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# Osteoporotic hip fractures: Bisphosphonates sales and observed turning point in trend. A population-based retrospective study

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ABSTRACT

The aim is to examine the temporal trends of hip fracture incidence in Portugal by sex and age groups, and explore the relation with anti-osteoporotic medication.
From the National Hospital Discharge Database, we selected from 1st January 2000 to 31st December 2008, 77,083 hospital admissions (77.4% women) caused by osteoporotic hip fractures (low energy, patients over 49 years-age), with diagnosis codes 820.x of ICD 9-CM. The 2001 Portuguese population was used as standard to calculate direct age-standardized incidence rates (ASIR) (100,000 inhabitants). Generalized additive and linear models were used to evaluate and quantify temporal trends of age specific rates (AR), by sex.
We identified 2003 as a turning point in the trend of ASIR of hip fractures in women. After 2003, the ASIR in women decreased on average by 10.3 cases/100,000 inhabitants, 95% CI (−15.7 to −4.8), per 100,000 anti-osteoporotic medication packages sold. For women aged 65–69 and 75–79 we identified the same turning point. However, for women aged over 80, the year 2004 marked a change in the trend, from an increase to a decrease. Among the population aged 70–74 a linear decrease of incidence rate (95% CI) was observed in both sexes, higher for women: −28.0% (−36.2 to −19.5) change vs −18.8%, (−32.6 to −2.3).
The abrupt turning point in the trend of ASIR of hip fractures in women is compatible with an intervention, such as a medication. The trends were different according to gender and age group, but compatible with the pattern of bisphosphonates sales.



## Introduction

Identifying and understanding trends of hip fracture incidence is important, not only as a way for planning future medical resources and treating patients but also in planning effective preventive measures [1]. Costs related to hip fractures are not only restricted to hospitalization but also to the long recovery time and assistance that these patients require [2,3]. Public health interventions can be taken using knowledge gathered from epidemiologic studies using secondary data. These studies can provide valuable information with the use of reliable data on a national basis [4,5].

The bone quality impairment is associated to aging and elevates the risk of osteoporotic fractures, particularly in post-menopausal women. Furthermore, an excessive pathologic decrease in bone strength can be prevented either by the use of medicaments or by changing activity and nutritional behaviour [6]. Osteoporotic hip fractures are more common among women over the age of 49 years and grows exponentially with aging. With the increase of life expectancy the range of population at risk is considerable, enhancing the need to analyze trends by age groups. In 2008, life expectancy at age 65 in the European Union (27 member states) was 17.2 and 20.7 years for males and females respectively [7]. In Portugal, the same indicator with data from 2009 to 2011 was 16.9 and 20.2 respectively (last available data) [7,8]. Moreover, the elderly form the fastest growing age group in most western countries thus aggravating the burden of osteoporosis.

In Portugal there are no national studies addressing the trend of hip fractures. However, internationally several studies have been conducted reporting trends of age-standardized incidence rates of hip fractures [1]. Nevertheless the results are not consensual: increasing, decreasing and

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stable trends have been reported, which may reflect different stages in the epidemic curve. The results regarding the shape of the trends as well an existing pattern in men have also differ. Studies in Finland [9] and Australia [10,11] have reported rates of hip fractures compatible with a non-linear trend. However in Finland the decrease pattern was observed in both genders, whereas in Australia only women presented a decreasing pattern. Rates presenting linear decreases have been reported by studies in Belgium [12], Denmark [13], Canada [14], United States [15] for both genders and Spain just for women [16]. Unique causes are impossible to assess, nevertheless studies have pointed out different plausible reasons, according to their results, namely medication for osteoporosis [10,11,16] or other interventions [13,14].

It is important to explore time trends of age-standardized incidence rates of hip fractures although they may hide different underlying trends by age groups thus leading to incorrect conclusions. And since hip fractures affect a wide range of ages, these studies may help uncover unequal patterns and meaningful associations with the preventive procedures undertaken by different countries.

The aim of this work is to examine the temporal trends of hip fracture incidence in Portugal by sex and age group, and explore its relation with anti-osteoporotic medication.

## Materials and methods

### *Study area*

The study area was Continental Portugal with a population of 10,135,309 inhabitants in 2008. In 2000 there were 3,298,922 inhabitants aged 50 years or over, increasing by 11.9% in 2008 (n = 3,691,104) [8], in contrast with a decrease of −0.6% in the population aged under 50 in the same period.

### *Data*

Population data was the annual official estimates, per sex and 5-year age groups, except for 2001, which was a census year.

We used data from the National Hospital Discharge Register (NHDR). The use of this administrative database is mandatory since 1997 in all Portuguese public hospitals, and compiles information on all discharges such as gender, age, admission and discharge date; first cause of admission (and up to 19 secondary causes) coded according to the International Classification of Diseases, version 9, Clinical Modification (ICD9-CM); main diagnosis (and up to 19 secondary diagnoses), also coded according to the ICD9-CM; clinical interventions (up to 20); surgical interventions; hospital providing the care; outcome (deceased, discharge to home, discharge to another hospital); length of stay (LOS) and patient's place of residence.

In Portugal, access to the national health-care system is free and universal and due to the high costs involved, hip fractures are primarily treated in public hospitals. Therefore hip fractures are highly documented and the NHDR records the total number of admissions with a diagnosis of hip fracture nationwide.

The quality of the NHDR is accessed regularly by both internal (hospitals) and external (ACSS — Central Administration of the National System) auditors [17].

We selected all discharges from 1st January 2000 to 31st December 2008 of individuals aged 50 years or over, with a diagnosis of hip fracture (codes ICD9-CM 820.x) caused by a low or moderate trauma. We excluded cases of bone cancer, readmissions for orthopedic after-care or complications in surgical and medical care (codes ICD9-CM: 170.x, 171.x, V54.x, 996.4), the exclusion expression was applied to all 20 fields containing diagnosis, and represented 0.8% of the cases. To account for misclassification on the diagnosis field other actions were taken, namely revisions were excluded based on procedures codes (81.53 Revision of hip replacement, not otherwise specified) representing a total of 0.08% of the cases. In addition we also excluded cases with length of stay inferior to 5 days, that did not went to a surgery and that were transferred to another hospital, because the first hospitalization could be just to stabilize the patient, these represent 1.1% of the cases.

In Portugal it is not possible to have database linkage between NHDR and prescriptions so the data on medication was only available for the entire population, and therefore it was not possible to access sales desegregated by sex and age groups, or have the number of patients treated. Data was provided by the National Authority of Medicines and Health Products (INFARMED). We analyzed, on a national level, the number of anti-osteoporotic medication packages sold from 2000 to 2008 through prescriptions made in the National Health System (NHS). We used the total number of anti-osteoporotic medication for the entire population to explain the trend of hip fractures in women, based on our preliminary results that showed no increasing or decreasing trends in ASIR for men. The stable incidence rates of hip fractures among men is compatible with the low prescription of anti-osteoporotic medication for men identified in other countries [12] and information contained in Portuguese national guidelines [18,19] which focus the prevention of osteoporosis in women. The medications analyzed were those indicated as agents that can act on the inhibition of bone loss or promote directly bone formation [20,21] with a high evidence level of reducing the risk of a hip fracture: bisphosphonates, calcitonin, hormonal replacement therapy (HRT), Strontium ranelate and Selective Estrogen Receptor Modulators (Reloxifene) as well as vitamin D (recommended to be prescribed in association with the medications mentioned [19]).

We used the Portuguese population from the 2001 census, available from the Statistics Portugal (Instituto Nacional de Estatística — INE) as the standard for calculating the direct age-standardized incidence rates (ASIR) per 100,000 inhabitants by gender.

We calculated age-specific rates (AR) by gender, using population counts in the census year of 2001 and official estimates for all the other years. Five-year age groups were used from 50 to 84 years of age and a wider group comprising all patients older than 84.

In addition, we calculated the 95% Confidence Intervals (95% CI) for each rate according to the methods described in Morris and Gardner (2000) [22].

### *Statistical analysis*

We used Generalized Additive Models (GAMs) to investigate changes in the trends of incidence rates. These models are flexible as they incorporate a non-parametric component that is implemented using spline functions (smoothers) and can reveal possible non-linearities in the

**Table 1**
Summary of statistics of in-patients characteristics in portugal (2000–2008).

| Variable | 2000 | 2001 | 2002 | 2003 | 2004 | 2005 | 2006 | 2007 | 2008 |
|---|---|---|---|---|---|---|---|---|---|
| *Men* | | | | | | | | | |
| No. of admissions | 1752 | 1947 | 1780 | 1989 | 1981 | 1961 | 2069 | 1913 | 2027 |
| Age (mean; (SD)) | 77.6 (10.02) | 77.4 (10.03) | 78.0 (9.92) | 77.6 (9.94) | 78.4 (10.26) | 78.1 (10.20) | 78.4 (9.99) | 78.2 (10.29) | 78.5 (10.14) |
| *Women* | | | | | | | | | |
| No. of admissions | 6086 | 6537 | 6295 | 6814 | 6820 | 6820 | 6892 | 6569 | 6831 |
| Age (mean; (SD)) | 80.3 (8.59) | 80.5 (8.64) | 80.9 (8.61) | 80.7 (8.72) | 81.3 (8.49) | 81.2 (8.46) | 81.2 (8.47) | 81.5 (8.30) | 81.8 (8.41) |