

# Antifracture drugs consumption in Tuscany Region before the Target Project: a valuable model for the analysis of administrative database

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## Summary

**Objectives.** As the Target Project of Tuscany Region is aimed to identify significant changes occurring during the time of the project compared to the previous years, we have analyzed antifracture drugs consumption in the years immediately preceding the start-up of the program. **Methods.** We have analyzed the regional administrative database to search for antifracture drugs delivered by the regional healthcare system to people living in Tuscany in the year 2009. Both drugs directly distributed by hospitals or local health authorities (direct distribution dataset, FED), and those delivered through pharmacies (pharmaceutical distribution dataset, SPF) were included in the analysis. Private expenditures were indirectly computed because total pharmaceutical expenditures were also known. A specific subgroup analysis has been carried out on elderly patients with femoral fractures (years 2006-2010), which represent the population of Target Project, in order to assess the evolution of all antifracture drug prescriptions before the start up of the project. **Results.** A total of 690,768 boxes of antifracture drugs (20 million defined daily doses, DDD) have been delivered in year 2009 for total expenditures of 23 million Euros. Public expenditures accounted for 71% of the total (16 million; 6% of regional pharmaceutical expenditures). Alendronate and risedronate were the most used drugs. The number of antifracture medications prescribed within the first 90 days to elderly people with hip fractures increased in the period before the start-up of the Target project but they remained under 14%. **Conclusions.** There is the need for an appropriate management of antifracture therapies, as they represent a valuable proportion of pharmaceutical expenditures. This need is pointed out also by the remarkable amount of direct private expenditures and by the few number of hip fractured people starting a treatment.

**KEY WORDS:** osteoporosis; antifracture drugs; public expenditures; private expenditures.

## Introduction

Life expectancy has remarkably increased in Italy from 1950 to 2005, reaching 78.4 years for men and 87.4 years for women, respectively (1, 2). However, this means that an increasing number of people will suffer from chronic and degenerative diseases, such as osteoporosis, which is considered by the World Health Organization (WHO) to be second only to cardiovascular diseases as a critical health problem (3). The main Epidemiological Study on the Prevalence of Osteoporosis in Italy (ESOPO), carried out in year 2000 on 16,000 subjects, reported a high prevalence of osteoporosis (Tables 1-3): 23% among all women, with age-specific rates ranging from 9% (40 to 49 year olds) up to 45% (70 to 79 or older), and almost 15% in men aged  $\geq 60$  years (4-5). According to these prevalence rates, about 4.5 million of Italian women and 1 million men are thought to be affected by osteoporosis (2). However, it must be taken into account that the ESOPO study was conducted by using QUS (Quantitative Ultra-Sounds) measurements and not DEXA (Dual Energy X-rays Absorbiometry), the gold standard tool in the diagnosis of osteoporosis (5-7). Our previous analyses have already shown that osteoporosis has a social relevance in Italy because of dramatic costs of hip fractures and the incidence of other fractures in different skeletal sites (8-16). This has been the starting point for the Target Project of Tuscany region (Appropriate Treatment of GERiatric Refractures in Tuscany), aimed to reduce the number of elderly people experiencing a hip fragility fracture, by providing them with the most appropriate antifracture treatment (considering time to prescription and patients' compliance as very important variables in the choice of the therapy). As the Target project needs to identify significant changes occurring during the time of the project compared to the previous years, we have analyzed antifracture drugs consumption (all drugs included within the Note 79 of the National Agency for Drugs, AIFA) in the year immediately preceding the start-up of the program thanks to the availability of institutional administrative datasets.

## Methods

We have analyzed all antifracture drug prescriptions (those included in the AIFA note 79) anonymously recorded in Tuscany regional pharmaceutical database in the years immediately preceding the start up of the Target project. We have included in the analysis both the drugs directly distributed by hospitals or local health authorities (direct distribution dataset, FED), and those delivered through pharmacies (pharmaceutical distribution dataset, SPF). The sample size consisted in all subjects (any age group) living in Tuscany who had at least one antifracture prescription, corresponding to almost 93,000 people in 2009 and over (males about 10% and females about 90%) for a total of 58,464,876 days of therapy. The analysis was carried out by considering defined daily dose (DDD), number of boxes, public and private expenditures for each drug. The analyzed antifracture therapies included: alendronic acid, alendronate plus vitamin D (colecalfiferol), risedronate, ibandronate, clodronate, neridronate, zolendronate, strontium ranelate, teriparatide, parathyroid hormone, and raloxifene. Neridronate has been included in the analysis, as it is used in Tuscany off-label for the treatment of osteoporosis. A specific subgroup analysis has

Table 1 - Prevalence % of osteopenia and osteoporosis per age groups according to the ESOP study (women).

Age Group	Normal	Osteopenia	Osteoporosis
40-49	52.8	37.8	9.4
50-59	40.0	44.2	15.8
60-69	23.0	44.8	32.1
70-79	14.0	40.3	45.7
Overall women	34.9	42.3	22.8

Table 2 - Prevalence % of osteopenia and osteoporosis per age groups according to the ESOP study (men).

Age Group	Normal	Osteopenia	Osteoporosis
60-64	53.9	34.3	11.8
65-69	50.8	35.1	14.1
70-74	47.9	34.3	17.9
75-79	48.7	33.0	18.3
Overall men	51.2	34.3	14.5

Table 3 - Number of people thought to be affected by osteoporosis in Italy per age group according to the ESOP study prevalence rates.

Age Group	Women	Men
40-49	363,400	NA
50-59	581,000	NA
60-69	1,093,000	386,350
70-79	1,260,300	340,750
80-100	1,311,700	256,080
Total	4,609,000	983,180

been carried out for years 2006-2010 on the patients with femoral fractures, which represent the population of Target Project, in order to assess the evolution of all antifracture drug prescriptions before the start up of the project.

## Results

A total of 690,768 boxes of antifracture drugs (DDD: 20 million) has been delivered in year 2009 to people living in Tuscany for total expenditures of 23,254,945 Euros (Tables 4-5). The regional healthcare system has paid for a total of 471,170 boxes (Table 6). Costs sustained by Tuscany Region for antifracture drugs were 16,553,153 Euros (71.2% of total expenditures), corresponding to 2.6% of total regional expenditures (620 million Euros). About 6.7 million Euros are paid directly by citizens to buy the prescribed medications. Among antifracture drugs, bisphosphonates represent 75% of all expenditures for this class of medications (included in AIFA Note 79), thus corresponding to 12 out of 16 million Euros. The majority of drug prescriptions (85%) was provided to people aged 60 to 90 years old. As showed in Table 4 and Table 5, alendronate was the most used antifracture drug (7 million DDD, 253,869 boxes or 36.8% of total prescriptions), followed by risendronate (4.7 million DDD, 170,423 boxes or 24.7% of prescriptions), and alendronate combined with vitamin D (3.4 million DDD, 122,531 boxes or 17.7% of prescriptions). Strontium ranelate and ibandronate accounted each one for 9.4% of prescriptions, with about 64,500 boxes sold (1.8 million DDD). If considering only patients with femoral fractures, which is specifically the population of Target Project, data concerning the years immediately preceding the start up of the project, elderly people provided with a proper antifracture therapy within 90 days from hospital discharge passed from 6.8 to 14.5% between 2006 and 2010 (Figure 1). This rate passed from 12.5% to 21.3% at one year, thus leaving the majority of hip fractured people without an adequate protection against the risk of refracture.

## Discussion

Tuscany has been the first Region to design and implement a specific project – known as Target project (Appropriate Treatment of Geriatric Refractures in Tuscany) – with the aim of reducing osteoporotic fractures by ensuring adequate treatment to all people aged ≥65 years old who experience a hip fragility fracture. The project has a 4-year prospective phase (2011-2014 with 2010 being considered as a start up year) and a retrospective control period (from 2006 to 2009). Since the project is expected to decrease the

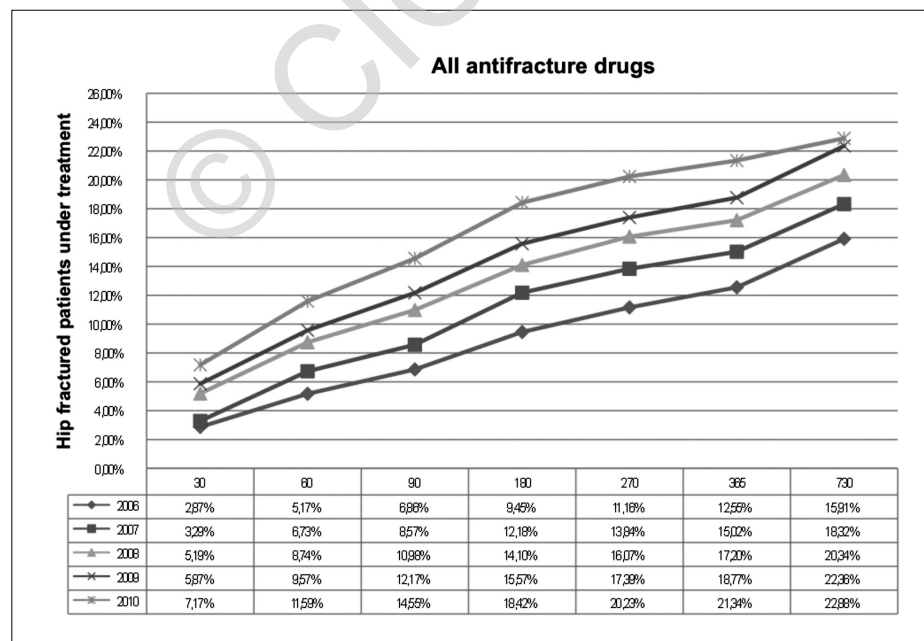


Figure 1 - Proportion of hip fractured elderly people receiving any antifracture therapy at 30, 60, 90, 180, 270, 365, and 730 days from hospital discharge (2006-2010).

Table 4 - Number of boxes and expenditures (public and private) per each antifracture drug in Tuscany (year 2009).

Medication	No. of boxes		Total expenditures (Euros)		Private expenditures (Euros)	
<b>Total</b>	690,768	100.0%	23,254,945	100.0%	6,701,792	100.0%
Risedronate	170,423	24.7%	6,223,303	26.8%	1,664,778	24.8%
Alendronate	253,869	36.8%	5,617,318	24.2%	2,055,267	30.7%
Strontium ranelate	64,364	9.3%	3,279,990	14.1%	778,975	11.6%
Alendronate+cholecalciferol	122,531	17.7%	3,101,260	13.3%	1,001,846	14.9%
Ibandronate	64,627	9.4%	2,824,200	12.1%	891,742	13.3%
Teriparatide	2,522	0.4%	1,439,331	6.2%	49,081	0.7%
Parathyroid Hormone	788	0.1%	394,370	1.7%	21,019	0.3%
Raloxifen	11,644	1.7%	375,175	1.6%	239,084	3.6%

Table 5 - Drug consumption (defined daily doses, DDDs) in Tuscany (year 2009).

Medication	DDDs	%
<b>Antiresorptive drugs</b>		
Risedronate	4,771,844	23.91%
Alendronate	7,108,332	35.61%
Alendronate + cholecalciferol	3,430,868	17.19%
Ibandronate	1,809,556	9.07%
Raloxifen	326,032	1.63%
Etidronate	18,000	0.09%
Clodronate	14,553	0.07%
Zoledronate	83,950	0.42%
Neridronate	502,768	2.52%
<b>Bone forming drugs</b>		
Strontium ranelate	1,802,192	9.03%
Teriparatide	70,606	0.35%
Parathyroid Hormone	22,064	0.11%
<b>Total DDDs</b>	<b>19,960,765</b>	<b>100.00%</b>

number of hip re-fractures, reductions of fractures incidence and costs sustained by the healthcare system needs to be compared. While analyzing antifracture drugs consumption in the year immediately preceding the start-up of the program, we have found that private expenditures accounted for 28.8% of the total expenditures for antifracture drugs, but in terms of boxes citizens directly buy 31.5% of total medications. This finding is quite impressive, although it is lower than that reported at national level (50%) by the OSMED report of Ministry of health (17). Actually, a relevant proportion of medication is not provided by the Healthcare system, thus originating different questions about the appropriateness of prescription in a percentage of patients who are not included in the restrictions determined by the national agency for drugs (AIFA). It could be also possible that these restrictions do not allow the access to a reimbursed therapy to a proportion of patients who really would benefit from that. It is not surprising that alendronate is the first drug in terms of prescriptions and expenditures, as in 2009 alendronate was already available as generic. Overall, the total value of antifracture drugs in Tuscany do not exceed 6% of total pharmaceutical expenditures. We can better understand the weight of these drugs on total regional budget by considering that statins represent 9% of total pharmaceutical expenditures in Tuscany (accounting for 53 million Euros). Beside costs and boxes of drugs, the most critical issue remains the compliance to the therapy, which makes the difference between wasting public money or contributing to improve people's quality of life by reducing the risk of fracture. The sub-analysis on elderly pa-

Table 6 - Number of boxes and public expenditures sustained by the regional healthcare system per each antifracture drug in Tuscany (year 2009).

Medication	No. boxes	Public expenditures (Euros)	% on total expenditures
Total Tuscany	471,170	16,553,153	71.20
<b>Antiresorptive</b>			
Risedronate	124,873	4,558,525	73.24
Ibandronate	44,221	1,932,458	68.42
Alendronate	162,632	3,562,051	63.41
Alendronate+ cholecalciferol	82,948	2,099,414	67.69
Raloxifen	4,236	136,091	36.27
<b>Bone forming drugs</b>			
Teriparatide	2,436	1,390,250	96.59
Parathyroid Hormone	746	373,351	95.67
Strontium ranelate	49,078	2,501,015	76.25

tients with femoral fractures, which represent the population of Target Project, has also pointed out the need for appropriateness in the prescription of these drugs. Actually, it is unacceptable that people with fracture do not receive a treatment. Target project will show in the next years the results, in terms of efficacy and effectiveness (including a cost-benefit evaluation), of adopting a disease management approach to these patients at higher risk of fracture.

## Conclusion

There is the need for an appropriate management of antifracture therapies, as they represent a valuable proportion of pharmaceutical expenditures. Specific projects should be adopted at regional level, as suggested by the Italian Senate inquiry commission on osteoporosis in 2002.

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