

# Pharmacological treatment of hip fractured patients in Italy: a simulation based on Tuscany regional database for the TARGET project

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## Summary

**Background:** Italy is the Country with the highest life expectancy in the world, and over 75,000 elderly people experience a hip fracture each year.

**Objective:** following the Tuscany TARGET protocol, we aimed to estimate the costs of pharmacological treatment in the hypothesis of treating all elderly Italian people with hip fractures.

**Methods:** we analyzed the Tuscany healthcare system databases at the beginning of the Tuscany TARGET project for the prevention of hip fractures in elderly patients, and the Italian national hospitalizations records and DRGs databases concerning hip fractures occurred between 2000 and 2005.

**Results:** costs sustained for pharmacological treatments effective in reducing the risk of subsequent hip fractures all over Italy would account for 17.5 million Euros, representing only 0.18% of the overall national pharmaceuticals expenditures, while the national healthcare service is currently spending more than 30% of the overall pharmaceuticals expenditures in providing cardiovascular-active drugs.

**Conclusions:** The burden of hip fractures in the Italian elderly population is substantial and must be acknowledged as an important health problem. Specific preventive strategies, such as the Tuscany TARGET project should be implemented in all Italian regions.

**KEY WORDS:** hip fractures; osteoporosis; incidence; costs; treatment; compliance.

## Introduction

Osteoporosis is a common skeletal disease in older populations, causing millions fractures annually in the United States (1) and Europe (2). Non vertebral fractures represent 75% of osteoporotic fractures seen in clinical practice (3). The incidence of non vertebral fractures, especially at the hip, increases rapidly with age (4). Fractures are a burden to society; in terms of costs, morbidity and mortality. In order to prevent these fractures, clinical guidelines recommend that candidates for osteoporosis therapy should be identified by screening the bone mineral density of all woman ages 65 and over (or earlier in case of high risk populations), in order to plan proper treatment strategies (5). Italy has one of the highest life expectancies in the world: according to the Italian National Institute for Statistics (ISTAT), life expectancy at birth increased at a rate of 4 months per year from 1950 to 2005, reaching 77.8 years for men and 86.9 years for women (6,7), but it is estimated to rise up to 78.4 and 87.4 years, respectively, by 2010 (6,7). In Italy, 20% of the population is actually over 65 years of age (6); within the next decade, this age group may exceed 22% of the population (8). Moreover, 4% of this group is already  $\geq 80$  years of age (6). For these reasons, Italy represents an interesting international case study for determining social and economic burden of aging-related diseases, because of the increasing weight of older age groups within the general population (resulting in the inversion of the age pyramid), which is a general phenomenon observed in all industrialized countries. Therefore, observations made in Italy in terms of osteoporosis prevalence and adoption of proper treatment strategies could be relevant for many other industrialized countries currently facing similar problems of ageing of their population. Increased life expectancy is associated with a greater frailty of elderly people and a higher prevalence of chronic and degenerative diseases. Osteoporosis and its complications - especially hip fractures - represent a challenge for health professionals and decision makers in the 21<sup>st</sup> century. The World Health Organization (WHO) considers osteoporosis to be second only to cardiovascular diseases as a critical health problem (9), and particularly in Italy the incidence and costs of hip fractures are already comparable to those of acute myocardial infarction (10). Furthermore, it must be always kept in mind that hip fractures have a 5% acute mortality rate and a 15–25% 1 year-mortality (11,12). Once hip fracture has occurred, the ability to walk is completely lost in 20% of cases, and only 30–40% of patients recover a degree of autonomy comparable to the period before the fracture (13–16). The main Epidemiological Study on the Prevalence of Osteoporosis in Italy (ESOPO) reported a high prevalence of osteoporosis: 23% among all women, with age-specific rates ranging from 9% (40 to 49 year olds) to 45% (70 to 79 year olds), and almost 15% in men aged  $\geq 60$  years (15, 16). According to these percentages, about 4 million of Italian women and 800 thousand men are thought to be affected by osteoporosis (7), while it is known that osteoporosis is a condition that enhances the risk of fracture, including hip fractures (17). Furthermore, one fifth of fractured patients will experience another hip fracture within few years, accounting for 20% of hip fractures costs (actually 200 millions €/year in Italy). Despite that, only a minority starts any treatment, and a relevant size of patients stops therapy within 2-3 months (18). In 2002, the conclusions of the official Senate inquiry on osteopo-

rosis encouraged the adoption of specific preventive strategies at regional level, to be implemented through institutional programs involving health authorities and the scientific community. Tuscany Region has designed a specific project (named TARGET: Appropriate Treatment of Geriatric Refractures in Tuscany) with the aim of ensuring adequate treatment to people aged  $\geq 65$  years old who experienced a hip fragility fracture in Tuscany region. TARGET project represents the first Italian program involving regional health authorities aimed to reduce the incidence of hip fragility fractures. This paper is aimed to provide preliminary evaluations and pharmaco-economic assessments fostering the start-up phase of the Tuscany regional TARGET project.

## Methods

We analyzed hospital discharge records, which are collected both at regional level and at the Italian Ministry of Health (national hospitalization database, SDO). These information are anonymous and include patient's age, diagnosis, procedures performed, and length of the hospitalization. The present manuscript focuses on the number of patients hospitalized because of hip fracture in Italy and subsequently treated with any antifracture drug during the years 2000 through 2005. First of all, we analyzed Tuscany regional databases and the national hospitalization database (SDO) in order to determine the number of hospitalizations due to hip fractures in the Italian and in Tuscany population aged  $\geq 65$  years. Population data were obtained from the National Institute for Statistics (ISTAT) for each of the considered years (1). Hip fractures were defined by the following ICD-9CM diagnosis codes (major diagnosis): 820.0–820.1 (femoral neck fractures), 820.2–820.3 (peritrochanteric femoral fractures) and 820.8, 820.9 and 821.1 (other femoral fractures). Data were stratified by gender and into three age groups (65–74 and  $\geq 75$  years) and were processed using Stata (StataCorp, College Station, USA) and Excel (Microsoft, Redmond, USA) softwares. Hip fractures in patients aged 45 to 64 represented about 8% of all fractures and were excluded from the analysis as conservatively considered as unlikely to be osteoporotic. We performed descriptive statistical analyses of the incidence in each gender and age subgroup across the 6 examined years. After having determined the number of hospitalizations due to hip fractures, we considered about 20% of these admissions as rehabilitation records of the same patients (8). Furthermore, we had to take into account a 5% acute mortality rate (within the first month) (8). We have preliminarily computed the number of hip fractured patients aged  $\geq 65$  and treated with any antifracture drug after the discharge from the hospital. Therefore, we have analyzed the Re-

gional Tuscany databases (hospital discharges records and pharmaceutical prescriptions records) in the latest available period (2005-2007) in order to calculate the incidence of hip fractures in people aged over 65 years old (both male and females) and medical prescriptions concerning those patients within one year after the fracture (18). We have used major diagnosis codes ICD9-CM 733.14, 733.15, 820 (all extensions), 821 (all extensions), 829 (all extensions). According to that, we have assumed that a proper antifracture therapy has been prescribed only to 13.1% (referring to the highest rate of the regional analysis) (18) of hip fractured patients all over Italy, in order to perform a national pharmaco-economic simulation concerning the treatment of severe osteoporosis, which is actually the condition leading to femoral fractures in elderly people. In order to be more conservative and to overcome possible inter-regional discrepancies, we have decided not to drop the 13.1% rate across the 6 years examined, although the analysis of Tuscany regional database had shown a 1.1% decrease across 3 years. Persistence on treatment at 1 year was found to be  $< 40\%$ . According to that, we assumed that only 40% of hip fractured patients in Italy have continued their therapy for 1 year, with 60% of them remaining on treatment just 6 months. The average cost considered for an antifracture therapy with bisphosphonates for 1 year has been computed in 250 Euros per patient, including supplementation with calcium and vitamin D, although some drugs could result in less expensive annual costs.

## Results

In Tuscany, almost 7,000 elderly patients were found to have experienced a hip fracture per each considered year, with expected direct costs being estimated in about 95 million euros. Annual costs sustained by the Italian healthcare system for treating hip fractured patients all over Italy has been estimated in 1 280 300 in year 2000, 1 365 000 in 2001, 1 407 875 in 2002, 1 564 400 in 2003, 1 581 125 in 2004, 1 645 875 in year 2005 (Table 1). The increasing costs are due just to the growing number of hip fractured patients. Sixty percent of these estimated costs can be considered as ineffective from a therapeutic point of view because patients were assuming their drug only for 6 months. Table 1 also shows the estimated number of hip fractured patients aged over 65 years old ranging from 58794 to 75577 between years 2000 and 2005, with an increase of 22.2% across six years. Table 2 shows the overall costs sustained for hospitalizations, rehabilitation and pharmacological treatment following hip fractures in people aged  $\geq 65$  years old, from year 2000 to 2005 as reported in previous Italian national studies (19, 20), including costs of phar-

Table 1 - Direct costs sustained for hospitalizations and rehabilitation following hip fractures in people aged  $\geq 65$  years old, from year 2000 to 2005.

	Patients (n) & costs (€) Year 2000	Patients (n) & costs (€) Year 2001	Patients (n) & costs (€) Year 2002	Patients (n) & costs (€) Year 2003	Patients (n) & costs (€) Year 2004	Patients (n) & costs (€) Year 2005
Hospitalizations due to hip fractures $>65$	73 493	78 354	80 804	89 796	90 753	94 471
Expected hip fractured patients $>65$ (no.)	58 794	62 683	64 643	71 837	72 602	75 577
<i>Pts (no.) discharged from the hospital*</i>	55 854	59 549	61 411	68 245	68 972	71 798
Patients starting any antifracture therapy	7 316	7 800	8 045	8 940	9 035	9 405
Costs of the therapies (euros) <sup>^</sup>	1,280,300	1,365,000	1,407,875	1,564,500	1,581,125	1,645,875

\* Assuming 5% acute mortality rate

<sup>^</sup> Assuming only 40% of treated patients to complete 1 year of treatment

Table 2 - Direct costs sustained for hospitalizations, rehabilitation and pharmacological treatment following hip fractures in people aged  $\geq 65$  years old, from year 2000 to 2005.

	Year 2000	Year 2001	Year 2002	Year 2003	Year 2004	Year 2005
Hospitalizations due to hip fractures	73 493	78 354	80 804	89 796	90 753	94 471
Expected hip fractured patients >65	58 794	62 683	64 643	71 837	72 602	75 577
Overall hospitalizations direct costs	343,000,000	373,000,000	394,000,000	433,000,000	448,000,000	467,500,000
Overall rehabilitation costs €	392,876,272	418,852,367	431,970,539	480,005,732	485,140,236	531,986,400
Costs of the therapies € <sup>^</sup>	1,280,300	1,365,000	1,407,875	1,564,500	1,581,125	1,645,875
<b>Total estimated costs €</b>	<b>738,436,872</b>	<b>794,582,367</b>	<b>828,786,289</b>	<b>916,134,732</b>	<b>936,302,486</b>	<b>1,002,778,150</b>

<sup>^</sup> Assuming only 40% of treated patients to complete 1 year of treatment

Table 3 - Simulation of pharmacological costs in the hypothesis of treating all hip fractured patients for 1 year with optimal compliance (100%).

	Year 2000	Year 2001	Year 2002	Year 2003	Year 2004	Year 2005
Hospitalizations due to hip fractures >65	73 493	78 354	80 804	89 796	90 753	94 471
Expected hip fractured patients >65 (no.)	58 794	62 683	64 643	71 837	72 602	75 577
Pts (no.) discharged from the hospital*	55 854	59 549	61 411	68 245	68 972	71 798
<b>Costs of the therapies (Euros)<sup>^</sup></b>	<b>13,963,500</b>	<b>14,887,250</b>	<b>15,352,750</b>	<b>17,061,250</b>	<b>17,243,000</b>	<b>17,949,500</b>

\* Assuming 5% acute mortality rate

<sup>^</sup> Assuming 100% of treated patients to complete 1 year of treatment

macological treatments as resulted from our analysis. According to that, costs of hip fractures in Italy have reached 1 billion Euros in year 2005. As shown in Table 2, costs sustained for pharmacological treatments effective in reducing the risk of subsequent hip fractures represent 0.3% of the overall costs related to hip fractures in Italy. Table 3 simulates the hypothesis of having treated with antifracture therapies for 1 year all the hip fractured patients in Italy. In this case, costs sustained for antifracture drugs would rise from about 13.9 (year 2000) to 17.9 (year 2005) million Euros across six years, thus accounting only for 1.8% of the overall yearly direct costs sustained for hip fractures occurring in Italy, and corresponding just to 0.18% of the overall national pharmaceutical expenditures.

Osteoporosis-related hip fractures do not only lead to high medical care costs but also to high rehabilitation costs, which represent more than 50% of total costs in our analyses. Other authors have also reported rehabilitation costs as the most important cost category accounting for 66% of the total annual costs, followed by medical care costs (31%), informal care (2%) and indirect costs (1%) (21). It must be pointed out that the treatment would result not only in expenditures, but would reduce the number of subsequent hip, vertebral and other non vertebral fractures suffered from the same patients. Therefore, costs sustained for drugs are expected to produce a reduction of direct and indirect costs associated with fractures which would occur without treatment. Furthermore, the entire hip fractured population should have been treated with antifracture drugs as stated by the Italian Pharmaceutical Agency.

## Discussion

Although in Italy is not currently available a codification for osteoporotic fragility fractures, the fact that more than 90% of hip fractures occurred among people aged >65 were actually suffered from people aged >75 years old (mainly women >75 with a rate of 82%) seems to prove the osteoporotic nature of these fractures. On the other hand, the 22.2% increase of hip fractured patients number between 2000 and 2005 strongly confirms the need for ensuring

proper pharmacological treatments to this population, which has the highest risk of subsequent fragility fractures. However, this objective can be achieved only by starting specific projects at regional level. There is also the need for a specific codification of osteoporotic fragility fractures at hospital admissions. As resulted from database analysis, 7,000 hip fractures in people aged >65 in Tuscany resulted in almost 10 million Euros expenditures (costs sustained by the Regional Healthcare System), and should be regarded as fragility fractures since they occurred most frequently in women aged >75 years old, the age group where the prevalence of osteoporosis is known to be higher. One out 5 patient suffers a new hip fracture during the following 4 years after the first event, thus presenting a higher disability and mortality risk. Nevertheless, in Tuscany the number of elderly hip fractured patients being treated with a drug effective in reducing the risk of fracture declined from 13.1% to 12.0% between 2005 and 2007 (18). Average Medication Possession Rate (MPR) was found to be 27%. According to the Tuscany Regional databases, 77.9% of hip fractured patients had a Medication Possession Ratio (MPR) <50% vs. 55% of the general population on treatment (just because of osteoporosis) (18). Only 2.0% of hip fractured patients had MPR >90% (which is required to maximize risk fracture reduction) vs. 18.6% of treated patients in the general population (all people assuming antiresorptive agents), thus meaning that patients who most need to be properly treated (i.e. elderly hip fractured people) are currently mistreated. To be noticed that ¼ of the costs sustained to treat the general population (approx. 55 millions €/year all over Italy) are wasted in providing very short treatment courses that unlikely reduce fracture risk (18). Given the need of ensuring a proper antifracture treatment to elderly hip fractured patients, and stopping short treatment courses, Regional databases would help for early identification of fractured patients showing low adherence to therapies, or identification of patients withdrawing their therapy before completing one year of treatment. Regional Healthcare System database allow us to follow the patient from the hospital admission following hip fracture to the discharge from orthopaedic division. Furthermore, it is possible to follow the medical prescriptions provided to individual patients, in order to be sure that hip fractured elderly people receive a proper therapy after leaving

the hospital. On these basis, University of Florence, University of Siena and Tuscany Region have developed the TARGET project, which is aimed to reduce the number of hip refractures in elderly patients by enrolling all people aged  $\geq 65$  years old who suffer a hip fracture in Tuscany and providing them with a long term anti-fracture treatment within 60 days. Orthopaedic surgeons are requested to cooperate with other specialists and GPs in order to get a complete clinical evaluation of the patient, and define the most appropriate treatment course for each individual patient. The aim of the project is to define a structured path where hip fractured patients aged  $\geq 65$  will automatically enter just because they are hospitalized. Regional databases will allow to register the fracture event of each individual patient almost in real time (all hospital records are sent to the Regional Healthcare Authority within few days after the hospital discharge). These institutional database will also allow us to know if the hip fractured patient has started any anti-fracture therapy: actually hip fractured patients have access to medications reimbursed from the Regional Healthcare Authority, who is able to follow the treatment compliance of each patient. The analysis of regional databases would help for early identification of fractured patients with low adherence to therapies. Databases will also record any other fracture events (both hip and non hip fractures) occurring in the same patient during the following years. The project has a 4-years prospective phase from 2010 to 2013 and a retrospective control period (from 2006 to 2009). Since the project is expected to decrease the number of hip re-fractures, reductions of fractures incidence and costs sustained from the healthcare system will be compared and analyzed. The TARGET patients database will also be integrated in the National registry of fragility fractures. Actually, Italian Ministry of Health has recognized the need for a specific codification of osteoporotic fragility fractures at hospital admissions, with Tuscany being involved as pilot Region in building up a National Registry of fragility fractures.

## Conclusion

Our simulation concerning the treatment of the overall hip fractured population has shown that costs sustained for pharmacological treatments effective in reducing the risk of subsequent hip fractures would account for just 0.18% of the overall national pharmaceutical expenditures, which is a very low rate if compared with the expenditures sustained by the national healthcare service for cardiovascular-active drugs, actually representing more than 30% of the overall pharmaceutical expenditures. In this perspective, preventive strategies should be carried out through specific regional programs, such as the Tuscany TARGET project, as stated in 2002 by the Italian Senate Commission during the official inquiry on osteoporosis.

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