Anti-Osteoporotic Therapy After Fragility Fracture Lowers Rate of Subsequent Fracture
Analysis of a Large Population Sample

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Background: This investigation assessed the effectiveness of initiating anti-osteoporotic therapy after a fragility fracture in preventing subsequent fractures.

Methods: The Truven Health MarketScan databases, which contain de-identified, integrated, person-specific claim data, were queried from 2003 to 2012. The study population included individuals fifty years of age or older who sustained a fragility fracture, defined as any fracture of the wrist, proximal part of the humerus, hip, or vertebra, and had three years of continuous enrollment following fracture. Patients were stratified into either an anti-osteoporotic therapy group or a no-treatment group. Subsequent fracture was defined as a fragility fracture occurring more than ninety days following the index fracture. Subjects were followed for three years. Unadjusted and age and sex-adjusted odds ratios for subsequent fracture were calculated for both groups.

Results: This investigation included 31,069 subjects, of whom 10.6% were treated with anti-osteoporotic therapy following the index fracture. The anti-osteoporotic therapy group was older and had a greater proportion of female patients compared with the no-treatment group. The three-year subsequent fracture rates were 7.5% in the anti-osteoporotic therapy group and 9.7% in the no-treatment group. Unadjusted odds ratios for subsequent fracture showed that the anti-osteoporotic therapy group experienced a risk reduction of 33% after an index wrist fracture, 48% after an index proximal humeral fracture, 28% after an index hip fracture, 20% after an index vertebral fracture, and 25% after all fractures combined. Age and sex-adjusted odds ratios showed that the anti-osteoporotic therapy group experienced a reduction in risk of 50% after an index wrist fracture, 52% after an index proximal humeral fracture, 34% after an index hip fracture, 43% after an index vertebral fracture, and 40% after all fractures combined. The number needed to treat to prevent a subsequent fragility fracture was twenty-eight after an index wrist fracture, twenty after an index proximal humeral fracture, twenty-six after an index hip fracture, twenty-five after an index vertebral fracture, and twenty-seven after all fractures combined.

Conclusions: Treatment with anti-osteoporotic therapy after a fragility fracture leads to a 40% decrease in the three-year risk of subsequent fracture, when adjusted for age and sex. Initiation of anti-osteoporotic therapy following a fragility fracture can prevent a subsequent fracture over the following three years in approximately one of every twenty-seven patients treated.

Level of Evidence: Therapeutic <u>Level III</u>. See Instructions for Authors for a complete description of levels of evidence.

Osteoporosis is the most common bone disease in humans and affects one in two women and one in five men older than fifty years of age in the United States[1,2]. In osteoporosis, an uncoupling of the balance between bone resorption and formation causes a disruption of osseous microarchitecture and corresponding low bone mineral density. Consequently, patients are at high risk of sustaining osteoporotic fragility fractures, most commonly at the wrist, proximal part of the humerus, hip, and vertebra[2]. Prior work has shown that the lifetime risk of osteoporotic fragility fracture is about 40% to 50% in women and 13% to 22% in men[3]. These fragility fractures have major effects on patient pain, function, and quality of life.

A fragility fracture at any location is a major risk factor for subsequent fractures[4-6]. One study showed that patients with a history of fractures have elevated risk ratios of sustaining subsequent fractures of 1.83 to 2.03[5]. Similarly, a meta-analysis revealed that a prior wrist, hip, or vertebral fracture doubles the risk of subsequent fractures in postmenopausal women[6]. Additionally, osteoporosis and osteoporotic fragility fractures cause considerable morbidity and mortality, leading to considerable individual and societal effects[7-9]. In 2005, costs relating to osteoporotic fragility fractures were more than $17 billion in the United States and were projected to be more than $25 billion by 2025[10]. One study reviewed the cost of a subsequent fracture following an initial fracture and found incremental increases in cost ranging from $23,852 to $47,351 at only one year following the index fracture. This study estimated the annual costs of a second fracture from 2002 to 2008 in Medicare patients alone to be approximately $1.13 billion[11]. These findings highlight the economic and public health benefits for improved prevention of secondary fragility fractures.

Anti-osteoporotic therapies are aimed at increasing bone mineral density and consequently decreasing the risk of fragility fracture. The most commonly employed anti-osteoporotic therapies are bisphosphonate medications that bind strongly to bone and inhibit osteoclast activity, thereby preventing bone resorption[12,13]. Clinical trials have shown that bisphosphonate treatment in patients with osteoporosis results in a 41% to 70% reduction in risk of an initial fragility fracture[14-17]. In a retrospective medical records review of 826 patients, increased compliance with bisphosphonate therapy has been found to reduce the risk of subsequent hip fracture after an initial hip fracture[18].

To our knowledge, no studies have examined large populations of patients to evaluate the effectiveness of initiating anti-osteoporotic therapies regardless of type in preventing subsequent fragility fractures regardless of site after an index fragility fracture. The purpose of this investigation was to assess the effectiveness, at a population level, of anti-osteoporotic therapies in preventing subsequent fractures. We hypothesized that patients receiving adequate anti-osteoporotic therapies after a fragility fracture will experience a decreased rate of subsequent fragility fracture compared with patients not receiving anti-osteoporotic therapies following a fragility fracture.

Materials and Methods

Data Source

This was a retrospective study performed with use of the Truven Health MarketScan databases (Truven Health Analytics, Ann Arbor, Michigan). The MarketScan databases provide de-identified, integrated, person-specific claim data for approximately seventeen to fifty-one million individuals per year; we examined data between 2003 and 2012. The data included claims made from both inpatient and outpatient clinical encounters and prescription medications. Claims made from both the Commercial Claims and Encounters Database and the Medicare Supplemental and Coordination of Benefits Database were included. International Classification of Diseases, Ninth Revision (ICD-9) diagnosis codes and Current Procedural Terminology (CPT) codes can be identified in individual claims. Outpatient prescription medication claims are organized according to National Drug Codes, which specify the type, dosage, and duration of medication prescribed. The data provided by the MarketScan databases used in this study were de-identified in compliance with Health Insurance Portability and Accountability Act (HIPAA) regulations. This study received exemption from the institutional review board at the study institution.

Study Sample

Subjects were included if they were fifty years of age or older, had sustained a fragility fracture, and had prescription medication coverage as a part of their insurance. A fragility fracture was defined according to the National Osteoporosis Foundation guidelines as any fracture of the wrist, proximal part of the humerus, hip, or vertebra[19]. The ICD-9 codes included in this definition are provided in Table I.

Patients who lacked twelve months of continuous enrollment in the database before the index fracture and three years of continuous enrollment after the index fracture were excluded to allow sufficient follow-up time for meaningful comparisons of subsequent fracture rates. Patients receiving anti-osteoporotic therapies (oral or injectable bisphosphonates, raloxifene, teriparatide, denosumab, or calcitonin) within twelve months prior to sustaining the index fragility fracture were excluded from the study. Patients who experienced multiple fractures at initial presentation or within fourteen days of the index fracture were excluded, as these were more likely to be secondary to higher-energy trauma and not true fragility fractures. Additionally, individuals with a diagnosis of Paget disease or cancer at any time were excluded to ensure that fractures were not pathologic.

The remaining individuals with index fragility fractures were then stratified into two groups for analysis. The anti-osteoporotic therapy group

TABLE I ICD-9 Codes for Each Fracture Site	
Fracture Site	ICD-9 Codes
Wrist	814.00, 813.40, 813.41, 813.42, 813.43, 813.44, 813.45, 813.46, 813.47, 813.50, 813.51, 813.52, 813.53, 813.54
Proximal part of the humerus	812.00, 812.01, 812.02, 812.03, 812.09, 812.10, 812.11, 812.12, 812.13, 812.19
Hip	820.00, 820.01, 820.02, 820.03, 820.09, 820.20, 820.21, 820.22, 820.8
Vertebra	805.00, 805.01, 805.02, 805.03, 805.04, 805.05, 805.06, 805.07, 805.08, 805.2, 805.4, 805.6, 805.8

TABLE II CPT Codes for Each Fracture Site	
Fracture Site	CPT Codes
Wrist	25600, 25605, 25606, 25607, 25608, 25609, 25611, 25620
Proximal part of the humerus	23600, 23605, 23615, 23616, 23620, 23625
Hip	27130, 27230, 27235, 27236, 27238, 27240, 27244, 27245
Vertebra	22310, 22315, 22325, 22326, 22327, 22328

included individuals who had sustained a fragility fracture and then were treated with anti-osteoporotic therapy as evidenced by prescription medication claims. Each prescription medication claim included the type of medication, the dosage, and the duration of treatment. From this information, the medication possession ratio was calculated with use of a well-described technique[20-22]. Using claims data, the total days of anti-osteoporotic therapy supplied to the patient were determined and then this sum was divided by the interval of days from the index prescription to the completion of the last prescription. We required that all patients in the anti-osteoporotic therapy group have a minimum medication possession ratio of 80% over six months. The 80% medication possession ratio cutoff has been commonly used in previous osteoporosis studies, as the medications have been reported to lose effectiveness at adherence levels of <80%[20-23]. Previous studies have shown anti-osteoporotic therapies to increase bone mineral density within six months of initiation[24-26]. Given that our goal was to study the role of adequate anti-osteoporotic therapies after an index fracture on subsequent fracture rates and that it takes time for anti-osteoporotic therapies to meaningfully improve bone mineral density, both criteria were utilized to establish a minimum of 80% medication possession ratio over six months. The control or no-treatment group contained those individuals who had sustained a fragility fracture and did not meet the 80% medication possession ratio minimum over six months.

Charlson Comorbidity Index scores were calculated for each subject in the study population with use of ICD-9 codes for comorbidities as used in previous studies[27]. The mean patient age, percentage of female patients, and mean Charlson Comorbidity Index were compared between the treated and untreated groups for each index fracture site. Chi-square tests were performed for categorical variables and Student t tests were performed for continuous variables.

Subsequent Fracture Identification

Identification of subsequent fracture utilized the same ICD-9 codes as for the index fragility fracture. Subsequent fractures could occur at the same site or at a different site than the index fragility fracture. To be counted as a subsequent fracture, an interval of more than ninety days between the index fracture claim and the subsequent fracture claim was required. In addition, if the subsequent fracture occurred at the same site as the initial fracture, a new CPT code charge was required to confirm that the subsequent fracture was truly a new fracture requiring treatment. CPT codes for each fracture site are included in Table II. The ninety-day interval requirement excluded individuals who may have sustained multiple fractures treated sequentially over a short interval from a specific injury or trauma. The end point for each subject in the study was three years following the index fragility fracture or the occurrence of a subsequent fracture, whichever occurred first.

Statistical Analysis

The main outcome studied was the three-year rate of subsequent fracture in the study population. Comparison of subsequent fracture rates between the anti-osteoporotic therapy group and the no-treatment group was performed with use of t tests, with a significant difference indicated by $p < 0.05$. Each fracture location was individually analyzed and was compared between the anti-osteoporotic therapy group and the no-treatment group. Multiple logistic regression analysis was performed to adjust for the effects of sex and age on the risk of subsequent fracture. Odds ratios for the risk of subsequent fracture in both groups were generated from the multiple logistic regression analysis and were reported with 95% confidence intervals (95% CIs). The number needed to treat with anti-osteoporotic therapies to prevent a subsequent fracture was calculated from age and sex-adjusted data with use of the methods described by Bender and Vervölgyi[28]. This calculation represents the number of patients who need to have anti-osteoporotic therapy initiated and maintained for six months to prevent a single subsequent fragility fracture. Stratification of the populations by age was performed to examine differential benefits by age. Statistical analysis was performed with SAS software (version 9.3; SAS Institute, Cary, North Carolina).

Source of Funding

TABLE III Patient Demographic Characteristics by Index Fracture Site										
	Wrist		Proximal Part of the Humerus		Hip		Vertebra		All	
	Treatment	No Treatment	Treatment	No Treatment	Treatment	No Treatment	Treatment	No Treatment	Treatment	No Treatment
No. of patients	744	9505	408	5069	931	6910	1195	6307	3278	27,791
Mean age (yr)	67.9	64.7*	69.0	68.0	77.3	76.4†	74.2	68.4*	73.0	69.1*
Female sex (%)	95.8	73.9*	96.1	74.4*	88.5	70.4*	80.8	56.8*	88.3	69.3*
Mean Charlson Comorbidity Index	0.105	0.089	0.140	0.119	0.118	0.135	0.161	0.137	0.133	0.117

*The values were significant at p < 0.001 for the comparison between patients who began anti-osteoporotic therapy after the index fracture and patients who did not begin anti-osteoporotic therapy after the index fracture. †The values were significant at p < 0.05 for the comparison between patients who began anti-osteoporotic therapy after the index fracture and patients who did not begin anti-osteoporotic therapy after the index fracture.

TABLE IV Three-Year Odds Ratio of Subsequent Fracture for the Anti-Osteoporotic Therapy Group Compared with the No-Treatment Group

Index Fracture	Unadjusted		Adjusted	
	Odds Ratio*	Odds Reduction with Treatment†	Odds Ratio*	Odds Reduction with Treatment†
Wrist	0.666‡ (0.478 to 0.927)	33.4%	0.505§ (0.360 to 0.708)	49.5%
Proximal part of the humerus	0.519§ (0.338 to 0.799)	48.1%	0.483§ (0.312 to 0.748)	51.7%
Hip	0.723§ (0.574 to 0.911)	27.7%	0.662§ (0.525 to 0.836)	33.8%
Vertebra	0.802 (0.640 to 1.005)	19.8%	0.569§ (0.452 to 0.717)	43.1%
All fractures combined	0.752§ (0.657 to 0.862)	24.8%	0.600§ (0.523 to 0.689)	40.0%

*The values are given as the odds ratio, with the 95% CI in parentheses. †Odds reduction of second fracture with anti-osteoporotic therapy treatment. ‡These values were significant at $p < 0.05$. §These values were significant at $p < 0.001$.

Results

Patient Characteristics

Eight groups were identified for analysis (four fracture locations each in the anti-osteoporotic therapy group and the no-treatment group) (Fig. 1). Of the 31,069 patients studied, 10.6% (3278 patients) were in the anti-osteoporotic therapy group. Significant differences ($p < 0.05$) in age were noted between the groups for every type of index fracture except index proximal humeral fractures. The mean age of patients in the anti-osteoporotic therapy group ranged from 67.9 to 77.3 years based on the index fracture location. In the no-treatment group, the mean age range of patients was 64.7 to 76.4 years. The anti-osteoporotic therapy group had significantly more female patients across all fracture types when compared with the no-treatment group (all $p < 0.01$). There was no significant difference ($p \geq 0.05$) in the Charlson Comorbidity Index between the groups (Table III).

Subsequent Fracture for the No-Treatment Group Compared with the Anti-Osteoporotic Therapy Group

The three-year subsequent fracture rates for patients in the no-treatment group were 7.7% for index wrist fractures, 10.3% for index proximal humeral fractures, 12.6% for index hip fractures, 9.7% for index vertebral fractures, and 9.7% for all fracture sites combined. In the anti-osteoporotic therapy group, subsequent fracture rates within three years of the index fracture were 5.2% for index wrist fractures, 5.6% for index proximal humeral fractures, 9.5% for index hip fractures, 8.0% for index vertebral fractures, and 7.5% for all fracture sites combined (Fig. 2). The lower rates of subsequent fracture observed in the anti-osteoporotic therapy group were significant for all index sites except vertebral fractures; the p values were <0.001 for any site, 0.02 for the wrist, 0.002 for the proximal part of the humerus, 0.006 for the hip, and 0.06 for the vertebrae.
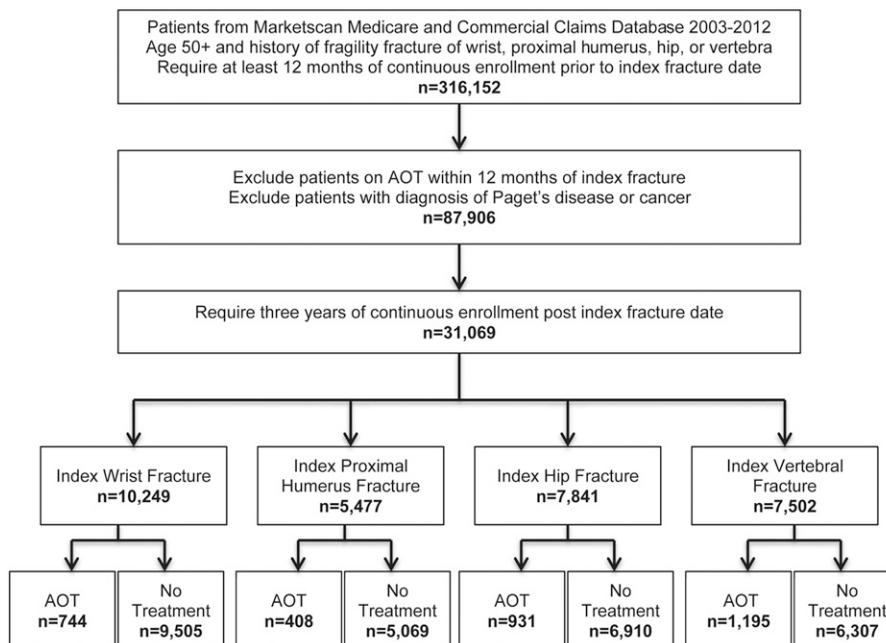

Fig. 1
Study sample selection from MarketScan databases from 2003 to 2012. AOT = anti-osteoporotic therapy.

ANTI-OSTEOPOROTIC THERAPY AFTER FRAGILITY FRACTURE
LOWERS RATE OF SUBSEQUENT FRACTURE

TABLE V Three-Year Number Needed to Treat with Anti–Osteoporotic Therapy After Index Fragility Fracture to Prevent a Subsequent Fracture	
Index Fracture	No. Needed to Treat*
Wrist	28 (20 to 45)
Proximal part of the humerus	20 (14 to 38)
Hip	26 (17 to 51)
Vertebra	25 (18 to 38)
All fractures combined	27 (22 to 35)

*The values are given as the number needed to treat, with the 95% CI in parentheses.

Of the entire cohort, twenty-seven patients had subsequent fractures within ninety days of the index fracture and were therefore excluded from the analysis. Additionally, 115 subsequent fractures occurred in patients who had been taking anti-osteoporotic therapy for a mean duration of 40.9 days but failed to meet the minimum medication possession ratio of 80% over six months. Within this subset, only forty patients had subsequent fractures with an anti-osteoporotic therapy prescription claim within thirty days prior to subsequent fracture and the remaining seventy-five patients discontinued anti-osteoporotic therapy at a mean time of 337 days prior to the subsequent fracture.

Odds ratios for subsequent fracture in both groups are presented in Table IV. Unadjusted analysis of subsequent fractures shows that the anti-osteoporotic therapy group had a decreased risk of subsequent fracture relative to the no-treatment group. Patients treated with anti-osteoporotic therapy had a reduction of risk of 33% after an index wrist fracture, 48% after an index proximal humeral fracture, 28% after an index hip fracture, and 25% when all index fracture sites were combined. Analysis of subsequent fracture risk after an index vertebral fracture did not reach significance (p = 0.056), with an odds ratio of 0.802 or an odds reduction of 20%. Adjusted odds ratios were calculated after multivariate regression to control for differences in age and sex between the anti-osteoporotic therapy group and the no-treatment group. Adjusted data showed that the anti-osteoporotic therapy group had a significantly decreased risk of subsequent fracture relative to the no-treatment group after an index fracture at any site (all p < 0.001). Patients' subsequent fracture risk was decreased by 50% after index wrist fractures, 52% after index proximal humeral fractures, 34% after index hip fractures, 43% after index vertebral fractures, and 40% when all index fracture sites were combined.

Number Needed to Treat

The values for the number needed to treat to prevent a single subsequent fragility fracture in the three years following the index fracture are presented in Table V. The number needed to treat to prevent a subsequent fragility fracture following all fractures combined in this study was twenty-seven (95% CI,
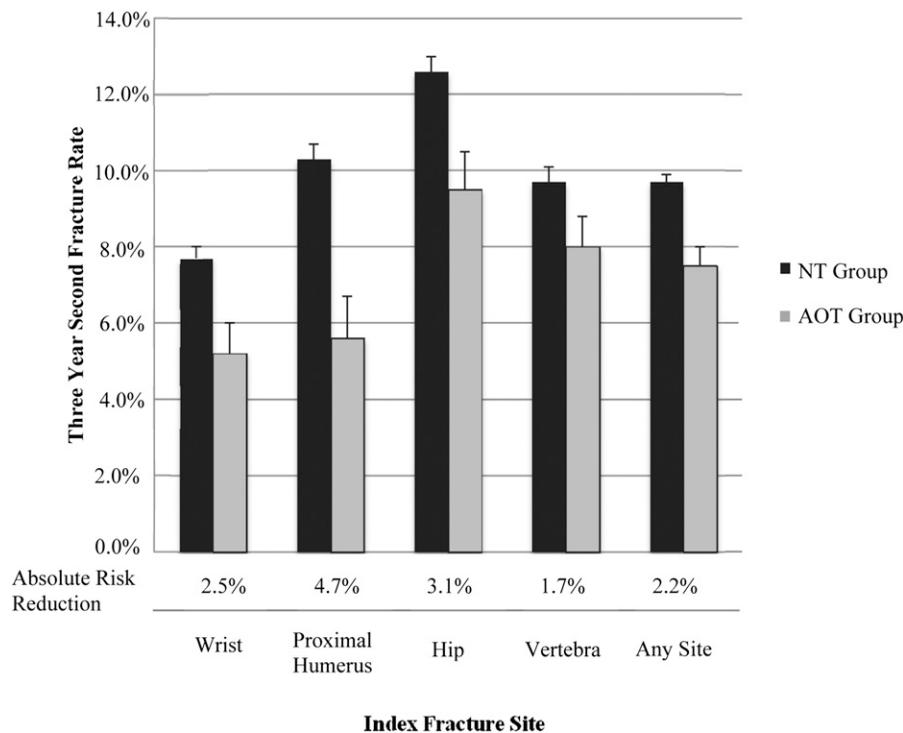

Fig. 2

Three-year subsequent fracture rates by index fracture site. The comparison of the anti-osteoporotic therapy (AOT) group and the no-treatment (NT) group showed significance at p < 0.05 for all rates except for index vertebral fracture. The error bars represent the standard error.

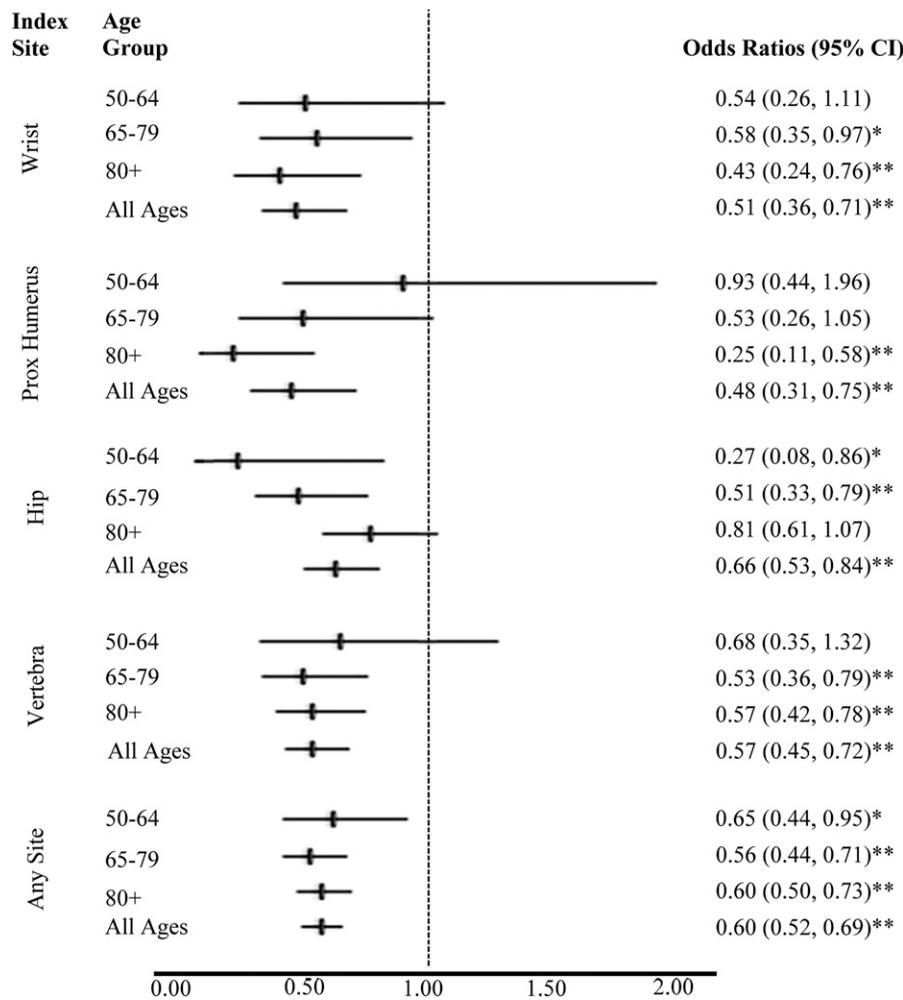| Index Site	Age Group		Odds Ratios (95% CI)
Wrist	50-64		0.54 (0.26, 1.11)
	65-79		0.58 (0.35, 0.97)*
	80+		0.43 (0.24, 0.76)**
	All Ages		0.51 (0.36, 0.71)**
Prox Humerus	50-64		0.93 (0.44, 1.96)
	65-79		0.53 (0.26, 1.05)
	80+		0.25 (0.11, 0.58)**
	All Ages		0.48 (0.31, 0.75)**
Hip	50-64		0.27 (0.08, 0.86)*
	65-79		0.51 (0.33, 0.79)**
	80+		0.81 (0.61, 1.07)
	All Ages		0.66 (0.53, 0.84)**
Vertebra	50-64		0.68 (0.35, 1.32)
	65-79		0.53 (0.36, 0.79)**
	80+		0.57 (0.42, 0.78)**
	All Ages		0.57 (0.45, 0.72)**
Any Site	50-64		0.65 (0.44, 0.95)*
	65-79		0.56 (0.44, 0.71)**
	80+		0.60 (0.50, 0.73)**
	All Ages		0.60 (0.52, 0.69)**

0.00   0.50   1.00   1.50   2.00

Fig. 3

Odds ratios (denoted by the tick marks) adjusted for sex for each age group and fracture type. The asterisk indicates significance at p < 0.05. The double asterisk indicates significance at p < 0.01. The bars represent the 95% CI.

twenty-two to thirty-five). Separate calculations based on index fracture site showed that the number needed to treat was twenty-eight (95% CI, twenty to forty-five) for index wrist, twenty (95% CI, fourteen to thirty-eight) for index proximal humeral, twenty-six (95% CI, seventeen to fifty-one) for index hip, and twenty-five (95% CI, eighteen to thirty-eight) for index vertebral fractures.

Stratification by Age

A stratified analysis of subsequent fractures demonstrated that all age groups in every fracture site had a decreased risk of subsequent fracture when they began anti-osteoporotic therapy after an index fracture compared with patients in the no-treatment group. Older patients (eighty years of age and older) had a lower risk of subsequent fracture when treated after index wrist (odds ratio, 0.43; p < 0.001) or proximal humeral fractures (odds ratio, 0.25; p < 0.001) than younger patients untreated after index wrist or proximal humeral fractures. Odds ratios for each age group and fracture type are presented in Figure 3.

Discussion

In this large study of commercial insurance and Medicare claims data, patients treated with anti-osteoporotic therapies after index fragility fractures were significantly less likely to sustain a subsequent fragility fracture within three years than patients who were not treated. The decrease in risk of subsequent fracture for patients treated with anti-osteoporotic therapies, after adjusting for age and sex, was 50% for an index wrist fracture, 52% for an index proximal humeral fracture, 34% for an index hip fracture, and 43% for an index vertebral fracture (Table IV). Stratification by age showed that nearly all subgroups experienced a significant decrease in risk of subsequent fracture in the anti-osteoporotic therapy group (Fig. 3).

Our results support the hypothesis that anti-osteoporotic therapy after an index fragility fracture decreases the likelihood of subsequent fracture. Age and female sex have been shown to be risk factors for fragility fractures. In our study, patients receiving anti-osteoporotic therapy were more likely to be older (the mean patient age was 73.0 years for the anti-osteoporotic therapy group and 69.1 years for the no-treatment group [p < 0.001]) and

female (the mean percentage of female sex for all index fractures was 88.3% in the anti-osteoporotic therapy group and 69.3% in the no-treatment group [p < 0.001]). Despite the anti-osteoporotic therapy group comprising a more at-risk population, a significant reduction in three-year subsequent fracture rates in both unadjusted and age and sex-adjusted analyses was observed. This finding further highlights the benefit of anti-osteoporotic therapy for patients with a history of fragility fracture.

It has been well established that anti-osteoporotic therapy reduces the risk of initial fragility fractures[29-32]. However, published data on the effectiveness of anti-osteoporotic therapy in preventing subsequent fragility fractures after an index fracture are limited. A recent retrospective review showed a significant reduction in the prevalence of subsequent hip fracture after an index hip fracture in patients compliant with bisphosphonate therapy[18]. In addition, a randomized controlled study showed that annual infusions of zoledronic acid after initial hip fractures significantly reduced the rates of subsequent fracture[33]. These findings are in agreement with the results of the current study. However, weaknesses of previous investigations include a focus on a single fracture type, a focus on a specific anti-osteoporotic therapy regimen, and a limited sample size. These limitations made it difficult to generalize these results across different fracture types and anti-osteoporotic therapy regimens. To our knowledge, the current study is the first to show the benefit of anti-osteoporotic therapy after an index fracture in preventing subsequent fragility fractures across multiple fracture sites and multiple anti-osteoporotic therapy treatments in a large cohort.

The findings of this study demonstrate substantial clinical effectiveness of anti-osteoporotic therapy in preventing subsequent fractures. Optimization of treatment to prevent subsequent fracture is necessary because of the burden that fragility fractures place on patients and the health-care system[10,11,34]. The number needed to treat to prevent a subsequent fracture ranged from twenty to twenty-eight based on the index fracture site and was twenty-seven when all fracture types were combined. The number-needed-to-treat values in this study are comparable with the number needed to treat in other major randomized controlled trials of anti-osteoporotic therapy medications in prevention of initial vertebral fractures (in which the number needed to treat ranges from four to sixty-four)[35]. In addition, the number-needed-to-treat values from our study compare favorably with established and accepted secondary prevention strategies, such as aspirin (150 needed to treat) and statins (ninety-four needed to treat) after myocardial infarction[36].

The use of claims data allows a large sample size but also has inherent limitations. The MarketScan database includes individuals with commercial insurance or Medicare coverage but does not contain information about uninsured individuals or those with Medicaid. The use of the medication possession ratio cannot truly determine whether the patients were compliant with the anti-osteoporotic therapy medication, only that prescriptions were filled. In our study, the minimum medication possession ratio was set at 80% over six months based on the prior literature on medication adherence and compliance[20,22,23]. Although grouping all anti-osteoporotic therapy regimens together, rather than stratifying them on the basis of the type of anti-osteoporotic therapy, led to stronger overall statements about the populationwide impact of anti-osteoporotic therapy use after a fragility fracture, it does not allow assessment of the relative efficacy of specific anti-osteoporotic therapies. Further investigation would be necessary to elucidate the effectiveness of specific regimens in preventing subsequent fragility fractures.

Optimizing care to prevent subsequent fractures in the elderly population is an important public health goal. This investigation has shown that anti-osteoporotic therapy after an index fracture leads to a significant decrease (approximately 40%) in the three-year risk of subsequent fracture across all index fracture sites in patients who are treated for a minimum of six months and are compliant (medication possession ratio, ≥80%). Consequently, physicians counseling patients about the relative reduction in risk of subsequent fracture after anti-osteoporotic therapy should emphasize the importance of compliance and duration of treatment. Furthermore, this study demonstrates the potential for anti-osteoporotic therapy to prevent a subsequent fracture in approximately one of every twenty-seven patients treated over the course of three years following an index fragility fracture, a ratio that compares favorably with other accepted preventative health strategies. These findings highlight the substantial benefits of anti-osteoporotic therapy initiation after osteoporotic fragility fractures. Anti-osteoporotic therapy should be accompanied by other accepted interventions in the fragility fracture risk modification armamentarium such as fall prevention or balance preservation interventions, resistance exercise, and optimization of serum vitamin D levels. ■

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