
 S72.019E Unsp intracap fx unsp femr, 7thE
 S72.021D Disp fx of epiphy (separation) (upper) of r femr, 7thD
 S72.022D Disp fx of epiphy (separation) (upper) of l femr, 7thD
 S72.023D Disp fx of epiphy (separation) (upper) of unsp femr, 7thD
 S72.023E Disp fx of epiphy (separation) (upper) of unsp femr, 7thE
 S72.024D Nondisp fx of epiphy (separation) (upper) of r femr, 7thD
 S72.025D Nondisp fx of epiphy (separation) (upper) of l femr, 7thD
 S72.026D Nondisp fx of epiphy (separation) (upper) of unsp femr, 7thD
 S72.026E Nondisp fx of epiphy (separation) (upper) of unsp femr, 7thE
 S72.031D Displ midcervical fx r femur, subs for clos fx w routn heal
 S72.032D Displ midcervical fx l femur, subs for clos fx w routn heal
 S72.033D Displ midcervical fx unsp femr, 7thD
 S72.033E Displ midcervical fx unsp femr, 7thE
 S72.034D Nondisp midcervical fx r femr, subs for clos fx w routn heal
 S72.035D Nondisp midcervical fx l femr, subs for clos fx w routn heal
 S72.036D Nondisp midcervical fx unsp femr, 7thD
 S72.036E Nondisp midcervical fx unsp femr, 7thE
 S72.041D Disp fx of base of nk of r femr, 7thD

Appendix A

S72.042D Disp fx of base of nk of l femr, 7thD
 S72.043D Disp fx of base of nk of unsp femr, 7thD
 S72.043E Disp fx of base of nk of unsp femr, 7thE
 S72.044D Nondisp fx of base of nk of r femr, 7thD
 S72.045D Nondisp fx of base of nk of l femr, 7thD
 S72.046D Nondisp fx of base of nk of unsp femr, 7thD
 S72.046E Nondisp fx of base of nk of unsp femr, 7thE
 S72.051D Unsp fx head of right femur, subs for clos fx w routn heal
 S72.052D Unsp fx head of left femur, subs for clos fx w routn heal
 S72.059D Unsp fx head of unsp femur, subs for clos fx w routn heal
 S72.061D Displ artic fx head of r femr, subs for clos fx w routn heal
 S72.062D Displ artic fx head of l femr, subs for clos fx w routn heal
 S72.063D Displ artic fx head of unsp femr, 7thD
 S72.064D Nondisp artic fx head of r femr, 7thD
 S72.065D Nondisp artic fx head of l femr, 7thD
 S72.066D Nondisp artic fx head of unsp femr, 7thD
 S72.091D Oth fx head/neck of r femur, subs for clos fx w routn heal
 S72.092D Oth fx head/neck of l femur, subs for clos fx w routn heal
 S72.099D Oth fx head/neck of unsp femr, subs for clos fx w routn heal
 S72.099E Oth fx head/neck of unsp femr, 7thE
 S72.101D Unsp trochan fx right femur, subs for clos fx w routn heal
 S72.102D Unsp trochan fx left femur, subs for clos fx w routn heal
 S72.109D Unsp trochan fx unsp femur, subs for clos fx w routn heal
 S72.109E Unsp trochan fx unsp femr, 7thE
 S72.111D Disp fx of greater trochanter of r femr, 7thD
 S72.112D Disp fx of greater trochanter of l femr, 7thD
 S72.113D Disp fx of greater trochanter of unsp femr, 7thD
 S72.114D Nondisp fx of greater trochanter of r femr, 7thD
 S72.115D Nondisp fx of greater trochanter of l femr, 7thD
 S72.116D Nondisp fx of greater trochanter of unsp femr, 7thD
 S72.121D Disp fx of less trochanter of r femr, 7thD
 S72.122D Disp fx of less trochanter of l femr, 7thD
 S72.123D Disp fx of less trochanter of unsp femr, 7thD
 S72.124D Nondisp fx of less trochanter of r femr, 7thD
 S72.125D Nondisp fx of less trochanter of l femr, 7thD
 S72.126D Nondisp fx of less trochanter of unsp femr, 7thD
 S72.131D Displ apophyseal fx r femur, subs for clos fx w routn heal
 S72.132D Displ apophyseal fx l femur, subs for clos fx w routn heal
 S72.133D Displ apophyseal fx unsp femr, subs for clos fx w routn heal
 S72.134D Nondisp apophyseal fx r femur, subs for clos fx w routn heal
 S72.135D Nondisp apophyseal fx l femur, subs for clos fx w routn heal
 S72.136D Nondisp apophyseal fx unsp femr, 7thD
 S72.141D Displ intertroch fx r femur, subs for clos fx w routn heal
 S72.142D Displ intertroch fx l femur, subs for clos fx w routn heal
 S72.143D Displ intertroch fx unsp femr, subs for clos fx w routn heal
 S72.144D Nondisp intertroch fx r femur, subs for clos fx w routn heal
 S72.145D Nondisp intertroch fx l femur, subs for clos fx w routn heal
 S72.146D Nondisp intertroch fx unsp femr, 7thD

Stress fracture

ICD9 Diagnosis Codes

733.96 Stress fracture of femoral neck
 733.97 Stress fracture of shaft of femur
 ICD10 diagnosis Codes (M84.3xxx Stress fracture)
 M84.351 Stress fracture, right femur
 M84.351A initial encounter for fracture
 M84.352 Stress fracture, left femur
 M84.352A initial encounter for fracture

Appendix A

M84.353 Stress fracture, unspecified femur
M84.353A initial encounter for fracture
M84.359 Stress fracture, hip, unspecified
M84.359A initial encounter for fracture

HIP AND FEMUR FRACTURES

ICD9 Procedure codes

78.55 Internal fixation of bone without fracture reduction, femur
79.05 Closed reduction of fracture without internal fixation, femur
79.15 Closed reduction of fracture with internal fixation, femur
79.25 Open reduction of fracture without internal fixation, femur
79.35 Open reduction of fracture with internal fixation, femur
79.65 Debridement of open fracture site, femur
815.1 Total hip replacement
815.2 Partial hip replacement

HIP AND FEMUR FRACTURES

ICD10 Procedure codes

REPOSITION

0QS6 Upper Femur, Right (ALL)
0QS604Z Reposition Right Upper Femur with Internal Fixation Device, Open Approach
0QS605Z Reposition Right Upper Femur with External Fixation Device, Open Approach
0QS606Z Reposition Right Upper Femur with Intramedullary Internal Fixation Device, Open Approach
0QS60BZ Reposition Right Upper Femur with Monoplanar External Fixation Device, Open Approach
0QS60CZ Reposition Right Upper Femur with Ring External Fixation Device, Open Approach
0QS60DZ Reposition Right Upper Femur with Hybrid External Fixation Device, Open Approach
0QS60ZZ Reposition Right Upper Femur, Open Approach
0QS634Z Reposition Right Upper Femur with Internal Fixation Device, Percutaneous Approach
0QS635Z Reposition Right Upper Femur with External Fixation Device, Percutaneous Approach
0QS636Z Reposition Right Upper Femur with Intramedullary Internal Fixation Device, Percutaneous Approach
0QS63BZ Reposition Right Upper Femur with Monoplanar External Fixation Device, Percutaneous Approach
0QS63CZ Reposition Right Upper Femur with Ring External Fixation Device, Percutaneous Approach
0QS63DZ Reposition Right Upper Femur with Hybrid External Fixation Device, Percutaneous Approach
0QS63ZZ Reposition Right Upper Femur, Percutaneous Approach
0QS644Z Reposition Right Upper Femur with Internal Fixation Device, Percutaneous Endoscopic Approach
0QS645Z Reposition Right Upper Femur with External Fixation Device, Percutaneous Endoscopic Approach
0QS646Z Reposition Right Upper Femur with Intramedullary Internal Fixation Device, Percutaneous Endoscopic Approach
0QS64BZ Reposition Right Upper Femur with Monoplanar External Fixation Device, Percutaneous Endoscopic Approach
0QS64CZ Reposition Right Upper Femur with Ring External Fixation Device, Percutaneous Endoscopic Approach
0QS64DZ Reposition Right Upper Femur with Hybrid External Fixation Device, Percutaneous Endoscopic Approach
0QS64ZZ Reposition Right Upper Femur, Percutaneous Endoscopic Approach
0QS6XZZ Reposition Right Upper Femur, External Approach
0QS7 Upper Femur, Left (ALL)
0QS704Z Reposition Left Upper Femur with Internal Fixation Device, Open Approach
0QS705Z Reposition Left Upper Femur with External Fixation Device, Open Approach
0QS706Z Reposition Left Upper Femur with Intramedullary Internal Fixation Device, Open Approach
0QS70BZ Reposition Left Upper Femur with Monoplanar External Fixation Device, Open Approach
0QS70CZ Reposition Left Upper Femur with Ring External Fixation Device, Open Approach
0QS70DZ Reposition Left Upper Femur with Hybrid External Fixation Device, Open Approach
0QS70ZZ Reposition Left Upper Femur, Open Approach
0QS734Z Reposition Left Upper Femur with Internal Fixation Device, Percutaneous Approach
0QS735Z Reposition Left Upper Femur with External Fixation Device, Percutaneous Approach
0QS736Z Reposition Left Upper Femur with Intramedullary Internal Fixation Device, Percutaneous Approach
0QS73BZ Reposition Left Upper Femur with Monoplanar External Fixation Device, Percutaneous Approach
0QS73CZ Reposition Left Upper Femur with Ring External Fixation Device, Percutaneous Approach
0QS73DZ Reposition Left Upper Femur with Hybrid External Fixation Device, Percutaneous Approach
0QS73ZZ Reposition Left Upper Femur, Percutaneous Approach
0QS744Z Reposition Left Upper Femur with Internal Fixation Device, Percutaneous Endoscopic Approach
0QS745Z Reposition Left Upper Femur with External Fixation Device, Percutaneous Endoscopic Approach

Appendix A

00S746Z Reposition Left Upper Femur with Intramedullary Internal Fixation Device, Percutaneous Endoscopic Approach
00S74BZ Reposition Left Upper Femur with Monoplanar External Fixation Device, Percutaneous Endoscopic Approach
00S74CZ Reposition Left Upper Femur with Ring External Fixation Device, Percutaneous Endoscopic Approach
00S74DZ Reposition Left Upper Femur with Hybrid External Fixation Device, Percutaneous Endoscopic Approach
00S74ZZ Reposition Left Upper Femur, Percutaneous Endoscopic Approach
00S7XZZ Reposition Left Upper Femur, External Approach
00S8 Femoral Shaft, Right (ALL)
00S804Z Reposition Right Femoral Shaft with Internal Fixation Device, Open Approach
00S805Z Reposition Right Femoral Shaft with External Fixation Device, Open Approach
00S806Z Reposition Right Femoral Shaft with Intramedullary Internal Fixation Device, Open Approach
00S80BZ Reposition Right Femoral Shaft with Monoplanar External Fixation Device, Open Approach
00S80CZ Reposition Right Femoral Shaft with Ring External Fixation Device, Open Approach
00S80DZ Reposition Right Femoral Shaft with Hybrid External Fixation Device, Open Approach
00S80ZZ Reposition Right Femoral Shaft, Open Approach
00S834Z Reposition Right Femoral Shaft with Internal Fixation Device, Percutaneous Approach
00S835Z Reposition Right Femoral Shaft with External Fixation Device, Percutaneous Approach
00S836Z Reposition Right Femoral Shaft with Intramedullary Internal Fixation Device, Percutaneous Approach
00S83BZ Reposition Right Femoral Shaft with Monoplanar External Fixation Device, Percutaneous Approach
00S83CZ Reposition Right Femoral Shaft with Ring External Fixation Device, Percutaneous Approach
00S83DZ Reposition Right Femoral Shaft with Hybrid External Fixation Device, Percutaneous Approach
00S83ZZ Reposition Right Femoral Shaft, Percutaneous Approach
00S844Z Reposition Right Femoral Shaft with Internal Fixation Device, Percutaneous Endoscopic Approach
00S845Z Reposition Right Femoral Shaft with External Fixation Device, Percutaneous Endoscopic Approach
00S846Z Reposition Right Femoral Shaft with Intramedullary Internal Fixation Device, Percutaneous Endoscopic Approach
00S84BZ Reposition Right Femoral Shaft with Monoplanar External Fixation Device, Percutaneous Endoscopic Approach
00S84CZ Reposition Right Femoral Shaft with Ring External Fixation Device, Percutaneous Endoscopic Approach
00S84DZ Reposition Right Femoral Shaft with Hybrid External Fixation Device, Percutaneous Endoscopic Approach
00S84ZZ Reposition Right Femoral Shaft, Percutaneous Endoscopic Approach
00S8XZZ Reposition Right Femoral Shaft, External Approach
00S9 Femoral Shaft, Left (ALL)
00S904Z Reposition Left Femoral Shaft with Internal Fixation Device, Open Approach
00S905Z Reposition Left Femoral Shaft with External Fixation Device, Open Approach
00S906Z Reposition Left Femoral Shaft with Intramedullary Internal Fixation Device, Open Approach
00S90BZ Reposition Left Femoral Shaft with Monoplanar External Fixation Device, Open Approach
00S90CZ Reposition Left Femoral Shaft with Ring External Fixation Device, Open Approach
00S90DZ Reposition Left Femoral Shaft with Hybrid External Fixation Device, Open Approach
00S90ZZ Reposition Left Femoral Shaft, Open Approach
00S934Z Reposition Left Femoral Shaft with Internal Fixation Device, Percutaneous Approach
00S935Z Reposition Left Femoral Shaft with External Fixation Device, Percutaneous Approach
00S936Z Reposition Left Femoral Shaft with Intramedullary Internal Fixation Device, Percutaneous Approach
00S93BZ Reposition Left Femoral Shaft with Monoplanar External Fixation Device, Percutaneous Approach
00S93CZ Reposition Left Femoral Shaft with Ring External Fixation Device, Percutaneous Approach
00S93DZ Reposition Left Femoral Shaft with Hybrid External Fixation Device, Percutaneous Approach
00S93ZZ Reposition Left Femoral Shaft, Percutaneous Approach
00S944Z Reposition Left Femoral Shaft with Internal Fixation Device, Percutaneous Endoscopic Approach
00S945Z Reposition Left Femoral Shaft with External Fixation Device, Percutaneous Endoscopic Approach
00S946Z Reposition Left Femoral Shaft with Intramedullary Internal Fixation Device, Percutaneous Endoscopic Approach
00S94BZ Reposition Left Femoral Shaft with Monoplanar External Fixation Device, Percutaneous Endoscopic Approach
00S94CZ Reposition Left Femoral Shaft with Ring External Fixation Device, Percutaneous Endoscopic Approach
00S94DZ Reposition Left Femoral Shaft with Hybrid External Fixation Device, Percutaneous Endoscopic Approach
00S94ZZ Reposition Left Femoral Shaft, Percutaneous Endoscopic Approach
00S9XZZ Reposition Left Femoral Shaft, External Approach
00S84ZZ Reposition Right Lower Femur, Percutaneous Endoscopic Approach
00S8XZZ Reposition Right Lower Femur, External Approach
00S8 Lower Femur, Right (ALL)
00S804Z Reposition Right Lower Femur with Internal Fixation Device, Open Approach
00S805Z Reposition Right Lower Femur with External Fixation Device, Open Approach
00S806Z Reposition Right Lower Femur with Intramedullary Internal Fixation Device, Open Approach

Appendix A

0QSB0BZ Reposition Right Lower Femur with Monoplanar External Fixation Device, Open Approach
0QSB0CZ Reposition Right Lower Femur with Ring External Fixation Device, Open Approach
0QSB0DZ Reposition Right Lower Femur with Hybrid External Fixation Device, Open Approach
0QSB0ZZ Reposition Right Lower Femur, Open Approach
0QSB34Z Reposition Right Lower Femur with Internal Fixation Device, Percutaneous Approach
0QSB35Z Reposition Right Lower Femur with External Fixation Device, Percutaneous Approach
0QSB36Z Reposition Right Lower Femur with Intramedullary Internal Fixation Device, Percutaneous Approach
0QSB3BZ Reposition Right Lower Femur with Monoplanar External Fixation Device, Percutaneous Approach
0QSB3CZ Reposition Right Lower Femur with Ring External Fixation Device, Percutaneous Approach
0QSB3DZ Reposition Right Lower Femur with Hybrid External Fixation Device, Percutaneous Approach
0QSB3ZZ Reposition Right Lower Femur, Percutaneous Approach
0QSB44Z Reposition Right Lower Femur with Internal Fixation Device, Percutaneous Endoscopic Approach
0QSB45Z Reposition Right Lower Femur with External Fixation Device, Percutaneous Endoscopic Approach
0QSB46Z Reposition Right Lower Femur with Intramedullary Internal Fixation Device, Percutaneous Endoscopic Approach
0QSB4BZ Reposition Right Lower Femur with Monoplanar External Fixation Device, Percutaneous Endoscopic Approach
0QSB4CZ Reposition Right Lower Femur with Ring External Fixation Device, Percutaneous Endoscopic Approach
0QSB4DZ Reposition Right Lower Femur with Hybrid External Fixation Device, Percutaneous Endoscopic Approach
0QSB4ZZ Reposition Right Lower Femur, Percutaneous Endoscopic Approach
0QSBXZZ Reposition Right Lower Femur, External Approach
0QSC Lower Femur, Left (all)
0QSC04Z Reposition Left Lower Femur with Internal Fixation Device, Open Approach
0QSC05Z Reposition Left Lower Femur with External Fixation Device, Open Approach
0QSC06Z Reposition Left Lower Femur with Intramedullary Internal Fixation Device, Open Approach
0QSC0BZ Reposition Left Lower Femur with Monoplanar External Fixation Device, Open Approach
0QSC0CZ Reposition Left Lower Femur with Ring External Fixation Device, Open Approach
0QSC0DZ Reposition Left Lower Femur with Hybrid External Fixation Device, Open Approach
0QSC0ZZ Reposition Left Lower Femur, Open Approach
0QSC34Z Reposition Left Lower Femur with Internal Fixation Device, Percutaneous Approach
0QSC35Z Reposition Left Lower Femur with External Fixation Device, Percutaneous Approach
0QSC36Z Reposition Left Lower Femur with Intramedullary Internal Fixation Device, Percutaneous Approach
0QSC3BZ Reposition Left Lower Femur with Monoplanar External Fixation Device, Percutaneous Approach
0QSC3CZ Reposition Left Lower Femur with Ring External Fixation Device, Percutaneous Approach
0QSC3DZ Reposition Left Lower Femur with Hybrid External Fixation Device, Percutaneous Approach
0QSC3ZZ Reposition Left Lower Femur, Percutaneous Approach
0QSC44Z Reposition Left Lower Femur with Internal Fixation Device, Percutaneous Endoscopic Approach
0QSC45Z Reposition Left Lower Femur with External Fixation Device, Percutaneous Endoscopic Approach
0QSC46Z Reposition Left Lower Femur with Intramedullary Internal Fixation Device, Percutaneous Endoscopic Approach
0QSC4BZ Reposition Left Lower Femur with Monoplanar External Fixation Device, Percutaneous Endoscopic Approach
0QSC4CZ Reposition Left Lower Femur with Ring External Fixation Device, Percutaneous Endoscopic Approach
0QSC4DZ Reposition Left Lower Femur with Hybrid External Fixation Device, Percutaneous Endoscopic Approach
0QSC4ZZ Reposition Left Lower Femur, Percutaneous Endoscopic Approach
0QSCXZZ Reposition Left Lower Femur, External Approach

INSERTION

0QH6 Upper Femur, Right (ALL)
0QH604Z Insertion of Internal Fixation Device into Right Upper Femur, Open Approach
0QH605Z Insertion of External Fixation Device into Right Upper Femur, Open Approach
0QH606Z Insertion of Intramedullary Internal Fixation Device into Right Upper Femur, Open Approach
0QH608Z Insertion of Limb Lengthening External Fixation Device into Right Upper Femur, Open Approach
0QH60BZ Insertion of Monoplanar External Fixation Device into Right Upper Femur, Open Approach
0QH60CZ Insertion of Ring External Fixation Device into Right Upper Femur, Open Approach
0QH60DZ Insertion of Hybrid External Fixation Device into Right Upper Femur, Open Approach
0QH634Z Insertion of Internal Fixation Device into Right Upper Femur, Percutaneous Approach
0QH635Z Insertion of External Fixation Device into Right Upper Femur, Percutaneous Approach
0QH636Z Insertion of Intramedullary Internal Fixation Device into Right Upper Femur, Percutaneous Approach
0QH638Z Insertion of Limb Lengthening External Fixation Device into Right Upper Femur, Percutaneous Approach
0QH63BZ Insertion of Monoplanar External Fixation Device into Right Upper Femur, Percutaneous Approach
0QH63CZ Insertion of Ring External Fixation Device into Right Upper Femur, Percutaneous Approach

Appendix A

0QHC3DZInsertion of Hybrid External Fixation Device into Left Lower Femur, Percutaneous Approach
 0QHC44ZInsertion of Internal Fixation Device into Left Lower Femur, Percutaneous Endoscopic Approach
 0QHC45ZInsertion of External Fixation Device into Left Lower Femur, Percutaneous Endoscopic Approach
 0QHC46ZInsertion of Intramedullary Internal Fixation Device into Left Lower Femur, Percutaneous Endoscopic A
 0QHC48ZInsertion of Limb Lengthening External Fixation Device into Left Lower Femur, Percutaneous Endoscopic
 0QHC4BZInsertion of Monoplanar External Fixation Device into Left Lower Femur, Percutaneous Endoscopic Appro
 0QHC4CZInsertion of Ring External Fixation Device into Left Lower Femur, Percutaneous Endoscopic Approach
 0QHC4DZInsertion of Hybrid External Fixation Device into Left Lower Femur, Percutaneous Endoscopic Approach

HIP AND FEMUR FRACTURES

HCPCS/CPT codes

27125Hemiarthroplasty, hip, partial (eg, femoral stem prosthesis, bipolar arthroplasty)
 27130Arthroplasty, acetabular and proximal femoral prosthetic replacement (total hip arthroplasty), with or without autograft por allograft
 27220Closed treatment of acetabulum (hip socket) fracture(s)
 27222Closed treatment of acetabulum (hip socket) fracture(s)
 27226Fracture and/or Dislocation Procedures on the Pelvis and Hip Joint
 27227Fracture and/or Dislocation Procedures on the Pelvis and Hip Joint
 27228Fracture and/or Dislocation Procedures on the Pelvis and Hip Joint
 27230Closed treatment of femoral fracture, proximal end, neck; without manipulation
 27232Closed treatment of femoral fracture, proximal end, neck; with manipulation, with or without skeletal traction
 27235Percutaneous skeletal fixation of femoral fracture, proximal end, neck
 27236Open treatment of femoral fracture, proximal end, neck, internal fixation or prosthetic replacement
 27238Closed treatment of intertrochanteric, peritrochanteric, or subtrochanteric femoral fracture; without manipulation
 27240Closed treatment of intertrochanteric, peritrochanteric, or subtrochanteric femoral fracture; with manipulation, with or without skin or skeletal traction
 27245Treatment of intertrochanteric, peritrochanteric, or subtrochanteric femoral fracture
 27244Treatment of intertrochanteric, peritrochanteric, or subtrochanteric femoral fracture; with plate/screw type implant, with or without cerclage
 27246Closed treatment of greater trochanteric fracture, without manipulation
 27248Open treatment of greater trochanteric fracture, includes internal fixation, when performed
 27254Fracture Procedures on the Pelvis and Hip Joint
 27267Closed treatment of femoral fracture, proximal end, head; without manipulation
 27268Closed treatment of femoral fracture, proximal end, head; with manipulation
 27269Open treatment of femoral fracture, proximal end, head, includes internal fixation, when performed
 27500Fracture Procedures on the Femur (Thigh Region) and Knee Joint
 27501Fracture Procedures on the Femur (Thigh Region) and Knee Joint
 27502Fracture Procedures on the Femur (Thigh Region) and Knee Joint
 27503Fracture Procedures on the Femur (Thigh Region) and Knee Joint
 27506Fracture Procedures on the Femur (Thigh Region) and Knee Joint
 27507Fracture Procedures on the Femur (Thigh Region) and Knee Joint
 27508Fracture Procedures on the Femur (Thigh Region) and Knee Joint
 27509Fracture Procedures on the Femur (Thigh Region) and Knee Joint
 27510Fracture Procedures on the Femur (Thigh Region) and Knee Joint
 27511Fracture Procedures on the Femur (Thigh Region) and Knee Joint
 27513Fracture Procedures on the Femur (Thigh Region) and Knee Joint
 27514Fracture Procedures on the Femur (Thigh Region) and Knee Joint

Appendix A

Pregnancy

Diagnosis Codes

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

Procedure Codes

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

Appendix A

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

Appendix A

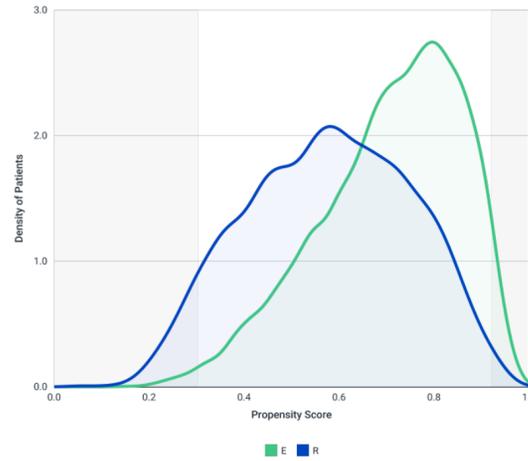
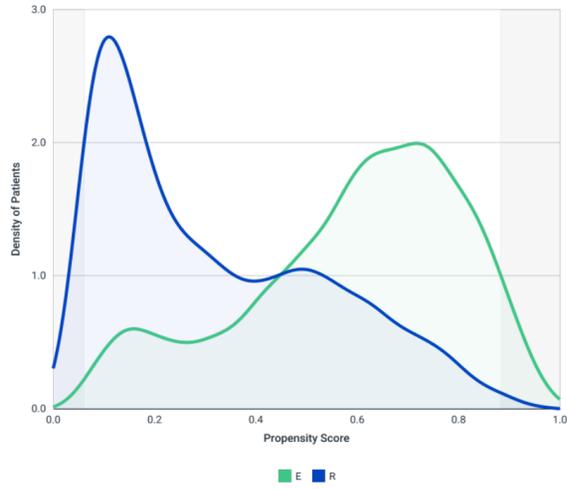
- 74.2 EXTRAPERITONEAL CESAREAN SECTION
- 74.3 REMOVAL OF EXTRATUBAL ECTOPIC PREGNANCY
- 74.4 CESAREAN SECTION OF OTHER SPECIFIED TYPE
- 74.9 CESAREAN SECTION OF UNSPECIFIED TYPE
- 74.91 HYSTEROTOMY TO TERMINATE PREGNANCY
- 74.99 OTHER CESAREAN SECTION OF UNSPECIFIED TYPE
- 75.4 MANUAL REMOVAL OF RETAINED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

Appendix B

Optum

MarketScan

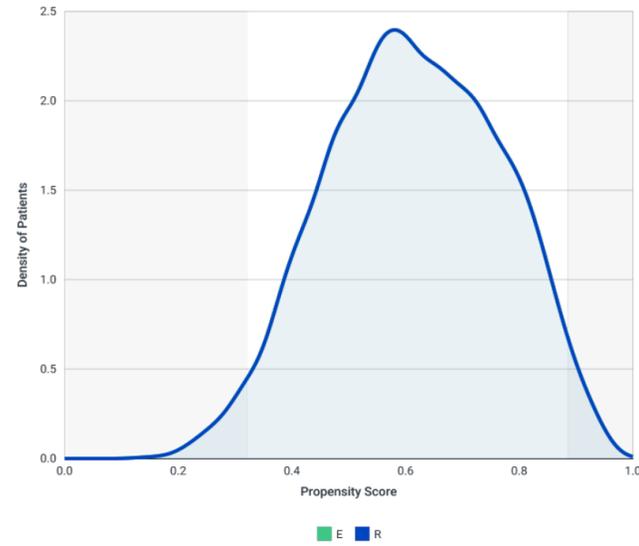
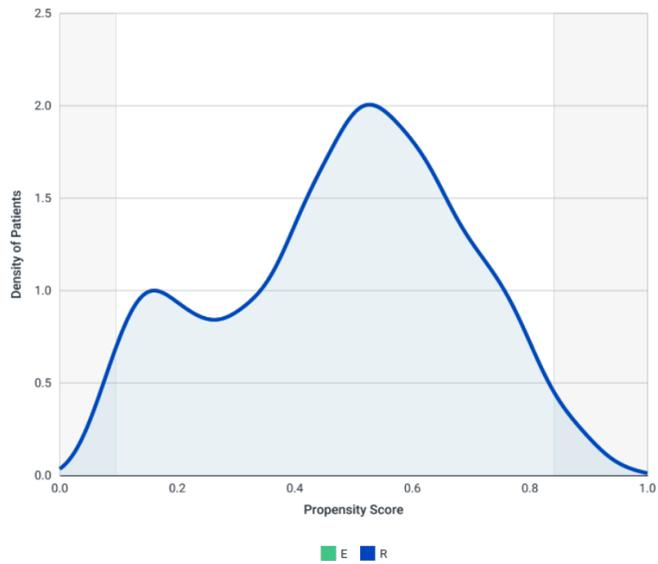
BEFORE PS MATCHING



The c-statistics for the propensity score model, pre-matching was 0.803.
The postmatching c-statistic was 0.533

The c-statistics for the propensity score model, pre-matching was 0.714.
The postmatching c-statistic was 0.526.

AFTER PS MATCHING



Appendix B

Variable	Unmatched								
	Optum			MarketScan			POOLED		
	Raloxifene	Zoledronic Acid	St. Diff.	Raloxifene	Zoledronic Acid	St. Diff.	Raloxifene	Zoledronic Acid	St. Diff.
Number of patients	6,815	6,605		6,694	13,997		13,509	20,602	
Demographic characteristics									
Age									
...mean (sd)	73.41 (5.90)	74.02 (5.52)	-0.107	73.81 (7.06)	75.61 (7.14)	-0.254	73.61 (6.50)	75.15 (6.71)	-0.233
...median [IQR]	73.00 [68.00, 78.00]	75.00 [69.00, 79.00]	-0.350	72.00 [68.00, 79.00]	75.00 [70.00, 81.00]	-0.423	72.50 (6.50)	75.00 (6.71)	-0.378
Age categories									
...< 70; n (%)	2,138 (31.4%)	1,714 (26.0%)	0.010	2,366 (35.3%)	3,498 (25.0%)	0.019	4,504 (33.4%)	5,212 (28.1%)	0.115
...70 - 74; n (%)	1,773 (26.0%)	1,575 (23.8%)	0.004	1,604 (24.0%)	3,134 (22.4%)	0.003	3,377 (25.0%)	4,709 (25.4%)	-0.009
...≥ 75; n (%)	2,904 (42.6%)	3,316 (50.2%)	-0.011	2,724 (40.7%)	7,365 (52.6%)	-0.017	5,628 (41.7%)	10,681 (57.6%)	-0.322
Region									
...Northeast; n (%)	1,052 (15.4%)	609 (9.2%)	0.018	1,226 (18.3%)	2,138 (15.3%)	0.007	2,278 (16.9%)	2,747 (14.8%)	0.058
...South; n (%)	2,873 (42.2%)	2,838 (43.0%)	-0.001	2,225 (33.2%)	4,693 (33.5%)	-0.001	5,098 (37.8%)	7,531 (40.6%)	-0.057
...Midwest; n (%)	776 (11.4%)	1,623 (24.6%)	-0.031	2,183 (32.6%)	5,245 (37.5%)	-0.008	2,959 (21.9%)	6,868 (37.0%)	-0.336
...West; n (%)	2,114 (31.0%)	1,535 (23.2%)	0.015	1,060 (15.8%)	1,921 (13.8%)	0.005	3,174 (23.5%)	3,456 (18.6%)	0.120
Calendar Time									
...Aug 2007 - Aug 2010; n (%)	1,729 (25.4%)	2,334 (35.3%)	-0.018	2,398 (35.8%)	3,308 (23.6%)	0.022	4,127 (30.6%)	5,642 (30.4%)	0.004
...Aug 2010 - Aug 2013; n (%)	1,436 (21.1%)	3,541 (53.6%)	-0.053	2,163 (32.3%)	5,934 (42.4%)	-0.017	3,599 (26.7%)	9,475 (51.1%)	-0.517
...Aug 2013 - Aug 2016; n (%)	1,570 (23.0%)	286 (4.3%)	0.051	1,587 (23.7%)	3,512 (25.1%)	-0.003	3,157 (23.4%)	3,798 (20.5%)	0.070
...Aug 2016 - Mar 2020; n (%)	2,080 (30.5%)	444 (6.7%)	0.055	546 (8.2%)	1,243 (8.9%)	-0.002	2,626 (19.4%)	1,687 (9.1%)	0.298
Metropolitan Statistical Area									
...Urban; n (%)	N/A	N/A	N/A	5,124 (76.5%)	10,520 (75.2%)	0.001	5,122 (76.6%)	9,932 (75.2%)	0.002
...Rural; n (%)	N/A	N/A	N/A	94 (1.4%)	256 (1.8%)	-0.003	94 (1.4%)	246 (1.6%)	-0.004
...Unknown/Missing; n (%)	N/A	N/A	N/A	1,476 (22.0%)	3,221 (23.0%)	-0.002	1,475 (22.0%)	3,030 (22.9%)	-0.002
General Health Related Measures									
Smoking; n (%)	525 (7.7%)	588 (8.9%)	-0.004	257 (3.8%)	800 (5.7%)	-0.009	782 (5.8%)	1,388 (7.5%)	-0.068
Alcohol/Drug abuse or dependence ; n (%)	21 (0.3%)	15 (0.2%)	0.002	5 (0.1%)	22 (0.2%)	-0.003	026 (0.2%)	037 (0.2%)	0.000
Obesity or Overweight; n (%)	770 (11.3%)	371 (5.6%)	0.020	277 (4.1%)	723 (5.2%)	-0.005	1,047 (7.8%)	1,094 (5.9%)	0.075
Obesity; n (%)	416 (6.1%)	277 (4.2%)	0.008	167 (2.5%)	509 (3.6%)	-0.006	583 (4.3%)	786 (4.2%)	0.005
Overweight; n (%)	414 (6.1%)	115 (1.7%)	0.022	127 (1.9%)	251 (1.8%)	0.001	541 (4.0%)	366 (2.0%)	0.117
Cardiovascular Measures									
Hypertension; n (%)	4,171 (61.2%)	4,326 (65.5%)	-0.005	3,474 (51.9%)	8,219 (58.7%)	-0.009	7,645 (56.6%)	12,545 (67.6%)	-0.228
Hyperlipidemia; n (%)	4,597 (67.5%)	4,422 (66.9%)	0.001	3,247 (48.5%)	7,278 (52.0%)	-0.005	7,844 (58.1%)	11,700 (63.1%)	-0.102
Coronary artery disease (MI, angina, Coronary atherosclerosis and other forms of chronic ischemic heart disease); n (%)	857 (12.6%)	1,130 (17.1%)	-0.012	813 (12.1%)	2,486 (17.8%)	-0.015	1,670 (12.4%)	3,616 (19.5%)	-0.195
Old MI; n (%)	98 (1.4%)	157 (2.4%)	-0.007	49 (0.7%)	190 (1.4%)	-0.007	147 (1.1%)	347 (1.9%)	-0.066
Acute MI; n (%)	39 (0.6%)	65 (1.0%)	-0.004	37 (0.6%)	150 (1.1%)	-0.005	076 (0.6%)	215 (1.2%)	-0.064
ACS/unstable angina; n (%)	53 (0.8%)	90 (1.4%)	-0.006	78 (1.2%)	213 (1.5%)	-0.003	131 (1.0%)	303 (1.6%)	-0.053
Stable angina; n (%)	223 (3.3%)	203 (3.1%)	0.001	145 (2.2%)	407 (2.9%)	-0.004	368 (2.7%)	610 (3.3%)	-0.035
Coronary atherosclerosis and other CHD; n (%)	719 (10.6%)	1,010 (15.3%)	-0.013	710 (10.6%)	2,205 (15.8%)	-0.014	1,429 (10.6%)	3,215 (17.3%)	-0.194
History of CABG or PTCA; n (%)	133 (2.0%)	222 (3.4%)	-0.009	60 (0.9%)	231 (1.7%)	-0.007	193 (1.4%)	453 (2.4%)	-0.073
Cerebrovascular disease (Stroke, TIA, Late effects); n (%)	281 (4.1%)	451 (6.8%)	-0.012	250 (3.7%)	948 (6.8%)	-0.014	531 (3.9%)	1,399 (7.5%)	-0.156
Stroke (Ischemic or hemorrhagic); n (%)	134 (2.0%)	228 (3.5%)	-0.009	114 (1.7%)	516 (3.7%)	-0.012	248 (1.8%)	744 (4.0%)	-0.131
TIA; n (%)	130 (1.9%)	230 (3.5%)	-0.010	129 (1.9%)	455 (3.3%)	-0.009	259 (1.9%)	685 (3.7%)	-0.109
Late effects of cerebrovascular disease; n (%)	91 (1.3%)	128 (1.9%)	-0.005	57 (0.9%)	227 (1.6%)	-0.006	148 (1.1%)	355 (1.9%)	-0.066
Heart Failure; n (%)	224 (3.3%)	373 (5.6%)	-0.011	218 (3.3%)	680 (4.9%)	-0.008	442 (3.3%)	1,053 (5.7%)	-0.116
Peripheral Vascular Disease (PVD) or PVD Surgery; n (%)	480 (7.0%)	563 (8.5%)	-0.005	348 (5.2%)	1,077 (7.7%)	-0.010	828 (6.1%)	1,640 (8.8%)	-0.103
Atrial fibrillation and Other cardiac dysrhythmia; n (%)	836 (12.3%)	1,086 (16.4%)	-0.011	686 (10.2%)	2,302 (16.4%)	-0.017	1,522 (11.3%)	3,388 (18.3%)	-0.198
Atrial fibrillation; n (%)	385 (5.6%)	582 (8.8%)	-0.012	294 (4.4%)	1,261 (9.0%)	-0.018	679 (5.0%)	1,843 (9.9%)	-0.187
Other cardiac dysrhythmia; n (%)	689 (10.1%)	774 (11.7%)	-0.005	529 (7.9%)	1,617 (11.6%)	-0.012	1,218 (9.0%)	2,391 (12.9%)	-0.125
Diabetes Related Measures									
Diabetes with or w/o complications; n (%)	1,348 (19.8%)	1,245 (18.8%)	0.002	1,035 (15.5%)	2,539 (18.1%)	-0.006	2,383 (17.6%)	3,784 (20.4%)	-0.071
Diabetes mellitus without mention of complications; n (%)	1,266 (18.6%)	1,140 (17.3%)	0.003	944 (14.1%)	2,305 (16.5%)	-0.006	2,210 (16.4%)	3,445 (18.6%)	-0.058
Diabetes with specified complications; n (%)	361 (5.3%)	402 (6.1%)	-0.003	230 (3.4%)	723 (5.2%)	-0.009	591 (4.4%)	1,125 (6.1%)	-0.076
Diabetes with unspecified complications; n (%)	83 (1.2%)	66 (1.0%)	0.002	36 (0.5%)	101 (0.7%)	-0.003	119 (0.9%)	167 (0.9%)	0.000
Hypoglycemia; n (%)	67 (1.0%)	77 (1.2%)	-0.002	54 (0.8%)	153 (1.1%)	-0.003	121 (0.9%)	230 (1.2%)	-0.029
GI Conditions									
Malabsorption disorders (Non-infective enteritis and colitis, other intestinal mal., operative-related disorders of the digestive system); n (%)	617 (9.1%)	947 (14.3%)	-0.015	667 (10.0%)	1,797 (12.8%)	-0.008	1,284 (9.5%)	2,744 (14.8%)	-0.163
Non-infective enteritis and colitis; n (%)	388 (5.7%)	638 (9.7%)	-0.014	424 (6.3%)	1,200 (8.6%)	-0.008	812 (6.0%)	1,838 (9.9%)	-0.145
Other intestinal malabsorption ; n (%)	39 (0.6%)	62 (0.9%)	-0.003	39 (0.6%)	134 (1.0%)	-0.004	078 (0.6%)	196 (1.1%)	-0.054

Appendix B

Intraoperative and postprocedural complications and disorders of digestive system; n (%)	259 (3.8%)	369 (5.6%)	-0.008	275 (4.1%)	683 (4.9%)	-0.004	534 (4.0%)	1,052 (5.7%)	-0.079
Upper GI (Diseases of esophagus, stomach and duodenum); n (%)	2,152 (31.6%)	2,650 (40.1%)	-0.014	1,566 (23.4%)	4,379 (31.3%)	-0.015	3,718 (27.5%)	7,029 (37.9%)	-0.223
GI bleeding; n (%)	303 (4.4%)	345 (5.2%)	-0.004	284 (4.2%)	655 (4.7%)	-0.002	587 (4.3%)	1,000 (5.4%)	-0.051
Disorders of gallbladder, biliary tract and pancreas; n (%)	225 (3.3%)	217 (3.3%)	0.000	153 (2.3%)	467 (3.3%)	-0.006	378 (2.8%)	684 (3.7%)	-0.051
Rheumatic Conditions									
Rheumatoid arthritis and other inflammatory polyarthropathies; n (%)	40 (0.6%)	44 (0.7%)	-0.001	18 (0.3%)	137 (1.0%)	-0.009	058 (0.4%)	181 (1.0%)	-0.072
Osteoarthritis; n (%)	2,073 (30.4%)	2,519 (38.1%)	-0.013	1,684 (25.2%)	4,966 (35.5%)	-0.019	3,757 (27.8%)	7,485 (40.3%)	-0.266
Other rheumatic disorders (including gout); n (%)	4,099 (60.1%)	4,410 (66.8%)	-0.008	3,608 (53.9%)	8,399 (60.0%)	-0.008	7,707 (57.1%)	12,809 (69.0%)	-0.248
Gout and other crystal arthropathies; n (%)	151 (2.2%)	135 (2.0%)	0.001	69 (1.0%)	222 (1.6%)	-0.005	220 (1.6%)	357 (1.9%)	-0.023
Other rheumatic disorders; n (%)	4,052 (59.5%)	4,388 (66.4%)	-0.009	3,579 (53.5%)	8,336 (59.6%)	-0.008	7,631 (56.5%)	12,724 (68.6%)	-0.252
Neuro Conditions									
Parkinson's disease; n (%)	26 (0.4%)	11 (0.2%)	0.004	18 (0.3%)	30 (0.2%)	0.002	044 (0.3%)	041 (0.2%)	0.020
Alzheimer and other Dementia Disease ; n (%)	366 (5.4%)	480 (7.3%)	-0.008	256 (3.8%)	911 (6.5%)	-0.012	622 (4.6%)	1,391 (7.5%)	-0.122
Seizure disorders (epilepsy); n (%)	53 (0.8%)	85 (1.3%)	-0.005	34 (0.5%)	143 (1.0%)	-0.006	087 (0.6%)	228 (1.2%)	-0.064
Delirium/Psychosis; n (%)	124 (1.8%)	162 (2.5%)	-0.005	112 (1.7%)	335 (2.4%)	-0.005	236 (1.7%)	497 (2.7%)	-0.068
Other Conditions									
Hypothyroidism; n (%)	1,800 (26.4%)	1,941 (29.4%)	-0.006	1,277 (19.1%)	3,187 (22.8%)	-0.008	3,077 (22.8%)	5,128 (27.6%)	-0.111
Liver disease; n (%)	356 (5.2%)	227 (3.4%)	0.009	191 (2.9%)	481 (3.4%)	-0.003	547 (4.1%)	708 (3.8%)	0.015
Chronic kidney disease stages I-III; n (%)	705 (10.3%)	485 (7.3%)	0.010	322 (4.8%)	591 (4.2%)	0.003	1,027 (7.6%)	1,076 (5.8%)	0.072
Chronic kidney disease stages IV-V, ESRD; n (%)	201 (2.9%)	124 (1.9%)	0.006	102 (1.5%)	149 (1.1%)	0.004	303 (2.2%)	273 (1.5%)	0.052
Premature menopause; n (%)	7 (0.1%)	16 (0.2%)	-0.003	7 (0.1%)	28 (0.2%)	-0.003	014 (0.1%)	044 (0.2%)	-0.026
Oophorectomy; n (%)	5 (0.1%)	16 (0.2%)	-0.003	7 (0.1%)	11 (0.1%)	0.000	012 (0.1%)	027 (0.1%)	0.000
COPD; n (%)	691 (10.1%)	1,006 (15.2%)	-0.014	619 (9.2%)	1,926 (13.8%)	-0.014	1,310 (9.7%)	2,932 (15.8%)	-0.184
Asthma; n (%)	563 (8.3%)	639 (9.7%)	-0.005	516 (7.7%)	1,319 (9.4%)	-0.006	1,079 (8.0%)	1,958 (10.6%)	-0.090
Obstructive sleep apnea; n (%)	222 (3.3%)	314 (4.8%)	-0.007	173 (2.6%)	651 (4.7%)	-0.011	395 (2.9%)	965 (5.2%)	-0.117
Syncope; n (%)	249 (3.7%)	350 (5.3%)	-0.008	249 (3.7%)	734 (5.2%)	-0.007	498 (3.7%)	1,084 (5.8%)	-0.099
Falls; n (%)	539 (7.9%)	640 (9.7%)	-0.006	152 (2.3%)	607 (4.3%)	-0.011	691 (5.1%)	1,247 (6.7%)	-0.068
VTE; n (%)	86 (1.3%)	200 (3.0%)	-0.012	81 (1.2%)	390 (2.8%)	-0.011	167 (1.2%)	590 (3.2%)	-0.137
Gait abnormality; n (%)	558 (8.2%)	802 (12.1%)	-0.012	422 (6.3%)	1,352 (9.7%)	-0.012	980 (7.3%)	2,154 (11.6%)	-0.147
Osteopenia; n (%)	2,470 (36.2%)	2,435 (36.9%)	-0.001	1,890 (28.2%)	3,578 (25.6%)	0.005	4,360 (32.3%)	6,013 (32.4%)	-0.002
Hip and femur fractures; n (%)	165 (2.4%)	234 (3.5%)	-0.006	116 (1.7%)	508 (3.6%)	-0.012	281 (2.1%)	742 (4.0%)	-0.111
Vertebral fractures; n (%)	485 (7.1%)	872 (13.2%)	-0.019	559 (8.4%)	1,814 (13.0%)	-0.014	1,044 (7.7%)	2,686 (14.5%)	-0.218
Other Fractures ; n (%)	270 (4.0%)	327 (5.0%)	-0.005	220 (3.3%)	710 (5.1%)	-0.009	490 (3.6%)	1,037 (5.6%)	-0.096
Combined comorbidity score, 450 days									
...mean (sd)	0.68 (1.77)	0.78 (1.84)	-0.055	0.34 (1.36)	0.66 (1.59)	-0.216	0.51 (1.58)	0.69 (1.67)	-0.111
...median [IQR]	0.00 [-1.00, 1.00]	0.00 [0.00, 2.00]	0.000	0.00 [-1.00, 1.00]	0.00 [0.00, 1.00]	0.000	0.00 (1.58)	0.00 (1.67)	0.000
Frailty Score: Empirical Version 365 days as Categories									
...< 0.12908; n (%)	4,286 (62.9%)	2,288 (34.6%)	0.041	3,514 (52.5%)	4,520 (32.3%)	0.031	7,800 (57.8%)	6,808 (36.7%)	0.432
...0.12908 - 0.1631167; n (%)	1,318 (19.3%)	1,889 (28.6%)	-0.019	1,639 (24.5%)	4,003 (28.6%)	-0.008	2,957 (21.9%)	5,892 (31.8%)	-0.225
...>= 0.1631167; n (%)	1,211 (17.8%)	2,428 (36.8%)	-0.036	1,541 (23.0%)	5,474 (39.1%)	-0.029	2,752 (20.4%)	7,902 (42.6%)	-0.492
Medication Use									
Use of Calcitonin (salmon); n (%)	1 (0.0%)	2 (0.0%)	0.000	275 (4.1%)	504 (3.6%)	0.003	276 (2.0%)	506 (2.7%)	-0.046
Use of oral corticosteroids; n (%)	1,595 (23.4%)	1,441 (21.8%)	0.003	1,652 (24.7%)	4,305 (30.8%)	-0.012	3,247 (24.0%)	5,746 (31.0%)	-0.157
Use of antidepressants; n (%)	1,511 (22.2%)	1,704 (25.8%)	-0.007	1,618 (24.2%)	4,513 (32.2%)	-0.015	3,129 (23.2%)	6,217 (33.5%)	-0.230
Use of anticonvulsants; n (%)	682 (10.0%)	761 (11.5%)	-0.005	702 (10.5%)	2,161 (15.4%)	-0.014	1,384 (10.2%)	2,922 (15.8%)	-0.167
Use of beta blocker OR calcium channel blocker; n (%)	1,947 (28.6%)	1,813 (27.4%)	0.002	2,048 (30.6%)	4,931 (35.2%)	-0.008	3,995 (29.6%)	6,744 (36.4%)	-0.145
Use of PPIs; n (%)	1,786 (26.2%)	1,883 (28.5%)	-0.004	1,983 (29.6%)	5,220 (37.3%)	-0.013	3,769 (27.9%)	7,103 (38.3%)	-0.222
Use of opioids; n (%)	1,927 (28.3%)	2,200 (33.3%)	-0.009	2,208 (33.0%)	6,037 (43.1%)	-0.016	4,135 (30.6%)	8,237 (44.4%)	-0.288
Use of antipsychotics; n (%)	105 (1.5%)	108 (1.6%)	-0.001	103 (1.5%)	302 (2.2%)	-0.005	208 (1.5%)	410 (2.2%)	-0.052
Use of anxiolytics/hypnotics; n (%)	526 (7.7%)	601 (9.1%)	-0.005	719 (10.7%)	1,682 (12.0%)	-0.004	1,245 (9.2%)	2,283 (12.3%)	-0.100
Use of dementia meds; n (%)	219 (3.2%)	232 (3.5%)	-0.002	192 (2.9%)	680 (4.9%)	-0.010	411 (3.0%)	912 (4.9%)	-0.098
Use of antiparkinsonian meds; n (%)	171 (2.5%)	211 (3.2%)	-0.004	168 (2.5%)	543 (3.9%)	-0.008	339 (2.5%)	754 (4.1%)	-0.090
Use of Benzodiazepine; n (%)	886 (13.0%)	686 (10.4%)	0.008	1,280 (19.1%)	3,137 (22.4%)	-0.007	2,166 (16.0%)	3,823 (20.6%)	-0.119
All antidiabetic medications; n (%)	762 (11.2%)	565 (8.6%)	0.008	645 (9.6%)	1,525 (10.9%)	-0.004	1,407 (10.4%)	2,090 (11.3%)	-0.029
ACEI/ARB; n (%)	2,651 (38.9%)	2,178 (33.0%)	0.010	2,539 (37.9%)	5,556 (39.7%)	-0.003	5,190 (38.4%)	7,734 (41.7%)	-0.067
Use of Anticoagulants; n (%)	297 (4.4%)	407 (6.2%)	-0.008	284 (4.2%)	1,223 (8.7%)	-0.018	581 (4.3%)	1,630 (8.8%)	-0.183
Use of Amiodarone; n (%)	41 (0.6%)	39 (0.6%)	0.000	48 (0.7%)	146 (1.0%)	-0.003	089 (0.7%)	185 (1.0%)	-0.033
Digoxin; n (%)	89 (1.3%)	112 (1.7%)	-0.003	104 (1.6%)	302 (2.2%)	-0.004	193 (1.4%)	414 (2.2%)	-0.060
Use of Diuretics; n (%)	1,978 (29.0%)	1,794 (27.2%)	0.003	2,103 (31.4%)	4,693 (33.5%)	-0.004	4,081 (30.2%)	6,487 (35.0%)	-0.103
Use of Aspirin; n (%)	37 (0.5%)	42 (0.6%)	-0.001	59 (0.9%)	158 (1.1%)	-0.002	096 (0.7%)	200 (1.1%)	-0.042
NSAIDs (NOT including aspirin); n (%)	1,374 (20.2%)	1,156 (17.5%)	0.006	1,314 (19.6%)	2,998 (21.4%)	-0.004	2,688 (19.9%)	4,154 (22.4%)	-0.061
Hormone replace therapy; n (%)	558 (8.2%)	598 (9.1%)	-0.003	840 (12.5%)	1,682 (12.0%)	0.001	1,398 (10.4%)	2,280 (12.3%)	-0.060
Other Pressors; n (%)	45 (0.7%)	38 (0.6%)	0.001	66 (1.0%)	134 (1.0%)	0.000	111 (0.8%)	172 (0.9%)	-0.011

Appendix B

Use of Statins ; n (%)	2,995 (43.9%)	2,448 (37.1%)	0.011	2,970 (44.4%)	6,633 (47.4%)	-0.004	5,965 (44.2%)	9,081 (48.9%)	-0.094
Prior bisphosphonate use; n (%)	1,625 (23.8%)	1,597 (24.2%)	-0.001	2,397 (35.8%)	5,368 (38.4%)	-0.004	4,022 (29.8%)	6,965 (37.5%)	-0.164
Healthcare Utilization Measures									
Number of any prescribed drug									
...mean (sd)	19.17 (16.44)	20.93 (19.56)	-0.097	19.38 (15.88)	25.07 (18.78)	-0.327	19.27 (16.16)	23.88 (19.01)	-0.261
...median [IQR]	15.00 [7.00, 27.00]	17.00 [4.50, 32.00]	-0.111	16.00 [8.00, 27.00]	22.00 [12.00, 35.00]	-0.345	15.50 (16.16)	20.56 (19.01)	-0.287
Number of office visits									
...mean (sd)	11.51 (8.82)	14.63 (10.41)	-0.323	9.55 (7.33)	12.46 (8.75)	-0.361	10.54 (8.12)	13.09 (9.26)	-0.293
...median [IQR]	10.00 [6.00, 15.00]	12.00 [8.00, 19.00]	-0.207	8.00 [4.00, 13.00]	11.00 [6.00, 16.00]	-0.372	9.01 (8.12)	11.29 (9.26)	-0.262
Number of ED visits									
...mean (sd)	0.36 (0.84)	0.53 (1.05)	-0.179	0.32 (0.82)	0.47 (1.03)	-0.161	0.34 (0.83)	0.49 (1.04)	-0.159
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 1.00]	0.000	0.00 [0.00, 0.00]	0.00 [0.00, 1.00]	0.000	0.00 (0.83)	0.00 (1.04)	0.000
Number of Hospitalizations									
...mean (sd)	0.15 (0.51)	0.25 (0.71)	-0.162	0.71 (2.75)	1.15 (3.69)	-0.135	0.43 (1.97)	0.89 (3.14)	-0.175
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.000	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.000	0.00 (1.97)	0.00 (3.14)	0.000
Recent hospitalization (-30 days to Index Rx date); n (%)	52 (0.8%)	40 (0.6%)	0.002	70 (1.0%)	88 (0.6%)	0.004	122 (0.9%)	128 (0.7%)	0.022
Old hospitalizations (-450 to -31 days); n (%)	591 (8.7%)	999 (15.1%)	-0.019	752 (11.2%)	2,464 (17.6%)	-0.017	1,343 (9.9%)	3,463 (18.7%)	-0.253
Number of Endocrinologist visits									
...mean (sd)	0.17 (0.88)	0.40 (1.32)	-0.205	1.64 (2.66)	1.94 (3.23)	-0.101	0.90 (1.97)	1.50 (2.82)	-0.247
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.000	1.00 [0.00, 2.00]	1.00 [0.00, 3.00]	0.000	0.50 (1.97)	0.71 (2.82)	-0.086
Number of DXA test performed									
...mean (sd)	0.70 (0.57)	0.76 (0.54)	-0.108	0.49 (0.53)	0.49 (0.54)	0.000	0.60 (0.55)	0.57 (0.54)	0.055
...median [IQR]	1.00 [0.00, 1.00]	1.00 [0.00, 1.00]	0.000	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	0.000	0.50 (0.55)	0.29 (0.54)	0.385
Number of days of hospitalization									
...mean (sd)	1.33 (7.94)	2.10 (9.94)	-0.086	0.71 (2.75)	1.15 (3.69)	-0.135	1.02 (5.96)	1.42 (6.18)	-0.066
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.000	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.000	0.00 (5.96)	0.00 (6.18)	0.000
Occurrence of basic or comprehensive metabolic blood chemistry test; n (%)									
	5,101 (74.8%)	5,289 (80.1%)	-0.006	2,173 (32.5%)	6,380 (45.6%)	-0.021	7,274 (53.9%)	11,669 (62.9%)	-0.183
Number of HbA1C test ordered									
...mean (sd)	0.67 (1.19)	0.50 (1.11)	0.148	0.21 (0.69)	0.23 (0.75)	-0.028	0.44 (0.97)	0.31 (0.87)	0.141
...median [IQR]	0.00 [0.00, 1.00]	0.00 [0.00, 0.00]	0.000	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.000	0.00 (0.97)	0.00 (0.87)	0.000
Occurrence of flexible Sigmoidoscopy or colonoscopy or CT virtual colonoscopy; n (%)									
	799 (11.7%)	882 (13.4%)	-0.005	848 (12.7%)	1,879 (13.4%)	-0.002	1,647 (12.2%)	2,761 (14.9%)	-0.079
Occurrence of Mammograms; n (%)									
	4,575 (67.1%)	4,379 (66.3%)	0.001	3,578 (53.5%)	6,460 (46.2%)	0.010	8,153 (60.4%)	10,839 (58.4%)	0.041
Occurrence of Pap smear; n (%)									
	1,595 (23.4%)	1,369 (20.7%)	0.006	1,557 (23.3%)	2,228 (15.9%)	0.017	3,152 (23.3%)	3,597 (19.4%)	0.095
Flu vaccine; n (%)									
	2,798 (41.1%)	3,017 (45.7%)	-0.007	1,593 (23.8%)	3,925 (28.0%)	-0.008	4,391 (32.5%)	6,942 (37.4%)	-0.103
Pneumococcal vaccine; n (%)									
	1,705 (25.0%)	827 (12.5%)	0.029	739 (11.0%)	1,691 (12.1%)	-0.003	2,444 (18.1%)	2,518 (13.6%)	0.123
Copay for pharmacy cost (charges in U.S. \$)									
...mean (sd)	36.83 (46.06)	31.00 (36.88)	0.140	23.13 (25.84)	20.45 (19.81)	0.116	30.04 (37.43)	23.49 (25.91)	0.203
...median [IQR]	24.21 [12.54, 43.97]	22.42 [10.81, 38.90]	0.043	17.50 [8.54, 30.00]	16.00 [8.28, 27.26]	0.065	20.89 (37.43)	17.85 (25.91)	0.094
Business Type									
...Commercial; n (%)	1,324 (19.4%)	1,589 (24.1%)	-0.010	N/A	N/A	N/A	1,324 (19.4%)	1,589 (24.1%)	-0.010
...Medicare; n (%)	5,491 (80.6%)	5,016 (75.9%)	0.005	N/A	N/A	N/A	5,491 (80.6%)	5,016 (75.9%)	0.005
Insurance Plan Type									
...Comprehensive; n (%)	N/A	N/A	N/A	2,485 (37.1%)	5,421 (38.7%)	-0.003	2,485 (37.1%)	5,421 (38.7%)	-0.003
...HMO; n (%)	N/A	N/A	N/A	698 (10.4%)	1,737 (12.4%)	-0.006	698 (10.4%)	1,737 (12.4%)	-0.006
...PPO; n (%)	N/A	N/A	N/A	3,108 (46.4%)	6,134 (43.8%)	0.004	3,108 (46.4%)	6,134 (43.8%)	0.004
...Others; n (%)	N/A	N/A	N/A	403 (6.0%)	705 (5.0%)	0.004	403 (6.0%)	705 (5.0%)	0.004

Optum (unmatched): <https://bwh-dope.aetion.com/projects/details/1406/results/64560/result/2>

Marketscan (unmatched): <https://bwh-dope.aetion.com/projects/details/1407/results/64559/result/2>

Appendix B

PS-matched									
Variable	Optum			MarketScan			POOLED		
	Raloxifene	Zoledronic Acid	St. Diff.	Raloxifene	Zoledronic Acid	St. Diff.	Raloxifene	Zoledronic Acid	St. Diff.
Number of patients	3,198	3,198		5,816	5,816		9,014	9,014	
Age									
...mean (sd)	73.50 (5.65)	73.62 (5.75)	-0.0211	74.24 (7.12)	74.29 (7.04)	-0.0071	73.98 (6.64)	74.05 (6.61)	-0.0106
...median [IQR]	74.00 [69.00, 78.00]	74.00 [69.00, 78.00]	0.0000	73.00 [68.00, 79.00]	73.00 [68.00, 79.00]	0.0000	73.35 (6.64)	73.35 (6.61)	0.0000
Age categories*									
...< 70; n (%)	923 (28.9%)	942 (29.5%)	-0.0011	1,882 (32.4%)	1,891 (32.5%)	-0.0002	2,805 (31.1%)	2,833 (31.4%)	-0.0065
...70 - 74; n (%)	790 (24.7%)	792 (24.8%)	-0.0002	1,402 (24.1%)	1,396 (24.0%)	0.0002	2,192 (24.3%)	2,188 (24.3%)	0.0000
...≥ 75; n (%)	1,485 (46.4%)	1,464 (45.8%)	0.0009	2,532 (43.5%)	2,529 (43.5%)	0.0000	4,017 (44.6%)	3,993 (44.3%)	0.0060
Region*									
...Northeast; n (%)	277 (8.7%)	300 (9.4%)	-0.0023	1,045 (18.0%)	1,029 (17.7%)	0.0007	1,322 (14.7%)	1,329 (14.7%)	0.0000
...South; n (%)	1,464 (45.8%)	1,511 (47.2%)	-0.0021	1,926 (33.1%)	1,966 (33.8%)	-0.0012	3,390 (37.6%)	3,477 (38.6%)	-0.0206
...Midwest; n (%)	457 (14.3%)	426 (13.3%)	0.0027	1,975 (34.0%)	1,953 (33.6%)	0.0007	2,432 (27.0%)	2,379 (26.4%)	0.0136
...West; n (%)	1,000 (31.3%)	961 (30.1%)	0.0022	870 (15.0%)	868 (14.9%)	0.0003	1,870 (20.7%)	1,829 (20.3%)	0.0099
Calendar Time*									
...Aug 2007 - Aug 2010; n (%)	1,153 (36.1%)	1,196 (37.4%)	-0.0021	1,797 (30.9%)	1,812 (31.2%)	-0.0005	2,950 (32.7%)	3,008 (33.4%)	-0.0149
...Aug 2010 - Aug 2013; n (%)	1,311 (41.0%)	1,285 (40.2%)	0.0013	2,047 (35.2%)	2,067 (35.5%)	-0.0005	3,358 (37.3%)	3,352 (37.2%)	0.0021
...Aug 2013 - Aug 2016; n (%)	295 (9.2%)	275 (8.6%)	0.0020	1,451 (24.9%)	1,460 (25.1%)	-0.0004	1,746 (19.4%)	1,735 (19.2%)	0.0051
...Aug 2016 - Mar 2020; n (%)	439 (13.7%)	442 (13.8%)	-0.0003	521 (9.0%)	477 (8.2%)	0.0027	960 (10.7%)	919 (10.2%)	0.0163
Metropolitan Statistical Area*									
...Urban; n (%)	N/A	N/A	N/A	4,395 (75.6%)	4,392 (75.5%)	0.0001	4,521 (75.6%)	4,515 (75.5%)	0.0001
...Rural; n (%)	N/A	N/A	N/A	92 (1.6%)	98 (1.7%)	-0.0008	93 (1.6%)	95 (1.6%)	0.0000
...Unknown/Missing; n (%)	N/A	N/A	N/A	1,329 (22.9%)	1,326 (22.8%)	0.0002	1,369 (22.9%)	1,373 (22.9%)	0.0000
General Health Related Measures									
Smoking; n (%)*	246 (7.7%)	267 (8.3%)	-0.0021	247 (4.2%)	267 (4.6%)	-0.0019	493 (5.5%)	534 (5.9%)	-0.0173
Alcohol/Drug abuse or dependence ; n (%)	11 (0.3%)	8 (0.3%)	0.0000	5 (0.1%)	5 (0.1%)	0.0000	016 (0.2%)	013 (0.1%)	0.0258
Obesity or Overweight; n (%)*	252 (7.9%)	233 (7.3%)	0.0022	267 (4.6%)	262 (4.5%)	0.0005	519 (5.8%)	495 (5.5%)	0.0130
Obesity; n (%)	158 (4.9%)	153 (4.8%)	0.0005	161 (2.8%)	178 (3.1%)	-0.0017	319 (3.5%)	331 (3.7%)	-0.0107
Overweight; n (%)	108 (3.4%)	96 (3.0%)	0.0022	123 (2.1%)	100 (1.7%)	0.0029	231 (2.6%)	196 (2.2%)	0.0261
Cardiovascular Measures									
Hypertension; n (%)*	2,020 (63.2%)	2,032 (63.5%)	-0.0004	3,125 (53.7%)	3,123 (53.7%)	0.0000	5,145 (57.1%)	5,155 (57.2%)	-0.0020
Hyperlipidemia; n (%)*	2,177 (68.1%)	2,218 (69.4%)	-0.0016	2,903 (49.9%)	2,946 (50.7%)	-0.0011	5,080 (56.4%)	5,164 (57.3%)	-0.0182
Coronary artery disease (MI, angina, Coronary atherosclerosis and other forms of chronic ischemic heart disease); n (%)*	490 (15.3%)	477 (14.9%)	0.0010	763 (13.1%)	769 (13.2%)	-0.0003	1,253 (13.9%)	1,246 (13.8%)	0.0029
Old MI; n (%)	56 (1.8%)	69 (2.2%)	-0.0028	49 (0.8%)	58 (1.0%)	-0.0021	105 (1.2%)	127 (1.4%)	-0.0177
Acute MI; n (%)	22 (0.7%)	28 (0.9%)	-0.0022	32 (0.6%)	37 (0.6%)	0.0000	054 (0.6%)	065 (0.7%)	-0.0124
ACS/unstable angina; n (%)	37 (1.2%)	33 (1.0%)	0.0019	70 (1.2%)	64 (1.1%)	0.0009	107 (1.2%)	097 (1.1%)	0.0094
Stable angina; n (%)	107 (3.3%)	96 (3.0%)	0.0017	134 (2.3%)	140 (2.4%)	-0.0007	241 (2.7%)	236 (2.6%)	0.0062
Coronary atherosclerosis and other CHD; n (%)	427 (13.4%)	416 (13.0%)	0.0011	671 (11.5%)	686 (11.8%)	-0.0009	1,098 (12.2%)	1,102 (12.2%)	0.0000
History of CABG or PTCA; n (%)	75 (2.3%)	81 (2.5%)	-0.0013	57 (1.0%)	70 (1.2%)	-0.0019	132 (1.5%)	151 (1.7%)	-0.0159
Cerebrovascular disease (Stroke, TIA, Late effects); n (%)*	162 (5.1%)	170 (5.3%)	-0.0009	241 (4.1%)	241 (4.1%)	0.0000	403 (4.5%)	411 (4.6%)	-0.0048
Stroke (Ischemic or hemorrhagic); n (%)	79 (2.5%)	96 (3.0%)	-0.0030	113 (1.9%)	129 (2.2%)	-0.0021	192 (2.1%)	225 (2.5%)	-0.0267
TIA; n (%)	72 (2.3%)	82 (2.6%)	-0.0019	125 (2.1%)	119 (2.0%)	0.0007	197 (2.2%)	201 (2.2%)	0.0000
Late effects of cerebrovascular disease; n (%)	56 (1.8%)	45 (1.4%)	0.0032	53 (0.9%)	49 (0.8%)	0.0011	109 (1.2%)	094 (1.0%)	0.0192
Heart Failure; n (%)*	143 (4.5%)	141 (4.4%)	0.0005	205 (3.5%)	196 (3.4%)	0.0005	348 (3.9%)	337 (3.7%)	0.0105
Peripheral Vascular Disease (PVD) or PVD Surgery; n (%)*	243 (7.6%)	227 (7.1%)	0.0018	333 (5.7%)	315 (5.4%)	0.0013	576 (6.4%)	542 (6.0%)	0.0166
Atrial fibrillation and Other cardiac dysrhythmia; n (%)*	446 (13.9%)	445 (13.9%)	0.0000	657 (11.3%)	671 (11.5%)	-0.0006	1,103 (12.2%)	1,116 (12.4%)	-0.0061
Atrial fibrillation; n (%)	207 (6.5%)	235 (7.3%)	-0.0030	287 (4.9%)	326 (5.6%)	-0.0031	494 (5.5%)	561 (6.2%)	-0.0298
Other cardiac dysrhythmia; n (%)	346 (10.8%)	334 (10.4%)	0.0012	504 (8.7%)	494 (8.5%)	0.0007	850 (9.4%)	828 (9.2%)	0.0069
Diabetes Related Measures									
Diabetes with or w/o complications; n (%)*	614 (19.2%)	635 (19.9%)	-0.0016	937 (16.1%)	916 (15.7%)	0.0010	1,551 (17.2%)	1,551 (17.2%)	0.0000
Diabetes mellitus without mention of complications; n (%)	568 (17.8%)	586 (18.3%)	-0.0012	854 (14.7%)	849 (14.6%)	0.0003	1,422 (15.8%)	1,435 (15.9%)	-0.0027
Diabetes with specified complications; n (%)	180 (5.6%)	192 (6.0%)	-0.0017	215 (3.7%)	219 (3.8%)	-0.0005	395 (4.4%)	411 (4.6%)	-0.0096
Diabetes with unspecified complications; n (%)	35 (1.1%)	34 (1.1%)	0.0000	32 (0.6%)	36 (0.6%)	0.0000	067 (0.7%)	070 (0.8%)	-0.0116
Hypoglycemia; n (%)	42 (1.3%)	40 (1.3%)	0.0000	52 (0.9%)	44 (0.8%)	0.0011	094 (1.0%)	084 (0.9%)	0.0103
GI Conditions									
Malabsorption disorders (Non-infective enteritis and colitis, other intestinal mal., operative-related disorders of the digestive system); n (%)*	363 (11.4%)	361 (11.3%)	0.0003	605 (10.4%)	625 (10.7%)	-0.0009	968 (10.7%)	986 (10.9%)	-0.0064
Non-infective enteritis and colitis; n (%)	230 (7.2%)	237 (7.4%)	-0.0007	390 (6.7%)	387 (6.7%)	0.0000	620 (6.9%)	624 (6.9%)	0.0000

Appendix B

Other intestinal malabsorption ; n (%)	16 (0.5%)	21 (0.7%)	-0.0026	37 (0.6%)	50 (0.9%)	-0.0035	053 (0.6%)	071 (0.8%)	-0.0240
Intraoperative and postprocedural complications and disorders of digestive system; n (%)	159 (5.0%)	146 (4.6%)	0.0018	248 (4.3%)	263 (4.5%)	-0.0010	407 (4.5%)	409 (4.5%)	0.0000
Upper GI (Diseases of esophagus, stomach and duodenum); n (%)*	1,141 (35.7%)	1,138 (35.6%)	0.0002	1,466 (25.2%)	1,430 (24.6%)	0.0012	2,607 (28.9%)	2,568 (28.5%)	0.0088
GI bleeding; n (%)*	161 (5.0%)	160 (5.0%)	0.0000	252 (4.3%)	269 (4.6%)	-0.0014	413 (4.6%)	429 (4.8%)	-0.0095
Disorders of gallbladder, biliary tract and pancreas; n (%)*	87 (2.7%)	88 (2.8%)	-0.0006	145 (2.5%)	148 (2.5%)	0.0000	232 (2.6%)	236 (2.6%)	0.0000
Rheumatic Conditions									
Rheumatoid arthritis and other inflammatory polyarthropathies; n (%)	16 (0.5%)	28 (0.9%)	-0.0048	18 (0.3%)	48 (0.8%)	-0.0067	034 (0.4%)	076 (0.8%)	-0.0518
Osteoarthritis; n (%)*	1,087 (34.0%)	1,111 (34.7%)	-0.0012	1,603 (27.6%)	1,636 (28.1%)	-0.0009	2,690 (29.8%)	2,747 (30.5%)	-0.0153
Other rheumatic disorders (including gout); n (%)*	2,019 (63.1%)	2,045 (63.9%)	-0.0010	3,198 (55.0%)	3,248 (55.8%)	-0.0011	5,217 (57.9%)	5,293 (58.7%)	-0.0162
Gout and other crystal arthropathies; n (%)	70 (2.2%)	55 (1.7%)	0.0036	65 (1.1%)	62 (1.1%)	0.0000	135 (1.5%)	117 (1.3%)	0.0170
Other rheumatic disorders; n (%)	1,999 (62.5%)	2,033 (63.6%)	-0.0014	3,170 (54.5%)	3,225 (55.5%)	-0.0014	5,169 (57.3%)	5,258 (58.3%)	-0.0202
Neuro Conditions									
Parkinson's disease; n (%)	8 (0.3%)	6 (0.2%)	0.0020	18 (0.3%)	10 (0.2%)	0.0020	026 (0.3%)	016 (0.2%)	0.0200
Alzheimer and other Dementia Disease ; n (%)*	193 (6.0%)	189 (5.9%)	0.0004	253 (4.4%)	257 (4.4%)	0.0000	446 (4.9%)	446 (4.9%)	0.0000
Seizure disorders (epilepsy); n (%)	29 (0.9%)	36 (1.1%)	-0.0020	31 (0.5%)	41 (0.7%)	-0.0026	060 (0.7%)	077 (0.9%)	-0.0225
Delirium/Psychosis; n (%)	64 (2.0%)	59 (1.8%)	0.0015	109 (1.9%)	84 (1.4%)	0.0039	173 (1.9%)	143 (1.6%)	0.0229
Other Conditions									
Hypothyroidism; n (%)*	900 (28.1%)	933 (29.2%)	-0.0021	1,179 (20.3%)	1,164 (20.0%)	0.0007	2,079 (23.1%)	2,097 (23.3%)	-0.0047
Liver disease; n (%)*	109 (3.4%)	121 (3.8%)	-0.0021	175 (3.0%)	164 (2.8%)	0.0012	284 (3.2%)	285 (3.2%)	0.0000
Chronic kidney disease stages I-III; n (%)*	284 (8.9%)	276 (8.6%)	0.0010	284 (4.9%)	272 (4.7%)	0.0009	568 (6.3%)	548 (6.1%)	0.0083
Chronic kidney disease stages IV-V, ESRD; n (%)	103 (3.2%)	70 (2.2%)	0.0061	89 (1.5%)	55 (0.9%)	0.0055	192 (2.1%)	125 (1.4%)	0.0534
Premature menopause; n (%)	3 (0.1%)	7 (0.2%)	-0.0026	5 (0.1%)	10 (0.2%)	-0.0026	008 (0.1%)	017 (0.2%)	-0.0258
Oophorectomy; n (%)	3 (0.1%)	5 (0.2%)	-0.0026	7 (0.1%)	3 (0.1%)	0.0000	010 (0.1%)	008 (0.1%)	0.0000
COPD; n (%)*	411 (12.9%)	401 (12.5%)	0.0011	584 (10.0%)	594 (10.2%)	-0.0006	995 (11.0%)	995 (11.0%)	0.0000
Asthma; n (%)*	294 (9.2%)	300 (9.4%)	-0.0007	461 (7.9%)	490 (8.4%)	-0.0018	755 (8.4%)	790 (8.8%)	-0.0143
Obstructive sleep apnea; n (%)*	123 (3.8%)	125 (3.9%)	-0.0005	171 (2.9%)	152 (2.6%)	0.0018	294 (3.3%)	277 (3.1%)	0.0114
Syncope; n (%)*	131 (4.1%)	139 (4.3%)	-0.0010	236 (4.1%)	236 (4.1%)	0.0000	367 (4.1%)	375 (4.2%)	-0.0050
Falls; n (%)*	266 (8.3%)	272 (8.5%)	-0.0007	146 (2.5%)	157 (2.7%)	-0.0012	412 (4.6%)	429 (4.8%)	-0.0095
VTE; n (%)	47 (1.5%)	72 (2.3%)	-0.0058	78 (1.3%)	119 (2.0%)	-0.0054	125 (1.4%)	191 (2.1%)	-0.0534
Gait abnormality; n (%)*	282 (8.8%)	305 (9.5%)	-0.0023	405 (7.0%)	373 (6.4%)	0.0023	687 (7.6%)	678 (7.5%)	0.0038
Osteopenia; n (%)*	1,200 (37.5%)	1,203 (37.6%)	-0.0002	1,585 (27.3%)	1,626 (28.0%)	-0.0013	2,785 (30.9%)	2,829 (31.4%)	-0.0108
Hip and femur fractures; n (%)*	86 (2.7%)	98 (3.1%)	-0.0023	113 (1.9%)	122 (2.1%)	-0.0014	199 (2.2%)	220 (2.4%)	-0.0133
Vertebral fractures; n (%)*	298 (9.3%)	304 (9.5%)	-0.0007	543 (9.3%)	527 (9.1%)	0.0007	841 (9.3%)	831 (9.2%)	0.0035
Other Fractures ; n (%)*	141 (4.4%)	142 (4.4%)	0.0000	206 (3.5%)	206 (3.5%)	0.0000	347 (3.8%)	348 (3.9%)	-0.0052
Combined comorbidity score, 450 days*									
...mean (sd)	0.70 (1.83)	0.68 (1.82)	0.0110	0.40 (1.40)	0.40 (1.37)	0.0000	0.51 (1.57)	0.50 (1.54)	0.0064
...median [IQR]	0.00 [-1.00, 1.00]	0.00 [-1.00, 1.00]	0.0000	0.00 [-1.00, 1.00]	0.00 [0.00, 1.00]	0.0000	0.00 (1.57)	0.00 (1.54)	0.0000
Frailty Score: Empirical Version 365 days as Categories*									
...< 0.12908; n (%)	1,492 (46.7%)	1,502 (47.0%)	-0.0004	2,738 (47.1%)	2,740 (47.1%)	0.0000	4,230 (46.9%)	4,242 (47.1%)	-0.0040
...0.12908 - 0.1631167; n (%)	866 (27.1%)	846 (26.5%)	0.0012	1,570 (27.0%)	1,563 (26.9%)	0.0002	2,436 (27.0%)	2,409 (26.7%)	0.0068
...≥ 0.1631167; n (%)	840 (26.3%)	850 (26.6%)	-0.0006	1,508 (25.9%)	1,513 (26.0%)	-0.0002	2,348 (26.0%)	2,363 (26.2%)	-0.0046
Medication Use									
Use of Calcitonin (salmon); n (%)	1 (0.0%)	0 (0.0%)	0.0000	243 (4.2%)	213 (3.7%)	0.0025	244 (2.7%)	213 (2.4%)	0.0190
Use of oral corticosteroids; n (%)*	779 (24.4%)	770 (24.1%)	0.0006	1,542 (26.5%)	1,540 (26.5%)	0.0000	2,321 (25.7%)	2,310 (25.6%)	0.0023
Use of antidepressants; n (%)*	836 (26.1%)	821 (25.7%)	0.0008	1,522 (26.2%)	1,542 (26.5%)	-0.0006	2,358 (26.2%)	2,363 (26.2%)	0.0000
Use of anticonvulsants; n (%)*	353 (11.0%)	387 (12.1%)	-0.0032	669 (11.5%)	689 (11.8%)	-0.0009	1,022 (11.3%)	1,076 (11.9%)	-0.0187
Use of beta blocker OR calcium channel blocker; n (%)*	1,013 (31.7%)	1,009 (31.6%)	0.0002	1,855 (31.9%)	1,884 (32.4%)	-0.0009	2,868 (31.8%)	2,893 (32.1%)	-0.0064
Use of PPIs; n (%)*	968 (30.3%)	962 (30.1%)	0.0004	1,845 (31.7%)	1,863 (32.0%)	-0.0005	2,813 (31.2%)	2,825 (31.3%)	-0.0022
Use of opioids; n (%)*	1,100 (34.4%)	1,111 (34.7%)	-0.0005	2,080 (35.8%)	2,074 (35.7%)	0.0002	3,180 (35.3%)	3,185 (35.3%)	0.0000
Use of antipsychotics; n (%)*	58 (1.8%)	56 (1.8%)	0.0000	97 (1.7%)	86 (1.5%)	0.0016	155 (1.7%)	142 (1.6%)	0.0079
Use of anxiolytics/hypnotics; n (%)*	301 (9.4%)	293 (9.2%)	0.0007	656 (11.3%)	660 (11.3%)	0.0000	957 (10.6%)	953 (10.6%)	0.0000
Use of dementia meds; n (%)*	109 (3.4%)	117 (3.7%)	-0.0016	188 (3.2%)	200 (3.4%)	-0.0011	297 (3.3%)	317 (3.5%)	-0.0110
Use of antiparkinsonian meds; n (%)*	103 (3.2%)	105 (3.3%)	-0.0006	157 (2.7%)	156 (2.7%)	0.0000	260 (2.9%)	261 (2.9%)	0.0000
Use of Benzodiazepine; n (%)*	403 (12.6%)	402 (12.6%)	0.0000	1,192 (20.5%)	1,196 (20.6%)	-0.0002	1,595 (17.7%)	1,598 (17.7%)	0.0000
All antidiabetic medications; n (%)*	341 (10.7%)	351 (11.0%)	-0.0009	589 (10.1%)	583 (10.0%)	0.0003	930 (10.3%)	934 (10.4%)	-0.0033
ACEI/ARB; n (%)*	1,218 (38.1%)	1,241 (38.8%)	-0.0011	2,250 (38.7%)	2,256 (38.8%)	-0.0002	3,468 (38.5%)	3,497 (38.8%)	-0.0062
Use of Anticoagulants; n (%)*	176 (5.5%)	183 (5.7%)	-0.0008	282 (4.8%)	315 (5.4%)	-0.0027	458 (5.1%)	498 (5.5%)	-0.0179
Use of Amiodarone; n (%)	25 (0.8%)	19 (0.6%)	0.0024	48 (0.8%)	37 (0.6%)	0.0024	073 (0.8%)	056 (0.6%)	0.0240
Digoxin; n (%)	52 (1.6%)	58 (1.8%)	-0.0015	97 (1.7%)	92 (1.6%)	0.0008	149 (1.7%)	150 (1.7%)	0.0000
Use of Diuretics; n (%)*	1,021 (31.9%)	1,041 (32.6%)	-0.0012	1,865 (32.1%)	1,857 (31.9%)	0.0004	2,886 (32.0%)	2,898 (32.1%)	-0.0021
Use of Aspirin; n (%)	25 (0.8%)	21 (0.7%)	0.0012	55 (0.9%)	56 (1.0%)	-0.0010	080 (0.9%)	077 (0.9%)	0.0000

Appendix B

NSAIDs (NOT including aspirin); n (%)	651 (20.4%)	643 (20.1%)	0.0007	1,198 (20.6%)	1,155 (19.9%)	0.0016	1,849 (20.5%)	1,798 (19.9%)	0.0149
Hormone replace therapy; n (%)*	315 (9.8%)	318 (9.9%)	-0.0003	743 (12.8%)	751 (12.9%)	-0.0003	1,058 (11.7%)	1,069 (11.9%)	-0.0062
Other Pressors; n (%)	23 (0.7%)	16 (0.5%)	0.0026	64 (1.1%)	66 (1.1%)	0.0000	087 (1.0%)	082 (0.9%)	0.0103
Use of Statins ; n (%)*	1,427 (44.6%)	1,443 (45.1%)	-0.0007	2,677 (46.0%)	2,656 (45.7%)	0.0004	4,104 (45.5%)	4,099 (45.5%)	0.0000
Prior bisphosphonate use; n (%)	746 (23.3%)	847 (26.5%)	-0.0064	2,079 (35.7%)	2,246 (38.6%)	-0.0048	2,825 (31.3%)	3,093 (34.3%)	-0.0639
Healthcare Utilization Measures									
Number of any prescribed drug*									
...mean (sd)	22.08 (18.32)	21.98 (16.47)	0.0057	20.71 (16.23)	20.85 (15.42)	-0.0088	21.20 (17.00)	21.25 (15.80)	-0.0030
...median [IQR]	18.00 [8.00, 31.00]	18.00 [10.00, 30.00]	0.0000	17.00 [9.00, 28.00]	18.00 [10.00, 28.00]	-0.0632	17.35 (17.00)	18.00 (15.80)	-0.0396
Number of office visits*									
...mean (sd)	12.76 (9.40)	12.86 (8.99)	-0.0109	10.14 (7.52)	10.11 (7.03)	0.0041	11.07 (8.24)	11.09 (7.78)	-0.0025
...median [IQR]	10.00 [6.00, 17.00]	11.00 [7.00, 16.25]	-0.1087	9.00 [5.00, 14.00]	9.00 [5.00, 13.00]	0.0000	9.35 (8.24)	9.71 (7.78)	-0.0449
Number of ED visits*									
...mean (sd)	0.42 (0.91)	0.42 (0.93)	0.0000	0.34 (0.85)	0.34 (0.89)	0.0000	0.37 (0.87)	0.37 (0.90)	0.0000
...median [IQR]	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	0.0000	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.0000	0.00 (0.87)	0.00 (0.90)	0.0000
Number of Hospitalizations*									
...mean (sd)	0.16 (0.53)	0.18 (0.61)	-0.0350	0.78 (2.88)	0.77 (2.89)	0.0035	0.56 (2.33)	0.56 (2.35)	0.0000
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.0000	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.0000	0.00 (2.33)	0.00 (2.35)	0.0000
Recent hospitalization (-30 days to index Rx date); n (%)	18 (0.6%)	20 (0.6%)	0.0000	54 (0.9%)	53 (0.9%)	0.0000	072 (0.8%)	073 (0.8%)	0.0000
Old hospitalizations (-450 to -31 days); n (%)	326 (10.2%)	347 (10.9%)	-0.0022	721 (12.4%)	732 (12.6%)	-0.0006	1,047 (11.6%)	1,079 (12.0%)	-0.0124
Number of Endocrinologist visits*									
...mean (sd)	0.23 (1.14)	0.26 (1.02)	-0.0277	1.72 (2.75)	1.71 (3.02)	0.0035	1.19 (2.31)	1.20 (2.50)	-0.0042
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.0000	1.00 [0.00, 2.00]	1.00 [0.00, 2.00]	0.0000	0.65 (2.31)	0.65 (2.50)	0.0000
Number of DXA test performed*									
...mean (sd)	0.73 (0.59)	0.73 (0.53)	0.0000	0.49 (0.53)	0.50 (0.54)	-0.0187	0.58 (0.55)	0.58 (0.54)	0.0000
...median [IQR]	1.00 [0.00, 1.00]	1.00 [0.00, 1.00]	0.0000	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	0.0000	0.35 (0.55)	0.35 (0.54)	0.0000
Number of days of hospitalization*									
...mean (sd)	1.35 (6.46)	1.58 (8.51)	-0.0304	0.78 (2.88)	0.77 (2.89)	0.0035	0.98 (4.49)	1.06 (5.57)	-0.0158
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.0000	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.0000	0.00 (4.49)	0.00 (5.57)	0.0000
Occurrence of basic or comprehensive metabolic blood chemistry test; n (%)*	2,462 (77.0%)	2,446 (76.5%)	0.0006	2,084 (35.8%)	2,096 (36.0%)	-0.0003	4,546 (50.4%)	4,542 (50.4%)	0.0000
Number of HbA1C test ordered*									
...mean (sd)	0.55 (1.10)	0.57 (1.15)	-0.0178	0.22 (0.71)	0.21 (0.71)	0.0141	0.34 (0.87)	0.34 (0.89)	0.0000
...median [IQR]	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	0.0000	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.0000	0.00 (0.87)	0.00 (0.89)	0.0000
Occurrence of flexible Sigmoidoscopy or colonoscopy or CT virtual colonoscopy; n (%)*	395 (12.4%)	401 (12.5%)	-0.0003	752 (12.9%)	763 (13.1%)	-0.0006	1,147 (12.7%)	1,164 (12.9%)	-0.0060
Occurrence of Mammograms; n (%)*	2,172 (67.9%)	2,175 (68.0%)	-0.0001	2,980 (51.2%)	3,031 (52.1%)	-0.0013	5,152 (57.2%)	5,206 (57.8%)	-0.0121
Occurrence of Pap smear; n (%)*	761 (23.8%)	771 (24.1%)	-0.0006	1,213 (20.9%)	1,262 (21.7%)	-0.0017	1,974 (21.9%)	2,033 (22.6%)	-0.0168
Flu vaccine; n (%)*	1,368 (42.8%)	1,331 (41.6%)	0.0019	1,458 (25.1%)	1,429 (24.6%)	0.0010	2,826 (31.4%)	2,760 (30.6%)	0.0173
Pneumococcal vaccine; n (%)*	536 (16.8%)	505 (15.8%)	0.0025	684 (11.8%)	672 (11.6%)	0.0006	1,220 (13.5%)	1,177 (13.1%)	0.0118
Copay for pharmacy cost (charges in U.S. \$)*									
...mean (sd)	32.98 (33.52)	32.63 (41.44)	0.0093	21.73 (21.64)	21.97 (23.47)	-0.0106	25.72 (26.47)	25.75 (31.06)	-0.0010
...median [IQR]	24.20 [13.60, 40.24]	23.21 [10.71, 40.75]	0.0263	16.93 [8.43, 28.46]	16.47 [8.00, 29.05]	0.0204	19.51 (26.47)	18.86 (31.06)	0.0225
Business Type*									
...Commercial; n (%)	754 (23.6%)	785 (24.5%)	-0.002	N/A	N/A	N/A	754 (23.6%)	785 (24.5%)	-0.002
...Medicare; n (%)	2,444 (76.4%)	2,413 (75.5%)	0.001	N/A	N/A	N/A	2,444 (76.4%)	2,413 (75.5%)	0.001
Insurance Plan Type*									
...Comprehensive; n (%)	N/A	N/A	N/A	2,179 (37.5%)	2,153 (37.0%)	0.001	2,179 (37.5%)	2,153 (37.0%)	0.001
...HMO; n (%)	N/A	N/A	N/A	636 (10.9%)	629 (10.8%)	0.000	636 (10.9%)	629 (10.8%)	0.000
...PPO; n (%)	N/A	N/A	N/A	2,686 (46.2%)	2,711 (46.6%)	-0.001	2,686 (46.2%)	2,711 (46.6%)	-0.001
...Others; n (%)	N/A	N/A	N/A	315 (5.4%)	323 (5.6%)	-0.001	315 (5.4%)	323 (5.6%)	-0.001

*Included in the 1:1 PS matching model

Optum (PS matched): <https://bwh-dope.aetion.com/projects/details/1406/results/63149/result/44>

Marketscan (PS matched): <https://bwh-dope.aetion.com/projects/details/1407/results/63153/result/44>