

## RESEARCH PAPER

# Factors associated with initiation of bone-health medication among older adults in primary care in Ireland

MARY E. WALSH<sup>1</sup>, MARI NERDRUM<sup>1,2</sup>, TOM FAHEY<sup>1</sup>, FRANK MORIARTY<sup>1,3</sup>

<sup>1</sup>HRB Centre for Primary Care Research, Department of General Practice, Royal College of Surgeons in Ireland, Dublin, Ireland

<sup>2</sup>Graduate Entry Medicine Royal College of Surgeons in Ireland, Dublin, Ireland

<sup>3</sup>School of Pharmacy and Biomolecular Sciences, Royal College of Surgeons in Ireland, Dublin, Ireland

Address correspondence to: Frank Moriarty. Email: [frankmoriarty@rcsi.com](mailto:frankmoriarty@rcsi.com)

## Abstract

**Background:** Adults at high risk of fragility fracture should be offered pharmacological treatment when not contraindicated, however, under-treatment is common.

**Objective:** This study aimed to investigate factors associated with bone-health medication initiation in older patients attending primary care.

**Design:** This was a retrospective cohort study.

**Setting:** The study used data from forty-four general practices in Ireland from 2011–2017.

**Subjects:** The study included adults aged  $\geq 65$  years who were naïve to bone-health medication for 12 months.

**Methods:** Overall fracture-risk (based on QFracture) and individual fracture-risk factors were described for patients initiated and not initiated onto medication and compared using generalised linear model regression with the Poisson distribution.

**Results:** Of 36,799 patients (51% female, mean age 75.4 (SD = 8.4)) included, 8% ( $n = 2,992$ ) were observed to initiate bone-health medication during the study. One-fifth of all patients ( $n = 8,193$ ) had osteoporosis or had high fracture-risk but only 21% of them ( $n = 1,687$ ) initiated on medication. Female sex, older age, state-funded health cover and osteoporosis were associated with initiation. Independently of osteoporosis and co-variates, high 5-year QFracture risk for hip (IRR = 1.33 (95% CI = 1.17–1.50),  $P < 0.01$ ) and all fractures (IRR = 1.30 (95% CI = 1.17–1.44),  $P < 0.01$ ) were associated with medication initiation. Previous fracture, rheumatoid arthritis and corticosteroid use were associated with initiation, while liver, kidney, cardiovascular disease, diabetes and oestrogen-only hormone replacement therapy showed an inverse association.

**Conclusions:** Bone-health medication initiation is targeted at patients at higher fracture-risk but much potential under-treatment remains, particularly in those  $>80$  years and with co-morbidities. This may reflect clinical uncertainty in older multimorbid patients, and further research should explore decision-making in preventive bone medication prescribing.

**Keywords:** Osteoporosis, Osteoporotic Fracture, Bone Density Conservation Agents, Primary Health Care, older people

## Key Points

- During this study, 23% of women and 11% of men defined as high-risk of fracture were newly initiated on bone-health medication.
- Rates of potential under-treatment were highest in patients over 80 years old.
- Fracture history, corticosteroid use and rheumatoid arthritis were independently associated with medication initiation.
- Patients with diabetes and liver, kidney, or cardiovascular disease were less likely to be initiated on medication.
- Clinical guidelines should provide advice on risk-benefit decisions in osteoporosis treatment where co-morbidities are present.

## Introduction

Fragility fractures, usually caused by falls in the presence of osteoporosis, are a prominent cause of morbidity and mortality, affecting approximately 3% of older adults annually [1,2]. Hip fractures are particularly serious with a 20% 1-year mortality rate [3].

International guidelines recommend that adults at high fracture-risk, including those with osteoporosis, previous fractures or taking long-term corticosteroids, be offered pharmacological treatment where no contraindication exists [4–6]. There is strong evidence that oral bisphosphonates reduce fracture incidence in men and women and they are the first line-therapeutic choice [4,7,8]. A common alternative treatment denosumab, which reduces fracture incidence in women and improves bone mass density (BMD) in men, involves six-monthly administration by subcutaneous injection [9–11].

It is well recorded that osteoporosis is under-diagnosed and under-treated. A nationally representative Irish study showed that 13% of women and 3% of men aged over 50 years had objective evidence of osteoporosis (albeit assessed via heel ultrasound) but only 28% of them were diagnosed [12]. Even in those diagnosed with osteoporosis, or identified as high fracture-risk, pharmacological treatment is not initiated in 23–72% of patients [9,13]. Reasons for non-initiation include GP and patient concerns about medication side effects (particularly gastrointestinal), perceived uncertainty about effectiveness, medicine administration restrictions and costs [9,13,14].

In primary care, it is recommended that fracture-risk be determined by risk prediction tools including FRAX and QFracture, which can be supplemented by BMD assessment [4,15,16]. Common factors included in these tools are older age, female sex, previous fracture, medications and conditions that affect bone quality and disorders that increase falls-risk [15,16]. Identification of factors associated with new initiation of bone-health medication in a large primary care population could reveal cases in which osteoporosis and high fracture-risk are potentially under-identified or under-treated in the Irish setting.

This study aims to investigate if older patients at higher fragility fracture risk had higher rates of new initiation of bone-health medication and to explore factors associated with initiation.

## Methods

### Study design

The REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) statement has been used for reporting this retrospective cohort study [17].

### Setting and data source

Data were collected as part of a larger study from 44 general practices (GP) (of approximately 1,600 practices nationally

in the Republic of Ireland using Socrates patient management software ([www.socrates.ie](http://www.socrates.ie)) between 2011 and 2017 [18]. These represented a range of practice sizes and locations, and Socrates is the most commonly used of three software options in Ireland. Data included demographic, clinical, prescribing and hospitalisation records of patients who were  $\geq 65$  years at the date of data extraction (2017). Ethical approval was obtained from the Irish College of General Practitioners.

### Participants

Patients were selected for inclusion in analysis if they had any records of prescriptions, hospitalisations or GP consultations over the study period (2011–2017) and were not prescribed any bone-health medication within 12 months of their first record. Patients were excluded if they had less than 12-months' data.

Prescriptions of bone-health medication were defined as bisphosphonates, denosumab, raloxifene, parathyroid hormone, strontium ranelate or calcitonin and identified from either GP prescription records or hospitalisation discharge summaries. WHO Anatomical Therapeutic Chemical (ATC) classification codes ([www.whocc.no/atc\\_ddd\\_index](http://www.whocc.no/atc_ddd_index)) were used to identify GP prescriptions (Supplementary Table A1). Medications in discharge summaries were identified with free-text search terms of trade and generic names based on the Irish Health Products Regulatory Authority ([www.hpra.ie](http://www.hpra.ie)) database (Supplementary Table A1).

### Outcome: bone-health medication initiation

Bone-health medication initiation was defined as receiving a bone-health prescription, where no such prescription was recorded in the preceding 12 months. The initiation date was defined as the 'index time-point'. Patients with no bone-health medication initiation were defined as a comparator group, and a random 'index time-point' assigned per patient after the initial 12-month period.

### Exposures

Exposures were defined in the pre-index time-point period and included age, sex, osteoporosis diagnosis, a calcium/vitamin D prescription, health cover type and fracture risk factors. Health cover type was grouped into three categories based on whether patients pay at point-of-care: General Medical Services scheme (GMS, covering GP care, hospitalisations and medications), Doctor Visit Card (DVC, covering GP care only), and Private.

The presence of 17 fracture risk factors (conditions and prescriptions) based on the QFracture tool [16] was identified for each patient prior to the index time-point. The QFracture tool was chosen as it is particularly suited to use in primary care databases in the UK and Ireland, has shown good accuracy for predicting fracture-risk, and the 2012 score is available for open source use

[4,19,20]. The presence of each condition was defined from consultations, GP prescriptions and hospitalisation records using previously validated ICD-10-AM, ICPC-2, ATC codes and free-text phrases (Supplementary Table A2). Prescriptions were defined from ATC codes in GP prescriptions and free-text phrases from hospitalisation records (Supplementary Table A2). Excessive alcohol use was defined dichotomously based on diagnostic indicators related to alcohol dependency.

Five-year QFracture hip fracture risk and all-fracture risk were calculated based on open source formulae ([www.qfracture.org](http://www.qfracture.org)). As data were not available for ethnicity, smoking status, body mass index (BMI), residence or family history of osteoporosis, these variables were set to the default value in the calculation (community-dwelling, white, non-smoker, no osteoporosis family history and BMI missing) [16]. Patients were categorised as ‘high-risk’ of fracture (top tenth percentile) based on QFracture cut-off values derived by Dagan *et al.* (4.0% for hip fracture and 6.7% for all fractures) [20].

### Co-variates

Co-variates in the analysis included total pre-index time-point observation in days, number of GP consultations and number of hospitalisations. The number of unique prescribed medications was calculated per person for 12-months prior to the index time-point. These are measures of access/exposure to healthcare, which may influence a patient’s likelihood of initiation. Polypharmacy has also been shown to be associated with fall risk [21].

### Statistical analysis

The number and proportion of patients with either an osteoporosis diagnosis or defined as high-risk on QFracture scores were presented by age, sex and bone-health medication initiation status to describe potential under- and over-treatment. Demographic and clinical variables were described for initiation and non-initiation groups and compared using t-tests,  $\chi^2$  and Wilcoxon rank-sum tests as appropriate.

Generalised linear model (GLM) regression using Poisson distribution was conducted to assess whether QFracture high 5-year risk of all fractures and hip fractures were associated with the initiation of bone-health medication univariably and adjusting for osteoporosis diagnosis, health cover type and co-variates. A pre-planned subgroup analysis was conducted to assess this relationship in males and females separately and a sensitivity analysis was conducted using a continuous QFracture score. GLM regression was conducted to assess whether each fracture risk factor was associated with initiation of bone-health medication, adjusting for osteoporosis diagnosis, age, sex, health cover type and co-variates.

Relative risks were calculated and 95% confidence intervals (CIs) were adjusted for clustering of patients within GP practices. Stata 16 (StataCorp. 2019) was used for analyses and statistical significance was assumed at  $P < 0.05$ .

## Results

### Participants

Among 36,799 patients (51.4% female) naïve for bone-health medication included in the analysis (Figure 1), mean age at the index time-point was 75.4 (SD = 8.4) years. Overall, 2,992 patients were initiated on bone-health medication during the study. In 62%, this involved oral bisphosphonates, 33% initiated denosumab and 3% initiated strontium. The remaining 2% initiated parathyroid hormone, raloxifene, bisphosphonate infusion or calcitonin. Most new-initiations (89%) were detected from GP prescriptions while 11% were based on hospital discharge summaries. Denosumab accounted for 20% of hospital initiations and 35% of GP initiations.

Almost 6% of patients ( $n = 2,053$ ) had an osteoporosis diagnosis but less than half of them ( $n = 1,004$ ; 49%) were initiated on bone-health medication. Furthermore, 22% of all patients ( $n = 8,193$ ) were found to either have osteoporosis or be high fracture-risk based on QFracture. Only 21% of them ( $n = 1,687$ ) were initiated on medication. Of 28,606 patients defined as lower fracture-risk with no osteoporosis diagnosis recorded, 5% ( $n = 1,305$ ) were initiated on medication. Table 1 shows this breakdown by sex and age-group.

### Factors associated with the initiation of bone-health medication

Those initiated on bone-health medication were more likely to be female, have an osteoporosis diagnosis or GMS/DVC scheme coverage, and were older by 2.2 years on average (Table 2). Over 80% of those initiated had a pre-initiation calcium/vitamin D prescription in comparison to 18% of those not initiated.

Independently of osteoporosis, health cover and co-variates, QFracture high 5-year risk for hip fractures (IRR = 1.33, 95% CI = 1.17–1.50,  $P < 0.01$ ) and all fractures (IRR = 1.30, 95% CI = 1.17–1.44,  $P < 0.01$ ) were associated with higher rates of medication initiation (Table 3). This relationship remained statistically significant in the subgroup analysis for males and hip fracture risk only. Results were similar in analysis of continuous QFracture scores and initiation (Supplementary Table A3), however, all-fracture risk was also associated with initiation in males.

Independently of age, sex, osteoporosis, health cover and co-variates, fracture history (IRR = 1.8, 95% CI = 1.6–2.0), Rheumatoid Arthritis (RA)/SLE diagnoses (IRR = 1.8, 95% CI = 1.5–2.2) and corticosteroid use (IRR = 1.6, 95% CI = 1.5–1.8) were associated with medication initiation (Table 4). Diabetes (IRR = 0.7, 95% CI = 0.6–0.7), chronic liver disease (IRR = 0.7, 95% CI = 0.5–0.8), chronic kidney disease (IRR = 0.8, 95% CI = 0.7–1.0), cardiovascular disease (IRR = 0.9, (95% CI = 0.8–0.9) and oestrogen-only hormone replacement therapy (HRT) use (IRR = 0.7, 95% CI = 0.6–0.9) had an inverse association with medication initiation.

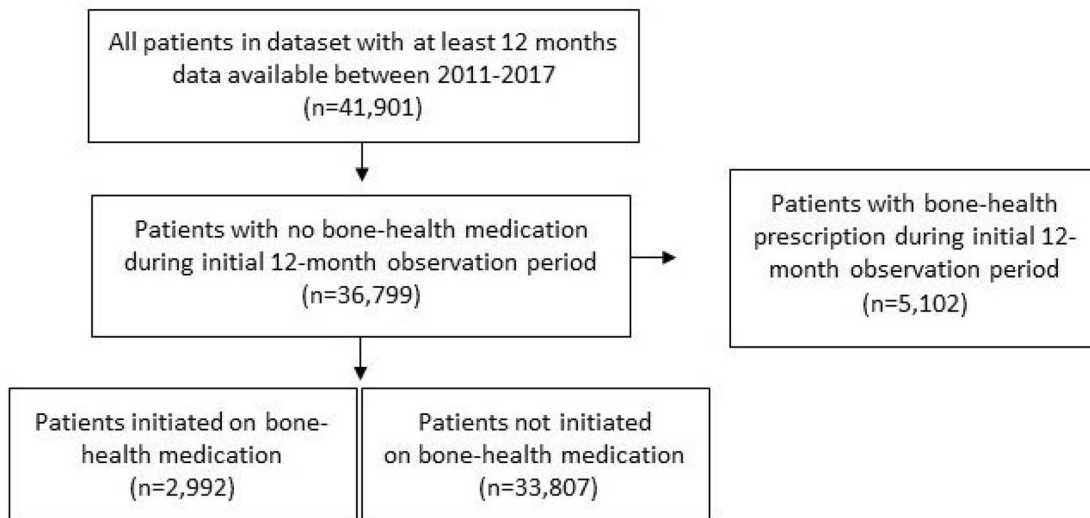


Figure 1. Flow-diagram of selected participants.

Table 1. Patients by fracture-risk age, sex and initiated group

	Potential under-treatment		Potential over-treatment	
	N (%) of group at higher risk of fracture <sup>a</sup>	N (%) of higher risk patients initiated on medication	N (%) of group at lower risk of fracture <sup>b</sup>	N (%) of lower-risk patients initiated on medication
Women < 70 years	593 (10.7)	262 (44.2)	4,948 (89.3)	299 (6.0)
Women 70–80 years	1,528 (21.4)	455 (29.8)	5,603 (78.6)	439 (7.8)
Women > 80 years	4,268 (68.3)	780 (18.3)	1,984 (31.7)	202 (10.2)
Women total	6,389 (33.7)	1,497 (23.4)	12,536 (66.3)	940 (7.5)
Men < 70 years	71 (1.3)	21 (29.6)	5,541 (99.0)	56 (1.0)
Men 70–80 years	318 (4.3)	56 (17.6)	6,981 (97.8)	158 (2.2)
Men > 80 years	1,412 (28.8)	112 (7.9)	3,485 (71.2)	150 (4.3)
Men total	1,801 (10.1)	189 (10.5)	16,007 (89.9)	364 (2.3)
Total	8,193 (22.3)	1,687 (20.6)	28,606 (77.7)	1,305 (4.6)

<sup>a</sup>Higher risk of fracture = High-risk on either QFracture score or recorded diagnosis of osteoporosis. <sup>b</sup>Lower risk of fracture = Low-risk on both QFracture scores and no recorded diagnosis of osteoporosis.

Table 2. Demographics and healthcare factors by bone-health medication initiation status

	Initiated (n = 2,992)	Not Initiated (n = 33,807)	P-value
Age at index time-point (mean (SD))	77.4 (8.2)	75.2 (8.5)	<0.01
Female sex (%)	2,437 (81.5)	16,488 (48.8)	<0.01
Osteoporosis diagnosis (n (%))	1,004 (33.6)	1,049 (3.1)	<0.01
On Calcium/Vitamin D (n (%))	2,453 (82.0)	5,977 (17.7)	<0.01
Health Cover (n (%)):			<0.01
Private or Other	537 (18.0%)	10,189 (30.2%)	
General Medical Services card	2,138 (71.5%)	20,554 (60.8%)	
Doctor Visit Card	316 (10.6%)	3,036 (9%)	
Observation time in days (mean (SD))	817 (587)	706 (597)	<0.01
Number of hospitalisations (mean (SD))	0.9 (2.4)	0.5 (1.7)	<0.01
Number of consultations (median (IQR))	33 (18–59)	22 (10–41)	<0.01
Number medications (median (IQR))	9 (5–14)	7 (3–11)	<0.01

## Discussion

This study of bone-health naïve older adults attending primary care practices in Ireland found that only 23% of

women and 11% of men at high-risk of fragility fracture were initiated on bone-health medication. In comparison, 5% of those not defined as high fracture-risk were initiated on medication.

## Factors associated with initiation of bone-health medication

**Table 3.** Association between fracture-risk and bone-health medication initiation in all patients and subgroups of females and males

QFracture 5-year risk	Initiated ( <i>n</i> = 2,992)	Not Initiated ( <i>n</i> = 33,807)	Univariable			Multivariable		
			IRR	95% CI <sup>a</sup>	<i>P</i> -value	IRR <sup>b</sup>	95% CI <sup>a</sup>	<i>P</i> -value
All fragility fractures								
High	864 (28.9%)	5,186 (15.4%)	2.06	(1.85–2.30)	<0.01	1.33	(1.17–1.50)	<0.01
Low	2,126 (71.1%)	28,557 (84.6%)						
Hip fractures								
High	808 (27.0%)	5,064 (15.0%)	1.95	(1.74–2.17)	<0.01	1.30	1.17–1.44	<0.01
Low	2,182 (73.0%)	28,679 (85.0%)						
Subgroup analysis by sex								
QFracture 5-year risk in Females	Initiated females ( <i>n</i> = 2,437)	Not Initiated females ( <i>n</i> = 16,488)	Univariable			Multivariable		
All fragility fractures								
High	787 (32.3%)	4,030 (24.4%)	1.40	(1.24–1.58)	<0.01	1.08	(0.96–1.21)	0.19
Low	1,650 (67.7%)	12,458 (75.6%)						
Hip fractures								
High	711 (29.2%)	3,598 (21.8%)	1.40	(1.24–1.57)	<0.01	1.10	(0.99–1.22)	0.06
Low	1,726 (70.8%)	12,890 (78.2%)						
QFracture 5-year risk in Males								
Initiated males ( <i>n</i> = 553) / Not Initiated males ( <i>n</i> = 17,255)								
All fragility fractures								
High	77 (13.9%)	1,156 (6.7%)	2.17	(1.74–2.71)	<0.01	1.19	0.97–1.46	0.10
Low	476 (86.1%)	16,099 (93.3%)						
Hip fractures								
High	97 (17.5%)	1,466 (8.5%)	2.21	(1.81–2.70)	<0.01	1.26	1.07–1.50	<0.01
Low	456 (82.5%)	15,789 (91.5%)						

<sup>a</sup>95% CIs adjusted by General Practice clusters. <sup>b</sup>IRR adjusted for osteoporosis diagnosis, health cover, observation time, number of hospitalisations (in four categories), number of consultations (in quartiles), number of medications in prior 12 months (in quartiles).

**Table 4.** Association between fracture risk factors and bone-health medication initiation

Conditions/prescriptions	Initiated ( <i>n</i> = 2,992) ( <i>n</i> (% of initiation group))	Not Initiated ( <i>n</i> = 33,807)	IRR <sup>a</sup>	95% CI <sup>b</sup>	<i>P</i> -value
Asthma or COPD	954 (31.9)	8,276 (24.5)	1.1	(1.0–1.1)	0.16
On antidepressants	755 (25.2)	6,145 (18.2)	1.0	(0.9–1.1)	0.91
On corticosteroids	582 (19.5)	2,772 (8.2)	1.6	(1.5–1.8)	<0.01
Cardiovascular disease	527 (17.6)	5,817 (17.2)	0.9	(0.8–0.9)	<0.01
Cancer	462 (15.4)	4,069 (12.0)	1.0	(0.9–1.1)	0.84
Fragility fracture	320 (10.7)	814 (2.4)	1.8	(1.6–2.0)	<0.01
Diabetes mellitus	274 (9.2)	4,744 (14.0)	0.7	(0.6–0.7)	<0.01
Dementia	205 (6.9)	1,930 (5.7)	1.0	(0.9–1.1)	0.68
Epilepsy	158 (5.3)	1,286 (3.8)	1.1	(0.9–1.3)	0.41
Chronic kidney disease	148 (5.0)	1,314 (3.9)	0.8	(0.7–1.0)	0.04
RA or SLE	140 (4.7)	447 (1.3)	1.8	(1.5–2.2)	<0.01
History of falls	62 (2.1)	360 (1.1)	1.1	(0.9–1.4)	0.46
Parkinson's disease	110 (3.7)	974 (2.9)	1.1	(1.0–1.4)	0.14
Endocrine disorders	96 (3.2)	537 (1.6)	1.1	(0.9–1.2)	0.50
Diseases of malabsorption	40 (1.3)	263 (0.8)	1.1	(0.8–1.4)	0.50
Oestrogen only HRT	45 (1.5)	402 (1.2)	0.7	(0.6–0.9)	<0.01
Chronic liver disease	34 (1.1)	423 (1.3)	0.7	(0.5–0.8)	<0.01
Alcohol dependency	38 (1.3)	473 (1.4)	1.0	(0.9–1.2)	0.52

COPD=Chronic Obstructive Pulmonary Disease; HRT = Hormone Replacement Therapy; RA = Rheumatoid Arthritis; SLE = Systemic Lupus Erythematosus. <sup>a</sup>IRR adjusted for osteoporosis diagnosis, sex, age, health cover type, pre-initiation observation time, number of hospitalisations (4 categories) and number of consultations (quartiles), number of medications in prior 12 months (quartiles). <sup>b</sup>95% CIs adjusted by General Practice clusters.

Patients who were newly initiated on bone-health medication were older, more likely to be female and to have state-funded health cover. While QFracture scores were associated with higher rates of medication initiation, this relationship was not observed in the female subgroup. This

may be due to a lack of statistical power or factors other than those used to estimate QFracture being considered by clinicians in prescribing for females. Independently of age, sex and osteoporosis diagnosis, specific fracture risk factors associated with medication initiation included fracture



history, corticosteroid use and RA/SLE diagnosis. In contrast, patients with diabetes, chronic liver or kidney disease, or cardiovascular disease, or prescribed HRT were less likely to be initiated.

The findings of this study are broadly in line with previous research in Ireland and internationally suggesting that fracture risk is under-identified and under-treated in older adults in primary care [9,12,13]. Potential under-treatment was particularly notable in men > 80 years old with only 8% of those at higher fracture-risk being initiated on medication. Irish GPs have previously reported having a good awareness of female osteoporosis but the condition in men is less recognised [22]. While men have lower hip fracture incidence, those who do fracture are younger with more comorbidities and experience worse outcomes including higher mortality [23]. Over-looking the assessment of fracture risk and primary and secondary fracture prevention in this vulnerable population could therefore have significant clinical consequences.

Factors identified in this study as most strongly associated with medication initiation are those most frequently described in guidelines, namely female sex, osteoporosis, fragility fracture history and corticosteroid use [4–7,10]. These factors have also been reported by Irish GPs as influencing their decision to consider an osteoporosis diagnosis [22]. It is not known to what extent Irish GPs take other clinical factors into account or use prediction tools including QFracture and FRAX, and warrants further research.

Lower levels of treatment in patients with specific medical conditions, including diabetes, kidney, liver and cardiovascular disease, may reflect previous findings that GP concerns about medication side effects and burden can influence decision-making [9,13,14]. The benefit of taking an additional medicine is likely to reduce in the presence of existing polypharmacy [24]. This is important, as older adults with the highest fracture-related mortality rates are more likely to have multi-morbidity. This may explain to some degree potential under-treatment observed in the oldest age group. However, contrary to this, we found a higher number of medicines were used by initiators compared to non-initiators (albeit not adjusted for factors such as age or sex).

There may be understandable clinical dilemmas for GPs deciding whether to prioritise pharmacological fracture-prevention in the presence of particular medical conditions. Adverse effects that could influence decision-making include upper gastrointestinal events for bisphosphonates [7] and risk of infections for denosumab [25]. While oesophageal symptoms are common in liver disease and stroke, these conditions also contribute significantly to osteoporosis and GPs could consider alternative medicine formulations in these circumstances [4,16,26]. Severe kidney impairment may complicate osteoporosis treatment due to calcium homeostasis disturbances and reduced drug excretion, and specialist referrals may be indicated for patients with high fracture risk [4,27]. Bisphosphonates or denosumab have not been found to increase the risk of cardiovascular events so the reasoning behind a lower prescription in patients

with these conditions as found in this study is not clear [7,28,29]. Small observational studies have linked diabetes to medication-related jaw osteonecrosis; however, this has been refuted in higher quality research [30]. HRT users being less likely to be initiated may be due to prescribers considering the bone-strengthening properties of HRT to offset the need for other fracture-preventive medications. Osteoporosis guidelines should provide clear advice regarding risk-benefit decisions in the presence of medical conditions, providing information on testing required and in which cases referral to specialists are indicated [4]. GPs may require further support and education in this area.

We were unable to consider lifestyle measures in osteoporosis management including exercise, smoking cessation, alcohol reduction and falls-prevention [4]. We did however find that over two-thirds of patients prescribed calcium and/or vitamin D supplements were not initiated on bone-health medication. While adequate dietary intake of these substances is important for maintaining BMD in older adults and as an adjunct to pharmacotherapy, GPs should be aware that supplementation without bone-health medication prescription has not been shown to reduce fracture incidence in those at high-risk [4].

### **Strengths and limitations**

This study includes a large cohort of older adults treated in primary care. We ascertained prescribing and fracture-risk factors from multiple sources (GP prescriptions, consultations and hospitalisation discharge summaries). Using data available, we were unable to include information on residence, osteoporosis family history, BMI and smoking status in calculating QFracture scores. In addition, as falls were identified based only on hospitalisation records, they are likely under-coded resulting in a 2% prevalence in comparison to the 20% that would be expected [12]. These factors likely led to an underestimation of fracture-risk, suggesting under-treatment may actually be higher. However, it is also possible that some initiations among apparently low-risk individuals were due to the presence of these risk factors we could not include. Furthermore, bisphosphonate use in cancer treatment could also explain a small proportion of such initiations. In sensitivity analysis using continuous QFracture score to assess potential bias due to systematic underestimation of fracture-risk due to absence of information such as BMI, the results were consistent with the primary analysis.

Using GP prescribing records, we could not determine if patients received prescriptions from consultant geriatricians or fracture liaison services; however, in the Irish setting patients would likely return to their GP for repeat prescriptions. We may still have underestimated the use of intravenous bisphosphonates where their GP is not involved in prescribing/administration, which could contribute to the rate of under-treatment identified. We were also unable to fully assess reasons for non-initiation of medication that may have been clinically appropriate and to what extent it reflects patient preferences.

### Clinical implications

We found a lower rate of initiation among those at high-fracture risk based on QFracture than among those with a previous osteoporosis diagnosis. Consideration should be given to the targeted screening of fracture risk as opposed to opportunistic case finding to address under-identification and treatment of osteoporosis, given evidence suggesting this reduces hip fracture among older women [31]. Interventions to improve appropriate initiation of bone-health medication in patients with high fracture-risk require investigation in the Irish primary care setting. International studies have shown benefits for complex interventions that include patient and practitioner education with feedback about test results/medication and encouragement for patients to follow-up with their practitioners [32]. This study's findings suggest that where GPs are managing fracture prevention, they may need particular support in making risk/benefit decisions about prioritising pharmacological treatment for fracture prevention, especially in adults >80 years old with medical co-morbidities.

### Conclusion

While there is a higher rate of bone-health medication initiation among older patients in primary care in Ireland who are at higher fracture-risk, there remains much potential under-treatment. This is particularly true among the oldest patients and those with chronic medical co-morbidities. Future research should assess reasons for non-prescription of bone-health medication in Ireland, including patient and GP concerns, and interventions to support appropriate prescribing in this setting.

---

**Supplementary Data:** Supplementary data mentioned in the text are available to subscribers in *Age and Ageing* online.

**Declaration of Conflicts of Interest:** None.

**Declaration of Sources of Funding:** Support was received from the Health Research Board (HRB) in Ireland through grant no. HRC/2014/1 (TF) and through the RCSI Research Summer School 2019 (MEW and MN).

### References

1. Amin S, Achenbach SJ, Atkinson EJ, Khosla S, Melton LJ 3rd. Trends in fracture incidence: a population-based study over 20 years. *J Bone Miner Res* 2014; 29: 581–9.
2. Kanis JA, On behalf of the World Health Organization Scientific Group. Assessment of osteoporosis at the primary health-care level. University of Sheffield, Sheffield, 2007.
3. Downey C, Kelly M, Quinlan JF. Changing trends in the mortality rate at 1-year post hip fracture—a systematic review. *World J Orthop* 2019; 10: 166–75.
4. Compston J, Cooper A, Cooper C *et al.* UK clinical guideline for the prevention and treatment of osteoporosis. *Arch Osteoporos* 2017; 12: 43.
5. Camacho PM, Petak SM, Binkley N *et al.* American association of clinical endocrinologists and American college of endocrinology clinical practice guidelines for the diagnosis and treatment of postmenopausal osteoporosis—2016. *Endocr Pract* 2016; 22: 1–42.
6. Watts NB, Adler RA, Bilezikian JP *et al.* Osteoporosis in men: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab* 2012; 97: 1802–22.
7. Davis S, Martyn-St James M, Sanders J *et al.* A systematic review and economic evaluation of bisphosphonates for the prevention of fragility fractures. *Health Technol Assess* 2016; 20: 1–406.
8. Nayak S, Greenspan SL. Osteoporosis treatment efficacy for men: a systematic review and meta-analysis. *J Am Geriatr Soc* 2017; 65: 490–5.
9. Naik-Panvelkar P, Norman S, Elgebaly Z *et al.* Osteoporosis management in Australian general practice: an analysis of current osteoporosis treatment patterns and gaps in practice. *BMC Fam Pract* 2020; 21: 32.
10. Davis S, Simpson E, Hamilton J *et al.* Denosumab, raloxifene, romosozumab and teriparatide to prevent osteoporotic fragility fractures: a systematic review and economic evaluation. *Health Technol Assess* 2020; 24: 1–314.
11. Langdahl BL, Tegljbjærg CS, Ho PR *et al.* A 24-month study evaluating the efficacy and safety of denosumab for the treatment of men with low bone mineral density: results from the ADAMO trial. *J Clin Endocrinol Metab* 2015; 100: 1335–42.
12. Cronin H, O'Regan C, Kenny R. Physical and behavioural health of older Irish adults. In: Barrett A, Savva G, Timonen V, Kenny R, editors. *Fifty Plus In Ireland 2011 first results from The Irish Longitudinal Study on Ageing (TILDA)*. 2011. doi: 10.38018/TildaRe.2011-00.c5. (25 August 2020, date last accessed).
13. Siris ES, Yu J, Bognar K *et al.* Undertreatment of osteoporosis and the role of gastrointestinal events among elderly osteoporotic women with Medicare part D drug coverage. *Clin Interv Aging* 2015; 10: 1813–24.
14. Swart KMA, van Vilsteren M, van Hout W *et al.* Factors related to intentional non-initiation of bisphosphonate treatment in patients with a high fracture risk in primary care: a qualitative study. *BMC Fam Pract* 2018; 19: 141.
15. McCloskey EV, Johansson H, Oden A, Kanis JA. From relative risk to absolute fracture risk calculation: the FRAX algorithm. *Curr Osteoporos Rep* 2009; 7: 77–83.
16. Hippisley-Cox J, Coupland C. Derivation and validation of updated QFracture algorithm to predict risk of osteoporotic fracture in primary care in the United Kingdom: prospective open cohort study. *BMJ* 2012; 344: e3427.
17. Benchimol EI, Smeeth L, Guttman A *et al.* The reporting of studies conducted using observational routinely-collected health data (RECORD) statement. *PLoS Med* 2015; 12: e1001885.
18. Sweeney J, Kearney P, Redmond P, Fahey T. Point of care morbidity coding: a feasibility study in primary care. *Forum J Irish Coll Gen Pract* 2017; 34: 52–4.
19. Marques A, Ferreira RJ, Santos E, Loza E, Carmona L, da Silva JA. The accuracy of osteoporotic fracture risk prediction tools: a systematic review and meta-analysis. *Ann Rheum Dis* 2015; 74: 1958–67.

20. Dagan N, Cohen-Stavi C, Leventer-Roberts M, Balicer RD. External validation and comparison of three prediction tools for risk of osteoporotic fractures using data from population based electronic health records: retrospective cohort study. *BMJ* 2017; 356: i6755.
21. Morin L, Calderon Larrañaga A, Welmer AK *et al.* Polypharmacy and injurious falls in older adults: a nationwide nested case-control study. *Clin Epidemiol* 2019; 11: 483–93.
22. Fay G, Cunningham C. Awareness and management of osteoporosis among general practitioners in Ireland. *Physiother Pract Res* 2015; 36: 107–13.
23. Saletti-Cuesta L, Tutton L, Wright J. The relevance of gender in the care of hip fracture patients. *Int J Orthop Trauma Nurs* 2016; 22: 3–12.
24. National Institute For Health and Care Excellence. Multimorbidity and polypharmacy (KTT18). 2017. <https://www.nice.org.uk/advice/ktt18/chapter/Evidence-context>. (8 September 2020, date last accessed)
25. Diker-Cohen T, Rosenberg D, Avni T, Shepshelovich D, Tsvetov G, Gafer-Gvili A. Risk for infections during treatment with denosumab for osteoporosis: a systematic review and meta-analysis. *J Clin Endocrinol Metab* 2020; 105: dgz322. doi: 10.1210/clinem/dgz322.
26. Santos LA, Romeiro FG. Diagnosis and management of cirrhosis-related osteoporosis. *Biomed Res Int* 2016; 2016: 1423462.
27. Wilson LM, Rebbholz CM, Jirru E *et al.* Benefits and harms of osteoporosis medications in patients with chronic kidney disease: a systematic review and meta-analysis. *Ann Intern Med* 2017; 166: 649–58.
28. Kim DH, Rogers JR, Fulchino LA, Kim CA, Solomon DH, Kim SC. Bisphosphonates and risk of cardiovascular events: a meta-analysis. *PLoS One* 2015; 10: e0122646.
29. Lv F, Cai X, Yang W *et al.* Denosumab or romosozumab therapy and risk of cardiovascular events in patients with primary osteoporosis: systematic review and meta-analysis. *Bone* 2020; 130: 115121.
30. Rahimi-Nedjat RK, Sagheb K, Pabst A, Olk L, Walter C. Diabetes mellitus and its association to the occurrence of medication-related osteonecrosis of the jaw. *Dent J (Basel)* 2016; 4.
31. Shepstone L, Lenaghan E, Cooper C *et al.* Screening in the community to reduce fractures in older women (SCOOP): a randomised controlled trial. *The Lancet* 2018; 391: 741–7.
32. Kastner M, Perrier L, Munce SEP *et al.* Complex interventions can increase osteoporosis investigations and treatment: a systematic review and meta-analysis. *Osteoporos Int* 2018; 29: 5–17.

**Received 10 September 2020; editorial decision 16 January 2021**