The Economic and Social Burden of Osteoporosis in Developed Countries: Health Policy Considerations Based on a Literature Review

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Abstract

Osteoporosis is a chronic disease affecting mostly women of post-menopausal age and characterized by bone mass loss and skeletal micro-architecture alteration, all conditions that imply significant consequences in terms of both mortality and disability. Direct healthcare costs for hospitalization, outpatient treatment and nursing home admissions saddle governments with a significant burden, which is destined to increase with population aging. Evidence exists on cost-effectiveness of osteoporosis treatment in reducing the risk of refracture, with positive effects not only for healthcare expenditure, but also in terms of premature mortality, reduced quality of life and autonomy loss. With the help of relevant literature, this paper analyses the economic and social burden of osteoporosis and provides policy measures to both reduce the risk of fragility fractures among the elderly and diminish the economic load on societies.

Keywords: Osteoporosis; Burden of disease; Fragility fractures; Social costs; Population aging;

1. Introduction

Osteoporosis is a chronic disease affecting mostly women of post-menopausal age and characterized by bone mass loss and skeletal micro-architecture alteration, all conditions that increase the risk of fractures. Due to its asymptomatic progression, it is frequently diagnosed after the first fracture, which represents the clinical manifestation of the disease (1). The burden worldwide is quite intensive, with more than 200 million people suffering from this disease (2). In Europe, about 22 million women and 5.6 million men were diagnosed with osteoporosis in 2010 (3), whilst in Italy people affected by this chronic disease are 5 million, of whom 80% are women at post-menopausal age (4). The examined literature agrees that, if no measures are taken to reduce the risk of fractures for osteoporotic patients, population aging will increase the disease burden on national healthcare systems. To provide some approximations, in 2005 the direct medical costs of osteoporosis in the United States were estimated to be 17 billion dollars with an expected increase to 25.3 billion dollars for 2025 (5). A study including Germany, France, Italy, Spain, Sweden and the UK, evaluated a total of 30.7 US billion euros being spent in 2010 in these countries (6). In Italy the overall healthcare costs due to hip fractures rose by 30% from 2000 to 2014, with an estimate of 961.6 million euro in 2014 (7).

Fragility fractures[1] due to osteoporosis have significant consequences, in terms of both mortality and disability, with high healthcare and social costs. Femoral fracture mortality is 5% in the period immediately following the episode and 15-25% at one year. In 20% of cases there is a definitive loss of autonomous ambulation and only 30-40% of the subjects return to the conditions preceding the fracture (4). Autonomy loss, chronic pain and decreased quality of life can represent the beginning of an irreversible process that brings the patient to ask for an external help to face daily activities' limitations (9). Caregiving costs, which may be temporary or permanent, are often underestimated when evaluating the economic burden of osteoporosis (10). Nursing home costs are to be considered too, since evidence shows that about 20% of patients who survive a hip fracture are subsequently admitted to residential long-term care structures (7).

The aim of the study is to describe and analyze, with the help of relevant literature, the economic and social burden of osteoporosis.

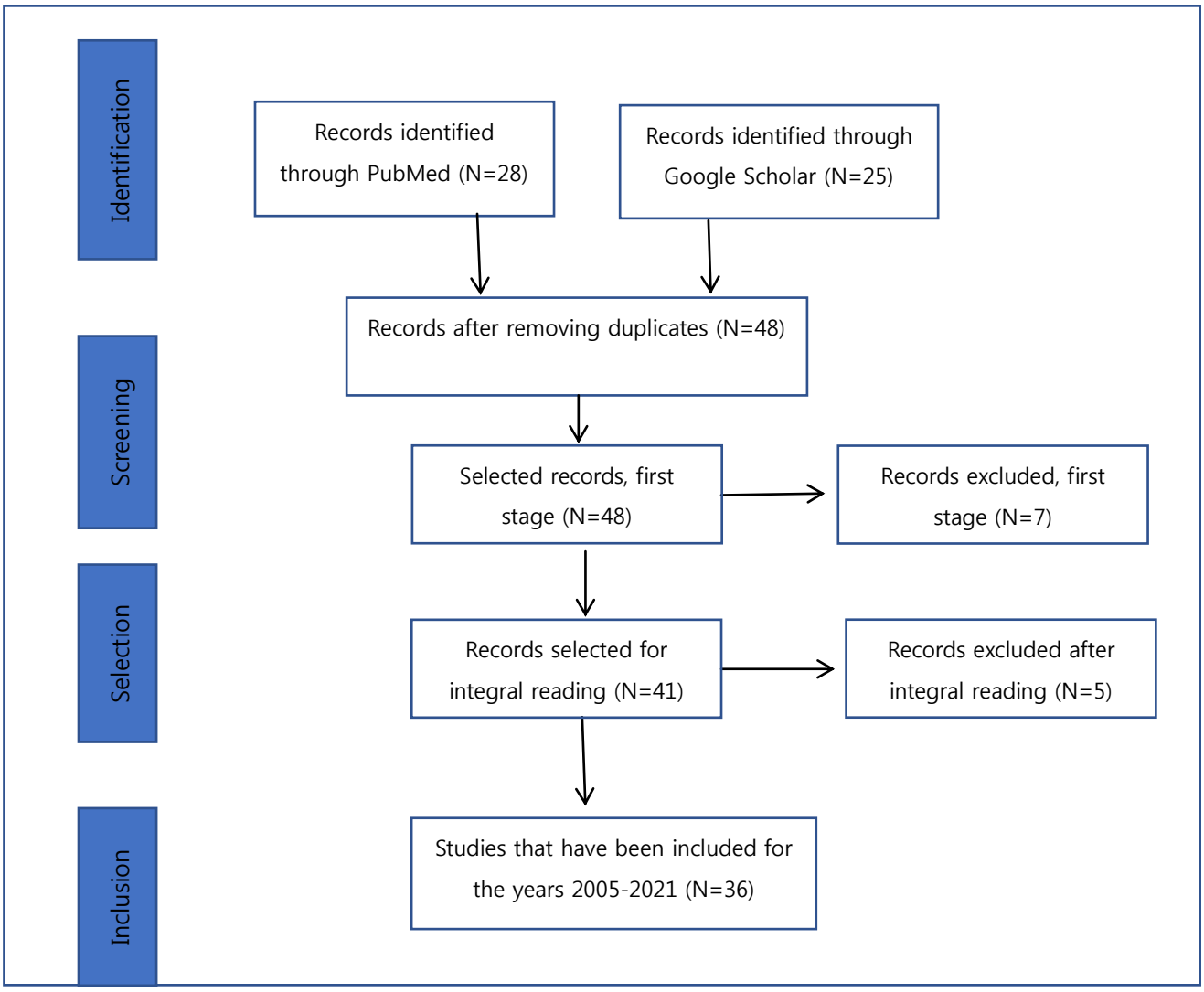
2. Materials and methods

The process of identification and selection of articles through PRISMA model (11) is reported in Figure 1.
The time span ranges from 2005 to 2020; the search on PubMed and Google Scholar employing search strings: "osteoporosis social costs", "osteoporosis economic burden", "osteoporosis cost- effectiveness", produced a high

[1]Defined by the World Health Organization (38) as "a fracture caused by an injury that would be insufficient to fracture a normal bone".

number of results. The first selection was made on title and abstract inspection, using as selecting criteria both the year of publication and the geographical location, with priority given to recently published studies and the exclusion of articles on developing countries: 28 papers were identified from PubMed and 25 from Google Scholar. After controlling for duplicates, the whole number of papers selected amounted to 48. Papers were subsequently screened according to their relevance to the main objective and using as privileging criteria the inclusion of articles showing strong empirical evidence: 7 articles were further excluded, and 41 articles remained for integral reading. After integral reading, only 36 articles were included in the final selection, because 5 of them did not add any relevant finding to the study.

Figure 1: PRISMA – Selection of articles for the years 2005-2020



3. Disease management: diagnosis, prevention, possible treatments

Fragility fractures represent the main clinical consequence of osteoporosis and often lead to a lower quality of life, loss of independence, greater premature mortality, and higher direct (e.g., hospitalization) and indirect (e.g., productivity loss and caregiving needs) costs (10,12,13).

Risk of refracture is very high in persons over 50 (14), therefore the need for an appropriate diagnosis and treatment across population is fundamental (7). Although General Practitioners (GPs) represent the first stage of care for their patients, their role in treating osteoporosis and reducing fragility fractures seems rather neglected in many countries. A recent study carried out in 8 European countries (Belgium, France, Germany, Ireland, Poland, Slovakia, Switzerland, and the UK) found that about 75% of elderly women visited in primary care who were at high risk of osteoporosis-related fractures were not receiving appropriate medication (15). This large treatment gap is mostly related to a low rate of osteoporosis diagnosis in routine primary care across Europe.

Another study from France reveals scarce awareness of osteoporosis among GPs (16); concern over the low level of knowledge on osteoporosis diagnosis and treatment is similarly expressed in a study on the Israeli population (17). The implementation of clinical guidelines on the disease management and treatment among GPs is considered a

valid tool to increase their involvement in contrasting negative effects of osteoporosis (18). Even in the absence of a fracture, around the age of 50, an assessment of risk factors (low body weight, early menopause, family history of osteoporosis, selected diseases and medications known to increase fracture risk) by the GPs could help in identifying the subjects at risk and initiating appropriate treatment (19).

At hospital level, a recent observational study on elderly Swiss patients (N=252) admitted to rehabilitation shows that 62.3% were lacking an appropriate diagnosis of osteoporosis. The mean age was 83.0 ± 6.5 years. 71.5% of the women were undiagnosed versus 44.8% of the men. Osteoporosis was identified through dual-energy X-ray absorptiometry (DXA), vertebral fracture assessment (VFA), and a history review of past fractures. Conclusions suggest that there might be a large share of elderly people who are undiagnosed. In order to prevent fragility fractures and higher healthcare costs, the combination of a history review of previous fractures with DXA in women and with VFA in men is recommended (20). Similar advice is offered by a retrospective study that examined 478 patients (424 W and 54 M) aged 65 years and over referred for fracture occurrence, mainly hip fractures, at an Italian Medical Center (21). Spine X-rays of patients treated for hip fragility fractures identified a large proportion of individuals who had previously experienced an unreported vertebral fracture. Fragility fractures were identified based on the history and fracture dynamic, as well as on radiographs (evaluation cortical index of the humerus and femur to upper or lower limb fractures) and blood tests. Of the 478 patients considered, 322 (67,6% of total fractures) were diagnosed with a fragility fracture (279 W and 43 M); 14.6% of fragility fractures (47 patients including 44 W and 3 M) were associated with earlier vertebral fractures (VFs), but only in 38% of cases, this had been previously reported. The residual 61.7% of cases were diagnosed during the outpatient visit for fractures in other locations, mostly femoral neck and humeral fractures. The authors suggest that this percentage of undiagnosed VFs is likely to be underestimated, due to the mean age of the sample, which is 80.25, whereas the association of VFs to other fragility fractures typically involves older patients (mean age 84.6 years). Conclusions recommend two radiographic projections of the spine in all patients with hip and humeral fractures in order to preserve the patient's quality of life and avoid higher healthcare costs due to the risk of refracture (21).

4. The economic burden of the disease: healthcare costs

Studies on the economic burden of osteoporosis are prevalently focused on direct healthcare expenditure, which is mainly represented by hospitalization costs for fragility fractures, outpatient services and pharmaceutical therapy. Noticeably, the resources to be attributed to this disease involve a wider sphere which includes intangible costs, measured in terms of chronic pain and decreased quality of life, indirect costs due to both patients' productivity loss and family members' informal caregiving, and other direct costs including medical devices that are temporarily or permanently required after a fracture, such as wheelchairs or walkers. Some studies also include bedroom equipment (rope ladder and mattress), home modifications (steps' alteration and ramps), and car modifications (seat alteration and steering devices), all costs that are often paid by the patients (22). Premature mortality costs and decreased quality of life are also to be included in the economic burden of osteoporosis (1, 23, 24).

A first outline of the direct healthcare costs related to the treatment of osteoporosis is reported in a quite comprehensive cost analysis carried out in the UK by Stevenson et al. over the years 2002 to 2004 (25). The cost-analysis is based on Hospital Episode statistics describing the occurrence of a fragility fracture in people aged 50 and over and it is performed through a bottom-up cost imputation. Total costs per fracture range from £144 (scapula) to £13,771 (other femoral fractures).

For hip, pelvis and other femoral fractures, hospital admission is always required and present a very extended length of stay (from 22 to 35 days), with consequent high average inpatient costs; in these cases, hospitalization absorbs 90% of total healthcare costs. For the other fractures, the average costs are lower due to a reduced admission rate.

A recent study from Italy provides the total and average healthcare costs for hip fracture in people aged 65 and over during the years 2000 to 2014 (7). This is one of the few studies including long term care costs within the analysis. Costs are associated with the different clinical paths of people admitted to hospital for a hip fracture in this period: given a 5% mortality rate after admission, only 95% patients are discharged, 13% of whom undergo hospital rehabilitation, 18.2% become institutionalized and 63.3% undergo home-based rehabilitation. These figures are central to understanding the long-run effects of a fragility fracture in aging population.

Each treatment is assigned a cost based on existing evidence, while hospitalization costs are directly driven from DRG tariffs[2]. A final total cost is then calculated (€ 961,649,800) which corresponds to an average cost of €10,173

[2]DRGs are cost related tariffs built on the average amount of resources necessary for specific hospital treatment, henceforth in the case of admission for fracture, and accordingly to the specific procedure, the DRG tariff, besides drug, laboratory test and inpatient costs, may include the cost of a surgical operation and an eventual prothesis.

per treated case. Community care (rehabilitation) costs are also accounted for and results show that overall rehabilitation costs slightly outweigh hospitalization costs.

Table 1: Direct costs for hip fracture -Italian patients aged 65 and over - values in euro

Year	**2000 (average in parenthesis)**	**2014 (average in parenthesis)**	**% increase**
N cases	73,493	94,525	28.6%
Hospitalization costs	343,000,000 (4,667.1)	457,039,034 (4,835.1)	33.2%
Rehabilitation costs	392,876,272 (5,345.8)	504,610,785 (5,338.4)	28.4%
Overall direct costs	***735,876,272 (10,012.9)***	***961,649,800 (10,173.5)***	30.7%

Source: adaptation from (7)

Table 1 presents the number of hip fractures among people aged 65 and over and the relative costs for the years 2000 and 2014 respectively. In 15 years, a large increase (28.6%) in the number of cases is shown, accompanied by a higher rise (30.7%) in healthcare costs, mainly driven by the increase in the costs of hospitalization. Italy experienced in the last decades a sizable aging process and presents now the highest share of elderly people across industrialized countries, rising concern over the dramatic burden of osteoporosis on the Italian National Health Service.

Keeping Italy as a reference, another clear-cut analysis on the direct healthcare costs attributable to fragility fractures is provided by Degli Esposti et al. (1). The study analyses the cost effectiveness of osteoporosis treatment in patients aged 50 and over: 3,475 individuals hospitalized for a refracture (vertebral or hip) and presenting a previous admission for a fragility fracture are retrospectively studied for a mean follow-up of three years. Patients are split between untreated and treated (patients following osteoporosis therapy) and the latter are further divided into two categories (patients using calcium and vitamin D as a supplementation to osteoporosis therapy vs patients treated with osteoporosis therapy only). Cost analysis includes hospitalization costs (based on DRG tariff), drug expenditure and outpatient service costs (outpatient specialist visit, diagnostic test and drug costs after discharge). The analysis is carried out from the Italian NHS perspective and healthcare expenditure is computed in terms of yearly average. Results are reported in table 2: total costs for the untreated patients are higher compared to costs associated to the treated (€9,299 vs €4,428 $p<0.001$); the main impact is attributable to hospitalization costs, which absorb 84% of the whole expenditure for the untreated group vs 59.3% for the treated group (€7,801.74 vs €2,627.77, respectively, $p<0.001$), due to the higher risk of refracture for the former. Conversely, drug costs are higher for the treated (€1,159) vs the untreated (€677.18 $p<0.001$). Additional cost-effectiveness is ascribed to osteoporosis treatment with the adjunction of calcium/vitamin D (annual overall cost € 4,125 vs € 5,977 for patients following osteoporosis treatment alone $p<0.001$). Conclusions clearly address specific osteoporosis treatment, especially when combined with calcium-vitamin D, as the most cost-effective procedure for osteoporotic patients. These results confirm existing evidence: previous studies carried out on postmenopausal women treated with bisphosphonates show a significant reduction in vertebral fractures compared to the control over a three-year follow up (26-27).

Table 2: Average costs for osteoporosis hip and vertebral fractures over three years follow up – Italian patients aged 50 and over, treated vs untreated -years 2011 to 2015 – values in euro

Costs (annual average)	**Untreated (n=1443)**	**Treated (n=2032)**	**Treated cohort**	
			Osteoporosis drug only (n = 333)	**Osteoporosis drug + calcium/vit D (n = 1699)**
Drugs	677.18	1,159.55	1,056.95	1,179.66
Hospitalization	7,801.74	2,627.77	4,407.92	2,278.86
Outpatient services	810.93	640.94	512	666.21
Overall direct costs	***9,298.85***	***4,428.26***	***5,976.88***	***4,124.74***

Source: adaptation from (1)

Slightly higher estimates for direct costs related to osteoporosis fractures are reported by Borgstrom et al. (8) in a study on the Swedish population aged 50 and over. A prospective data analysis is carried out on 635 male and female patients surviving a year after fracture. The mean cost for a hip, vertebral and wrist fracture in the 12 months following the event is computed. Direct costs include both special living arrangements due to the fracture (e.g., nursing home) and other community care after discharge. Data on resource use and quality of life are collected through questionnaires at baseline, 4 months and 12 months. The average direct cost attributed to a hip, vertebral and wrist fracture for the year following the event is estimated respectively at €13,775, €11,941 and

€1,950 (2004 prices, in euro). Healthcare costs are quantified through a very detailed bottom-up technique and include hospitalization costs, which represent the main share, outpatient care, pharmaceuticals and community care (including special living accommodation). Details are reported in table 3.

Table 3: Average annual costs for osteoporosis fractures– Swedish population aged 50 and over – year 2004 – values in euro

Parameter	*Hip fracture; n= 278*	*Vertebral fracture; n=81*	*Wrist fracture; n = 276*
Inpatient care	8,805	5,533	357
Outpatient care	616	527	1,275
Pharmaceuticals	170	294	124
Community care - special living accommodation - other community care	 1,897 2,287	 2,127 3,460	 - 194
Overall direct costs	**13,775**	**11,941**	**1,950**

Source: adaptation from (8)

Table 4 summarizes the findings of the reviewed literature; despite the heterogeneity in either method, therapies and variables adopted, the average cost for a hip fracture, which is the most frequent osteoporosis site, does not present relevant differences across studies. The estimate ranges from €10,173 for the Italian case to €13,775 for the Swedish healthcare system; a slightly lower estimate (€9,290) is provided by Degli Esposti (1), but this study analyses jointly hip and vertebral fractures and provides an annual average estimate, through a three-year follow up.

All the studies, except the Piscitelli article (7), focusing on the long-term effects, address hospital costs as the most sizeable expenditure. Concern is expressed over the increase in fragility fractures due to population aging, which is destined to heavily impact on the national health systems of developed countries.

Table 4: Direct costs for hip fracture - comparison from reported studies

Country (year)	**Sample**	**Method**	**Total cost for hip fracture**	**ref**
UK (2002 to 2004)	Hospital Episode Statistics 2002-2004	Bottom-up cost analysis. Hospital and outpatient costs.	£ 10,760 = €12,060* Cost per treated case	(25)
Italy (2000 and 2014)	Males and females aged 65+	Clinical pathway of people admitted for hip fracture. Long run perspective which includes admission in nursing homes. Hospital costs from DRG – other costs from existing evidence.	€ 10,173 Average cost per treated case	(7)
Italy (2011 to 2015)	3475 males and females with refracture, aged 50+	Cost-effectiveness analysis (treated vs untreated) **. Three years retrospective follow up. Drugs, hospital (through DRG) and outpatient costs.	€ 9,299 Annual average cost	(1)
Sweden (2004)	635 males and females surviving one year after the fracture	Bottom-up technique including hospital costs, outpatient care, drugs, community care.	€ 13,775 Average cost per treated case	(8)

* At current change; ** hip and vertebral fractures

5. The social costs of osteoporosis: caregiving costs, premature mortality and reduced Quality of life

While direct costs of osteoporosis are well debated in literature, there is a paucity of evidence on indirect costs. The principal motivation is that indirect costs are mainly related to patients' productivity loss and this disease is prevalent among retired individuals; the few studies analyzing productivity loss among people less than 65 years of age, found rather negligible values (8); nonetheless, some studies include early retirement as a consequence of osteoporosis (24). Other relevant social costs are seldom included in the overall impact of osteoporosis: these are

represented by informal caregiving, premature mortality, decreased quality of life and the cost of residential care following a fragility fracture.

In terms of caregiving costs, fragility fractures very frequently lead to increased dependency: after a femoral fracture, only 30-40% of the subjects return to the conditions preceding the event and 20% of patients show a definitive loss of autonomous ambulation (4). Informal care is frequently provided by a family member (very often adult offspring), with possible effects on both his own health and labor profile. Assisting a dependent relative may provoke stress and burn-out with negative outcomes on mental health (28); on the job side, absence from work, career breaks or job abandonment are the most frequent effects (29). Nonetheless, caregivers' costs are hardly included in the economic burden of osteoporosis (6,10) and the few studies including them apply the salary of a home help (30-31), without considering the societal costs due to the choice of assisting a family member.

Similarly, premature mortality due to osteoporosis is frequently mentioned, but hardly ever quantified in terms of economic costs to society (10). For example, the Dubbo study, which provides 25 years follow up on a population (men and women) aged 60 and over, measures the risk of premature mortality and its persistence over the years without furnishing the economic evaluation of the phenomenon (23). Many studies have shown that mortality rate is higher among people with osteoporotic fractures, especially hip (32-34) and vertebral fractures (35), but it is difficult to find an economic assessment of premature mortality due to osteoporosis.

Another aspect seldom included in the analysis of social costs is the reduction in quality-of-life following a fragility fracture. Borgstrom et al. (9) show an estimate of the average costs related to the decreased quality of life due, respectively, to hip (€ 14,221), vertebral (€ 12,544) and wrist fracture (€ 2,147) in population aged 65 and over.

A recent and rather detailed systematic literature review on studies analyzing the indirect costs of osteoporosis in the years between 1998 and 2019 reports that only 43.7% of the selected articles included measurements on quality of life (10). Among them, an estimate on the disease burden in Europe in terms of QALY loss, suggests 1,180,000 QALYs were lost in Europe in 2010 (36). Adopting a conservative estimate between £20,000 and £30,000 (€ 22,231 to € 33,423 at the current exchange-rate) per QALY gained, an economic burden between 26.2 US billion and 39.4 US billion euro can be attributed to osteoporosis. The previous study is corroborated by an article including France, Germany, Italy, Spain, Sweden and the UK, which provides an estimate of 845,401 QALYs lost in 2010, due to hip fracture with a suggested total annual value of € 47 US billion (6).

Other studies on cost-effectiveness include the cost of treatment for QALYs gained. These studies are to be preferred by policy makers because they provide good grounding to choose the most cost-effective treatment within a perspective that includes patients' quality of life.

For example, Liu et al. (37) investigate the cost-effectiveness of teriparatide compared with alendronate in post-menopausal white US women with severe osteoporosis; a 70-year-old woman is chosen as base-case. Three different therapies are compared with usual care (defined as calcium or vitamin D supplementation), namely i) five years of alendronate, ii) two years of teriparatide followed by five years of alendronate (sequential therapy) and iii) two years of teriparatide. For the base-case analysis, the cost of alendronate treatment was $11,600 per QALY gained compared with usual care, while the cost of sequential teriparatide/alendronate therapy was $156,500 per QALY compared with alendronate. Both strategies outperform teriparatide monotherapy which costs more and increased QALYs less than alendronate.

Lastly, long-term care costs due to nursing home admission after a fragility fracture are seldom quantified, despite representing a direct cost of osteoporosis. Most studies prefer to focus on the short run costs (hospitalization, drugs and outpatient services) without considering the consequences in the long run. However, especially among older individuals, a fragility fracture can lead to nursing home admission, with a persistency in costs that is to be shouldered by the collectivity. To provide some figures, after a hip fracture the residential admission rate is 4% in people aged 60 years and rises to 12% in individuals aged 80 years (25). Estimates from Sweden are 6% at the age of 50 and rise to 23% for patients older than 90. Caution is however expressed in analyzing these figures since the risk exists that patients are admitted to residential care due to causes unrelated to the hip fractures themselves.

Strom et al. (6), analyze residential facility admission costs one year after a hip fracture in a few European countries, specifically France, Germany, Italy, Spain, Sweden and the UK. Results are reported in table 5 and show a heterogeneous framework, with Sweden, Italy and Spain surmounting the annual cost of 50,000 euro.

Concern over the likelihood of these costs remaining until death would of course recommend the adoption of any treatment able to reduce fragility fractures in older ages.

Table 5: average annual cost for nursing home 1 year after a hip fracture, 2010

Country	**Long-term care costs, €**
France	31,512
Germany	34,534
Italy	50,202
Spain	51,786
Sweden	57,247
UK	33,756

Source: (6)

6. Discussion

With the aging of population in developed countries, osteoporosis is destined to increasingly impact on both national healthcare systems and collectivity as a whole. Direct healthcare costs for hospitalization, outpatient treatment and nursing home admissions impose governments a relevant burden, which has been quantified by several studies. Hip fracture costs range from about €10,000 to €13,800 euro per treated case, raising concern over longer life expectancy increasing the number of fractures. Prevention of fragility fractures, through correct diagnosis and treatment, is confirmed to be the most valuable policy. Diagnosis in individuals aged 55 years or more, with or without a previous fracture, should be promoted at both community care and hospital level and osteoporosis detection must be followed by adequate treatment, which should be monitored over the years.

Although scholars agree in recognizing that general practitioners (GPs) play a key role in detecting individuals at high risk of osteoporosis, in prescribing the appropriate treatments and in monitoring patients over the years, their involvement in managing the disease is still marginal. GPs also play a fundamental role in informing elderly patients, especially women, through the promotion of healthy habits that reduce the risk of osteoporosis. For these reasons, the implementation of appropriate guidelines at primary care level is highly recommended to reduce the burden of osteoporosis and save resources for the collectivity.

Clear protocols should likewise be introduced at hospital level. In patients aged 65 and over accessing the hospital for a fracture, diagnostic tests such as DXA, VFA, and history review for past fractures have been proven to effectively detect possible unreported previous fractures and consequently prevent the risk of refracture. These tests are strongly recommended in such occurrences. Beneficial effects have also been observed for public screening programs aimed at identifying individuals at risk of osteoporosis.

As for the most cost-effective therapy, many variables play a role: among them, age, therapy adherence, comorbidity, time of diagnosis, fracture sites and previous fragility fractures, consistently influence the final result. To this extent, there is still room for research and investigation: sensitivity analysis helps in designing the most appropriate and effective treatment for each specific risk profile.

In the reviewed literature, the social costs of the disease are often underestimated, despite their impact at both individual and societal level. Loss of autonomy, chronic pain and decreased quality of life are seldom quantified, even if they represent a high cost to the patients and their families. Informal caregiving, mostly provided by family members, impose a significant cost on society, because carers are more subject to mental health problems and may well suffer financial limitations in their old age, if they quit their job or break their carrier. These mostly unexplored effects should be considered, especially in view of an increased life expectancy. Aging itself involves a number of limitations and chronic conditions; it is then advisable to reduce the risk of osteoporosis and avoid fragility fractures and their consequences in order to promote an active aging.

7. Conclusions

Existing literature agrees in expressing concern over the economic and social burden of osteoporosis in developed countries, which is destined to increase with population aging. Early detection and appropriate pharmaceutical treatments tailored on specific risk profiles are highly recommended to control healthcare expenditure, reduce premature mortality and secure adequate autonomy for elderly people.

Cost effectiveness studies, especially those including patient quality of life, should be considered when establishing priority setting in the allocation of healthcare resources. The promotion of both a healthy diet and correct lifestyle remains a valuable means to reduce the risk of fragility fractures.

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