Economic Burden of Osteoporosis in the World: A Systematic Review

Asma Rashki kemmak
Iran University of Medical Sciences

Aziz Rezapour (rezapour.a@iums.ac.ir)
Health Management and Economics Research center, Iran University of medical sciences

Reza Jahangiri
Iran University of Medical Sciences

Shima Nikjoo
Iran University of Medical Sciences

Hiro Farabi
Iran University of Medical Sciences

Samira Soleimanpour
Iran University of Medical Sciences

Research

Keywords: economic burden, direct costs, lost productivity costs, osteoporosis, osteoporotic fractures

Posted Date: January 31st, 2020

DOI: https://doi.org/10.21203/rs.2.22372/v1

Abstract

Background

Osteoporosis is a skeletal disease that is associated with a reduction in bone mass and microstructures and deterioration of bone tissue. It is also associated with an increased risk of fracture that is the most important complication of osteoporosis. Osteoporosis and consequent fractures not only have a major impact on the health and quality of life, but also impose a significant economic burden on the health system of countries.

Objective

Since the population of many countries around the world is aging, the incidence of fractures due to osteoporosis is increasing too. The knowledge about costs and economic aspects of osteoporosis plays an important role in making policies and planning measures for the prevention and management of this disease, hence, this study systematically investigated the available evidence on the costs associated with osteoporosis worldwide.

Methods

Considering language, year of publication, and the research question, electronic searches were conducted in multiple databases and different sources. After selecting articles based on inclusion and exclusion criteria, the data were extracted and the results were summarized. To prevent bias, the whole procedure was performed by three researchers.

Results

Of a total of 1989 papers, 28 papers were included in the study on the basis of inclusion criteria. Among the selected studies, 13 papers reported direct and indirect costs. Based on the data extracted from the mentioned studies, the mean age of people with osteoporotic fractures was 50 years, with the highest costs associated with hip fractures.

Conclusion

There is a paucity of studies investigating the burden of osteoporosis in the world. The available studies indicate a lack of standardization in the methodological approach of assessing the economic burden of this disease. It is necessary to highlight the importance of studies on osteoporosis to inform policymakers and enhance health care planning.

Background

Osteoporosis is a skeletal disease characterized by a reduction in bone mass and microstructures and a decline in bone tissue that is associated with increased fragility and increased risk of fracture (1). Osteoporosis is one of the main threats of aging, and its prevalence among people aged over 50 years is 30% in women and 15% in men (2). Osteoporosis is characterized by a decrease in bone mineral content along with bone matrix, so that bone loss is reduced but bone composition remains normal(3).

Bone fractures are the most important complication of osteoporosis (1). The fractures lead to increased mortality, disability, and increased medical costs. Osteoporosis is more common in women than in men. The disease is manifested when bone fractures occur, especially in the vertebral and pelvic areas (4).

In 2010, the estimated number of osteoporotic fractures in the European Union was 3.5 million cases, which included 620,000 cases of hip fractures, 520,000 cases of spine fractures, 560,000 cases of forearm fractures, and 1,800,000 cases of other types of fracture. The number of annual cases of osteoporotic fractures is expected to reach 4.5 million cases by 2025 (5).

Osteoporosis and its fractures not only have a major impact on health and quality of life, but also impose a significant economic burden on the health system (1). The economic costs of a disease can be used to estimate the burden of that disease. The costs in the economy are divided into two groups, including direct and indirect costs. The direct costs are the treatment costs and the indirect costs are the costs associated with days off from work or school due to illness (6). The costs associated with osteoporosis in the European Union in 2010 were estimated to be 37 billion euros, more than 70% of which is related to the costs of fractures caused by osteoporosis (2). In 2005, the direct medical costs of osteoporosis in the United States were estimated to be 13.7 to 20.3 billion dollars. It is also projected that by 2025, more than 3 million cases of osteoporotic fracture will occur annually, with an estimated cost of 25.3 billion dollars (7, 8). In 2005, the cost of every case of hip fracture in the United States was estimated to be 13,240 to 35,600 dollars annually, and the cost of osteoporotic fractures in the United States is estimated to be 20 billion dollars annually (1). Pelvic bone fractures are the most common type of fracture and are most prevalent type associated with mortality (7). This type of fracture is also the most expensive type of fracture (1).

Among the different components of health care systems, hospitals are facing a shortage of resources as a challenge, and every type of shortage of resources leads to a competition. Under such a condition and competition, only the organizations that could reduce the costs while paying attention to the quality of services provided can be successful. Therefore, cost information in the hospital can be of great value in optimizing resource allocation, modifying budgets, reducing waste costs, and making more efficient use of available resources. The objective of every cost detection and cost management system is to provide accurate and practical information to help organizations deliver quality goods and services under a competitive setting (9).

The prevalence of osteoporosis increases with aging that is due to decreased bone tissue. Due to the decline of ovarian function in women during the post-menopausal period, the loss of bone mass is accelerated and as a result most of women have the indications for the diagnosis of osteoporosis at the age of 70-80 years (10).

Since the population of most Asian countries is aging, the incidence of fractures due to osteoporosis is also increasing in these countries. More than 50% of hip fractures are projected to occur in Asian countries by 2050 (5). The average prevalence of osteoporosis in Iran in 2012 was 17% (11).

Osteoporosis is preventable and treatable, but since it is a latent disease it is usually undetectable until the final stages (12). Osteoporosis is a complex disease that is influenced by several factors, some of which are uncontrollable, such as age, sex, race, family history, menopause, and some other factors such as weight, mobility, nutrition, and smoking (10). Bone ability to cope with fracture is dependent on several factors including bone mass, bone shape, and intrinsic characteristics of bone (13). There are several recommendations for preventing osteoporosis, for instance it is recommended to adopt a diet high in calcium and vitamin D and have a daily intake of calcium-rich foods, especially low-fat and pasteurized dairy products (9). Different treatment strategies such as behavioral changes, use of pelvic protectors and analgesics, and use of muscle relaxants, heat, massage, and rest can reduce the risk of osteoporotic fractures (10). The risk and frequency of fractures vary by race, so they should be investigated individually in every population group (14).

Half of women and one-fifth of men aged over 50 years are at risk of fractures in their life. The serious complications of fracture are mortality, pain, and loss of quality of life (15). The rate of mortality from hip and spine fractures is approximately 20%. The total DALY due to osteoporotic fractures in 2000 was 5.8 million years, which is somewhat higher than that of hypertension and rheumatism. The economic burden on this disease in women is higher than that in men, with 64% of DALY observed in women. In a study on osteoporosis burden in Iran in 2001, the years of life lost (YLL) due to osteoporotic fractures was 32,375 years for hip fractures, 3,493 years for spine fractures, and 158 years for forearm fractures. In total, osteoporosis resulted in 36,027 years of life lost due to premature death and disability (14).

According to the latest statistics, in Iran about 25,969,046 people suffer from osteopenia and 3,024,798 people suffer from osteoporosis, which respectively will reach 40,303,730 and 3,592,708 by 2020. Based on the results of studies conducted by Tehran University of Medical Sciences in 2001 and 2004, considering the DALY scale, osteoporosis was responsible for the loss of more than 36,000 years of life among Iranian men and women. Thus, Iran accounts for about 0.85% of the global burden of osteoporosis and 12.4% of the burden of osteoporotic fractures in the Middle East (10).

As mentioned above, due to increased life expectancy and an increasing percentage of the elderly population in recent years, the incidence and prevalence of osteoporosis and related fractures have been increasing, and this disease has become one of the most common diseases. In addition, advances in medical technology and the introduction of new and sometimes costly preventive and therapeutic methods have made the disease economically striking. Studies carried out in Western and some Asian countries have shown that osteoporosis imposes a significant economic burden on communities, and its related costs are rising in most countries, especially Asian countries, including Iran. Given the important role of information about the costs and economic aspects of osteoporosis in making policies and planning measures for the prevention and management of this disease, this study systematically investigated the evidence and data on the costs of osteoporosis in the world. The data was analyzed through reviewing existing studies and it aimed at better assessing the economic burden of osteoporosis in different countries around the world.

Methods

This study was conducted as a systematic review to examine the economic burden of osteoporosis in the world. First, all relevant terms related to economic burden and osteoporosis were identified. The search strategy was designed via utilizing keyword combinations. Search keywords, search terms, synonyms, and combinations with OR and AND operators were used to improve the sensitivity of the search. The related literature was then searched in related journal databases and references based on the search strategy. Screening was performed through considering the inclusion and exclusion criteria and relevant articles were identified. Finally, the required data were extracted from the selected articles and the evidence was compared and summarized.

Literature Search and Screening

To find suitable studies for analysis, several databases including PubMed, Embase, Scopus, web of science, ProQuest, and Cochrane were searched using the keywords of economic burden, cost of illness, and osteoporosis. The following strategy was also used to search the databse: (Cost of Illness OR Economic Burden) AND (Osteoporosis (

The search strategy for Pubmed database was as follows:

("Economic burden"[tiab] OR "Cost of Illness"[tiab] OR "Burden of Illness"[tiab]) AND ("osteoporosis "[tiab])

Inclusion and exclusion criteria

in this study inclusion criteria were as follows: economic burden of disease, including direct and indirect costs and different types of fractures associated with osteoporosis; studies with available full-text papers; Scientific research and studies written in English and published between 1980 to 2018 years.

This study excluded papers that did not meet the following criteria: studies written in languages other than English; and all protocols, conference abstracts, review articles and letters to the editor.

Data Extraction and Quality Assessment

After searching different databases, all the detected articles were imported into EndNote software and the duplicates were removed. The rest of the papers were independently reviewed individually by two experts in this field. At this stage, the PRISMA principles were followed to retrieve the final articles.

In the first stage the title and abstract of the papers were reviewed and on the basis of the inclusion and exclusion criteria mentioned above, the relevant papers were selected. Then, if the full text of the selected studies was accessible, the studies were carefully reviewed and the final papers were selected. In each of these stages, in case of disagreement between the two researchers, the papers were reviewed by a third researcher. After final selection of articles, data extraction was performed using a data extraction form. Taking into consideration the nature of studies on the economic burden and cost of the disease and the impossibility of meta-analysis and quantitative analysis of studies, the results were analyzed and the discussion and conclusion were presented via narrative synthesis method. In addition, in order to compare costs in different studies, all the costs were converted to dollars based on purchasing power parity index in 2018. For each study investigated in the final step, a sheet was designed in the Excel file and the basic information including the author's name, article title, year of publication, country of origin, study design and duration of study, study population, study outlook, direct costs, and indirect costs were entered into each sheet.

Results

The initial results of search in the databases provided a total of 3113 articles. Of these, after removing duplicates, 1989 article entered the study, which was reduced to 612 papers after reviewing the title. Then, the abstracts of the articles were reviewed and 163 articles met the inclusion criteria. The full texts of the 163 articles were reviewed, out of which 135 were selected based on the inclusion and exclusion criteria. Finally, 28 papers were selected for more meticulous examination. No new relevant studies were found in the review of the references of the finally selected articles.

The quality of the 28 selected studies was assessed using the PRISMA checklist. To avoid bias when evaluating the quality of the selected papers, the researchers had become blinded to the basic information on the article, such as author's name, country, and year of publication. The results of the quality assessment of the studies were acceptable and no study was excluded based on the results of the quality assessment of the study. The results of the quality assessment of the studies were presented on the basis of the PRISMA checklist. After evaluating the quality of data of the selected articles, data were extracted using a data extraction form and arranged in a table format. Because studies could only be categorized by cost types, the data were categorized by cost types (direct, indirect, etc.).

Direct costs:

Studies that only investigated direct costs had been published between 1993 and 2017. Most of the studies in this category were conducted in developed countries such as Canada, Germany, and the United States. The sample sizes were different. The cost perspectives in the reviewed studies included the perspective of patients, community, government, etc. As presented in Table 1, the studies in this category reported direct costs, costs per case of fracture, average cost, total cost, or annual cost of fracture for the country under the study.

Table 1- Direct costs

Reference	Year	Country	perspective	Sample size	Type of fracture	Type of direct cost	Cost value
Lia Gutie´ rrez (18)	2011	UK	Unknown	2427 cases	Hip	Cost of hospitalization per case of fracture	$ 5248
Morteza Saeb (19)	2014	Iran	societal	103 cases	Hip	Cost of surgery per case of fracture	$ 43,502 per case
Simin HEPGÜLER (20)	2011	Turkey	societal	1118 cases	Hip	Costs from a providers perspective	$2,249,885 per year and $3,119 per patient
Yong-Chan Ha (21)	2017	South Korea	societal	2035639 cases	No investigation of fracture	Cost of surgery	$ 5,125,585 annually
RB Hopkins (22)	2012	Canada	societal	284108 cases	Unknown	Cost of hospitalization	$ 551770 annually
RB Hopkins (23)	2016	Canada	Unknown	164763 cases	Hip, wrist , spine, arm	Costs from a providers perspective	$ 426,000 annually
B. Haussler (1)	2006	Germany	health insurance system	3243445 cases	Hip , wrist, spine, arm, rib, forearm, hip, chest, thigh	Annual fee	$ 6065 billion
P. LEVY (24)	2002	France	societal	Unknown	Unknown	Annual fee	$ 222 million
Jorge Morales-Torres (25)	2003	Latin America	Unknown	507932043 cases	Hip	Hospital costs	$ 6,000
Sabine Berghaus (26)	2014	Germany	payer’s perspective	40540 cases	Hip , wrist, spine, arm, rib, forearm, chest	Cost of surgery	$ 1284 million annually
C. Pike (27)	2010	America	societal	3536 cases	No fracture examination	Annual fee	$ 19000
Crystal Pike, (28)	2010	America	societal	526572 cases	Hip , wrist, spine, arm, rib, forearm, hip, chest	Annual fee	$ 12000
Matthew D (29)	2007	America	Unknown	7626 cases	Unknown	Cost of hospitalization per case	$ 5370
Luminita Mihalache (30)	2013	Romania	Unknown	150 cases	Hip , wrist , spine	Cost of hospitalization	$ 1077 annually

A. LOPES VAZ (31)	1993	Portugal	Unknown	88690 cases	Hip	Cost of hospitalization and cost of surgery per case	354000 $
Amgen Inc (32)	2012	America	insurer	49680 cases	Hip and wrist	Cost of hospitalization and cost of surgery per case	$ 19225

Indirect and direct costs:

Among the selected studies, there was no study that reported only indirect costs. As presented in Table 2, some of the selected studies had reported the results of direct and indirect costs together and had been published between 2002 and 2017.

Table 2- Indirect costs and direct costs

Reference	Year	Country	perspective	Sample size	Type of fracture	Type of cost	Cost value
Biljana Dzajkovska (33)	2007	Slovenia	social	355100 cases	Hip , wrist, spine	Costs from a community perspective per case	$ 9 million in direct costs and $ 10 million in indirect costs
Jinhyun Kim (34)	2016	South Korea	social	244798 cases	Hip , wrist, spine, arm, forearm	Cost per case for hospitalization, medical requirements , medication, personnel	$ 645 million in direct costs and $ 647 million in indirect costs
Charmaine Shuyu Ng (35)	2017	Singapore	hospital's and patient's	67 cases	Hip , wrist, spine	Direct costs per case	$ 5545 in direct costs and $ 3697 in indirect costs
Hans Peter Dimai (22)	2012	Australia	societal	119911 cases	Hip , arm, spine, forearm, rib	Direct and indirect costs	$ 550 million in direct costs and $ 253 million in indirect costs
P. Clark (36)	2008	Mexico	patient and provider	493 cases	Hip	Direct and indirect costs per case	$ 31000 in direct costs and $ 97000 in indirect costs
DA Eekman (37)	2014	Netherlands	societal	116 cases	Hip , arm, spine, forearm, rib ,	Direct costs (hospitalization and surgery) and indirect costs	$ 328 million in annual direct costs and $ 437 million in annual indirect costs
Oskar Ström (38)	2008	Sweden		684 patients from 7 hospitals	Hip , wrist spine	Costs of diagnosis and treatment	$ 6566 in annual direct costs and $ 150 in indirect costs

			societal				
W. Max (39)	2002	California	societal	10254774 cases	Hip , arm, spine	Direct costs and indirect costs	$ 3 million in direct costs and $ 4353 in indirect costs
B. Qu (17)	2014	China	societal	938 cases	Hip , arm, spine	Direct costs and indirect costs	$ 7860 in direct costs and $ 410 in indirect costs
V. Rabenda (40)	2006	Belgium	payer’s perspective	1811 cases	Unknown	Direct costs and indirect costs	$ 52 in annual direct costs and $ 40 in indirect annual costs
J.-E. Tarride (41)	2011	Canada	social	12706 cases	Hip , arm, spine, forearm, rib	Direct costs and indirect costs	$ 200 billion in annual direct costs and $ 115 million in annual indirect costs
A. Marques (42)	2015	Portugal	societal	186 cases	Hip	Direct costs and indirect costs	$ 3800 annual direct costs and $ 194 annual indirect costs

The twenty-eight articles selected for the study had been published between 1980 and 2018. Of all, 4 articles were from USA (27, 28, 29, 32), three articles were from Canada (22,23, 41), two articles were from South Korea (21,34), two articles were from Portugal (31, 42) , and two articles were from Germany (1, 26). In addition, there was one article from each of the countries of Belgium, China, California, Sweden, Netherlands, Mexico, Australia, Singapore, Slovenia, Romania, France, Turkey, England, Iran, and Latin America. Of all, five articles reported a retrospective research, 3 articles reported a prospective research, 2 articles reported bottom-up costing, 2 articles reported prevalence-based investigation, 2 articles reported top-down costing, one article reported an observational research, and one article had a descriptive design. The sample size ranged from 67 to 30,243,445 cases. In addition, 18 out of 28 studies had been carried out after 2010, indicating the increasing importance of the disease in recent years. Target groups in these studies had various fractures including hip, spine, wrist, shoulder, ankle, and rib fractures; except for five studies that did not investigate fractures (30, 22, 24, 27, 40), hip fracture had been investigated in all studies and was reported as a costly complication. Cost data were mainly collected from hospital bills and patient records. These studies included direct medical costs, direct non-medical costs, and indirect costs, and in most studies direct medical costs, including the costs of outpatient services, drugs, and surgeries were included. The cost components of most studies were clearly stated, although the descriptions varied widely among studies. Indirect costs were also reported in 12 studies. Other types of costs, including home care costs, equipment, etc. were also reported in some studies. In four studies, indirect costs were higher than direct costs. Qiu et al.'s study estimated indirect costs such as early retirement and job loss (17), while Kim et al.’s study estimated the

rate of lost productivity (34). Only Chang's study reported incremental costs of treatment (21). Since all the studies included patient-level data, it was not useful to conduct sensitivity analysis.

The average cost of treatment of osteoporosis was US $ 5,258,741, which accounts for 20 percent of the GDP of countries in 2018. The studies conducted in Singapore, Iran, and Korea reported less than 20% of the GDP per capita for osteoporotic care (18, 34, 35), while in most other studies it accounted for more than 30% of the GDP.

Cost components analysis showed that hospitalization and surgery accounted for the largest part of the total costs. The length of hospital stay varied from 2 to 89 days. In studies that reported direct non-medical costs (n = 9), the average transportation cost was US $ 20, indicating a small proportion of the total costs. As reported in Que's study, the indirect costs of job loss, early retirement, and unemployment were $ 11, $ 48, and $ 60, respectively (17).

Discussion

The economic consequences of osteoporosis are divided into two categories, including direct costs for the healthcare providers as well as indirect costs for families and the community. In this systematic review, we reviewed studies that reported different types of osteoporosis costs. South Korea incurs 645 million dollars for direct costs and 647 million dollars for indirect costs (34). According to another study conducted in South Korean, this country also spends 5,125,585 dollars annually for outpatient treatment (21). The annual cost of outpatient treatment in Australia was reported to be 350 million dollars in 2008 for direct cost (16). In Portugal and the US, annual costs of hospital and surgical services range from 354000 to 19000 dollars (31, 32).

Based on the results of studies investigated in this systematic review, regardless of the approach of cost detection used by different studies, the average cost of each case of treatment is reported to be between 5000 doller and 6500 billion dollars. To justify this finding, it might be said that many studies on osteoporosis have been conducted in developed countries where the cost of inputs is relatively high in such countries and they usually follow the proper treatment procedures and guidelines.

The majority of studies investigated in this systematic review which investigated the costs of osteoporosis had been conducted in developed countries. Concerning osteoporosis with fractures, regardless of the type of cost detection, the USA spends between 5,000 and 19000 dollars for each case of fracture (27,28,29,32). Also in the US studies only direct costs were reported. In the UK, 5248 dollars is spent per case for the treatment of osteoporotic fractures(18).

Phillips et al. in 1986 investigated the direct medical costs spent by women with osteoporosis in the United States. According to the results of the mentioned study, the direct medical costs of osteoporosis in women aged 45 and older were estimated at about 2.5 dollars. The mentioned study used secondary data to investigate costs in the study group, and 67,000 patients with osteoporosis were enrolled into the study based on diagnostic codes, the majority of whom were women aged over 75 years of age. The mean length of hospital stay of the patients was 1.7 days longer than other patients. The highest cost share in these patients in the hospital was attributed to the room and physician visits, while the cost of surgical operations had accounted for the lowest share. Nursing homes and physician referrals accounted for about 40.5% of costs and outpatient service accounted for 3.6% of direct medical costs. According to this study, changing lifestyle as well as providing women with over-the-counter calcium medication could greatly help to delay osteoporosis and ultimately reduce costs (43). According to the present study, the length of stay of these patients was longer than others that attributed to hospitalization in ICU after the operation. In the present study, surgery was one of the cost types that accounted for a large part of the costs. The difference between this findings with the results of the mentioned study can be attributed to the differences between treatment processes in various countries.

Our findings showed that few studies have fully investigated the total costs (direct and indirect costs) to estimate the economic burden of osteoporosis, and this limitation reduces investment in health care resources to prevent the disease. In addition, although all the studies aimed to determine the economic burden of osteoporosis fractures, there were many differences in the cost estimation methods that prevent the direct comparison of results.

In the present studies, economic evaluations of indirect and intangible costs were very scarce, which leads to uncertainty in the estimation of the economic burden of osteoporosis. Although, productivity loss due to absenteeism might be very infrequent in the elderly patients, the indirect costs incurred by other family members can be significant.

Limitation

In this study it was tried to avoid any bias through conducting a comprehensive and systematic search. However, the failure to follow a standard cost detection approach in the selected studies had reduced the consistency of the reported results; hence, it might prevent the analysis of the reported results on the basis of different dimensions. The papers investigated in this systematic review had reported costs in different years and on the basis of different countries' currencies and examined different cost items. In addition, some studies have reported the costs in a general form while some other studies have reported the details on costs, thus, in some cases it was not possible to compare them.

Conclusion

Because of the recruitment of skilled personnel, surgical procedures, expensive medications, and long-term treatment service delivery and hospital stays, the process of treating people with osteoporosis and related fractures is often expensive. Prevention of this disease can significantly reduce the costs incurred by the health system, especially in developing countries where osteoporosis is common and associated with fractures. Developed countries, such as the United States, provide treatment for osteoporosis and associated fractures at high costs that is due to the high cost of inputs used in the treatment process. The current systematic review study included a cost detection method which included both direct medical costs and direct non-medical costs, and future studies that examine other costs may reveal newer dimensions of disease burden and more cost-effective methods of osteoporosis therapies. Most studies focusing on direct costs had been conducted in developed countries such as the United States and Canada and they had not considered non-monetary costs of care (such as lost quality of life), which may be an important issue in future studies. This systematic review study undoubtedly provides valuable information about the osteoporosis burden for individuals and communities, and also shows that many resources are being spent on this disease in the world. Some of the studies investigated in this systematic reviews have shown that the provision of osteoporosis prevention services is less expensive than its treatment. Therefore, it is necessary to work with providers and payers to provide preventive care, especially in developing countries where osteoporosis is prevalent. Such services can be included in the basic services package and provided at lower costs in hospitals or designated centers.

Declarations

Ethical Approval and Consent to participat The manuscript does not contain clinical studies or patient data.

Consent for publication all authors consent to the publication of the manuscript in Syst. Rev should the article be accepted by the Editor-in-chief upon completion of the refereeing process.

Availability of data and material Not applicable

Competing interests The authors declare that they have no conflict of interest

Funding This study was part of a research project that is supported by the health management and economics research center affiliated to Iran University of Medical Sciences (Project No. 97-3-48- 12618 and Ethical Code. IR.IUMS.REC.1397.926).

Authors' contributions Authors make substantial contributions to conception and acquisition of data, and analysis and interpretation of data.

Acknowledgements Not applicable

References

1. Häussler B, Gothe H, Göl D, Glaeske G, Pientka L, Felsenberg D. Epidemiology, treatmentand costs of osteoporosis in Germany—the BoneEVA Study. Osteoporos Int. 2007;18(1):77-84. https://doi.org/ 10.1007/s00198-006-0206-y
2. Zamani, B., Ebadi, S., Ahmadvand, A., Mousavi, G. "The Frequency of Osteoporosis in hip fracture following minor trauma and the resulting mortality rate and direct treatment costs in patients over 45 years old in Kashan Naghavi Hospital during 2005-2007." JKMU. 2010;17(2): 137-144. http://jkmu.kmu.ac.ir/article_17302.html
3. Aghamohammadzadeh, N., et al. Evaluation of effective factors in decreased bone density in patients with osteoporosis and osteopenia. Gorgan Univ Med Sci. 2009;11(2):61-7. http://www.goums.ac.ir/journal
4. Ahmadzadeh A, et al. Comparative evaluation of the OST and SCORE for prediction of osteoporosis in post menopausal women. SBUMS. 2010; 15 (4) :165-170. http://pajoohande.sbmu.ac.ir/article-1-990-en.html
5. Hernlund E, Svedbom A, Ivergård M, Compston J, Cooper C, Stenmark J, et al. Osteoporosis in the European Union: medical management, epidemiology and economic burden. Archives of osteoporosis. 2013;8(1-2):136. URL:http://pajoohande.sbmu.ac.ir/article-1-990-en.html
6. Heydarpour F AsA, Mohebali M, Bokaie S. Economic Burden of Cutaneous and VisceralLishmaniasis in Iran in 2013. Iran J Immunol. 2017; 12(4); 1-13. URL: http://irje.tums.ac.ir/article-1-5686-en.html
7. Burge R, Dawson-Hughes B, Solomon DH, Wong JB, King A, Tosteson A. Incidence and economic burden of osteoporosis-related fractures in the United States, 2005–2025. J BONE MINER RES. 2007;22(3):465-75. https://doi.org/ 10.1359/jbmr.061113
8. Roche J, Wenn RT, Sahota O, Moran CG. Effect of comorbidities and postoperative complications on mortality after hip fracture in elderly people: prospective observational cohort study. BMJ 2005;331(7529):1374. https://doi.org/10.1136/bmj.38643.663843.55
9. Bangeman T. Shared Services in Finance and Accounting, Gower Publishing Limited. 2005.(Book)
10. Hodsman A, Papaioannou A, Cranney A. Clinical practice guidelines for the use of parathyroid hormone in the treatment of osteoporosis. CMAJ. 2006;175(1):48-. https://doi.org/10.1503/cmaj.060624
11. Irani AD, Poorolajal J, Khalilian A, Esmailnasab N, Cheraghi Z. Prevalence of osteoporosis in Iran: A meta-analysis. J Res Med Sci .2013; 18(9): 759–766. https://doi.org/10.1016/j.dsx.2019.07.036

12. Naghavi M, et al. The burden of disease and injury in Iran 2003. Popul Health Metr. 2009;7(1):9. https://dx.doi.org/10.1186%2F1478-7954-7-9
13. Dempster DW. Osteoporosis and the burden of osteoporosis-related fractures. Am J Manag Care. 2011;17(6):S164-9. https://www.ajmc.com/journals/supplement/2011/a357_may11/a357_11ma7__dempster_s164to169
14. Larijani B, et al. "Peak bone mass of Iranian population: The Iranian multicenter osteoporosis study. J Clin Densitom. 2006; 9(3): 367-374. https://doi.org/10.1016/j.jocd.2006.05.001
15. Maghbooli Z, et al. Direct costs of osteoporosis-related hip fractures: protocol for a cross-sectional analysis of a national database. BMJ open. 2017; 7(4):e014898. https://dx.doi.org/10.1136%2Fbmjopen-2016-014898
16. Dimai HP, Redlich K, Peretz M, Borgström F, Siebert U, Mahlich J. Economic burden of osteoporotic fractures in Austria. Health Econ. Rev. 2012; 2(1):12. https://doi.org/10.1186/2191-1991-2-12
17. Qu B, et al. The economic burden of fracture patients with osteoporosis in western China. Osteoporos Int. 2014; 25(7):1853-60. https://doi.org/10.1007/s00198-014-2699-0
18. Gutiérrez L, et al. "Study of the incremental cost and clinical burden of hip fractures in postmenopausal women in the United Kingdom. J. Med. Econ. 2011;14(1): 99-107. https://doi.org/10.3111/13696998.2010.547967
19. Saeb M, Beyranvand M, Basiri Z, Haghparast-Bidgoli H. The hospital resource utilization associated with osteoporotic hip fractures in Kermanshah, Iran. JIVR. 2014; 6(1):16. https://doi.org/10.5249/jivr.v6i1.492
20. Hepgüler S, et al. "Osteoporotic hip fracture costs in the elderly Turkish population." Acta Orthop Traumatol Turc. 2011; 45(5): 316-325. https://doi.org/10.3944/AOTT.2011.2543
21. H Yong-Chan, et al. Economic burden of osteoporosis in South Korea: claim data of the National Health Insurance Service from 2008 to 2011. Calcif. Tissue Int. 2017;101 (6): 623-630. https://doi.org/10.1007/s00223-017-0320-1
22. HOPKINS R. B, et al. Estimating the excess costs for patients with incident fractures, prevalent fractures, and nonfracture osteoporosis. Osteoporos Int. 2013; 24(2): 581-593. https://doi.org/10.1007/s00198-012-1997-7
23. 23. HOPKINS R. B, et al. The current economic burden of illness of osteoporosis in Canada. Osteoporos Int .2016; 27(10): 3023-3032. https://doi.org/10.1007/s00198-016-3631-6
24. LEVY P, et al. The cost of osteoporosis in men: the French situation. Bone. 2002; 30(4): 631-636. https://doi.org/10.1016/s8756-3282(01)00708-6
25. Morales-Torres J, et al. The burden of osteoporosis in Latin America. Osteoporos Int. 2004; 15(8): 625-632. https://doi.org/10.1007/s00198-004-1596-3
26. Berghaus S, et al. "Osteoporosis in German men: a cost-of-illness study." EXPERT REV PHARM OUT.2015; 15(3): 531-537. https://doi.org/10.1586/14737167.2015.990885
27. Pike C, et al. "Economic burden of privately insured non-vertebral fracture patients with osteoporosis over a 2-year period in the US." Osteoporos Int. 2011;22(1): 47-56. https://doi.org/10.1007/s00198-010-1267-5
28. Pike, Crystal, et al. "Direct and indirect costs of non-vertebral fracture patients with osteoporosis in the US." Pharmacoeconomics.2010; 28(5): 395-409. https://doi.org/10.2165/11531040-000000000-00000
29. Matthew D, et al. "Economic burden of osteoporosis-related fractures in Medicaid." Value Health.2007; 10(2): 144-152. https://doi.org/10.1111/j.1524-4733.2006.00161.x
30. Mihalache L, et al. "The cost of osteoporotic fractures in the Romanian postmenopausal women population. Value Health .2013; 16: A323–A636
31. Vaz, A. Lopes. "Epidemiology and costs of osteoporotic hip fractures in Portugal." Bone. 1993; (14): S9. https://doi.org/10.1016/8756-3282(93)90342-8
32. Viswanathan N, et al. "Direct healthcare costs of osteoporosis-related fractures in managed care patients receiving pharmacological osteoporosis therapy." APPL HEALTH ECON HEA.2012; 10(3): 163-173.

https://doi.org/10.2165/11598590-000000000-00000

33. Dzajkovska B, Albert I, Wertheimer, and Ales Mrhar. "The burden-of-illness study on osteoporosis in the Slovenian female population." PHARM WORLD SCI. 2007; 29(4): 404-411. https://doi.org/10.1007/s11096-007-9091-5
34. Kim J, et al. "Economic burden of osteoporotic fracture of the elderly in South Korea: a national survey." Value Health Reg Issues.2016; 9: 36-41. https://doi.org/10.1016/j.vhri.2015.09.007
35. Wong, M, et al. "Osteoporotic hip fractures in Singapore–costs and patient's outcome." Ann Acad Med Singapore. 2016; 31(1): 3-7. https://doi.org/10.1016/j.vhri.2016.12.002
36. Clark, P, et al. "Direct costs of osteoporosis and hip fracture: an analysis for the Mexican healthcare system." Osteoporos Int. 2008;19(3): 269-276. https://doi.org/10.1590/s0036-36342009000700014
37. Eekman, D. A, et al. "Indirect costs account for half of the total costs of an osteoporotic fracture: a prospective evaluation." Osteoporos Int. 2014; 25(1): 195-204. https://doi.org/10.1007/s00198-013-2505-4
38. Oskar S, et al. "Long-term cost and effect on quality of life of osteoporosis-related fractures in Sweden." Acta orthopaedica. 2008;79(2): 269-280. https://doi.org/10.1080/17453670710015094
39. Max W, et al. "The burden of osteoporosis in California", 1998." Osteoporos Int. 2002; 13(6):493-500. https://doi.org/10.1007/s001980200060
40. Rabenda V, et al. "The direct and indirect costs of the chronic management of osteoporosis: a prospective follow-up of 3440 active subjects". Osteoporos Int. 2006;17(9) :1346-1352. https://doi.org/10.1007/s00198-005-0066-x
41. Tarride J, et al. "The burden of illness of osteoporosis in Canada." ." Osteoporos Int. 2012; 23(11):2591-2600. https://doi.org/10.1007/s00198-012-1931-z
42. Marques A, Ó Lourenço, J. A. P. da Silva. "The burden of osteoporotic hip fractures in Portugal: costs, health related quality of life and mortality." Osteoporos Int. 2015; 26(11) :2623-2630. https://doi.org/10.1007/s00198-015-3171-5
43. Phillips S, et al., The direct medical costs of osteoporosis for American women aged 45 and older, 1986. Bone, 1988. 9(5): p. 271-279. https://doi.org/10.1016/8756-3282(88)90009-9

Figures

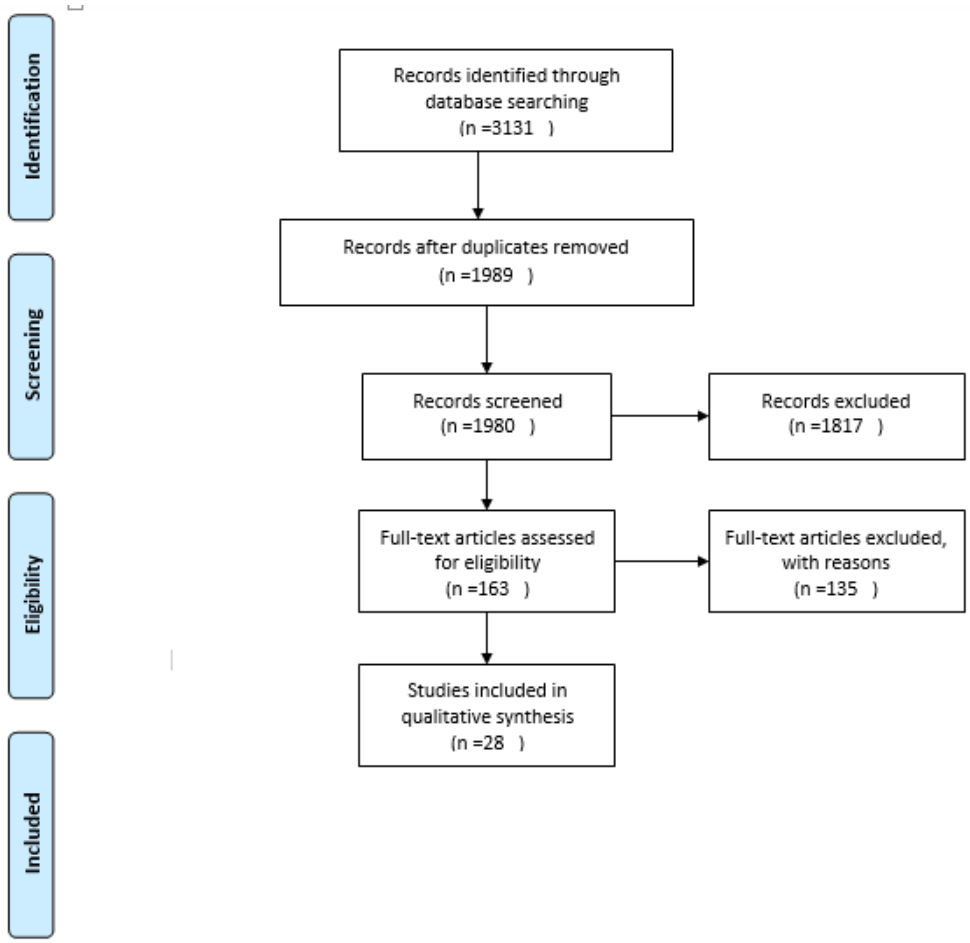

Figure 1

Flow chart.