osteology

MDPI

Article

Exploring Disparities in Post-Fracture Osteoporosis Pharmacotherapy Initiation: A Retrospective Cohort Study Utilizing the *All of Us* Research Database

Roban Shabbir [1,*], Shums Lareef [1], Zion Kang [1], Brendan Layton [1], Robert Hoy [2] and Saqib Rehman [2]

[1] Lewis Katz School of Medicine at Temple University, Philadelphia, PA 19140, USA; shums.lareef@temple.edu (S.L.); zion.kang@temple.edu (Z.K.); tuj67333@temple.edu (B.L.)
[2] Department of Orthopedic Surgery, Temple University Hospital, Philadelphia, PA 19140, USA; robert.hoy@tuhs.temple.edu (R.H.); saqib.rehman@tuhs.temple.edu (S.R.)
* Correspondence: mdrobans@gmail.com

Abstract

Background/Objectives: Osteoporosis-related fragility fractures are sentinel events that should trigger timely secondary prevention, yet post-fracture care remains inconsistent. Leveraging the NIH All of Us Research Program, we quantified initiation of osteoporosis pharmacotherapy after fragility fracture and explored associations by age, sex at birth, race, and ethnicity. **Methods**: Retrospective cohort study using All of Us Controlled Tier data (v8) included adults aged 45 to 100 years with an index fragility fracture using prespecified OMOP concept sets intended to capture fractures commonly associated with osteoporosis. A new-user design excluded participants with any osteoporosis pharmacotherapy in the 365 days before fracture; participants required at least 180 days of follow-up. The primary outcome was initiation of osteoporosis pharmacotherapy (bisphosphonates, denosumab, or anabolic agents) within 180 days. Secondary outcomes were completion of dual-energy x-ray absorptiometry (DXA) and bone-health laboratory testing within 180 days. Multivariable logistic regression estimated adjusted odds ratios (OR) for each outcome by age at fracture, sex at birth, race, and ethnicity. **Results**: Among 1492 eligible participants, 87 initiated pharmacotherapy within 180 days (5.83%). After adjustment, older age was associated with higher odds of initiation (OR 1.04 per year; 95% CI 1.02 to 1.05). Male participants had markedly lower odds of pharmacotherapy initiation (OR 0.20; 95% CI 0.11 to 0.37) and DXA screening (OR 0.22; 95% CI 0.15 to 0.32) compared with female participants. In exploratory adjusted models, we did not detect an independent association between race and pharmacotherapy initiation (White vs. Black/African American OR 1.01; 95% CI 0.49 to 2.09), while White participants had higher odds of DXA screening than Black/African American participants (OR 1.79; 95% CI 1.02 to 3.28). **Conclusions**: In this diverse national EHR-based cohort, initiation of osteoporosis pharmacotherapy after fracture was uncommon, highlighting a substantial secondary prevention gap. In exploratory adjusted models, male sex was associated with lower odds of pharmacotherapy initiation and DXA receipt, while White participants had higher odds of DXA receipt than Black participants. System-level post-fracture pathways, including fracture liaison services and EHR-based prompts, may improve equitable identification and treatment of osteoporosis for All of Us participants and their communities.

Keywords: osteoporosis; fragility fracture; secondary prevention; treatment gap; pharmacotherapy; health disparities; All of Us; EHR

Check for updates

Academic Editors: Rui Soles Gonçalves and Samo Karel Fokter

Received: 28 February 2026
Revised: 27 April 2026
Accepted: 29 May 2026
Published: 2 June 2026

Copyright: © 2026 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license.

1. Introduction

Osteoporosis is a systemic skeletal disorder characterized by reduced bone mass and microarchitectural deterioration of bone tissue, leading to increased fracture risk [1]. The first manifestation of disease is often a fragility fracture resulting from low-energy trauma [2]. These fractures serve as sentinel events that identify individuals at high risk for subsequent fractures and fracture-related morbidity [3].

Osteoporosis-related fractures represent a major public health burden. Globally, one in three women and one in five men over the age of 50 will sustain an osteoporotic fracture during their lifetime [4]. Fragility fractures are associated with chronic pain, functional decline, loss of independence, and increased mortality, particularly following hip and vertebral fractures [3,5,6]. Importantly, a prior fragility fracture is among the strongest predictors of future fracture, making timely secondary prevention critical [7].

Despite the availability of effective diagnostic tools and pharmacologic therapies, osteoporosis care following fracture remains inconsistent. Dual-energy x-ray absorptiometry (DXA) enables objective assessment of bone mineral density, and medications such as bisphosphonates, denosumab, and anabolic agents reduce fracture risk [2]. However, the gap between guideline recommendations and real-world practice (i.e., the osteoporosis care gap), is most pronounced after fracture, when patients are at their highest risk. Prior studies have consistently shown that fewer than 20 to 30 percent of patients receive osteoporosis pharmacotherapy in the year following a fragility fracture [1,8,9].

Differences in osteoporosis care by sex have been reported previously and may contribute to variation in post-fracture management. Although osteoporosis is more prevalent in women, men account for approximately 25 to 30 percent of osteoporotic fractures and experience higher mortality in the year following injury [9,10]. Nevertheless, men are significantly less likely to undergo bone density testing or receive osteoprotective pharmacotherapy after fracture, reflecting persistent underrecognition of osteoporosis in male patients [11].

The National Institutes of Health All of Us Research Program provides a unique platform to evaluate post-fracture osteoporosis care across a diverse U.S. population. By integrating longitudinal electronic health records with detailed sociodemographic data and harmonizing information to the Observational Medical Outcomes Partnership (OMOP) Common Data Model (CDM), the program enables assessment of real-world post-fracture care patterns and variation in treatment delivery [12].

Using data from All of Us, we conducted a retrospective cohort study to characterize post-fracture osteoporosis care, including diagnosis/testing and initiation of osteoporosis pharmacotherapy, within 180 days of an index fracture among adults with adequate post-fracture follow-up. We aimed to characterize post-fracture osteoporosis care patterns in a diverse national EHR cohort, including initiation of pharmacotherapy, diagnostic evaluation, and laboratory assessment. We additionally explored whether care patterns varied across demographic subgroups, recognizing that subgroup analyses were exploratory given the limited number of treatment events.

2. Methods

2.1. Study Design and Data Source

We performed a retrospective cohort study using the All of Us Research Program Controlled Tier Dataset (v8). The Controlled Tier provides access to row-level EHR data with unshifted dates, allowing for precise temporal analysis of the interval between fracture events and medication dispensing. The data are harmonized to the OMOP CDM v5.2, which standardizes diverse coding systems (e.g., ICD-9, ICD-10, CPT, SNOMED, RxNorm) into standard concepts.

All analyses were executed within the All of Us Researcher Workbench, a secure, cloud-based environment. Data extraction utilized BigQuery-backed SQL, and statistical analyses were performed using Python 3.12.4 (Python Software Foundation, Wilmington, DE, USA) (libraries: *pandas* for data manipulation, *statsmodels* for regression analysis). The study protocol adhered to the All of Us Data User Code of Conduct. As the data were de-identified and the study involved no direct participant contact, Institutional Review Board (IRB) approval was not required by the local institution, consistent with program governance.

2.2. Study Population and Cohort Construction

Participants were identified using the All of Us Cohort Builder and subsequent SQL filtering. The inclusion criteria were designed to capture a broad population of adults at risk for osteoporotic fractures while ensuring sufficient data density for analysis.

2.2.1. Inclusion Criteria

Inclusion required linked EHR data within the dataset. Eligible participants were 45 to 100 years old at the time of the curated data repository (CDR) snapshot. This age range was used to capture the most relevant population for primary and secondary osteoporosis prevention. Fragility fracture was assigned as the presence of at least one condition occurrence record representing a likely fragility fracture. Because structured EHR data did not reliably capture the low-energy injury mechanism, the index event was defined using a prespecified OMOP concept set of fractures at sites commonly associated with osteoporosis. This site-based proxy included classical osteoporotic fracture locations and additional fracture sites captured by the concept set; accordingly, the cohort should be interpreted as enriched for likely fragility fractures rather than confirmed low-energy fractures.

We utilized standard concepts and their descendants to capture all relevant diagnostic codes (e.g., ICD-10 M80.x for pathological fracture, S72.x for femur fracture). Pathological fractures due to malignancy or high-impact trauma were excluded where distinguishable by specific codes. Because structured EHR data incompletely capture injury mechanisms, fracture classification relies on diagnosis-code concept sets and anatomic site rather than direct confirmation of low-energy trauma. The Index Fracture Date was defined as the date of the earliest qualifying fragility fracture event recorded during the observation period. If multiple fractures were present, the earliest-occurring fracture served as the index case.

2.2.2. Observation Time and New-User Design

To accurately characterize the cohort as "new users" of osteoporosis therapy and to ensure sufficient follow-up, strict observation time criteria were applied using the OMOP observation_period table. For baseline lookback, participants were required to have at least 365 days of continuous EHR observation before the index fracture date. This window was used to assess baseline comorbidities and, crucially, to exclude prior medication use. For follow-up, participants were required to have at least 180 days of continuous EHR observation after the index fracture date to allow sufficient time for the primary outcome (treatment initiation) to occur.

2.2.3. Exclusion of Prevalent Users

To focus the analysis on the clinical decision-making process triggered by the fracture event itself, we excluded participants with any evidence of osteoporosis pharmacotherapy exposure in the 365 days preceding the index fracture. This created a "treatment-naïve" or "new-user" analytic cohort, ensuring that the outcome measures represent de novo initiation of secondary prevention rather than the continuation of existing therapy. After applying these attrition criteria, the final analytic cohort consisted of 1492 eligible participants.

Demographic variables were extracted from the OMOP person table and linked survey data. These included sex at birth, race, ethnicity, and age at fracture.

2.3. Outcomes

2.3.1. Primary Outcome: Pharmacotherapy Initiation

The primary outcome was the initiation of an osteoporosis-specific pharmacological agent within 180 days following the index fracture date. This window was selected to align with quality measures (e.g., HEDIS) that typically assess care within 6 months of a fracture. Medications were identified from the OMOP drug_exposure table using standard RxNorm concept IDs and descendant concepts. These drugs included bisphosphonates (Alendronate, risedronate, ibandronate, zoledronic acid, pamidronate), RANK Ligand inhibitors (denosumab), and anabolic agents (teriparatide, abaloparatide, romosozumab). Calcium and vitamin D supplements were excluded because they are generally considered adjunctive rather than primary anti-fracture therapy. Selective Estrogen Receptor Modulators (SERMs) such as raloxifene were tracked separately but were not included in the primary pharmacotherapy outcome.

2.3.2. Secondary Outcomes

To understand where the breakdown in care occurs, we evaluated intermediate steps in the management pathway within the same 180-day window. This included DXA Scan for evidence of a dual-energy X-ray absorptiometry scan (CPT codes 77080, 77081, etc.) in the procedure_occurrence or measurement tables, Bone Health Labs for evidence of relevant metabolic bone labs (serum calcium, 25-hydroxyvitamin D, PTH) in the measurement table, and Osteoporosis Diagnosis for documentation of a specific osteoporosis diagnosis code (e.g., ICD-10 M81.0) in the condition_occurrence table.

2.4. Statistical Analysis

Descriptive Analysis:

We summarized participant characteristics using counts and percentages for categorical variables and means or medians for continuous variables. The proportion of participants meeting the primary and secondary outcomes was calculated for the overall cohort and stratified by race, ethnicity, and sex. Participants with unknown sex at birth, race, or ethnicity were retained as separate analytic categories, and no imputation was performed. Retaining these categories allowed inclusion of participants with incomplete demographic ascertainment and enabled transparent reporting of missingness across demographic variables.

To explore associations between sociodemographic factors and treatment initiation, we fitted multivariable logistic regression models and estimated odds ratios (ORs) for treatment receipt. A separate model was run for the secondary outcomes of Bone Lab testing and DXA screening to compare predictors across the care cascade. Given the limited number of pharmacotherapy initiators, these adjusted models were considered exploratory and were restricted to prespecified sociodemographic covariates. All statistical tests were two-sided with an alpha level of 0.05. Confidence intervals (95% CI) were calculated for all point estimates.

3. Results

3.1. Cohort Flow and Demographics

The initial query identified 1853 participants with a qualifying index fragility fracture. Of these, 361 (19.5%) were excluded due to evidence of osteoporosis pharmacotherapy in the year prior to the fracture. The final analytic "new-user" cohort comprised 1492 participants.

The cohort was predominantly female (59.4%) and White (65.4%). A substantial proportion of participants had missing demographic data, including 18.0% with unknown sex and 24.2% with unknown race, which are reported as separate analytic categories. Specifically, the sample included 886 females (59.4%), 338 males (22.7%), and 268 individuals with unknown sex (18.0%). In terms of race, 976 participants identified as White (65.4%), 88 as Black or African American (5.9%), 67 as Other (4.5%), and 361 were categorized as Unknown (24.2%). Regarding ethnicity, 1107 participants were not Hispanic (74.2%), 98 were Hispanic (6.6%), and 287 had unknown ethnicity (19.2%). The proportion of participants with unknown demographic information was substantial, particularly for race and sex at birth, and should be considered when interpreting subgroup comparisons.

3.2. Index Fracture Site Distribution

Hip fractures were the most prevalent injury in the cohort, accounting for 55.6% of cases (n = 830). Fractures of the shoulder or humerus comprised 13.2% (n = 197), followed by fractures of the spine at 8.0% (n = 120) and hand or wrist fractures at 3.5% (n = 52). The remaining 18.6% (n = 278) included fractures of the pelvis or acetabulum, ribs or sternum, clavicle or scapula, femoral shaft or distal femur, tibia or fibula, and ankle or foot. These additional fracture sites reflect the broader range of injuries captured by the prespecified concept set and should be interpreted with caution when considering the cohort as representing classical fragility fractures.

3.3. Primary Outcome: Pharmacotherapy Initiation Rates

Among the 1492 patients with a new fragility fracture, only 87 patients initiated osteoporosis pharmacotherapy within 180 days. Given the small number of treated patients, subgroup comparisons should be interpreted with caution. Initiation rates stratified by demographic characteristics are presented in Table 1.

Table 1. Unadjusted rates of osteoporosis pharmacotherapy initiation within 180 days after an index fracture, stratified by race, ethnicity, and sex at birth, with ≥180 days of post-fracture EHR follow-up.

Group	Sub-Category	Number of Patients (*n*)	Initiated Pharmacotherapy (*n*)	Initiation Rate (%)
Race	White	976	75	7.68%
	Black/African American	88	3	3.41%
	Other	67	3	4.48%
	Unknown	361	6	1.66%
Ethnicity	Hispanic	98	5	5.10%
	Not Hispanic	1107	72	6.50%
	Unknown	287	5	1.74%
Sex	Female	886	76	8.60%
	Male	338	11	3.30%
	Unknown	268	0	0.00%

Initiation reflects a new prescription for a bisphosphonate, denosumab, or an anabolic agent; values are shown as *n*, number initiated, and initiation rate (%). Subgroup comparisons may be interpreted cautiously because some strata had few treatment initiators.

Medication Choice

Among patients who initiated therapy, oral bisphosphonates were the most commonly prescribed agents. Alendronate accounted for 41.4% of first prescriptions, followed closely by zoledronic acid (IV) at 37.2%. Denosumab was the first choice in 4.6% of cases.

3.4. Secondary Outcomes

Within six months of the index event, fewer than one quarter of patients in the cohort received a formal ICD diagnosis of osteoporosis (M81.x), with an observed diagnosis rate of 22.38%. Evaluation of bone health was more common than diagnostic labeling, with 53.62% of patients undergoing relevant laboratory testing, including serum vitamin D and calcium measurements. In contrast, documentation of dual-energy X-ray absorptiometry (DXA) screening was relatively infrequent. To further evaluate factors associated with receipt of post-fracture care, multivariable logistic regression models were constructed (Table 2). Taken together, the observed pattern of laboratory testing, osteoporosis diagnosis, DXA use, and pharmacotherapy initiation suggests attrition at multiple steps of the post-fracture care pathway, with the largest shortfall at transition to documented pharmacologic treatment.

Table 2. Multivariable Odds Ratios for Post-Fracture Care.

Predictor	Rx Initiation OR (95% CI)	*p*-Value	Bone Lab OR (95% CI)	*p*-Value	DXA OR (95% CI)	*p*-Value
Age at Fracture (per year)	**1.04 (1.02–1.05)**	**<0.001**	**1.01 (1.01–1.02)**	**0.006**	**1.05 (1.04–1.07)**	**<0.001**
Male (vs. Female)	**0.20 (0.11–0.37)**	**<0.001**	1.09 (0.86–1.37)	0.487	**0.22 (0.15–0.32)**	**<0.001**
Unknown Sex (vs. Female)	0.90 (0.26–3.11)	0.862	0.72 (0.32–1.63)	0.431	0.73 (0.28–1.92)	0.521
White (vs. Black)	1.01 (0.49–2.09)	0.980	**0.73 (0.39–0.97)**	**0.049**	**1.79 (1.02–3.28)**	**0.040**
Other Race (vs. Black)	0.66 (0.21–2.13)	0.488	1.04 (0.58–1.89)	0.889	1.63 (0.72–3.72)	0.244
Unknown Race (vs. Black)	2.65 (0.29–24.68)	0.391	0.84 (0.33–2.16)	0.722	1.70 (0.52–5.54)	0.375
Not Hispanic (vs. Hispanic)	2.52 (0.31–20.62)	0.388	1.05 (0.45–2.44)	0.903	0.74 (0.27–2.01)	0.558

Data in bold are findings with statistical significance.

Adjusted odds ratios (OR) from multivariable logistic regression models evaluating associations of age at fracture, sex at birth, race, and ethnicity with receipt of post-fracture osteoporosis care within 180 days: (1) pharmacotherapy initiation, (2) bone-health laboratory testing (serum calcium, 25-hydroxyvitamin D, and/or PTH), and (3) DXA testing. Results are presented as OR (95% CI) with *p*-values.

In exploratory adjusted analyses, male participants demonstrated lower odds of pharmacotherapy initiation and DXA receipt. After adjustment for prespecified sociodemographic covariates, male participants had lower odds of pharmacotherapy initiation (OR = 0.20) and DXA receipt (OR = 0.22) compared to female participants. Age is positively associated with care, with every additional year of age increasing the odds of initiating treatment by 4% (OR = 1.04). The adjusted odds of treatment for White participants compared to Black participants were 1.01 (95% CI 0.49–2.09), which was not statistically significant, suggesting that the differences observed in unadjusted rates (7.68% vs. 3.41%) may be explained by differences in age and sex distribution. DXA receipt differed by race, with White participants having higher odds of screening compared to Black participants (OR = 1.79; $p = 0.040$).

4. Discussion

4.1. Variation in Pharmacotherapy Initiation

The primary finding of this study is the low rate of osteoporosis pharmacotherapy initiation following a fragility fracture, measured at 5.83%. This rate is below previously reported benchmarks, as earlier studies using Medicare claims data have documented post-fracture treatment rates ranging from 10% to 25%, although differences in data sources and methodology should be considered when making such comparisons [13,14]. The lower

treatment rates observed in the All of Us cohort may reflect differences in data capture, cohort composition, or care patterns compared to prior studies. Although the cohort is smaller than national administrative datasets, its broad geographic and demographic composition may offer insight into treatment patterns in segments of the population that have been underrepresented in prior studies focused on insured or older adult populations. However, differences in cohort characteristics and data capture methods should be considered when interpreting this finding.

These findings suggest a potential gap in osteoporosis care that persists despite evidence that initiation of pharmacotherapy may reduce the risk of recurrent fractures [15]. The lack of timely initiation of osteoporosis treatment following a fragility fracture is associated with an increased risk of subsequent fractures. The observed discrepancy between the treatment initiation rate (5.83%) and the diagnosis rate (22.38%) suggests that, even when osteoporosis is identified and coded by clinicians, it is not consistently followed by pharmacologic intervention. This potential gap in care may reflect systemic factors, such as care coordination challenges. For example, osteoporosis management may be deferred across specialties, with orthopedic surgeons primarily addressing surgical needs and primary care providers potentially unaware of or delaying post-fracture treatment due to competing clinical demands [16].

4.2. Variation by Sex

In this analysis, male sex appeared to be a strong predictor of undertreatment, with men approximately 80 percent less likely than women to receive osteoporosis pharmacotherapy. This finding is consistent with prior research indicating a persistent pattern of under-recognition and undertreatment of osteoporosis in men [17]. When considered alongside evidence that men experience significantly higher mortality rates following hip fractures compared to women [18], this treatment gap warrants further attention. Several factors may contribute to this disparity. Osteoporosis is often perceived as a condition primarily affecting postmenopausal women, a perspective reflected in current screening guidelines. The 2025 US Preventive Services Task Force recommends screening for osteoporosis in women aged 65 and older but concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening in men [9]. As a result, fractures in men may be more readily attributed to higher-energy trauma or other non-osteoporotic causes rather than to underlying bone fragility. This perception may be one factor contributing to the decreased rates of diagnostic imaging, such as DXA scans (odds ratio 0.22), and reduced pharmacologic treatment observed among men in the cohort. These findings underscore the importance of improving awareness of osteoporosis risk in men and evaluating whether current screening and treatment approaches adequately address this population.

4.3. Variation by Race

In the unadjusted analysis, White participants were more than twice as likely as Black participants to receive osteoporosis treatment, a pattern that is consistent with national data showing lower screening and treatment rates among Black women [19]. However, after adjusting for age and sex in the multivariable analysis (Table 2), the difference in treatment initiation between White and Black participants was no longer statistically significant (OR 1.01). This suggests that demographic factors, such as differences in age distribution and sex, which are both associated with a higher likelihood of treatment, may partially explain the observed post-fracture care in treatment rates.

Despite the absence of a statistically significant difference in adjusted treatment rates, a notable disparity remained in diagnostic evaluation. White participants were significantly

more likely to undergo DXA screening compared to Black participants (OR 1.79), indicating that differences in assessment practices may persist. This finding is consistent with longstanding perceptions, sometimes referred to as the "myth of high bone density," which have been interpreted to suggest that Black individuals are at inherently lower risk for osteoporosis due to higher average bone mineral density [20,21]. Individuals of any racial background who sustain a fragility fracture remain at elevated risk for subsequent fractures and may benefit from secondary prevention strategies. The lower use of diagnostic imaging in Black patients may contribute to underdiagnosis and may represent an important area for further investigation and intervention to reduce disparities in osteoporosis care. Interpretation of race-specific treatment estimates should remain cautious because the number of treatment initiators in several subgroups was small, limiting precision.

4.4. Variation by Age

The positive association between age and treatment initiation (OR = 1.04) suggests that older patients may be more likely to be identified and managed for osteoporosis. In contrast, individuals aged 45 to 65 years who experience fragility fractures may be less consistently evaluated or treated for underlying bone health. For instance, distal radius fractures in women in their mid-50s are not always recognized as potential indicators of osteoporosis, despite evidence linking such fractures to an increased risk of subsequent hip fracture [22]. The lower treatment rates observed in younger cohorts may reflect uncertainty about when to initiate evaluation and intervention, which could limit opportunities for secondary prevention and risk reduction before more serious fracture events occur, and warrants investigation.

4.5. Limitations

This study has limitations inherent to its retrospective design and reliance on electronic health record data from the All of Us Research Program. As an observational analysis, causal inferences cannot be made. Although multivariable adjustment was performed, residual confounding is likely from factors not reliably captured in structured EHR data, including fracture severity and mechanism, functional status, provider specialty, patient preferences, and competing clinical priorities in the post-fracture period. In addition, the current models included a limited set of covariates, and the absence of key clinical and system-level factors (e.g., comorbidities, healthcare utilization, and fracture site) may result in residual confounding and limit interpretation of observed associations, particularly for disparity analyses.

The number of participants who initiated osteoporosis pharmacotherapy was small, limiting statistical power for subgroup analyses, particularly across racial and ethnic groups and less common fracture sites. As a result, some analyses yielded wide confidence intervals, and nonsignificant findings should be interpreted cautiously.

Misclassification is possible due to reliance on diagnostic, procedural, and medication codes. Fragility fractures were defined by anatomic site rather than by a confirmed mechanism, which may have led to the inclusion of some higher-energy injuries or the exclusion of true fragility fractures not explicitly coded as such. Additionally, inconsistency in coding practices across contributing sites may further affect cohort definition and fracture classification. Medication exposure records may not fully capture prescriptions or administrations outside participating health systems or account for patient nonadherence, potentially underestimating treatment rates. Furthermore, the drug_exposure data may reflect prescriptions, dispensing, or administration events without distinction, and injectable therapies may be variably captured, introducing additional uncertainty in outcome ascertainment. We were unable to apply a reliable mechanism-of-injury proxy or perform a mechanism-based

sensitivity analysis because external-cause and trauma-context fields were incompletely captured across contributing sites.

The use of a new-user design with requirements for continuous pre- and post-fracture observation strengthens internal validity by isolating treatment decisions following fracture but may exclude patients who were appropriately re-initiated on therapy or received care across fragmented health systems, leading to conservative estimates of post-fracture osteoporosis management. Additionally, the requirement for at least 180 days of follow-up may exclude patients with early mortality following fracture, potentially biasing the cohort toward healthier individuals.

Incomplete demographic data represent an additional limitation. A substantial proportion of participants had unknown race, ethnicity, or sex at birth, reflecting known limitations of EHR-derived variables. Although these categories were retained to minimize selection bias, missingness may have attenuated observed associations. Because participants with unknown demographic categories were retained rather than excluded, estimates may be less vulnerable to selection bias; however, incomplete demographic ascertainment may still influence interpretation of subgroup findings. Furthermore, sample sizes for non-white demographics were somewhat limited. Moreover, race and ethnicity reflect social constructs, and unmeasured structural factors such as access to care and healthcare utilization could not be fully accounted for.

Finally, while the All of Us cohort is intentionally diverse, it is not population-representative and may differ from the broader fracture population. This analysis was limited to diagnostic evaluation and pharmacotherapy initiation within 180 days of fracture and did not assess treatment persistence, adherence, or subsequent fracture outcomes, capturing only the initial step in secondary fracture prevention. Given these limitations, findings should be interpreted as descriptive associations rather than definitive evidence of causal relationships or system-level disparities.

5. Conclusions

This retrospective analysis of All of Us Research Program data highlights a potential post-fracture osteoporosis care gap: fewer than 6% of patients may have initiated guideline-concordant pharmacotherapy after a likely fragility fracture, leaving what could be a majority of the relevant patient population without evidence-based pharmacologic protection against subsequent fractures. This study primarily highlights a substantial post-fracture osteoporosis care gap across a diverse national cohort. Exploratory subgroup analyses suggested variation in care by demographic characteristics; however, these findings should be interpreted cautiously given limited event counts, missing demographic information, and restricted covariate adjustment. These findings support standardized, system-level secondary prevention strategies rather than reliance on individual clinician initiative. Pragmatic interventions may include automated EHR identification of qualifying fractures, standardized discharge order sets for DXA and bone-health laboratory testing, and fracture liaison service workflows that ensure referral and timely treatment initiation across specialties. Future work should evaluate whether these pathways improve equitable post-fracture osteoporosis care in diverse populations.

Author Contributions: Conceptualization, R.S., R.H., S.R.; methodology, R.S., R.H., S.R.; software, R.S.; formal analysis, R.S., S.L., Z.K., B.L.; data curation, R.S., S.L.; writing—original draft preparation, R.S., S.L., Z.K., B.L.; writing—review and editing, R.S., S.L., Z.K., B.L.; visualization, R.S.; supervision, R.S., R.H., S.R.; project administration, R.S., R.H., S.R. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: Not applicable. This study used fully de-identified data from the All of Us Research Program Controlled Tier dataset. According to NIH program governance and U.S. federal regulations (45 CFR 46), research involving de-identified datasets does not constitute human subjects research and therefore does not require IRB approval [23]. No identifiable private information was accessed.

Informed Consent Statement: Not applicable. All data used in this study were originally collected by the All of Us Research Program under its informed consent process. Only de-identified data were accessed for the present analysis, and no direct contact with participants occurred.

Data Availability Statement: The data presented in this study are available upon reasonable request from the corresponding author; access is subject to the All of Us Research Program policies and may require approval through the All of Us Researcher Workbench.

Conflicts of Interest: The authors declare no conflicts of interest.

References

1. Ayers, C.; Ward, R.; Kansagara, D. Update alert: Effectiveness and safety of treatments to prevent fractures in people with low bone mass or primary osteoporosis: A living systematic review and network meta-analysis for the American College of Physicians. *Ann. Intern. Med.* **2024**, *177*, eL230118. [CrossRef]
2. Camacho, P.M.; Petak, S.M.; Binkley, N.; Diab, D.L.; Eldeiry, L.S.; Farooki, A.; Harris, S.T.; Hurley, D.L.; Kelly, J.; Lewiecki, E.M.; et al. American Association of Clinical Endocrinologists/American College of Endocrinology Clinical Practice Guidelines for the Diagnosis and Treatment of Postmenopausal Osteoporosis-2020 Update. *Endocr. Pract.* **2020**, *26*, 1–46. [CrossRef]
3. Cosman, F.; Lewiecki, E.M.; Eastell, R.; Ebeling, P.R.; Jan De Beur, S.; Langdahl, B.; Rhee, Y.; Fuleihan, G.E.; Kiel, D.P.; Schousboe, J.T.; et al. Goal-directed osteoporosis treatment: ASBMR/BHOF task force position statement 2024. *J. Bone Miner. Res.* **2024**, *39*, 1393–1405. [CrossRef]
4. Morin, S.N.; Leslie, W.D.; Schousboe, J.T. Osteoporosis: A Review. *JAMA* **2025**, *334*, 894–907. [CrossRef] [PubMed]
5. Cummings, S.R.; Melton, L.J. Epidemiology and outcomes of osteoporotic fractures. *Lancet* **2002**, *359*, 1761–1767. [CrossRef]
6. Brown, J.P.; Adachi, J.D.; Schemitsch, E.; Tarride, J.E.; Brown, V.; Bell, A.; Reiner, M.; Oliveira, T.; Motsepe-Ditshego, P.; Burke, N.; et al. Mortality in older adults following a fragility fracture: Real-world retrospective matched-cohort study in Ontario. *BMC Musculoskelet. Disord.* **2021**, *22*, 105. [CrossRef] [PubMed]
7. Wong, R.M.Y.; Wong, P.Y.; Liu, C.; Wong, H.W.; Chung, Y.L.; Chow, S.K.H.; Law, S.W.; Cheung, W.H. The imminent risk of a fracture-existing worldwide data: A systematic review and meta-analysis. *Osteoporos. Int.* **2022**, *33*, 2453–2466. [CrossRef] [PubMed]
8. Dimai, H.P. Use of dual-energy X-ray absorptiometry (DXA) for diagnosis and fracture risk assessment; WHO-criteria, T- and Z-score, and reference databases. *Bone* **2017**, *104*, 39–43. [CrossRef]
9. US Preventive Services Task Force; Nicholson, W.K.; Silverstein, M.; Wong, J.B.; Chelmow, D.; Coker, T.R.; Davis, E.M.; Jaén, C.R.; Krousel-Wood, M.; Lee, S.; et al. Screening for Osteoporosis to Prevent Fractures: US Preventive Services Task Force Recommendation Statement. *JAMA* **2025**, *333*, 498–508. [CrossRef]
10. Björnsdottir, S.; Clarke, B.L.; Mannstadt, M.; Langdahl, B.L. Male osteoporosis-what are the causes, diagnostic challenges, and management. *Best Pract. Res. Clin. Rheumatol.* **2022**, *36*, 101766. [CrossRef]
11. De Almeida, R.J.R.; Grover, A.; Agarwal, S.; Dhaliwal, R. Inequities Across the Spectrum of Osteoporosis Care and Post-Fracture Management in Men. *Curr. Osteoporos. Rep.* **2025**, *23*, 49. [CrossRef]
12. All of Us Research Program Investigators; Denny, J.C.; Rutter, J.L.; Goldstein, D.B.; Philippakis, A.; Smoller, J.W.; Jenkins, G.; Dishman, E. The "All of Us" Research Program. *N. Engl. J. Med.* **2019**, *381*, 668–676. [CrossRef]
13. Wu, H.; Liu, Y.; Zhang, J.; Sen, B.; Curtis, J.R. Individual and Community-level Determinants of Osteoporosis Treatment Following Fracture Among Medicare Beneficiaries. *J. Gen. Intern. Med.* **2025**. [CrossRef] [PubMed]
14. Liu, S.K.; Munson, J.C.; Bell, J.E.; Zaha, R.L.; Mecchella, J.N.; Tosteson, A.N.; Morden, N.E. Quality of osteoporosis care of older Medicare recipients with fragility fractures: 2006 to 2010. *J. Am. Geriatr. Soc.* **2013**, *61*, 1855–1862. [CrossRef] [PubMed]
15. Ye, C.; Ebeling, P.; Kline, G. Osteoporosis. *Lancet* **2025**, *406*, 2003–2016. [CrossRef]
16. Silverstein, W.K.; Wang, S.; Alavinejad, M.; Sarnocinska, A.; Stall, N.M.; Malikov, K.; Hillmer, M.P.; Zipursky, J.S. Antiosteoporosis Medication Prescriptions After Fragility Fractures. *JAMA Netw. Open* **2024**, *7*, e2438393. [CrossRef]
17. Rinonapoli, G.; Ruggiero, C.; Meccariello, L.; Bisaccia, M.; Ceccarini, P.; Caraffa, A. Osteoporosis in Men: A Review of an Underestimated Bone Condition. *Int. J. Mol. Sci.* **2021**, *22*, 2105. [CrossRef] [PubMed]

18. Bajracharya, R.; Guralnik, J.M.; Shardell, M.D.; Rathbun, A.M.; Yamashita, T.; Hochberg, M.C.; Gruber-Baldini, A.L.; Magaziner, J.S.; Orwig, D.L. Long-term sex differences in all-cause and infection-specific mortality post hip fracture. *J. Am. Geriatr. Soc.* **2022**, *70*, 2107–2114. [CrossRef]
19. White, L. Osteoporosis Prevention, Screening, and Diagnosis: ACOG Recommendations. *Am. Fam. Physician* **2022**, *106*, 587–588.
20. Noel, S.E.; Santos, M.P.; Wright, N.C. Racial and Ethnic Disparities in Bone Health and Outcomes in the United States. *J. Bone Miner. Res.* **2021**, *36*, 1881–1905. [CrossRef]
21. Aloia, J.F. African Americans, 25-hydroxyvitamin D, and osteoporosis: A paradox. *Am. J. Clin. Nutr.* **2008**, *88*, 545S–550S. [CrossRef] [PubMed]
22. Crandall, C.J.; Hovey, K.M.; Cauley, J.A.; Andrews, C.A.; Curtis, J.R.; Wactawski-Wende, J.; Wright, N.C.; Li, W.; LeBoff, M.S. Wrist Fracture and Risk of Subsequent Fracture: Findings from the Women's Health Initiative Study. *J. Bone Miner. Res.* **2015**, *30*, 2086–2095. [CrossRef] [PubMed]
23. Department of Health and Human Services. Code of Federal Regulations Title 45 Part 46 Protection of Human Subjects. Available online: https://www.ecfr.gov/current/title-45/part-46 (accessed on 10 January 2026).

Disclaimer/Publisher's Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.