

# Trends and Geographical Variability in Osteoporosis Treatment After Hip Fracture: A Multilevel Analysis of 30,965 Patients in the Region of Valencia, Spain

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#### ABSTRACT

Despite improvements in the therapeutic arsenal and the recommendations of guidelines, low rates of prescribing osteoporosis medications are being reported worldwide for patients surviving a hip fracture, and important geographical variation remain. We aimed to describe trends in the proportion of patients that receive osteoporosis medication after hip fracture and to analyze the geographical variation in the prescription of drug therapy and its associated factors in the region of Valencia, Spain. We studied a populationbased retrospective cohort of 30,965 patients aged 65 years and older, discharged from hospital after a hip fracture from January 2008 to December 2015, who were followed up for 3 months after discharge to identify the presence of any prescription of osteoporosis medication. We conducted a multilevel multiple logistic regression analysis with two levels (individuals and health departments [HD]) to determine which individual covariates were associated with receiving a prescription of osteoporosis medication in the 3 months after discharge, as well as the importance of the HD of hospitalization. The percentage of patients treated in the region decreased from a maximum of 28.9% in 2009 to 16.4% in 2015. By sex, the proportion of women treated reached a maximum of 33.4% in 2009 and declined to 19% in 2015, while the proportion of men reached a maximum of 14% in 2011 and reduced to 8.1% in 2015. By health department, there was a noticeable variability in the rate of patients treated, ranging from 40.9% to 11.1% in the whole period (intraclass correlation coefficient [ICC] = 7.54%; median odds ratio [MOR] = 1.64). Proportion of treated patients decreased in 20 of the 24 HDs. Variability could be also observed with regard to choice of medication by HD. This situation pressingly demands action (both at the organizational and professional levels) focused on populations at a higher risk (such as hip fracture patients) that particularly address underutilization and unwarranted variation. © 2020 The Authors. Journal of Bone and Mineral Research published by American Society for Bone and Mineral Research.

KEY WORDS: OSTEOPOROSIS; HEALTH SERVICES RESEARCH; FRACTURE PREVENTION; THERAPEUTICS; STATISTICAL METHODS

## Introduction

O steoporotic hip fracture is associated with important morbidity, elevated risk of recurrent falls and refracture, as well as with increased mortality.<sup>(1-3)</sup> After hip fracture, effective treatment with osteoporosis medication is available and recommended by every clinical guideline in order to prevent subsequent fractures.<sup>(4)</sup> Significant advances in osteoporosis pharmacological treatment to reduce fracture risk<sup>(5)</sup> have occurred in the last 13 years. Taking into account the clear clinical indication to hip fracture patients, it would be reasonable to expect high rates of treatment in the real world, although the frailty and comorbidities that often come along with hip fracture could also contribute inversely to lowering the rates of treatment observed. However, and despite progress in pharmacological therapies and the recommendations of guidelines,<sup>(6)</sup> real-world evidence shows that translating research evidence and guidance into routine clinical care is insufficient, with low rates of prescribing being reported worldwide for patients surviving a hip fracture. Evidence of this post-fracture gap in care is abundant and comes from multiple health care settings, countries, and populations.<sup>(7–12)</sup> Accordingly, there is growing public health concern in that fewer individuals with previous osteoporotic hip fracture are receiving effective drug treatment to prevent further osteoporotic fractures.<sup>(13)</sup>

Evidence from the US, both in Medicare and commercially insured patients, states that in 2011 only 21% of patients

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received effective drug therapy after a hip fracture.<sup>(7)</sup> A crossnational study in the US found even lower rates (11% Medicare, 13% commercial) and there are higher but still concerning rates in Korea (39%) and Spain (25%).<sup>(14)</sup> More recently, Desai and colleagues<sup>(15)</sup> echoed these previous reports in a large US population of commercially insured individuals by reporting rates of post-hip fracture treatment and associated treatment effectiveness. The rate of effective drug treatment in the 180 days after hip fracture was 9.8% in 2004, decreasing to 3.3% in 2015, with additional analyses showing that low treatment rates were even worse in men. In the UK, Klop and colleagues found that 32% of patients received medication in the year after the hip fracture in the period 2000 to 2010,<sup>(16)</sup> whereas Shah and colleagues provided data of patients treated in the 4 months after the fracture and found that the percentage of patients treated was as low as 9% in 1999, rising to 51% in 2011 and decreasing to 39% in 2013.(17)

Interestingly, Shah and colleagues also point out the existence of important geographical variations in the prescribing of antiosteoporotic drugs after a hip fracture.<sup>(17)</sup> Geographic variability in the provision of health care has been used to inform health care policy,<sup>(18)</sup> as any variation that remains after adjustment for demographic factors is unlikely to be due to differences in disease prevalence or patient characteristics or preferences, with health services being responsible for inequalities in access to health care services and treatments.

The aim of this study is to describe trends in the proportion of patients that receive osteoporosis medication after hip fracture during the period 2008 to 2015 and to analyze the geographical variation in the prescription of osteoporosis drug therapy and its associated factors in the region of Valencia, Spain.

## **Materials and Methods**

#### Design

The retrospective study includes a population-based cohort of all patients aged 65 years and older, discharged from hospital after hip fracture from January 1, 2008, to December 31, 2015. Patients were followed up for 3 months after discharge to identify the presence of any prescription of osteoporosis medication.

#### Setting

The study was conducted in the Valencia Health System (VHS), a comprehensive structure of hospitals, primary care facilities, and other public resources managed by the government of the region of Valencia in Spain (more than 5 million inhabitants registered in 2010) providing free, universal health care services (besides drug cost-sharing) to 97% of the region's population The VHS is organized territorially into health departments (HDs). Each HD is composed of one hospital and several primary care centers serving a population of between 150,000 and 250,000 people. The number of HDs increased from 22 in 2008 to 23 in 2009 and to 24 for the rest of the study period, due to the opening of two new hospitals in the region.

#### Population

We included all patients aged 65 years and older discharged from VHS hospitals after a hip fracture (International Classification of Diseases 9th revision Clinical Modification [ICD9CM] codes: 820.xx and 733.14) and without a diagnosis of road accident, multiple fracture, or active bone cancer (Supplemental



Fig. 1. Flowchart of participants.

Table S1) between January 1, 2008, and December 31, 2015, and we followed them up for 3 months after the date of discharge to identify those with at least one osteoporotic treatment prescribed (either by primary care doctors or any hospital specialist) in that period. We excluded patients who died within the first 3 months after the index date, non-residents in the region, or those excluded from pharmaceutical coverage (Fig. 1).

#### Data sources

Data were obtained from the Valencia Health System Integrated Database (VID). The VID is the result of the linkage, by means of a single personal identification number, of a set of publicly owned population-wide health care, clinical, and administrative electronic databases in the region of Valencia, Spain, which has provided comprehensive information about the region's 5 million inhabitants since 2008. The VID includes sociodemographic and administrative information (sex, age, nationality, etc.) and health care information such as diagnoses, procedures, lab data, pharmaceutical prescriptions and dispensations, hospitalizations, mortality, health care utilization, and public health data. It also includes a set of specific associated databases with population-wide information on significant care areas such as cancer, rare disease, vaccines, or imaging data.<sup>(19)</sup>

## Study endpoints

The primary outcome was the individual level binary outcome (yes/no) of receiving at least one prescription for osteoporosis medication in the 3 months after discharge for an osteoporotic hip fracture in the period 2008 to 2015, for the whole region, by sex and by HD. We further described the choice of osteoporosis medication (bisphosphonates, calcitonin, denosumab, para-thyroid hormone [PTH, 1–34 and 1–84], raloxifene, or strontium ranelate) for treated patients by year and HD (Supplemental Table S1).

### Covariates

Potentially relevant variables with regard to the risk of hip fracture and to the use of osteoporosis medication were included, with a look-back period of 365 days before the index hospital discharge. These variables included sociodemographic information, comorbidities, use of osteoporosis medication and other concomitant treatments before the fracture, and health care resources use (Supplemental Table S2).

## Ethics approval and consent to participate

Our study was observational and used retrospective data pseudo-anonymized before being transferred to the research team in accordance with Spanish laws on data protection for health research (Act 3/2018 transposing the 2015 European Data Protection Regulation). It was approved by the Ethics Committee for Clinical Research of the General Directorate of Public Health and the Centre for Public Health Research (approval resolution numbers 20160224 and 20160930).

## Analysis

We first described baseline patient characteristics for patients treated and untreated after a hip fracture. Second, we described the yearly percentage of patients treated within 3 months of discharge for the whole region, by sex, and for the 24 HDs. We also performed a sensitivity analysis using a 6-month window instead of a 3-month window. Third, we conducted two multilevel multiple logistic regression analyses with two levels, individuals and HDs: an empty model (a model considering only the general contextual effect of the HD level on treatment initiation, which informs about the variability of treatment attributable to the HD component without the interaction of other variables), and a second model including both the HD and individual-level variables, which informs about the variability in treatment initiation attributable to the interaction of the individual and HD levels. We further used the model with individual variables to determine which individual covariates were associated with receiving a prescription of osteoporosis medication in the 3 months after discharge, as well as the importance of the HD of hospitalization. We estimated these associations using regression coefficients expressed as odds ratios (ORs) with 95% confidence intervals (Cls) for individual covariates, and the median odds ratio (MOR) and the intraclass correlation coefficient (ICC) for the effect of the HDs. The MOR translates the HD variance into the OR scale. which makes the MOR comparable with the OR of individual covariates. The MOR can be interpreted as the amount by which the odds of receiving a prescription by a randomly selected patient would increase (in average) if this patient moved to a HD with a higher probability of being treated. At MOR = 1, there would be no differences between HDs in the odds of being treated after

hip fracture. The ICC informs on the proportion of total variance in the probability of being treated after hip fracture that is attributable to the HD level. An ICC = 0 would reflect that the HD level does not affect the individual probability of being treated, and thus there would be no general contextual effects.<sup>(20-24)</sup> We also provided the area under the receiver-operating characteristic (ROC) curve to inform about the discriminatory accuracy of the models. Fourth, we plotted adjusted differences between HDs in the percentage of patients treated obtained from the multilevel logistic regression analysis. These differences were expressed as ORs and 95% Cls. Fifth, we described the trends in the choice of osteoporosis drugs in those patients actually receiving medication within 3 months of discharge, per year and by HD. Zoledronic acid is not included in figures because inpatient medication is not recorded in the electronic medical record. The same applies to over-the-counter medication and other treatments prescribed by private doctors that are not publicly reimbursed. All the analyses were performed using the Stata 13.0 (StataCorp, College Station, TX, USA) statistical software. We used the command from Stata xtmelogit to run the model in Stata and the command xtmrho to compute the ICC and MOR.(22)

# Results

## Patient characteristics

After taking into account the exclusion criteria, we ended up with a cohort of 30,965 patients who were discharged alive after a hip fracture in the whole period. From those, 6938 (22.4%) received an osteoporosis medication within 3 months of discharge. Treated patients were younger than untreated patients (81.9 versus 83.4 years old, p < 0.001), were more likely to be female (87.9% versus 72.9%, p < 0.001), had used health services less in the year before the fracture, had fewer comorbidities except for osteoporosis, rheumatoid arthritis, and depression (p < 0.001), but had received more previous medication (opioids, hypnotics, corticoids, anxiolytics, and cardiovascular drugs) overall (p < 0.001; Table 1).

# Trends of treatment after hip fracture

The percentage of patients treated in the region declined from a maximum of 28.9% in 2009 to 16.4% in 2015. By sex, women treated reached a maximum of 33.4% in 2009 to 19% in 2015, whereas men reached a maximum of 14% in 2011 to 8.1% in 2015 (Fig. 2). By health department, there was a noticeable variability in the rate of patients treated, ranging from 40.9% to 11.1% in the whole period. Proportion of treated patients decreased from 2008 to 2015 in 20 of the 24 HDs. In 2008, 15 HDs were treating more than 20% of the patients at discharge (six of them treating more than 30%, with three treating more than 40% of the patients), whereas in 2015 only six HDs treated more than 20% of the patients (and only one HD more than 40% of patients). In nine of the 24 HDs, the percentage of patients treated fell by more than 50% (Fig. 3). Proportion of treatment at 6 months was only marginally higher (Supplemental Fig. S1).

## Factors associated with receiving treatment

Table 2 presents the results of the two multilevel models, showing the specific associations between contextual (HDs) characteristics and treatment within 3 months of hip fracture (empty model) and between individual and contextual characteristics and treatment **Table 1.** Baseline Characteristics in the 365 Days Before the Index Hip of Patients Who Received Pharmacologic Treatment for Osteoporosis at 3 Months from Index Date

		Treated ( <i>n</i> = 6938)		Untreated ( $n = 24,027$ )		Total ( <i>n</i> = 30,965)	
Characteristics		N	%	N	%	N	<i>p</i> Value
		0	Sociodemogr	aphics			
Sex	Women	6097	87.9	17,508	72.9	23,605	0.000
	Men	841	12.1	6519	27.1	7360	
Age (years)	65–74	1053	15.2	3061	12.7	4114	0.000
	75–84	3557	51.3	10,354	43.1	13,911	
	≥85	2328	33.6	10,612	44.2	12,940	
	Mean (SD)	81.9 (6.5)		83.4 (7.0)		83.1 (6.9)	0.000
		U	se of health :	services			
Primary care visits	0–4	2644	38.1	10,008	41.7	12,652	0.000
	5–12	2912	42.0	9855	41.0	12,767	
	13	1382	19.9	4164	17.3	5546	
ER visits	0-1	4408	63.5	15,413	64.2	19,821	0.348
	≥2	2530	36.5	8614	35.9	11,144	
Hospital admission	Yes	1302	18.8	5006	20.8	6308	0.000
•	No	5636	81.2	19,021	79.2	24,657	
Polypharmacy	0–5	3289	47.4	12,782	53.2	16,071	0.000
	6–12	3592	51.8	11,126	46.3	14,718	
	≥13	57	0.8	119	0.5	176	
	Mean (SD)	5.88 (4.3)		4.74 (4.4)		4.99 (4.4)	0.000
		,	Comorbidi				
Previous fracture		1734	25.0	4959	20.6	6693	0.000
Osteoporosis		1717	24.8	2424	10.1	4141	0.000
Parkinson's		408	5.9	1523	6.3	1931	0.165
Dementia		1445	20.8	6677	27.8	8122	0.000
Diabetes		2030	29.3	7710	32.1	9740	0.000
Rheumatoid arthritis		322	4.6	642	2.7	964	0.000
Stroke		687	9.9	3118	13.0	3805	0.000
Myocardial infarction		778	11.2	3209	13.4	3987	0.000
Heart failure		750	10.8	3092	12.9	3842	0.000
Depression		1492	21.5	4468	18.6	5960	0.000
Cancer		975	14.1	3851	16.0	4826	0.000
Malnutrition		98	1.4	434	1.8	532	0.026
		20	Medication			001	0.020
Opioid treatment		2482	35.8	6021	25.0	8503	0.000
Hypnotic treatment		1204	17.4	4233	17.6	5437	0.611
Oral corticoids		794	11.4	2261	9.4	3055	0.000
Antipsychotics		1112	16.0	4570	19.0	5682	0.000
Anxiolytics		3409	49.1	10,503	43.7	13,912	0.000
Antiarrythmics		325	4.7	117	4.9	1495	0.526
Antihypertensive treatment		5255	75.7	17,612	73.3	22,867	0.000
Diuretic treatment		2330	33.6	8201	34.1	10,531	0.395
Osteoporosis treatment		3805	54.8	1453	6.1	5258	0.000

ER = emergency room.

(model with HD and individual variables), as well as the analysis of variance (MOR) and the values of the intraclass correlation statistic (ICC). ICC, informing on the proportion of total variance in treatment initiation attributable to the HD component, was 5.33% in the empty model and 7.57% in the model with individual variables, showing that variability among HDs was statistically significant. The median odds ratio, that translates the area level variance in the widely used odds ratio scale, was 1.51 for the empty model and 1.64 for the model with covariates, showing differences in the probability of receiving treatment between HDs.

Regarding discriminatory accuracy, the area under the ROC curve (AUC) in the empty model was 0.62. Information provided

by individual variables resulted in an increase of the AUC to a value of 0.84. In the model with individual covariates, patients treated within 3 months of hip fracture discharge were more likely to be female (OR = 1.80, 95% CI 1.64–1.98), to have had previous osteoporosis treatment (OR = 17.12, 95% CI 15.80–18.56), to have a diagnosis of osteoporosis (OR = 1.31, 95% CI 1.19–1.44) and rheumatoid arthritis (OR = 1.23, 95% CI 1.03–1.48), and to use oral corticoids (OR = 1.13, 95% CI 1.01–1.27). Patients at an increased risk of remaining untreated after a hip fracture were more prone to being older than 85 years (versus 65 years and younger, OR = 0.76, 95% CI 0.68–0.84), having a prior stroke (OR = 0.88, 95% CI 0.79–0.99) and dementia

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Ű	2008	2009	2010	2011	2012	2013	2014	2015
- All	25,0	28,8	25,6	25,7	21,7	19,4	16,2	16,5
••••• Male	12,3	14,2	13,6	14,2	11,5	9,8	7,9	8,4
– – – Female			29,3	29,2	25,0	22,4	19,0	19,3

Fig. 2. Percentage of patients treated in the region, for the whole cohort and by sex, 2008 to 2015.

(OR = 0.72, 95% CI 0.66–0.78), and were more likely to use antipsychotic drugs, antiarrhythmic drugs, diuretics, anxiolytics, and hypnotics (OR = 0.83, 95% CI 0.76–0.92; OR = 0.82, 95% CI 0.68–0.98; OR = 0.86, 95% CI 0.78–0.94; OR = 0.92, 95% CI 0.86–0.99; OR = 0.88, 95% CI 0.80–0.96, respectively), as well as to have a previous hospital admission for any cause (OR = 0.82, 95% CI 0.75–0.90). In 10 HDs, the probability of being treated was below the regional average, 8 were above it, and 6 showed no difference with the regional average (Fig. 4). With respect to

year 2008, patients were more likely to be treated in 2009 (OR = 1.14, 95% Cl 1.01–1.30) but less likely during other years (p < 0.001), except for 2011 (Table 2).

#### Choice of medication according to health departments

In 2008, patients receiving bisphosphonates in the 22 HDs existing that year ranged from 38.1% to 6.7% of patients treated. For PTH, percentages ranged from 14.3% to 0% and from 10.8% to 0% for strontium ranelate. In 2015, with 24 HDs, 44.4% to 3.2% patients received a bisphosphonate depending on the HD of discharge, 7.3% to 0% were treated with PTH, and 6.9% to 0% were treated with denosumab. Overall, among treated patients, an important variability between HDs can be observed in the percentage of use of bisphosphonates (from 81.4% to 47.7%), PTH (from 26.7% to 4.2%), or denosumab (from 11.3% to 0.8%; Supplemental Fig. S2).

#### Discussion

Our results showed that secondary prevention after an osteoporotic hip fracture in the region of Valencia was not only suboptimal but followed a deteriorating trend in the period 2008 to 2015. Only 1 in 4 patients were treated at the beginning of the follow-up, whereas only 1 in 6 were treated at the end of the



Fig. 3. Percentage of patients treated per health department, 2008 to 2015.

**Table 2.** Factors Associated with Receiving Treatment: Multilevel

 Analysis Results

Analysis Results					
			Model with individual variables		
	Empty model	OR	95% CI		
Sociodemographics					
Female		1.80	1.64–1.98		
Aged 85 years and older		0.76	0.68-0.84		
Osteoporosis treatment		17.12	15.80–18.56		
Year of discharge					
2009		1.14	1.01-1.29		
2010		0.86	0.76-0.97		
2012		0.64	0.56-0.73		
2013		0.57	0.50-0.65		
2014		0.53	0.46-0.61		
2015		0.56	0.49-0.64		
Comorbidities					
Prior stroke		0.88	0.79–0.99		
Osteoporosis		1.31	1.19–1.44		
Dementia		0.72	0.66-0.78		
Rheumatoid arthritis		1.23	1.03–1.47		
Medication use					
Antipsychotics		0.83	0.75-0.91		
Antiarrythmics		0.83	0.71–0.98		
Diuretics		0.90	0.83-0.98		
Anxiolytics		0.92	0.86-0.99		
Oral corticoids		1.13	1.01–1.27		
Hypnotics		0.88	0.80-0.96		
Use of health services					
Hospital admission		0.82	0.75-0.90		
Random effects					
Intraclass correlation (ICC)	5.33%	7.54%			
Median odds ratio (MOR)	1.51	1.64			
Area under ROC curve (AUC)	0.62	0.84			

OR = odds ratio; CI = confidence interval.

Only significant variables are shown. Nonsignificant variables: aged 75 to 84 years, year 2011, previous fracture, heart failure, diabetes, Parkinson's, cancer, depression, malnutrition, myocardial infarction, use of opioids, use of antihypertensives, emergency room visits, polypharmacy.

period. Systematically, men were treated less than women throughout the study period. Moreover, ICC indicates that significant differences between HDs exist with regard to percentage of patients treated and the choice of drug.

Our study provides relevant and original information on the temporal evolution of secondary prevention of hip fracture in a large, population-based cohort, combined with the analysis of the general contextual effect of HD variation and the individual level variables associated with receiving treatment. We showed that HDs are contextual factors that influence significantly patterns of treatment in patients after a hip fracture, irrespective of individual characteristics. The HD of discharge was one of the most prominent factors related to the decision to treat, as well as some individual variables, and our model showed a good discriminative ability. At patient level, being a female and having a previous osteoporosis diagnosis, previous osteoporosis treatment, as well as rheumatoid arthritis were associated with receiving post-discharge treatment, whereas factors associated with a lower chance of being treated were older age, patients with



**Fig. 4.** Ranking of adjusted differences between health departments. Differences are expressed as odds ratios (ORs), and 95% confidence intervals (Cls) are shown.

prior stroke and dementia, use of antipsychotics, antiarrhythmic drugs, diuretics, anxiolytics, or hypnotics, and previous hospitalization for any reason. With regard to the choice of drug by health department, important variations could be observed, with an almost twofold difference in the use of bisphosphonates, a sevenfold difference in the use of PTH, or a 14-fold difference in the use of denosumab.

A series of elements, mainly supply-side factors, may be associated with such different behaviors among HDs: physician preferences based on clinical experience, risk aversion, or safety warning awareness, HD-specific health care policies and protocols (or their absence) influencing both specialist and primary care prescription, or different promotional intensity over time and districts. Qualitative research is warranted to identify specific HD characteristics that may explain such differential trends.

The overall decline in the use of medication after a hip fracture is consistent with the observed downward trend of osteoporosis medication in many countries such as the UK, Australia, or the US.<sup>(13,15,25-28)</sup> This trend has been linked to the safety warning issued in 2010 by the FDA with regard to the association between long-term use of bisphosphonates and atypical fractures. In Spain, the Spanish Agency for Medicines and Medicinal Products did not publish the warning on atypical fractures (simultaneously with the European Medicines Agency [EMA]) until mid-2011. That may explain why the drop observed in the consumption of osteoporosis drugs happened at a later moment-2011-in Spain. In 2009, a previous decline can be also observed, coinciding in time with the EMA safety warning on osteonecrosis of the jaw. However, in a recent study evaluating the impact of these warnings on the use of osteoporosis medication for primary and secondary prevention, we did not find a significant impact of the 2009 warning on drug consumption.<sup>(29)</sup> In that study, we found that the decline in medication use was similar for both high- and low-risk patients in the same period, which is consistent with our current results based on a

cohort of high-risk patients, where the general trend is clearly downward. Only in four of the 24 health departments in the region of Valencia does the percentage of treated patients increase over time. Finally, a further drop can be observed around 2012, coinciding with a change in the pharmaceutical cost-sharing system, which we showed in the aforementioned study as impacting on the overall consumption of antiosteoporotic drugs in the region.<sup>(29)</sup>

Our study is subject to some limitations. First, VID databases gather real-world clinical practice data and contain information as registered by health professionals during routine clinical practice; these are not specifically prepared for research. In this sense, studies based on real-world clinical information like VID may be subject to well-known biases such a differential recording, misclassification bias, or missing data. This is a common feature in studies based on real-word data. However, diagnostic accuracy for hospital discharge diagnoses due to acute surgical conditions (such as hip fracture, our main inclusion criterion) is expected to be very high, and prescription and dispensation information (the essential data to define our main endpoint) is also very accurate as it is used for billing purposes. Second, we lack information on zoledronic acid, which is provided in-hospital in Spain. Even if some patients may be prescribed this drug (resulting in an underestimation of the proportion of patients treated in our study), international evidence suggest that zoledronic acid consumption has declined in the same way as other bisphosphonates.<sup>(30)</sup> Third, we analyzed the simplest possible multilevel structure of individuals within health departments, but we recognize that other care levels or contexts, for instance primary care zones or physicians, may influence patterns of prescription. Notwithstanding, this design is commonly used in multilevel health care studies, (20-24,31) and our analyses included appropriate variables for evaluating differences in the prescription of anti-osteoporotic drugs. Fourth, despite using many relevant patient variables, we cannot discard the existence of missing clinical factors relevant for treatment decisions, such as treatment contraindications. Fifth, we have not analyzed the impact of the decrease in prescription on clinical outcomes, but current evidence shows relevant benefits of osteoporosis treatment after hip fracture, reducing refracture rates by about 50%.<sup>(32–34)</sup> Finally, the generalization of our results to other settings outside, or even to other regions within, the Spanish National Health System should be done with great caution, especially considering the importance of contextual factors.

The main findings of this study are the acknowledgment of a suboptimal and worrying trend in the treatment of patients after a hip fracture in the region of Valencia between 2008 and 2015 and that the decision regarding treatment was influenced by provider factors. The identification of factors that are not related to clinical appropriateness but are conditioning choices regarding initiation of treatment brings to light important management issues. Although we have evidence that an important problem of osteoporosis treatment overuse in primary prevention in low-risk populations still remains in Spain,<sup>(29)</sup> the problem of underuse in high-risk populations is aggravated. This situation pressingly demands action (both at the organizational and professional levels) focused on populations at a higher risk (such as hip fracture patients) that particularly address underutilization.

## **Disclosures**

The FISABIO Foundation (a nonprofit research institution depending on the Valencia Ministry of Health) had a collaboration agreement with Amgen SA to conduct nonconditioned independent research on osteoporosis (ESOSVAL and PREV2FO cohorts) during 2014.

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Authors' roles: Study design: AG, GS, IH, and SP. Study conduct: IH and AG. Data collection: IH. Data analysis: IH, AG, SP, and GS. Data interpretation: AG, IH, SP, and GS. Drafting manuscript: AG. Revising manuscript content: SP, GS, AG, and IH. Approving final version of the manuscript: AG, IH, SP, GS, CR, and JS.

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