

# Anti-osteoporosis drug prescribing after hip fracture in the UK: 2000–2010

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## Abstract

**Summary** The probability of initiating with anti-osteoporosis therapy increased from 7 % in 2000 to 46 % in 2010. This improvement was greater for patients over the age of 75 years. Men, those overweight, having dementia or exposed to anti-psychotics, sedatives/hypnotics or opioid analgesics were significantly less likely to receive anti-osteoporosis drugs.

**Introduction** The objective of this study was to examine trends and determinants of anti-osteoporosis drug prescribing after hip fracture in the UK between 2000 and 2010.

**Methods** Data were extracted from the UK Clinical Practice Research Datalink for patients  $\geq 50$  years who had a first hip fracture between 2000 and 2010 and who did not currently ( $\leq 6$  months prior) receive anti-osteoporosis drugs (bisphosphonates, strontium ranelate, parathyroid hormone, calcitonin and raloxifene) ( $n=27,542$ ). The cumulative incidence probability of being prescribed anti-osteoporosis drugs within 1 year after hip fracture was estimated by Kaplan-

Meier life-table analyses. Determinants for treatment initiation were estimated by Cox proportional hazards models.

**Results** The probability of being prescribed any anti-osteoporosis drug after hip fracture increased from 7 % in 2000 to 46 % in 2010. This trend was more marked in patients  $\geq 75$  years. The increase in prescribing of anti-osteoporosis drugs was complemented by a similar increase in vitamin D/calcium provision. Cumulative incidence of receiving anti-osteoporosis therapy was greater at any given point in time in women (8 % in 2000, 51 % in 2010) compared to men (4 % in 2000, 34 % in 2010). In addition to male gender, multivariable Cox regression identified reduced likelihood of receiving anti-osteoporosis drugs for those being overweight, having dementia and exposed to psychotropic drugs (antipsychotics, sedatives/hypnotics) or opioid analgesics.

**Conclusion** Although the prescribing of anti-osteoporosis drugs after hip fracture has increased substantially since 2000, the overall rate remained inadequate, particularly in

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men. With the continuing increase in the absolute number of hip fractures, further research should be made into the barriers to optimise osteoporosis management.

**Keywords** Anti-osteoporotic drugs · Bisphosphonate · Osteoporosis · Osteoporotic fracture

## Introduction

Osteoporosis is a growing public health issue affecting an estimated 2.8 million people within the UK [1]. Osteoporosis results in fragility fractures, the most serious of which are hip fractures. In the last decade, absolute numbers of hospital admissions for hip fractures have increased by 15.5 %, despite age- and sex-standardised rates remaining stable since 2003 [2]. A history of hip fracture increases the risk of future fracture 3.2 times when compared to patients without a hip fracture [3], and this risk is greatest in the first year and remains elevated for at least 5 years [4, 5].

Hence, post-fracture treatment with anti-osteoporosis drugs is important to prevent the occurrence of new fragility fractures. Over the decade 2000–2010, the therapies available for treatment of osteoporosis have changed markedly. Initially, hormone replacement therapy (HRT) was the first-line osteoporosis treatment [6]. However, since the Woman's Health Initiative trial in 2002 demonstrated that the risk of coronary heart disease, pulmonary embolism, stroke and breast cancer was greater than the benefits conferred by this therapy, its use has been limited to the short-term relief of menopausal symptoms [7]. Since then, bisphosphonates have been the mainstay of treatment for osteoporosis. Bisphosphonates have been shown to reduce the risk of hip fractures by 30–50 % and vertebral fractures by 30–70 % [8]. From 2005 onwards, the National Institute for Health and Clinical Excellence (NICE) has also endorsed the use of raloxifene, teriparatide, strontium ranelate and calcitonin (although now withdrawn) for secondary fracture prevention. Despite these readily available, effective treatments, a care gap in pharmacological prevention of subsequent fractures has been documented worldwide [9–11].

Given the ageing population and therefore the increasing number of hip fractures, it is important to know the trend in prescribing practice for anti-osteoporosis drugs and to identify patients at risk of not receiving these drugs. Fortunately, several, but not all, studies have shown an improvement in anti-osteoporosis drug prescribing between the late 1990s and the first half of the twenty-first century, where few studies have investigated prescribing practices over more recent years [12–20] or have concerned concomitant prescribing of anti-osteoporosis drugs with vitamin D and/or calcium supplements [21–23]. The latter is important since clinical trials demonstrating efficacy of anti-osteoporosis drugs were all conducted among participants receiving adequate levels of

calcium and vitamin D. In 2010, a national clinical audit in the UK showed that as many as 40 % of all hip fracture patients did not receive any form of anti-osteoporosis drug treatment within 12 weeks [24]. Numbers for concomitant or solely prescribing of anti-osteoporosis drugs and calcium/vitamin D were not provided, and prescribing practices were not presented beyond age and gender while other patient characteristics may influence prescribing practice as well. Individual data linking drug prescribing and patient characteristics (e.g. previous fractures, lifestyle variables, co-morbidities, poly-pharmacy) would greatly assist in determining which patient groups are at increased risk of not receiving anti-osteoporosis drug treatment after hip fracture.

Therefore, the objective of the present study was to investigate the trends in prescribing of anti-osteoporosis drugs and co-prescribing with vitamin D/calcium supplements in hip fracture patients, who were not currently in receipt of anti-osteoporosis drugs, within a primary care setting in the UK between 2000 and 2010. Additionally, we aimed to examine which patient characteristics influenced the initialisation of anti-osteoporosis drug treatment.

## Methods

### Source population

The population was sourced from the Clinical Practice Research Datalink (CPRD) which contains anonymised electronic health records from 625 primary care practices from across the UK representing around 8 % of the population. The records include details of all diagnoses and prescriptions issued by NHS general practitioners, specialist referrals, hospital admissions and lifestyle variables (e.g. body mass index, smoking status) for community-dwelling, but not institutionalized, patients.

### Study population

The study population comprised patients aged  $\geq 50$  years who suffered an incident hip fracture between 1 January 2000 and 31 December 2010 and who did not receive a prescription for any anti-osteoporosis drug (bisphosphonates, calcitonin, strontium ranelate, raloxifene, parathyroid hormone analogues [teriparatide]) in the 6 months prior to the index hip fracture. A 6-month period was chosen since previous studies have shown that the vast majority of patients who stop with anti-osteoporosis treatment restart their treatment within 6 months [25] and is also in line with previous studies [16]. To ensure that the hip fracture was the first hip fracture, patients with a record of non-specified fractures any time prior to the index hip fracture date were excluded. Approval for this study was given by the Independent Scientific Advisory

Committee for MHRA Database Research (protocol number 13\_113, amendment 2).

### Outcome

The outcome of interest was a prescription for an anti-osteoporosis drug in the year following hip fracture. This was defined as a prescription for either: bisphosphonates (alendronic acid, risedronic acid, ibandronic acid, etidronic acid and zoledronic acid), calcitonin, strontium ranelate, raloxifene or parathyroid hormone analogues (teriparatide) based upon the NICE guidelines for secondary osteoporosis treatment [26]. Additionally, prescribing trends for calcium/vitamin D (separately and in combination with anti-osteoporosis drugs) and hormone replacement therapy (HRT) were described. Patients were followed from the date of index hip fracture until the date of the first prescription or censoring, whichever came first. Patients were censored upon death, exit from the database or end of the follow-up period (365 days after the index hip fracture, 31 December 2011 at the latest).

### Determinants

Factors identified as potential determinants for anti-osteoporosis drug prescribing were largely based on risk factors for osteoporosis or fracture: age; sex; smoking status (non-smoker, ex-smoker, current smoker, missing); the most recent record of body mass index ([BMI]; <18, 18–25, >25 kg/m<sup>2</sup>, missing); history of major fracture (clinical vertebrae, forearm, humerus); falls (3–12 months before); a history of secondary osteoporosis in accordance with the FRAX definition [27]; inflammatory bowel disease (Crohn's disease and ulcerative colitis); rheumatoid arthritis; Parkinson's disease; cerebrovascular disease; ischaemic heart disease; and the use in the 6 months prior of corticosteroids, antipsychotics, antidepressants, opioid analgesics stronger than tramadol, anti-convulsants and benzodiazepines and other sedatives/hypnotics or calcium/vitamin D. In addition to these, a history of dementia or malignant neoplasms and the total number of different prescriptions (poly-pharmacy) in the 6 months prior to hip fracture may also influence prescribing practice. Indication for osteoporosis treatment is historically based on bone mineral density (BMD); however, this data is not routinely available within the CPRD and so could not be included in this analysis.

### Statistical analysis

Sex-specific descriptive characteristics were calculated at baseline. Kaplan-Meier life-table analyses were used to estimate the cumulative incidence probability for receiving a prescription for anti-osteoporosis drugs within 1 year of hip fracture. The

analysis was done separately for each calendar year and stratified by age categories (50–74, 75–84, ≥85 years), region (England, Scotland, Wales and Northern Ireland) and sex. We also examined prescribing trends over time for the individual drug classes, type of bisphosphonate, and for calcium/vitamin D both separately and in combination with anti-osteoporosis drugs. For the latter analysis, patients were required to not have received both anti-osteoporosis drugs and calcium/vitamin D in the 6 months before hip fracture.

Univariate and multivariate Cox proportional hazard models were used to identify which factors (including the year of index hip fracture) were determinants of anti-osteoporosis drug initiation. Since for some of the covariates' (BMI, smoking status) missing data were present, multiple imputation was used to create five imputed datasets. Analyses were performed separately for the five imputed datasets, and hazard ratios (HRs) were pooled using the MIANALYZE procedure. All analyses were carried out using SAS 9.2 (SAS, Cary NC, USA).

## Results

### Trends in anti-osteoporosis drug prescribing

Over the 10-year period, 30,516 patients aged 50 years or older suffered a hip fracture. Of these, 2974 (9.7 %) had received at least one prescription for anti-osteoporosis drugs in the 6 months prior to the index fracture. Table 1 shows the characteristics of the study population. The median age (interquartile range) was 83 (76–88) and 79 years (71–85) for females and males, respectively.

After index hip fracture, 6684 patients received some form of anti-osteoporosis therapy, of which 94 % of the prescriptions were for bisphosphonates. The mean time to receiving a prescription was 88 days (SD80). The remaining patients, 20,858 (68 %), had no record of receiving osteoporosis medication in either the 6 months prior or in the year following hip fracture.

During the study period, there was a steady rise in anti-osteoporosis drug prescribing following a hip fracture. Among patients who were not currently on treatment, the probability of receiving an anti-osteoporosis drug increased from 7.4 % in 2000 to 45.5 % in 2010. Cumulative incidence of receiving anti-osteoporosis drugs was greater at any given point in time in women compared to men. The proportion of women that was prescribed an anti-osteoporosis drug in 2000 was 8.2 % and increased to 51.3 % in 2010. These numbers were 4.1 and 33.6 % for men, respectively. By 2010, a female hip fracture patient was 1.5 times more likely to be prescribed an anti-osteoporosis drug when compared to males (Fig. 1a). Figure 1b demonstrates that this trend also differed between age categories, with a more pronounced trend for patients aged 75 years and older than for those under the age of 75 years,

**Table 1** Baseline characteristics of hip fracture patients who were not in receipt of anti-osteoporosis drugs

Characteristic	Male (n=7051)		Female (n=20,491)		Total (n=27,542)	
Age category, n, %						
50–74	2348	33.3	4177	20.4	6525	23.7
75–84	2801	39.7	7860	38.3	10,661	38.7
85+	1902	27.0	8454	41.3	10,356	37.6
BMI category, n, %						
<18 kg/m <sup>2</sup>	590	8.4	2547	12.4	3137	11.4
18–25 kg/m <sup>2</sup>	2390	33.9	6384	31.2	8774	31.9
>25 kg/m <sup>2</sup>	2470	35.0	5703	27.8	8173	29.7
Missing <sup>a</sup>	1601	22.7	5857	28.6	7458	27.1
Smoking category, n, %						
Non-smoker	2393	33.9	10,595	51.7	12,988	47.2
Ex-smoker	2068	29.3	3010	14.7	5078	18.4
Current smoker	1879	26.7	4058	19.8	5937	21.6
Missing <sup>a</sup>	711	10.1	2828	13.8	3539	12.8
Disease history, n, %						
≥1 fall (3–12 months prior hip fracture)	494	7.0	1792	8.7	2286	8.3
History of major fracture	689	9.8	4152	20.3	4841	17.5
Secondary osteoporosis <sup>b</sup>	511	7.2	1023	5.0	1534	5.6
Inflammatory bowel disease	95	1.3	224	1.1	319	1.2
Rheumatoid arthritis	160	2.3	652	3.2	812	2.9
Parkinson's disease	368	5.2	579	2.8	947	3.4
Dementia	679	9.6	2747	13.4	3426	12.4
Cerebrovascular disease	1545	21.9	3444	16.8	4989	18.1
Ischaemic heart disease	1683	23.9	3624	17.7	5307	19.3
Malignant neoplasms	1296	18.4	2818	13.8	4114	14.9
Drugs history (6 months prior), n, %						
Antipsychotics	445	6.3	1667	8.1	2112	7.7
Antidepressants	1323	18.8	4945	24.1	6268	22.8
Anti-epileptics	403	5.7	810	4.0	1213	4.4
Corticosteroids	1249	17.7	2907	14.2	4156	15.1
Opioid analgesics	1248	17.7	3933	19.2	5181	18.8
Sedatives and hypnotics	1004	14.2	4074	19.9	5078	18.4
Calcium/vitamin D	360	5.1	2069	10.1	2429	8.8
Hormone replacement therapy	3	0	274	1.3	277	1.0
Number of different prescriptions, n, %						
<5 different prescriptions	2110	29.9	6285	30.7	8395	30.5
5–9 different prescriptions	2300	32.6	7214	35.2	9514	34.5
10–14 different prescriptions	1490	21.1	4198	20.5	5688	20.7
>14 different prescriptions	1151	16.3	2794	13.6	3945	14.3

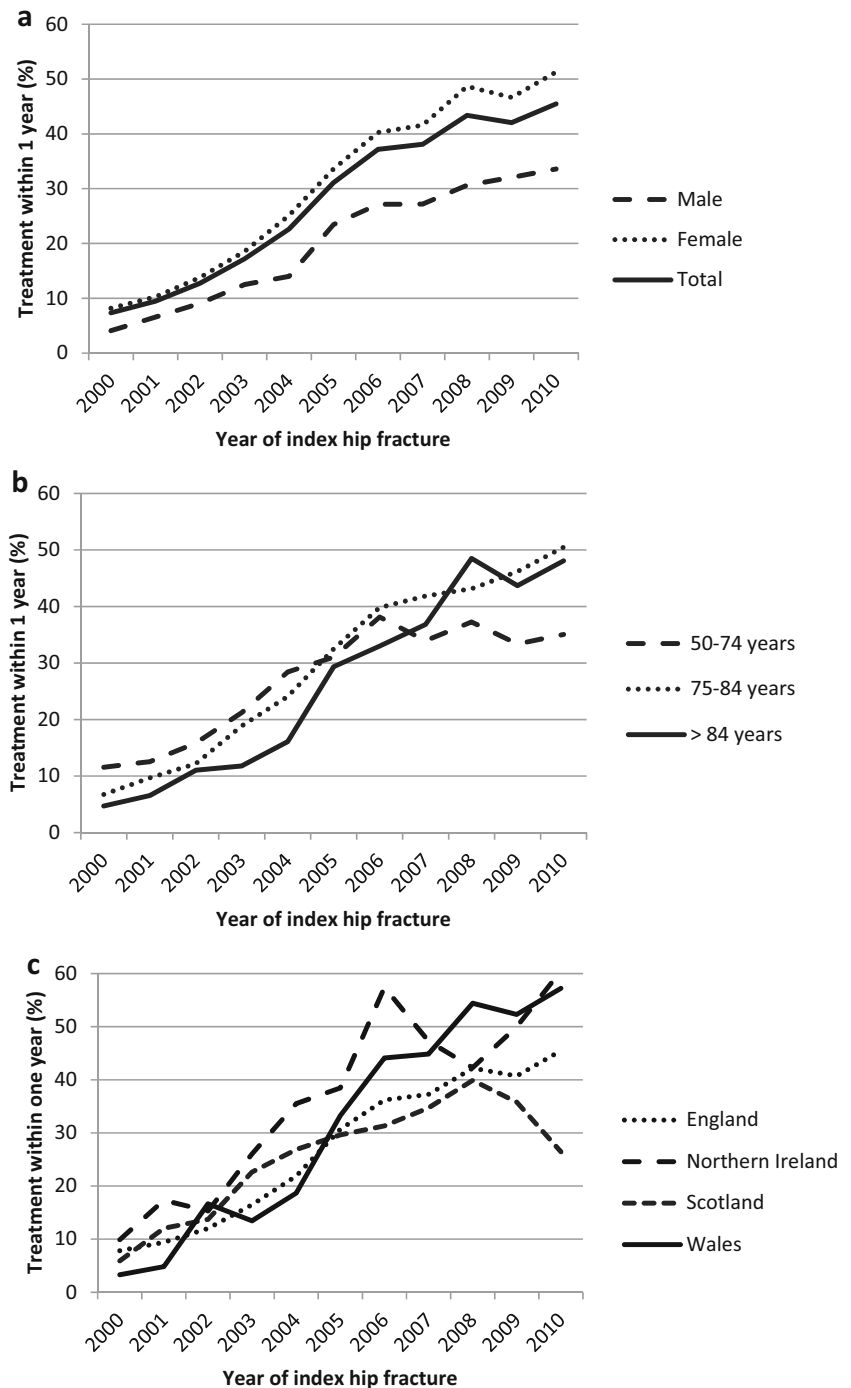
<sup>a</sup> Imputed values were used for regression models

<sup>b</sup> As defined by FRAX; anorexia nervosa, coeliac disease, diabetes mellitus (type 1), hypogonadism, osteogenesis imperfecta, osteomalacia, liver disease (cirrhosis, hepatitis and neoplasms), malnutrition, malabsorption and premature menopause

particularly after 2005 where the prescribing rates continued to increase for the older population but stabilised for patients under the age of 75 years. Figure 1c shows that there was a general improvement in anti-osteoporosis prescribing for all four UK regions (England, Scotland, Wales and Northern Ireland), but levels of prescribing varied considerable across these regions. From 2008, these rates diverged with an increase in Northern Ireland and a decrease in Scotland.

Evaluation of the medication classes individually demonstrated a substantial rise in the prescribing of bisphosphonates within 1 year after hip fracture (Fig. 2a). Figure 2b shows the trend in the prescribing of bisphosphonates, stratified by the type of bisphosphonate. Alendronic acid was the most frequently prescribed bisphosphonate followed by risedronic acid, and after 2006, this disparity became markedly greater. Zoledronic acid was not included in the figure as numbers

**Fig. 1** Trends in anti-osteoporosis drug prescribing after hip fracture (by Kaplan-Meier method), stratified by sex (a), age categories (b) and region (c)



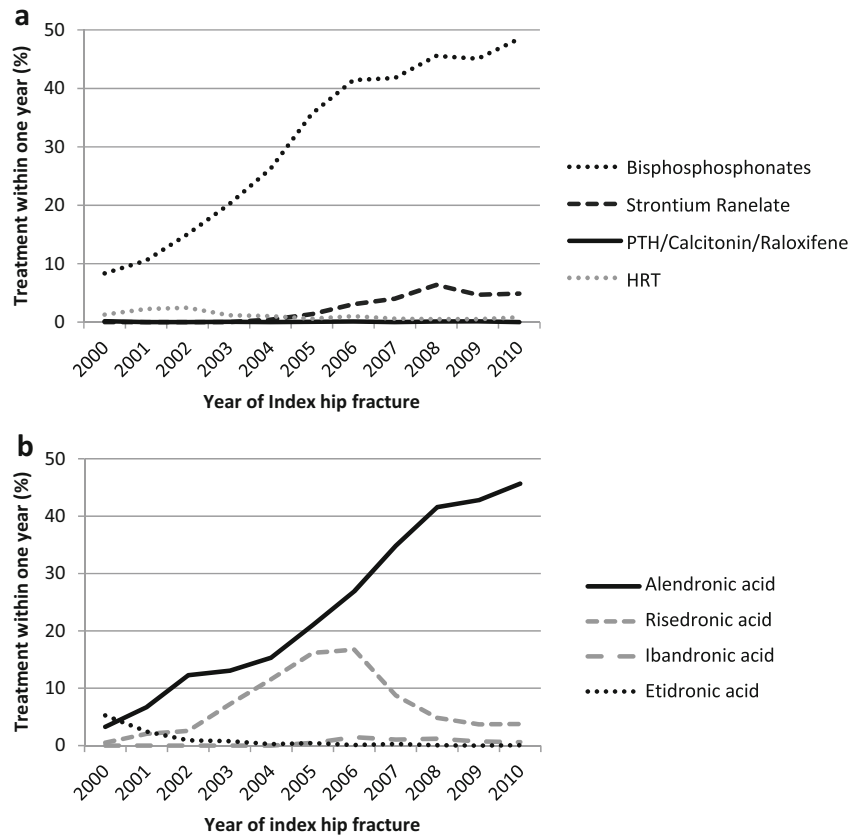
were too low ( $n=2$ ). Finally, from Fig. 3, it can be seen that there has been a dramatic increase in the combined prescribing of anti-osteoporosis drugs together with vitamin D/calcium supplementation.

#### Determinants of anti-osteoporosis drug prescribing

Multivariable Cox regression identified increased likelihood of being prescribed an anti-osteoporosis drug after hip fracture for increasing calendar year, female sex (adj. HR=1.74, 95 %

confidence interval (CI) 1.64–1.86), rheumatoid arthritis (HR=1.26, 95 % CI 1.11–1.42) and the presence of secondary osteoporosis (HR=1.13, 95 % CI 1.03–1.26), corticosteroid use and a history of major osteoporotic fracture. When compared to patients younger than 60 years, patients between the ages of 60–90 years were significantly more likely to receive osteoporosis therapy. Conversely, having dementia, a BMI >25 kg/m<sup>2</sup> or using antipsychotics, sedatives/hypnotics, or opioid analgesics were negatively associated with the initiation of osteoporosis therapy (Table 2).

**Fig. 2** Trends in anti-osteoporosis drug prescribing after hip fracture (by Kaplan-Meier method), stratified by drug class (a) and type of bisphosphonate (b)



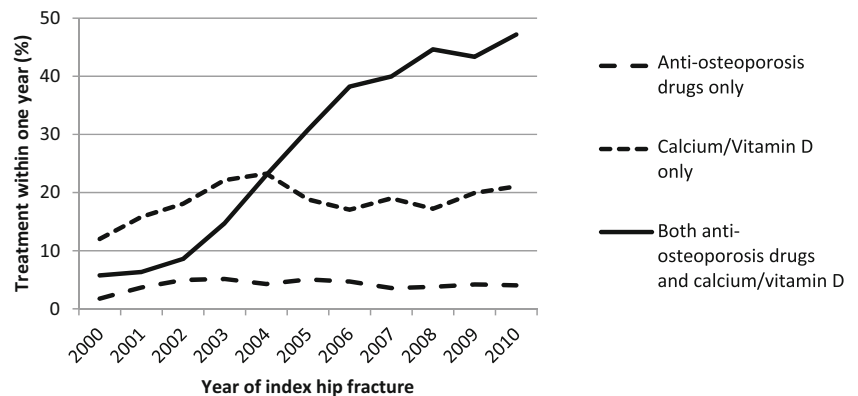
**Discussion**

The last decade has seen a striking change in prescribing practices for anti-osteoporosis drugs following a hip fracture. The probability of initiating anti-osteoporotic treatment has increased dramatically, particularly for patients over the age of 75 years. It was also apparent that the initiation of anti-osteoporosis drugs was paired with the initiation of calcium/vitamin D supplementation. However, this encouraging trend slowed down from 2006 onwards. Ultimately, the overall prescribing rate has remained inadequate with just over 50 % of hip fracture patients not receiving any anti-osteoporosis drug in 2010. The factors which were associated with reduced

likelihood of receiving anti-osteoporosis drug therapy were male gender, being overweight, having dementia or exposed to certain psychotropic drugs (antipsychotics, sedatives/hypnotics) or opioid analgesics.

Our findings of a steady increase in the prescribing of anti-osteoporosis drugs up until 2005 are consistent with most studies performed in other countries [15–19] and form an extension to the study performed on the former version of the CPRD (GPRD) for the period 1991–2005 by Watson et al. [20]. The pattern of anti-osteoporosis drug prescribing may be reflective of changes in bisphosphonate formulation, advice from various committees and changes to NHS guidelines. As from 2005, there was a pronounced difference in

**Fig. 3** Trends in anti-osteoporosis drug and calcium/vitamin D prescribing individually or combined (by Kaplan-Meier method)



**Table 2** Cox proportional hazard ratios (95 % CI) for anti-osteoporosis drug initiation within 12 months of incident hip fracture.

Characteristic	Age-sex-adjusted HR (95 % CI)		Fully adjusted HR (95 % CI)	
<b>Index year of hip fracture</b>				
2001 vs. 2000	1.33	(1.05–1.68)	1.33	(1.06–1.68)
2002 vs. 2000	1.88	(1.51–2.33)	1.88	(1.51–2.34)
2003 vs. 2000	2.60	(2.12–3.18)	2.61	(2.13–3.20)
2004 vs. 2000	3.54	(2.91–4.32)	3.57	(2.93–4.36)
2005 vs. 2000	5.46	(4.51–6.62)	5.49	(4.53–6.66)
2006 vs. 2000	6.79	(5.61–8.21)	6.83	(5.65–8.27)
2007 vs. 2000	7.15	(5.91–8.64)	7.19	(5.95–8.70)
2008 vs. 2000	8.50	(7.04–10.3)	8.72	(7.21–10.5)
2009 vs. 2000	8.50	(7.02–10.3)	8.63	(7.13–10.5)
2010 vs. 2000	9.77	(8.08–11.8)	9.87	(8.15–11.9)
<b>Age (years)</b>				
60–69 vs. 50–59	1.10	(0.96–1.26)	1.18	(1.03–1.35)
70–80 vs. 50–59	1.21	(1.08–1.37)	1.48	(1.30–1.67)
80–89 vs. 50–59	1.19	(1.05–1.33)	1.43	(1.73–1.61)
≥90 vs. 50–59	0.89	(0.78–1.02)	1.04	(0.91–1.20)
<b>Gender</b>				
Female vs. male	1.52	(1.43–1.62)	1.74	(1.64–1.86)
<b>BMI category (kg/m<sup>2</sup>)</b>				
<18 vs. 18–25	0.93	(0.83–1.04)	0.95	(0.84–1.07)
>25 vs. 18–25	0.87	(0.83–0.92)	0.86	(0.82–0.91)
<b>Smoking category</b>				
Ex-smoker vs. non-smoker	1.16	(1.09–1.24)	0.98	(0.92–1.05)
Current smoker vs. non-smoker	0.84	(0.79–0.90)	1.00	(0.93–1.07)
<b>Disease history<sup>a</sup> (%)</b>				
≥1 fall (3–12 months prior)	0.94	(0.86–1.04)	0.91	(0.83–1.00)
History of major fracture	1.13	(1.07–1.21)	1.12	(1.05–1.19)
Secondary osteoporosis <sup>b</sup>	1.23	(1.12–1.36)	1.13	(1.03–1.26)
Inflammatory bowel disease	1.16	(0.94–1.43)	1.03	(0.83–1.27)
Rheumatoid arthritis	1.31	(1.16–1.48)	1.26	(1.11–1.42)
Parkinson's disease	0.94	(0.82–1.08)	1.03	(0.90–1.18)
Dementia	0.66	(0.61–0.72)	0.65	(0.59–0.71)
Cerebrovascular disease	0.96	(0.90–1.02)	0.99	(0.93–1.06)
Ischemic heart disease	1.01	(0.95–1.07)	0.98	(0.92–1.04)
Malignant neoplasms	1.03	(0.96–1.10)	0.92	(0.87–1.00)
<b>Drugs history<sup>a</sup> (in 6 month prior to hip fracture) (%)</b>				
Antipsychotics	0.53	(0.47–0.60)	0.66	(0.58–0.74)
Antidepressants	0.95	(0.89–1.00)	0.98	(0.92–1.04)
Anti-epileptics	1.02	(0.90–1.14)	0.96	(0.85–1.08)
Corticosteroids	1.22	(1.14–1.30)	1.16	(1.08–1.25)
Opioid analgesics	0.86	(0.80–0.91)	0.93	(0.86–0.99)
Sedatives and hypnotics	0.83	(0.77–0.88)	0.92	(0.86–0.99)
Calcium/vitamin D	1.21	(1.12–1.31)	1.04	(0.96–1.13)
Number of prescriptions	1.01	(1.01–1.01)	1.00	(0.99–1.01)

HR hazard ratio, CI confidence interval

<sup>a</sup> Reference category is no history of disease or exposure to a drug

<sup>b</sup> Anorexia nervosa, coeliac disease, diabetes mellitus I, hypogonadism, osteogenesis imperfecta, osteomalacia, liver disease (cirrhosis, hepatitis and neoplasms), malnutrition, malabsorption, and premature menopause

prescribing of anti-osteoporosis medications between patients under and over 75 years. This is most likely a consequence of the NICE Technology Appraisal 87 published in 2005 [28], which advocated the use of anti-osteoporosis therapies without the need for prior dual energy X-ray absorptiometry (DXA) scanning for women over the age of 75 years who had already suffered a hip fracture. This, however, does not explain why the prescribing rate plateaued for those <75 years. We have no clear explanation for this phenomenon, but it may be partly related to the actual proportion of hip fractures that was attributable to osteoporotic BMD. This proportion has been reported to a range between 28 and 64 %, depending on age and sex [29, 30]. Since DXA-derived diagnosis of osteoporosis has been the cornerstone for indicating anti-osteoporosis drug therapy, an increase in DXA referrals may not necessarily have resulted in a further increase in anti-osteoporosis drug prescribing as osteoporosis may subsequently not have been diagnosed for many younger hip fracture patients. Furthermore, the cost of anti-osteoporotic drugs has been reduced further since the release of generic forms of alendronic acid in August 2005. Subsequently, NICE guidance (TA161) endorsed alendronic acid as the first-line therapy. This resulted in the stabilisation in the prescribing of risedronic acid in 2005 whose use then went into decline [26]. The majority of anti-osteoporosis drug prescribing was paired with the prescribing of vitamin D/calcium supplements which is in line with clinical guidelines. Another UK study that was conducted in 2006 among nine general practitioner practices showed that 34 % of patients were co-prescribed calcium and/or vitamin D with anti-osteoporosis drugs [23]. This coincides well with our results with a cumulative incidence probability of 39 % in 2006. Unfortunately, there was a considerable number of patients who only received vitamin D/calcium supplementation.

Inline with the results by Wang et al. [31], we found a slowing down in the increasing prescribing trend from 2006 onwards, while an Australian study showed a decline between 2007 and 2010 [32]. Reasons for the stagnation or even decline in anti-osteoporosis drug prescribing may coincide with revised labelling of bisphosphonates for risk of osteonecrosis of the jaw in 2005 and reports for increased risk of atypical femoral fractures and atrial fibrillation, with increasing publicity in the years thereafter. A US study showed a decline in use of anti-osteoporosis drugs after hip fracture from 2002 onwards (40.2 % in 2002 to 20.5 % in 2011) [12]. Together with the possible influence of safety issue reports, this could have been attributed to a fragmented health care system with a lack of, or insufficient, communication between emergency/orthopaedic departments and outpatient care for follow-up osteoporosis assessment. A service model to bridge this gap, the Fracture Liaison Service (FLS), now exists for over a decade in the UK which has proven to reduce the care gap for secondary fracture prevention [33]. However, this care model has been developed

in 27 % of UK NHS Hospital Trusts prior to 2006, which has barely increased to 29 % by 2009. This is in line with the flattening in prescribing rates for this period.

Few studies have examined which factors lead to the initiation of anti-osteoporosis drugs after hip fracture. Many of the factors which increase the risk of fracture were also significant determinants for initiation of anti-osteoporosis drug therapy. Hence, female gender, increasing age (except for very old age), a history of major osteoporotic fracture, rheumatoid arthritis, secondary osteoporosis and the use of corticosteroids all increased the likelihood of receiving osteoporosis treatment which is in line with previous studies [12, 34–37]. Conversely, patients who were suffering from mental illness (i.e. using antipsychotics, sedatives and hypnotics or having dementia) or patients who were overweight or used opioid analgesics were less likely to receive osteoporosis therapy. Other factors which have been associated with the initiation of anti-osteoporosis drug treatment are patients' self-perception of osteoporosis risk [34] and their appraisal for their treatment need [38], but these could not be identified in our data. The fact that an increasing number of prescriptions was not inversely associated with the instigation of osteoporosis therapy was unexpected given the findings of Duyvendak et al. [39] who found that poly-pharmacy was a barrier to osteoporosis treatment in long-term corticosteroid users. The study of Solomon et al. [12] even found an increased likelihood of being prescribed anti-osteoporosis drugs with increasing number of prescriptions which was also conducted among hip fracture patients. Consistent with other findings is the observation that male hip fracture patients were less likely to be prescribed anti-osteoporosis drugs than female patients [12, 16, 40]. The difference in prescribing patterns between men and women is likely partly due to osteoporosis primarily being considered a health problem of older women [41, 42], rather than of men; consequently, men often have poor knowledge of the condition and therefore do not consider themselves as susceptible [43, 44] and hence would not consider asking their GP for treatment. Furthermore, the number of clinical trials examining the effect of bisphosphonates on fracture reduction in men is limited, where the majority of trials used change in bone mineral density (BMD) as the primary end point [45, 46]. The few trials into the effects of bisphosphonate use on fracture reduction in men and lack of clinical guidance for anti-osteoporosis drug prescribing for men may explain why GPs do not habitually provide bisphosphonate treatment to men. However, seeing as the bisphosphonate has a similar effect on bone turnover and density in both men and women, the difference in prescribing habits is likely unjustified.

We studied a large community-dwelling population representative of the UK as a whole. However, there are several limitations that should be considered in the interpretation of our results. By studying hip fracture patients, we have assumed that all of our study population was eligible for anti-

osteoporosis medication according to a confirmed diagnosis of osteoporosis, while this may not necessarily have been the case. BMD measurements are not routinely available in the CPRD which limits our interpretation as to the eligibility for treatment. Additionally, it is possible that some fractures were pathological or due to trauma. Furthermore, we have only considered initial prescription rates and did not include repeat prescriptions. Therefore, we cannot make any comments regarding adherence with treatment. It is well known that a large proportion of patients do not adhere to their treatment regimen, although the exact reasons for this phenomenon remain poorly understood [47]. Zoledronic acid as well as PTH analogues (teriparatide) and denosumab are not fully captured in CPRD records as this database only includes prescriptions issued by general practitioners and not specialists. This may have resulted in an underestimate of anti-osteoporosis therapy initiation. However, denosumab became available in the UK at the end of the study period (2010), and although we cannot directly estimate the magnitude of this limitation for PTH analogues and zoledronic acid, indirect evidence from other countries has shown that the utilisation of these drugs remained limited until the year 2010 [12, 32]. Furthermore, NICE guidance places teriparatide under restrictive conditions for the secondary prevention of fragility fractures. Similarly, data for non-prescription over-the-counter vitamin D or calcium were not available in our database, which may have resulted in an underestimate of use of these drugs. Finally, the generalisability of this study is limited to free-living individuals as it excluded those who were institutionalized. Just under 10 % of the patients transferred out of the database, most likely to nursing homes where prescribing practices could differ.

In conclusion, our study has shown that although the prescribing rate for anti-osteoporosis medications has increased substantially since 2000, the overall rate in 2010 was still markedly inadequate. This was particularly so in men, where the prescribing of anti-osteoporosis drugs was notably less than that observed in women at any given point in time. Other patient characteristics that were associated with decreased likelihood of receiving anti-osteoporosis drugs were being overweight, having dementia and exposed to antipsychotics, sedatives/hypnotics or opioid analgesics. Increase in the prescribing of anti-osteoporosis medications may be facilitated by recent major advances in risk assessment, such as the FRAX calculator [48], linked to treatment thresholds, as exemplified by the UK NOGG Guidelines [49]. There is much work to promote secondary fracture prevention services [50], notably by the current International Osteoporosis Foundation Capture the Fracture initiative [51]. With the absolute number of hip fractures expected to increase inexorably across the world over coming decades, our findings clearly demonstrate the acute need for such activity and for the generally increased awareness of osteoporosis and prevention of fragility fracture.



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