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ORIGINAL ARTICLE

Trends in Hip Fracture Incidence and in the Prescription of Antiosteoporosis Medications During the Same Time Period in Belgium (2000–2007)

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Objective. **To examine the secular trend of hip fracture incidence in Belgium between 2000 and 2007 and the concomitant change in the prescriptions of antiosteoporosis medications.**

Methods. **The incidence of hip fractures and the number of prescriptions were determined using national databases. A logistic regression including years and 5-year age range was performed to assess the secular trend of hip fracture incidence, and Pearson's correlation coefficient was calculated to examine the relationship between hip fracture incidence and the prescriptions of antiosteoporosis medications.**

Results. **The annual number of hip fractures increased in Belgium from 13,512 in 2000 to 14,744 in 2007, with a more marked increased in men (20.4%) than in women (5.7%). The age-adjusted incidence of hip fractures was significantly decreased by 1.12% per year in women, but declined nonsignificantly by 0.34% per year in men. An increase in the prescriptions of antiosteoporosis medications in women was observed during the same time period.**

Conclusion. **Despite an increase in the number of hip fractures in Belgium between 2000 and 2007, there was a significant decrease in age-adjusted incidence in women but not in men. Although our results suggest that the decrease may be related to the extent of antiosteoporosis medications, a causal relationship cannot be ascertained and many other factors may have contributed to the decrease in age-adjusted incidence.**

INTRODUCTION

Hip fractures constitute a major public health concern and are considered the most serious consequences of osteoporosis in terms of morbidity, mortality, and health care expenditures. Approximately 15–25% of patients will die within 1 year (1), and hip fractures result in chronic pain, reduced mobility, increasing dependence, and long-term mortality excess (2,3).

Accurate estimates of the epidemiology and secular changes of hip fracture incidence may be useful for decision makers to predict the future burden of hip fractures and to set priorities regarding large-scale public health interventions. Given there is large country-to-country variation in hip fracture incidence (4), national data are required. In Belgium, no recent data on the incidence of hip

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Significance & Innovations

- Despite an increase in the number of hip fractures in Belgium between 2000 and 2007, there was a significant decrease in age-adjusted incidence in women but not in men. These results may suggest a reversal of the previously observed secular trend.
- Although a causal relationship cannot be ascertained and many factors may have contributed to the decrease in age-adjusted incidence in women, an increase in the prescriptions of antiosteoporosis medications was observed during the same time period.
- Our results may be useful to set priorities regarding large-scale public health interventions and suggest that, even if less common than in women, hip fractures in men should not be underestimated and will become a major burden.

fractures are available. The last report available suggested that there was an increase (2.07% per year) in age-adjusted hip fracture incidence between 1984 and 1996 (5). In contrast to that observation, a leveling off and even a decrease in age-adjusted hip fracture incidence has been suggested in some countries over the past years (6–13). Reasons for this decrease, however, are largely unknown (13,14). Recent studies have suggested that this change may be related to the extended use of antiosteoporosis medications over the last 2 decades (15–17). This trend, however, would not fully explain the entire decline in incidence rates that has been observed (15,18). Further studies have been recommended to confirm, or not, the relationship between the use of antiosteoporosis medications and hip fracture incidence (17).

This study was designed to assess how the age-adjusted incidence of hip fractures evolved in Belgium between 2000 and 2007, and the concomitant changes in prescriptions of antiosteoporosis medications by sex and age groups. We also estimated the expected number of hip fractures by projecting the observed changes on population estimates until 2025.

MATERIALS AND METHODS

The incidence of hip fractures was determined using the national hospital database, which fully covers the annual hospital stays in Belgium (source: INAMI-RIZIV [Institut National d'Assurance Maladie Invalidité–Rijksinstituut voor Ziekte en Invaliditeitsverzekerin] and SPF Public Health). All patients ages ≥50 years with an International Classification of Diseases, Ninth Revision code for hip fracture (820) were included in the study. Patients' sex and age at the fracture event were recorded. As patients may have multiple registrations for the same diagnosis, it is important to adjust fracture incidence. Overall, yearly multiple registrations of patients accounted for 3.6% of the records (data not shown). Based on this, a correction factor of 0.964 was used to adjust the incidence calculations over the entire period.

For validation purposes, a random sample of claim data collected between 2002 and 2008 by sickness funds was analyzed. The permanent sample (EPS) is a representative random sample of 2.5% of all persons covered by the compulsory health insurance, stratified by age and sex (with a supplementary sampling of another 2.5% for people ages ≥65 years). The EPS contains all reimbursement data and some demographic and socioeconomic characteristics of individuals (for a maximum period of 10 years). We extracted from the EPS data on all individuals ages ≥40 years who during the period 2002–2008 experienced a hip fracture, under the assumption that the majority of bone fractures occurring at age ≥40 years are associated with osteoporosis. When 2 nomenclature codes for fractures were separated by less than 30 days, the 2 codes were considered to correspond to the same event.

Using population data obtained from the Directorate-general Statistics and Economic information–SPF Economy (19), we calculated 5-year and sex-specific incidence rates. Age-specific rates were calculated as the number of hip fractures by age group divided by the total number of individuals in the group, and were expressed as the number of hip fractures per 1,000. To allow comparison over time, hip fracture incidence was standardized to the age distribution of the year 2005. We also examined the changes of hip fractures between 2000 and 2007 for all men and women ages >50 years and by 5-year age range. A logistic regression including years and 5-year age group was performed in both sexes to assess the significance of the secular change within the period. By including age groups, any differences between hip fracture incidences cannot be attributed to different age distribution, but must be attributed to some other factors.

Data on the annual prescriptions of antiosteoporosis medications in populations ages >50 years were obtained from the INAMI-RIZIV–Pharmanet database. Prescriptions by 5-year age and sex groups were available from the year 2002. The defined daily doses were provided for bisphosphonates, raloxifene, parathyroid hormone analog, and strontium ranelate. As no significant differences between these drugs in terms of efficacy have been shown, we kept all medications together. However, in a separate analysis, raloxifene was deleted because the effect of this treatment on hip fractures has not been demonstrated. Oral bisphosphonates are the most widely prescribed medications for the treatment and prevention of postmenopausal osteoporosis in Belgium, representing 84% market shares between 2002 and 2007. A Pearson's correlation coefficient was calculated to examine the relationship between hip fracture incidence and the number of antiosteoporosis prescriptions.

Finally, the Belgian population projections for the period 2010–2025, made by the Federal Planning Bureau and the Directorate-general Statistics and Economic information–SPF Economy (19) and based on current population demographics (2000–2007) and fertility and immigration assumptions, were used to estimate the expected number of hip fractures. Changes in hip fracture incidence ob-

Table 1. Annual absolute number of hip fractures, total population, and age-standardized incidences of hip fracture per 1,000 for the Belgian population (age ≥50 years) over an 8-year period (2000–2007)*

Year	Absolute number of hip fractures			Total population (men and women), no.	Standardized incidence of hip fracture	
	Women	Men	Total		Women	Men
2000	10,349	3,164	13,513	3,429,058	5.60	2.15
2001	10,517	3,326	13,843	3,469,201	5.64	2.20
2002	10,671	3,404	14,074	3,511,588	5.63	2.20
2003	10,787	3,423	14,210	3,557,211	5.62	2.16
2004	10,560	3,443	14,003	3,601,888	5.43	2.13
2005	10,682	3,602	14,284	3,653,614	5.38	2.16
2006	10,754	3,675	14,429	3,706,447	5.27	2.12
2007	10,937	3,808	14,745	3,763,606	5.22	2.13
2000–2007	85,257	27,844	113,101	28,692,813	5.48	2.16

* A direct method of standardization was used, with the year 2005 as the reference.

served between 2000 and 2007 were projected to population estimates and lower and upper bounds of the 95% confidence intervals (95% CIs) of the secular changes were used in sensitivity analysis.

All statistical tests were considered significant at a level of 0.05. Data were processed on a Windows Excel spreadsheet format (Microsoft) and analyses were carried out using SAS software, version 9.

RESULTS

A total of 113,101 hip fractures were recorded in the Belgian population age >50 years between 2000 and 2007, with an average annual number of 14,138 hip fractures per year. The results based on claim data from sickness funds were very similar. For example, in 2005, the numbers of hip fractures based on the abstracted clinical files were 14,285 and 14,000 when the reporting was based on claim data, i.e., a difference of 2%. More than three-quarters of hip fractures (85,256 [75.4%]) occurred in women. The overall absolute number of hip fractures (Table 1) increased by 9.1%, and more in men (20.4%) than in women (5.7%). The age-standardized incidence rates of hip fractures remained stable for men and substantially decreased for women, especially from the year 2003.

The distribution of hip fractures in Belgian men and women by age group is shown in Figure 1. The highest number of hip fractures was found in individuals in the population between ages 81 and 85 years, either men or women. More than one-half of hip fractures occurred at age >80 years, 50.3% in men and 65.6% in women. The incidence of hip fractures increases with age and follows the same pattern for men and women, with approximately a 5-year delay in men.

Between 2000 and 2007, the number of hip fractures increased by 20.4% in men and by 5.7% in women. The population age >50 years increased by 9.9% in men and by 8.3% in women. After standardization to the 2005 Belgian population, the age-adjusted incidence of hip fractures significantly decreased by 1.12% (95% CI −1.41%, −0.31%; $P < 0.0001$) per year in women, but nonsignificantly decreased by 0.34% (95% CI −0.88%, 0.25%; $P = 0.1983$) per year in men. According to age-specific analyses, a drop in fracture incidence in women was observed mainly among women ages >70 years and in particular among some age groups (66–70, 71–75, 76–80, and 91–95

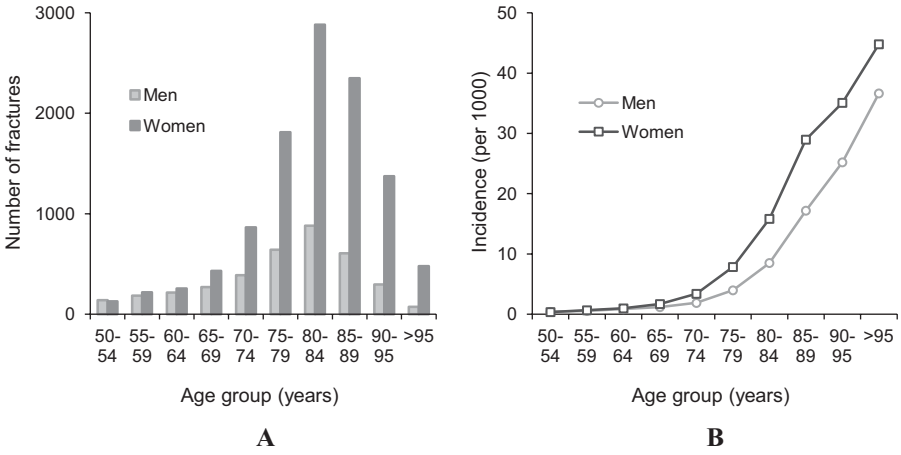

Figure 1. A, average yearly number of and **B,** incidence per 1,000 hip fractures in Belgian men and women by age groups.

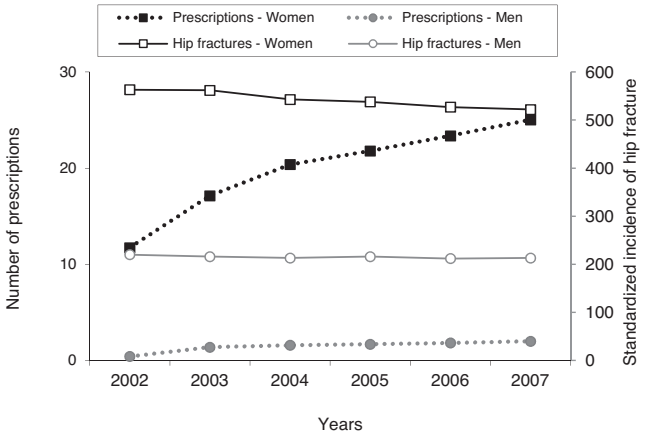

Figure 2. Age-standardized hip fracture incidence (per 1,000) and prescription of antiosteoporosis therapy (expressed in defined daily doses per patient) in Belgian women and men (ages ≥50 years) over a 6-year period (2002–2007).

years) with an annual decrease of at least 1.5%. In men, a decrease was observed in some particular groups (71–75, 76–80, and >95 years). The female:male ratio of hip fractures significantly decreased from 3.12 to 2.95 between 2000 and 2007 (linear trend, $P = 0.0041$).

The number of antiosteoporosis prescriptions substantially increased between 2002 and 2007 in Belgium (Figure 2). In women, a doubling of these medications was observed with a more marked increase (at least 200%) observed among elderly age groups (86–90, 91–95, and >95 years). Although there was an almost 4-fold increase in these medications among men, the actual numbers are very small compared with women. Approximately 65–70% of antiosteoporosis medications occurred in people between ages 61 and 80 years (Figure 3).

The Pearson's tests showed a significant negative correlation between the prescriptions of antiosteoporosis and age-standardized hip fracture incidence in the entire female population age >50 years ($r = -0.93$, $P = 0.0063$). According to age-specific analyses, a significant inverse relationship was found in some age groups of women (66–70, 71–75, 76–80, 81–85, and 86–90 years). When excluding raloxifene from the analysis, the Pearson's correlation coefficient between age-standardized hip fracture incidence and prescriptions of antiosteoporosis medications was estimated at −0.95 ($P = 0.0036$).

The number of fractures is expected to increase in the future (Table 2). By assuming the sex-specific secular change observed between 2000 and 2007 will be maintained, the total number of hip fractures from the year 2007 would increase by 18.5% by the year 2025, with a more marked increase in men (36.1%) than in women (12.3%). The female:male ratio of hip fractures would substantially decrease in the future, and was estimated at 2.37:1 in 2025. Hip fracture projections were highly sensitive to the secular changes of hip fracture incidence. For example, by the year 2025, the expected number of fractures was reduced by 6.7% or increased by 15.3%, assuming the lower and the upper bounds of the 95% CIs of the sex-specific changes observed between 2000 and 2007.

DISCUSSION

The findings of this study suggest a changing trend in the incidence of hip fractures in Belgian women. In contrast to a prior Belgian analysis (5) reporting a secular increase in the incidence of hip fractures between 1984 and 1996 (+2.1% per year), we found a significant decrease between 2000 and 2007 (−1.1% per year). Similar downward trends have been reported in other countries. A recent review by a scientific working group of the International Osteoporosis Foundation showed that in western populations (whether in North America, Europe, or Oceania), the rates of hip fracture incidence have reached a plateau or even decreased over the last 2 decades (13). For example, the age-adjusted incidence of hip fractures annually increased by 0.9% over the period 1985–1995 in US women and then decreased by 2.5% per year between 1996 and 2005 (11).

Understanding the reasons for the decline in hip fracture incidence may be useful to prevent hip fractures (13). Studies in other countries have suggested that this change may be related to the extent of use of antiosteoporosis

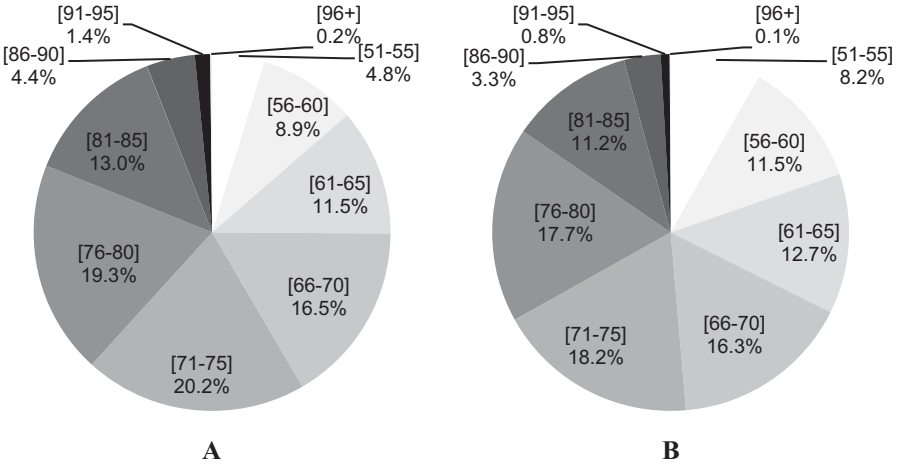

Figure 3. Distribution of antiosteoporosis medications (%) by age groups in **A,** Belgian women and **B,** Belgian men ages >50 years (2002–2007).

Table 2. Expected number and age-standardized incidence of hip fractures per 1,000 in Belgium until 2025 assuming sex-specific changes observed between 2000 and 2007 will be maintained in the future*

Year	Women		Men		Total no. of fractures (95% CI)	Total population, no. (19)
	No. of fractures (95% CI)	Incidence (95% CI)	No. of fractures (95% CI)	Incidence (95% CI)		
2010	11,347 (11,214, 11,723)	4.92 (4.87, 5.09)	4,031 (3,944, 4,127)	2.11 (2.07, 2.16)	15,378 (15,159, 15,851)	3,945,864
2015	11,906 (11,595, 12,813)	4.65 (4.53, 5.01)	4,492 (4,277, 4,737)	2.08 (1.98, 2.19)	16,398 (15,873, 17,550)	4,264,322
2020	12,127 (11,638, 13,594)	4.40 (4.22, 4.93)	4,810 (4,458, 5,225)	2.04 (1.89, 2.22)	16,937 (16,096, 18,819)	4,531,767
2025	12,285 (11,618, 14,344)	4.16 (3.93, 4.86)	5,184 (4,675, 5,799)	2.01 (1.81, 2.24)	17,469 (16,293, 20,144)	4,750,778

* Age-adjusted annual change between 2000 and 2007: women, −1.12% (95% confidence interval [95% CI] −1.41, −0.31) and men, −0.34 (95% CI −0.88, 0.25).

medications over the last 2 decades (15–17). In this study, we have observed a significant negative correlation between the increase in the prescriptions of medications and the decrease in the incidence of hip fractures observed in Belgian women. A causal relationship, however, cannot be ascertained because the 2 study findings are from 2 different databases and the use of osteoporosis medication is unknown among people who sustained fractures. It should also be noted that, despite an inverse correlation between hip fracture incidence and the number of prescriptions, the decrease in hip fracture incidence was modest in comparison with those observed in other countries (15,18).

In addition, other factors, such as concomitant changes in physical activity, dietary intake of calcium and vitamin D, or the implementation of prevention programs for falls, may contribute to or be responsible for the decrease in the age-adjusted incidence of hip fractures. Unfortunately, no national data are routinely collected on these parameters. An increased awareness of osteoporosis in the medical profession and the general population may also be a contributing factor. The age of starting therapy against osteoporosis might also be a critical issue, since if treatment is initiated in the very elderly, sarcopenia and frailty may be major determinants for falls, a well-accepted risk factor for hip fracture. In the risedronate Hip Intervention Program study, although the primary outcome (hip fracture reduction) was achieved in the overall population, the effect was mainly driven by the population age 70–79 years with low bone mineral density (BMD). Patients ages >80 years, selected on the presence of risk factors for falls and not specifically on low BMD or prevalent fractures, were not affected by the treatment. In the present study, we should therefore acknowledge that osteoporosis medications can only act in patients presenting with quantitative and/or qualitative disorders of bone and not on falls by themselves.

In men, despite the increase in the use of antiosteoporosis medications, the incidence of hip fractures did not significantly decrease. This result is also consistent with other reports (12,13). The use of antiosteoporosis medications, however, remained limited in the male population, and their recent introduction and/or their inappropriate use may also explain the current limited impact on incidence rates.

Our analysis also suggests that, even if the decreasing trend continues in the future, the number of hip fractures is expected to substantially increase in Belgium. Consequently, efforts should be pursued and more efficient preventive measures should be adopted. Actual treatment for osteoporosis is far from optimal, and further reductions in age-adjusted incidence can be expected. Indeed, only a small proportion of patients receive therapy after a fracture (20), and persistence and compliance with osteoporosis medications remain poor and suboptimal (21). More than one-half of the potential clinical benefits from oral bisphosphonates in patients with osteoporosis have been shown to be lost due to poor adherence with treatment (22). On the other hand, changes in patient identification may result in better identification and subsequent management of individuals at high fracture risk. It has been increasingly suggested that treatment should be based on absolute fracture risk rather than on the BMD threshold (23). Many agencies have adopted a low BMD as one of the criteria for treatment based on the operational definition of osteoporosis (BMD T score below −2.5) (23). Although low BMD is a major risk factor for fractures (24), most fractures occur in patients with a BMD T score above the operational threshold for osteoporosis (25,26). Recent developments in fracture risk assessment, including the FRAX tool, which estimates the 10-year probability of fracture (27,28), may certainly improve identification of patients at an increased risk of fractures and therefore further decrease the age-adjusted incidence. In addition, numerous studies have shown that a prior fracture greatly increases the risk for future fractures (29–31), whereas a male patient post–hip fracture has a 60% risk of future fracture within the next 4 years (32,33). This suggests the importance of developing secondary prevention of osteoporotic fractures.

We also would like to emphasize that, even if less common than in women, hip fractures in men should not be underestimated and will become a major burden. The female:male ratio significantly decreased between 2000 and 2007 and is expected to further decrease in the future. This is important for decision makers, especially since mortality excess (2) and fracture costs (34) have been shown to be higher in men than in women.

One strength of this study was its reliance on accurate national data for hip fractures and utilization of antiosteoporosis drugs. However, information on other factors that could be involved in the reduction of hip fractures such as lifestyle changes was not available. Moreover, we were unable to know whether a patient experienced a first or

subsequent hip fracture. A further reduction in the likelihood of a recurrent hip fracture among survivors of the first fracture has been suggested (35). Another potential source of inaccuracy is the use of a national hospital database to estimate hip fracture incidence. We could not check the diagnosis of hip fractures directly in the patients' files. The accuracy of the database, however, was studied and demonstrated in a representative random sample of 2.5% of all persons covered by the compulsory health insurance.

It is also a limitation of the present study that hormone replacement therapy (HRT) was not accounted for in our study as an osteoporosis medication because of the pleiotropic actions of substitution therapy in elderly women. Although HRT is no longer considered as a first-line treatment for osteoporosis, in postmenopausal women without climacteric symptoms, it is well recognized that HRT has a protective effect on fracture risk (36), with variation in the efficacy according to risk factors (37,38). One cannot rule out that part of the reduction in fracture incidence observed in women is related to the widespread use of estrogens, particularly before the publication of the Women's Health Initiative study. This might, at least partially, explain why fractures in men were not decreased to a similar extent as in women, whereas a 4-fold increase in antiosteoporosis medications among men was recorded during the study. In some countries, however, a modest decline has been observed in the prescription of HRT in postmenopausal women (39,40) that may therefore not explain the reversal in age-adjusted incidence observed in women. On the other hand, the use of vitamin D and calcium supplements is unknown. Low vitamin D and calcium are risk factors for osteoporosis, and supplementations may reduce the risk of hip fractures (41,42). We also acknowledged that projections should be interpreted with caution and showed that any projections are sensitive to secular trends in fracture incidence rates. In a prior Belgian analysis (5), 20,000 hip fractures were estimated for 2007, whereas approximately 15,000 occurred effectively with the changing trend in hip fracture incidence.

In conclusion, despite an increase in the number of hip fractures in Belgium between 2000 and 2007, there was a significant decrease in the age-adjusted incidence in women but not in men. Although our results suggest that the decrease may be related to the extent of antiosteoporosis medications, the factors responsible for this decrease remain largely unknown. Optimizing patient selection and patient compliance as well as developing secondary prevention programs may certainly contribute to further decreasing the age-adjusted incidence of hip fractures.

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AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be published. Dr. Hiligsmann had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Study conception and design. Hiligsmann, Bruyère, Reginster.
Acquisition of data. Hiligsmann, Roberfroid, Dubois, Parmentier, Carton, Gillet.
Analysis and interpretation of data. Hiligsmann, Bruyère, Roberfroid, Detilleux, Reginster.

ROLE OF THE STUDY SPONSOR

Servier had no role in the study design; in the collection, analysis, and interpretation of data; in the writing of the report; and in the decision to submit the article for publication. Publication of this article was not contingent on the approval of Servier.

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