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Mapping theme trends and recognizing hot spots on postmenopausal osteoporosis: a bibliometric analysis

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Abstract

Background: Due to the high morbidity and correlated with age-related fractures, postmenopausal osteoporosis is a crucial clinical and public health burden, but the bibliometric studies on such field remain unclear. This study was summarized the research progress on postmenopausal osteoporosis in recent five years.

Methods: Scientific papers published on postmenopausal osteoporosis were extracted from Jan 1st, 2013 to Dec 31st, 2017. Extracted information were analyzed quantitatively with Bibliographic Item Co-Occurrence Matrix Builder (BICOMB) and extremely frequent MeSH terms/MeSH subheadings terms were confirmed. To explore the hot spots in this field, co-word biclustering analysis was conducted by gCLUTO based on major MeSH terms/MeSH subheadings terms-source articles matrix.

Results: The research findings covered 2089 publications, and eight authors published twenty or more articles. A total of 720 publications (34.47%) came from England, 700 publications included (33.51%) were from the United States, and 1972 of the 2089 articles (94.22%) were published in English. The ranking of top ten most productive journals brought out 37.48% (783/2089) of the articles on this theme. Eight research hot spots were identified.

Conclusions: Eight major research hot spots identified provide basic information that can be used in further research regarding the treatment of osteoporosis. On the side, comparison with England and the United States, the correspondingly small amount of literature extracted via PubMed from other countries suggests to a certain degree that the area might be less developed in these regions. Additional Studies on postmenopausal osteoporosis could give some references for the health of the elderly women.

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Key words: Postmenopausal osteoporosis; Mapping theme trends; Hot spots; Co-word analysis; Bibliometric analysis; Biclustering;

Introduction

The health of the elderly has received more and more attention this year. With the aggravation of population aging, the incidence of primary osteoporosis increases sharply. Osteoporosis causes high rates of age-related fractures, peculiarly the hip fractures and Vertebral fracture, which shape into a considerable burden to public health [1].

Osteoporosis, attributed by microstructural degeneration of bone tissue and low bone mass, has been defined as a systemic skeletal disease with an incremental consequent in bone fragility and sensitivity to fracture [2]. The most common osteoporotic fractures are the proximal femur, the vertebrae and the distal radius fracture. Owing to the ageing population, their life quality seriously impacted by fractures, which is becoming a primary public health problem. With the increasing incidence of osteoporotic fractures at all ages, women have twice the risk of fractures as men. It is particularly important to pay attention to postmenopausal osteoporosis.

Primary osteoporosis mainly points to postmenopausal osteoporosis, resulting from estrogen deficiency, accounts for a large portion of osteoporosis [3]. Estrogen deficiency leads to an increase in bone turnover on account of effects on all types of bone cells. To repair microdamage and adapt to mechanical and metabolic needs, bone is being remodeled continuously. Consequently, remodeling of bone is fulfilled by two specialised cells: bone-forming osteoblasts and bone-resorbing osteoclasts. Trabecular bone (loss of connectivity) and cortical bone (cortical thinning and porosity) is effected by the imbalance of bone formation and resorption.

Bone mineral density (BMD) — measured by dual-energy X-ray absorptiometry (DXA) — is a golden key to diagnose osteoporosis. According to the WHO, osteoporosis is defined by a BMD of 2.5 standard deviations (T-score) below the average BMD of healthy young women [4]. The decision on whom to treat is made based on treatment algorithms (such as the WHO Fracture Risk Assessment Tool (FRAX)) that take into account the BMD together with pivotal risk factors for fractures (for example, prior fractures and age). A 10-year hip fracture risk of 3% is usually regarded as a cut-off to initiate treatment [5]. Diphosphonates are given as first-line treatment, followed by denosumab (a RANKL inhibitor). Teriparatide (a fragment of parathyroid hormone) is the only approved anabolic agent. Estrogen replacement therapy or selective estrogen receptor modulators can be considered in specific conditions [6]. According to improved understanding of the cellular basis for osteoporosis, new drugs targeted to key pathways are under development.

Prevention of osteoporosis is directed at gaining maximum peak bone mass and minimizing postmenopausal and age-related bone loss through nutrition, maintenance of a normal body mass index, regular physical activity and absence of smoking [7]. The main complication of osteoporosis is fractures. By reducing falls in high-risk populations, fractures may also be restrained [8].

While the above reviews to a certain extent, reflects the research status on postmenopausal osteoporosis, different scholars have different research contents and views in this field, and lack of long-term bibliometric research. In recent years, the method of bibliometric is a quantitative analysis, which has been widely applied to the decision on the development of scientific research. The statistical index measuring the contribution of a subject or scientific publications in the area of research may on behalf of the research trends and hotspots [9]. A research hot spot points to research focus on which the researchers conducted a lot of research and numerous relevant articles published.

The hot spots of the field can generally be recognized by estimating the relationship and frequencies of words that reflect the substance of articles in a field. Back in the late 1970s, French bibliometric scientists put forward the co-word analysis, which utilized to find knowledge and recognize hot spots in scholarly literature [10]. It is based on the principle that two professional terms expressing a specific subject may have a certain internal relationship if they appear in the same article. These two terms in the same article appear more frequently, they are connected closer [11]. Based on this "distance", to further summarize the focus of the research and structure of the subject by statistical analysis, such as factor analysis, cluster analysis, multivariate analysis or multidimensional scaling analysis, the significant keywords of a theme are categorized. As is known to all, it has been widely used cluster analysis to extract an area of research theme. For instance, with clustering algorithms, Yu, Z et al characterized the important research topics in cancer discovery using gene expression profiles and Bae HW et al identified the progression patterns in open-angle glaucoma patients with medical treatment [12]. Unlike the conventional clustering, biclustering permits coinstantaneous clustering of rows and columns of matrices, not merely cluster the global information, but also to detect local message in high-dimensional data efficiently. Hartigan came up with the creativity that coinstantaneous clustering could be carried out for the rows and columns of matrices firstly until 1972.The frame and algorithm of biclustering officially rendered by Cheng and Church in 2000[13]. From then on, scientists have developed more and more preeminent algorithms and frames. The field of bibliometric recommended biclustering analysis in more recent years. Fiannaca, A et al revealed miRNA expression profiles in breast cancer using biclustering [14]. Li F et al applied biclustering to probe into subject areas and hot spots of research on Internet health information seeking behavior [11]. Their research findings suggested that using the biclustering method can snatch central research focus and representative literature or researches in a field.

To the best knowledge of the authors, for the time being, there have been few bibliometric articles on postmenopausal osteoporosis. In this study, an integrated analysis on external features and content patterns of pertinent literature was performed to make clear the research status and progress on postmenopausal osteoporosis in recent five years. Particularly, co-word biclustering analysis was exploited to confirm the research hot spots of postmenopausal osteoporosis. It is hoped that this research will provide some basis for future study on postmenopausal osteoporosis.

Materials & Methods

Data collection

PubMed, providing free access to MEDLINE, OLDMEDLINE, and other related databases and developed by the national center for biotechnology information (NCBI) of the national library of medicine (NLM), from which related data were extracted and downloaded without the restriction of language. MeSH (Medical Subject Headings) terms, a series of standardized words

that can map the content of articles. According to those MeSH words, the co-word clustering analysis can be carried out continuously [11]. The search strategy applied was "Osteoporosis, Postmenopausal"[Mesh]. Publication date was set from Jan 1st, 2013- Dec 31st, 2017 and a total of 2089 literature were extracted. Two investigators independently conducted the primary search by screening these articles ground on the full text, titles and abstracts in some cases. The agreement rate between them was 0.90, showing a strong accordance [15]. Before the agreement reaching, any differences are discussed particularly. From PubMed, each downloaded article comprised the following key items: PubMed Unique Identifiers (PMIDs), MeSH terms, country, institution, language, author, publication year, source and title. These data were saved as file in XML format.

Data extraction and matrix setup

Bibliographic Item Co-Occurrence Matrix Builder (BICOMB)(developed by Professor Cui from China Medical University and securable online freely) [16] and Microsoft Excel were utilized to identify the proportion of the frequency permutation of major MeSH terms/MeSH subheadings terms, countries, languages, authors, publication year, the first author and the journals of the involved literature.

In this study, the tendencies of the extremely frequent major MeSH terms/MeSH subheadings terms were stated visually in the meanwhile. So as to detect the hot spots of postmenopausal osteoporosis, biclustering for involved publications and extremely frequent major MeSH terms/MeSH subheadings terms was carried out. Applying biclustering, the relationship between source articles and extremely frequent words and the relationship among extremely frequent words could be. Whereafter, from BICOMB, a binary matrix with source articles as the columns and extremely frequent major MeSH terms/MeSH subheadings terms as the rows was structured for further biclustering by means of the software "gCLUTO", version 1.0 (Graphical CLUstering TOolkit, a graphical front-end for the CLUTO data clustering library, developed by Rasmussen, Newman, and Karypis from University of Minnesota) [17]. Based on the literature, parameters of biclustering in gCLUTO were set, which were suitable for biclustering analysis. Then, I2 was selected for criterion function, Cosine was chosen for similarity function and repeated bisection for clustering method. The biclustering result of the matrix of source articles - extremely frequent major MeSH terms/MeSH subheadings terms was displayed by matrix visualization and mountain visualization. In order to identify the appropriate number of clusters, the biclustering with different numbers of clusters were redirected until the matrix visualization and mountain visualization reach the optimal result. With semantic relationships between major MeSH terms/MeSH subheadings terms and the typical source articles in clusters, the fundamental structure of research focus on postmenopausal osteoporosis was mapped and establish.

Results

Growth of the relevant Literature

In total, 2089 literature (Jan. 1st, 2013-Dec. 31st, 2017) were involved in this research based on the search strategy and inclusion criteria. Over the past five years, investigators are concerned about postmenopausal osteoporosis less and less. It is demonstrated that the annual output of literature has decreased bit by bit from 498 in 2013, to 320 in 2017 in the area of postmenopausal osteoporosis. (Fig. 1)

Distribution characteristics of literature

In all of the articles that provided by PubMed on postmenopausal osteoporosis, 98.95% (2067/2089) furnished the addresses of authors. Thus, based on the ough statistics, articles on postmenopausal osteoporosis downloaded from PubMed stemmed from at least 52 different countries. In Fig. 2, the number of research findings on postmenopausal osteoporosis in different countries or regions has been enumerated. So far, England（34.47%）and the United States（33.51%）have been the largest contributors to postmenopausal osteoporosis.

Of all 12587 authors contained in this subject, individually, eight authors published twenty or more articles. Reginster JY topped the list with 28 articles, five of which were printed as the first author. Roux C brought out 26 articles come off second best, publishing four articles as the first author. As for ranking of the first author, the top place with seven articles on postmenopausal osteoporosis were Palacios S from Spain and McClung MR from the United States.

Majority of these literature were published in English (94.22%,1972/2089), the remaining articles were published in Chinese (1.15%, 24/2089), Spanish (1.10%, 23/2089), German (0.91%, 19/2089), , French (0.67%, 14/2089), Japanese (0.57%, 12/2089) Russian (0.33%, 7/2089), Hungarian (0.24%, 5/2089), Portuguese (0.14%, 3/2089) Polish(0.14%, 3/2089) and Bulgarian (0.14%, 3/2089), in several. [Note, four articles were published in both English and Norwegian, English and French, English and Spanish [18-21].]

Most Active Journals

Thoroughly, 587 journals have emerged in this area. The ten most active journals published 783 publications on postmenopausal osteoporosis, accounting for 37.48% of all 2089 publications. Ranking of the top ten active journals, which are recognized as the core journals in this field, spread out in Table 1. Throughout the top ten journals, the top three journals are Osteoporosis international, Menopause and The Journal of clinical endocrinology and metabolism, at the same time, these three journals make up more than 22.55% of the entire indexed articles in this area.

Research Hot Spots of postmenopausal osteoporosis

As far as the involved literature, 2439 major MeSH terms/MeSH subheadings terms were computed with an accumulated frequency of 9372 times. After H index standard evaluation, with a frequency of 36 or more times' appearance, a major MeSH term/MeSH subheadings term was defined as an extremely frequent one. Then, 36 extremely frequent major MeSH terms/MeSH subheadings terms abstracting from the involved publications with an accumulated percentage of 38.22% (3582/9372) were displayed in Table 2. Different numbers of clusters were performed by biclustering; mountain visualization and matrix visualization shown the biclustering result of the matrix of source articles - extremely frequent major MeSH terms/MeSH subheadings terms. The mountain visualization and the extremely frequent major MeSH terms/MeSH subheadings terms in each cluster when they were classified into eight clusters was illustrated in Fig. 3. The intention of the mountain visualization is to visibly facilitate the consumer in grasping the result of biclustering and the essence of high-dimensional datasets. Fig. 3 displays each cluster as a peak in the 3D landform marking with the cluster number (from 0 to 7, totally eight clusters in this study). The information about the associated cluster was reflected by location on the plane, altitude, color and volume of a peak. With respect to other peaks, the location on the plane is the most informative attribute of a peak. The relative similarity of their clusters is represented by the interval between a couple of peaks on the plane. The altitude of a peak is often in direct proportion to the internal similarity of the cluster. The internal standard deviation of objects in each cluster revealed by color of each peak. Blue means high deviation, while red means low deviation. Finally, the volume of a peak is in direct proportion to the amount of major extremely frequent major MeSH terms/MeSH subheadings terms stored within the cluster. Based on the knowledge of authors, at lowest 30 publications should be contained in each independent cluster and triplet peaks should not appear in the mountain visualization. The matrix visualization is illustrated in Fig. 4, in which the column tags are PMIDs of source articles, and the row tags on behalf of extremely frequent major MeSH terms/MeSH subheadings terms, separately on the bottom and the right of the matrix. The values present in the matrix are graphically represented by colors. The color of each reseau paints the proportional emergence frequency of a major MeSH term/MeSH subheading term in a publication. The cumulatively deeper red indicates greater significance, while the white indicates the significance closer to none. In Table 3, with the biclustering, gCLUTO replumed the rows of the initial matrix so that analogous rows in the same cluster are converged; these clusters are partition by black horizontal lines. 36 extremely frequent major MeSH terms/MeSH subheadings terms are clustered into eight clusters exposited in the matrix visualization. The top layered cluster tree describes the relationships between articles and the left layered cluster tree demonstrates the relationships between extremely frequent major MeSH terms/MeSH subheadings terms. In each cluster, it also shows each of the major MeSH term/MeSH subheading term exists in matching articles. A deeper exploration of the typical articles in each cluster conduced to the project of discerning and outlining the themes of each cluster. According to the above standards discussed by the research team, the major MeSH terms/MeSH subheadings terms were categorized into eight clusters (Fig. 3). These clusters include:

Genetics related researches on bone metabolisms of postmenopausal osteoporosis (Cluster 0),
Adverse effects of Diphosphonates (Cluster 1),
Therapeutic use of postmenopausal osteoporosis (Cluster 2),
Administration and dosage of Clinical therapy drug——Diphosphonates (Cluster 3),
Study on epidemiology and etiology of complications on postmenopausal osteoporosis (Cluster 4),
Physiology and physiopathology of postmenopausal osteoporosis (Cluster 5),
Risk factors associated with BMD in the diagnosis of postmenopausal osteoporosis (Cluster 6),
Clinical drug effects of Dietary Supplements on postmenopausal osteoporosis (Cluster 7),
These eight clusters could stand for the major research hot spots in recent five years.

Discussion

MeSH terms can image the content of articles and a great quantity of MeSH terms can map the current research status and trends of the field. According to the statistical and co-word analysis by software BICOMB, the research output on "Osteoporosis, Postmenopausal"[Mesh] in recent five years keeps a gradually decrease. Additionally, our analysis suggested that the biggest participants of the research in this field are England and the US, which is accord with the bibliometric results in other fields [22]. English is the official language in these two countries may explain these results. According to a quantitative and co-word biclustering analysis by gCLUTO software, similar MeSH terms can be identified and categorized into clusters. Then, the research hot spots on postmenopausal osteoporosis were generated on end, so that the essential knowledge structure and trends in this field can be examined systematically.

Cluster 0 relates to the genetics researches on bone metabolisms of postmenopausal osteoporosis. Postmenopausal osteoporosis is a common polygenic health problem. Genetic factors play an important role in the bone metabolisms of postmenopausal osteoporosis. BMD, a crucial risk factor for osteoporosis, is under strong genetic control with estimates of heritability scoping from 0.5 to 0.9. To date, several studies have reported that some functional genes, for instance, the CYP11A1 in vitamin D and estrogen hormone-response pathways, the estrogen receptorα (ERα) gene, tumor necrosis factor (TNF)-α gene and the TNFSF11, TNFRSF11A in the RANKL/RANK/OPG pathway, are implied to be associated with BMD on postmenopausal osteoporosis [23]. Exploring different genetic variants underlying development of osteoporosis would make it possible to early prophylactics of osteoporosis as well as manage individual-based symptomatic treatment.

Cluster 1 relates to adverse effects of diphosphonates. For the treatment of osteoporosis, the most widely used medications is diphosphonates, which are divided into two groups on the basis of their structures. First generation diphosphonates do not contain nitrogen, while new generation diphosphonates have a nitrogen-containing side chain. The structure has a high-affinity for the hydroxyapatite at the bone surface, so the diphosphonates can preserve for months or even years. After years of evolution, diphosphonates, including alendronate (ALN), risedronate sodium, ibandronate sodium (IBN) and zoledronic(ZOL), are more durable and stable. The adverse

effects of diphosphonates, however, are unavoidable. On the one hand, the first intravenous dose of diphosphonates, such as IBN and ZOL, may be trigger an acute-phase response (APR). After their first diphosphonates infusion, patients had a fever and pain. Commonly, these symptoms were transient in duration and mild to moderate in intensity. By means of NSAID, the incidence and intension of such APR could retarded efficiently [24]. On the other hand, an unusual atraumatic or minimal-trauma fracture, the atypical femoral fracture (AFF), has been reported with increasing frequency in long-term diphosphonates users since the first case reports were published in 2005[25]. A unique case of AFF after diphosphonates therapy the patient had a successful recovery through conservative treatment [26]. To summarize, it is essential to assess the possibility of atypical fractures in osteoporotic patients when they beef about lower extremity pain and to take into account alternative treatments instead of diphosphonates.

Cluster 2 relates to the therapeutic use of postmenopausal osteoporosis. According to the mechanism, drug therapy for osteoporosis can be divided into antiresorptive agents and anabolic agents. Antiresorptive agents are composed of raloxifene (RAL), diphosphonates, and denosumab. Teriparatide is the only anabolic agent for osteoporosis treatment approved by Food and Drug Administration. Studies have shown that cortical turnover and cortical bone formation in patients who were either treatment naïve (TN) or had previous ALN therapy increase with 24 months of teriparatide treatment [27]. In other clinical studies, synergistic effects of combination therapy with an antiresorptive agent and teriparatide have been proposed [28]. The addition of ALN to ongoing teriparatide and continuing ALN after teriparatide was stopped may be beneficial for patients in terms of areal and volumetric BMD increases [29]. What is more, the treatment of combining teriparatide with diphosphonates can reflect faster bony union and highly improved BMD scores [30]. Although combination therapy has obvious advantages, the best time to start the combination therapy should be further studied to prevent osteoporotic fractures.

Cluster 3 relates to the administration and dosage of Diphosphonates. Diphosphonates as an antiresorptive agent have been accepted for the treatment and prevention of postmenopausal osteoporosis. While the official guidance on the dosage and the length of treatment is lacking. Curative effect of diphosphonates is not very ideal. Firstly, Long-term users with ten dose years or more of a diphosphonates are rare due to periods of low compliance and gaps, with a discrepancy between the length of treatment and dose taken [31]. Then, Long-term diphosphonates treatment of postmenopausal women does not impair the response to subsequently administered intravenous pamidronate suggesting that inadequate response to long-term diphosphonates treatment is not responsible for treatment failure [32]. What's more, over the past decade, several reports have highlighted the increased risk of AFF in patients treated with long-term diphosphonates. On the basis of this recommendation, patients may be advised to stop taking diphosphonates for a while. BMD at the total hip declines significantly within 1 year of diphosphonates discontinuation, particularly in lean patients [33]. Hence, additional studies are needed to identify reasonable treatment of diphosphonates.

Cluster 4 relates to epidemiology and etiology of complications on postmenopausal osteoporosis. The essential complication of postmenopausal osteoporosis is fractures. Accurate

Assessment and prediction for the risk of fracture is particularly crucial. DXA regarded as the gold standard for the diagnosis of osteoporosis at the lumbar spine and hip worldwide. Whereas, BMD reveals merely a portion of an individual's fracture risk by reason that the multi-factor of fragility fracture. Accordingly, consideration must be taken into the identification of patients at high risk of fracture, and many clinical risk factors predict the risk of fracture, independently of the BMD. The combine of BMD with risk factors can enhance the precaution of patients at high risk of osteoporotic fractures. A real-world study found teriparatide to be more effective in reducing risk of fragility fractures as early as 6 months with continuous treatment benefit up to 24 months [34]. A FRAX, using nine clinical risk factors: age, sex, BMI, prior fragility fracture history, family history of hip fracture, the existence of secondary osteoporosis, exposure to systemic glucocorticoids, current smoking and three or more units of alcohol per day, has been developed and acknowledged by the WHO to predict an individual 10-year risk of major or hip osteoporotic fractures. In addition, the International Osteoporosis Foundation (IOF) One Minute Test, though with the lowest predicting rate compared to other tested tools, had competent precision for predicting yet [35,36]. Moreover, there is an increasing risk for hip fracture in postmenopausal women with type 2 diabetes [37]. From what has been discussed above, further etiology studies should be conducted to prevent the occurrence of complications.

Cluster 5 relates to the physiology and physiopathology of postmenopausal osteoporosis. A strong correlation between BMD scores and the probability of fragility fractures is well-documented. BMD is affected by multiple factors. Higher BMI scores and moderate levels of physical activity have been found significant in avoiding a decline in BMD [38]. Life satisfaction and its improvement are longitudinally linked with reduced bone loss in postmenopausal women [39].

Cluster 6 relates to risk factors associated with BMD in the diagnosis of postmenopausal osteoporosis. With the increasing incidence of postmenopausal osteoporosis, it is important to identify risk factors for the prevention of postmenopausal osteoporosis. As the cause of postmenopausal osteoporosis is multiple factors, it is difficult to accurately reveal its risk factors. Exercise is consistently effective in favorably affecting BMD in (initially) early-postmenopausal women without any leveling-off effect after 16 years of exercise [40]. Duration of fertility (years of menstruation) longer than 33 years and a BMI greater than 32 seem to prevent postmenopausal osteoporosis. Age is also an independent risk factor for postmenopausal osteoporosis [41]. When it comes to diagnostic imaging, in probabilistic sensitivity analysis, DXA and quantitative CT at age 55 years with quantitative CT screening every 5 years was the best strategy. Furthermore, combined assessment of bone strength and BMD is a cost-effective strategy for osteoporosis screening in postmenopausal women and has the potential to prevent a large number of osteoporosis fractures.

Cluster 7 relates to the drug effect of alternative therapy— Dietary Supplements. In spite of pharmacotherapy, for instance, diphosphonates, have been widely used to alleviate the risk of fractures and remedy osteoporosis. With low compliance with long-term medication and related adverse effects, it is instant and crucial to develop new alternative medicine to treat osteoporosis.

Additionally, many people admire alternative and complementary therapies. A calcium collagen chelate (CC) dietary supplement was effective in improving BMD and blood biomarkers of bone turnover in osteopenic postmenopausal women [42,43]. Context Eucommiae Cortex and Radix Dipsaci, occurring in a ratio of 1:1 in Du-Zhong-Wan (DZW) and Puerarin 600-O-xyloside can also achieve the above effect on ovariectomy mice [44,45].

In addition, we realize that several latent restrictions that may stimulate intensive study. First of all, although co-word biclustering, based on extremely frequent MeSH terms, is a highly beneficial way to determine research hot spots in a field, the number of MeSH terms might have some effect on the result of biclustering analysis. However, the updated emerging themes with low attention may not have been involved. Thus, in the future studies, analysis combining updated emerging themes and multiple databases should be considered. Secondly, complete affiliation data did not appear in 1.05% (22/2089) of publications, so the countries of these articles were blank. It may lead to bias that understate in some countries. Finally, publications were merely extracted and downloaded from the PubMed, which may not cover all publications associated with postmenopausal osteoporosis, peculiarly non-English and some grey literature, that's probably why the decline in the research output.

Conclusions

In this study, the visualization of research hot spots in the area of postmenopausal osteoporosis was carried out by content analysis with co-word biclustering. Eight major research hot spots identified provide basic information that can be used in further research regarding the treatment of osteoporosis. Furthermore, other bibliometric information suggests the research condition in this field; the research findings is decreasing stage by stage. Osteoporosis international is the most active chief journal, which publishing primary articles on postmenopausal osteoporosis. On the side, comparison with the United States and England, the correspondingly small amount of literature extracted by PubMed from other countries suggests to a certain degree that the area might be less developed in these regions. Additional Studies on postmenopausal osteoporosis could give some references for the health of the elderly women.

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Compliance with ethical standards

Conflicts of interest Siming Zhou, Zhengbo Tao,Yue Zhu and Lin Tao declare that they have no conflict of interest.

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Figure 1

All the literature involved in this research based on the search strategy and inclusion criteria.

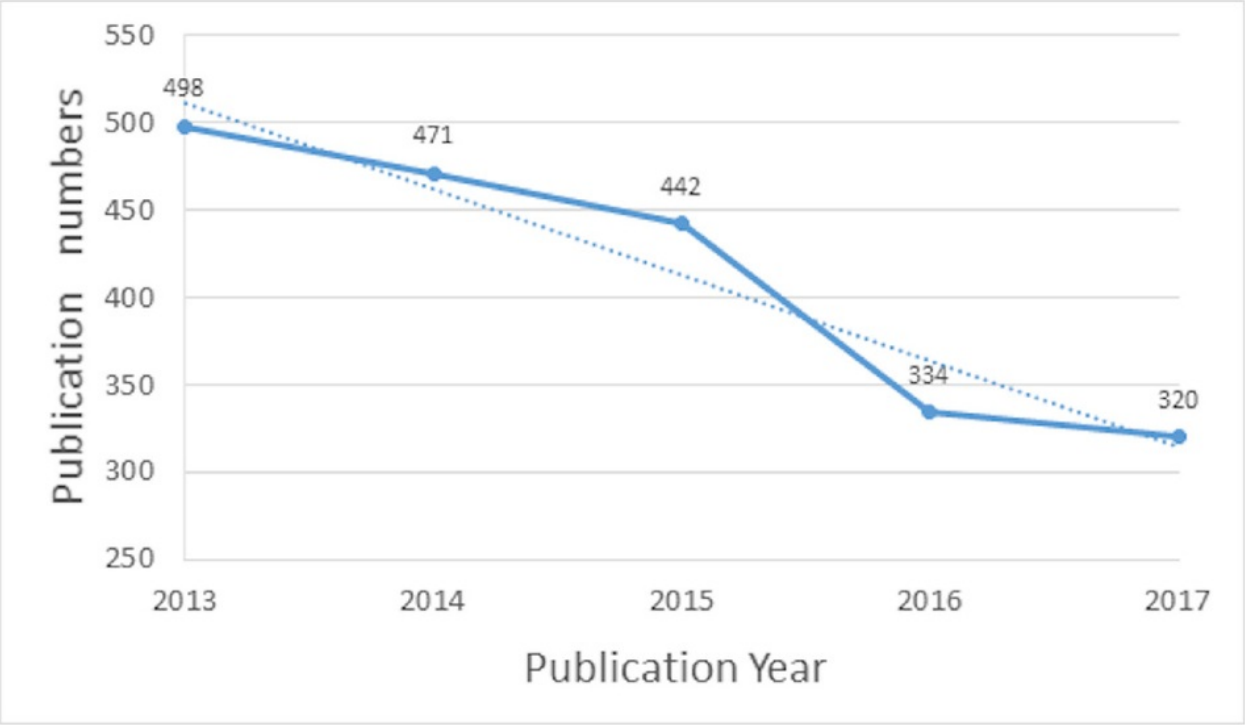

Figure 2

Geographic distribution of research output on postmenopausal osteoporosis

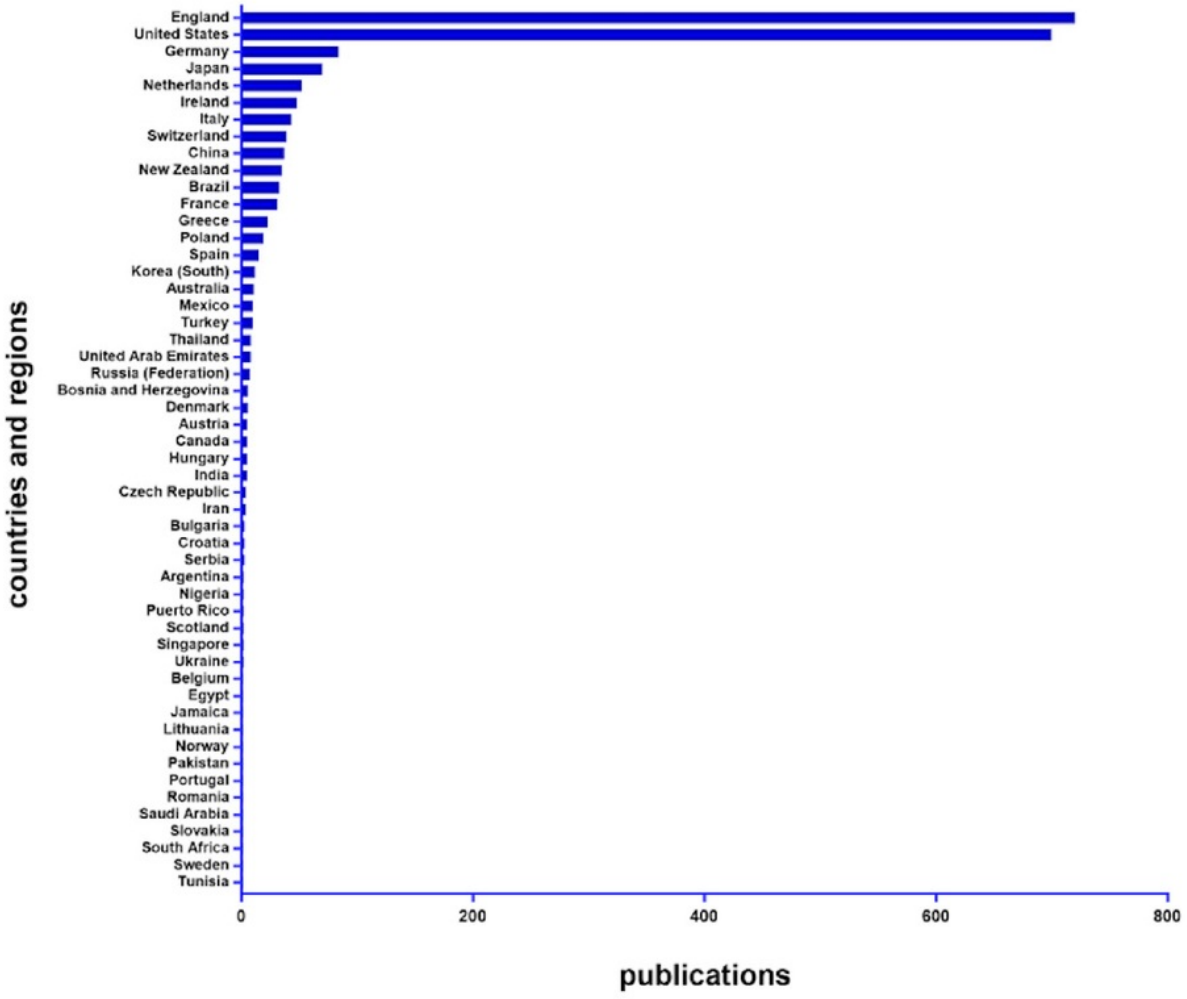

Figure 3

Mountain visualization of biclustering of highly frequent major MeSH terms and articles on postmenopausal osteoporosis

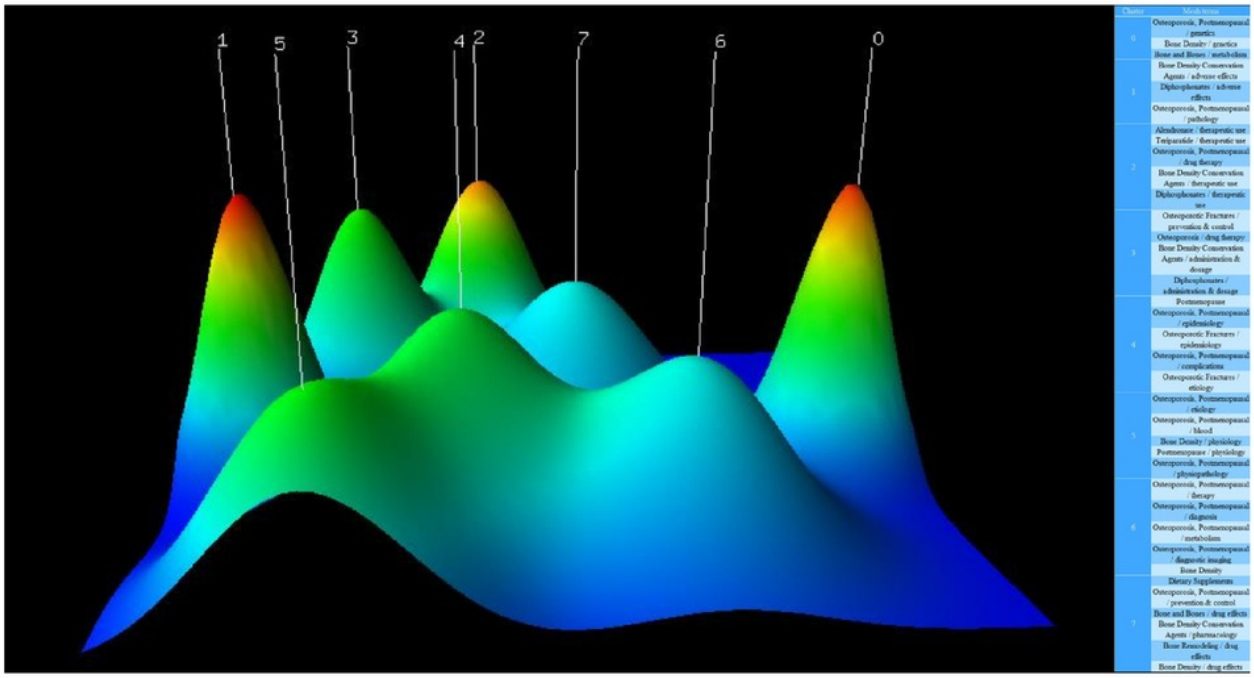

Figure 4

1

Visualized matrix of biclustering of highly frequent major MeSH terms and PubMed Unique Identifiers (PMIDs) of articles on postmenopausal osteoporosis.

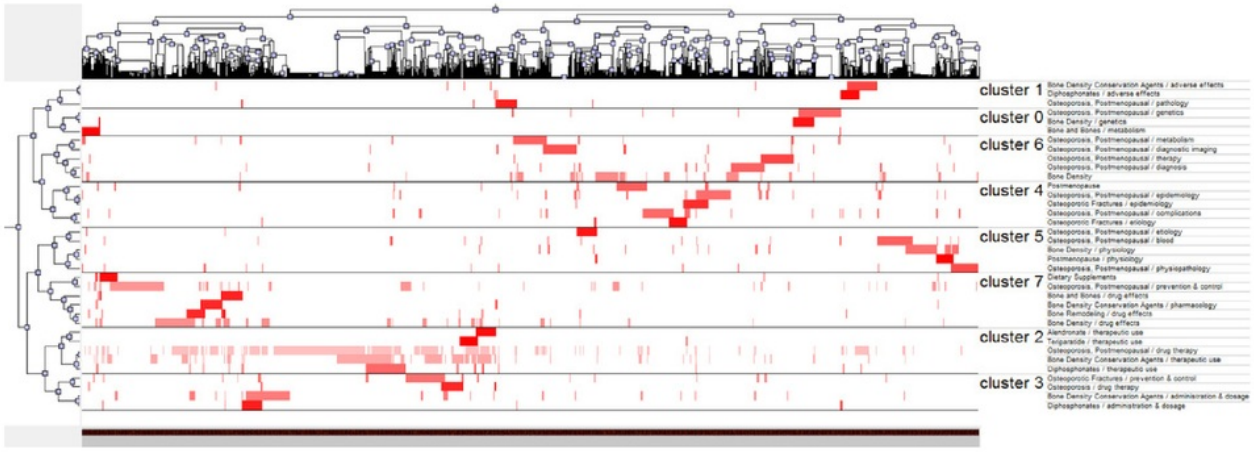

Table 1(on next page)

Most active journals on the topic of postmenopausal osteoporosis (PubMed sourced until Dec 2017) (n=2089).

No.	Top journals	Publications n (%)
1	Osteoporosis international	341（16.32）
2	Menopause	71（3.40）
3	The Journal of clinical endocrinology and metabolism	59（2.82）
4	Climacteric	58（2.78）
5	Calcified tissue international	48（2.30）
6	Journal of bone and mineral research	46（2.20）
7	Bone	46（2.20）
8	PloS one	45（2.15）
9	Maturitas	39（1.87）
10	Journal of bone and mineral metabolism	30（1.44）
Total		783(37.48)

1

Table 2(on next page)

Highly frequent major MeSH[1] terms from the included publications on postmenopausal osteoporosis (n=9372).

Rank	Major MeSH terms/ MeSH subheadings	Frequency	Proportion of frequency (%)	Cumulative percentage (%)
1	Osteoporosis, Postmenopausal / drug therapy	577	6.1566	6.1566
2	Bone Density Conservation Agents / therapeutic use	305	3.2544	9.4110
3	Osteoporosis, Postmenopausal / prevention & control	208	2.2194	11.6304
4	Bone Density / drug effects	185	1.9740	13.6044
5	Bone Density	172	1.8353	15.4396
6	Bone Density Conservation Agents / administration & dosage	135	1.4405	16.8801
7	Bone Density / physiology	116	1.2377	18.1178
8	Osteoporotic Fractures / prevention & control	113	1.2057	19.3235
9	Osteoporosis, Postmenopausal / epidemiology	110	1.1737	20.4972
10	Osteoporosis, Postmenopausal / complications	104	1.1097	21.6069
11	Diphosphonates / therapeutic use	102	1.0883	22.6953
12	Osteoporosis, Postmenopausal / genetics	96	1.0243	23.7196
13	Osteoporosis, Postmenopausal / diagnosis	94	1.0030	24.7226
14	Osteoporosis, Postmenopausal / metabolism	94	1.0030	25.7256
15	Postmenopause	92	0.9816	26.7072
16	Osteoporosis, Postmenopausal / blood	91	0.9710	27.6782
17	Osteoporosis, Postmenopausal / diagnostic imaging	80	0.8536	28.5318
18	Osteoporosis, Postmenopausal / physiopathology	72	0.7682	29.3000
19	Osteoporosis, Postmenopausal / therapy	68	0.7256	30.0256
20	Bone Density Conservation Agents / adverse effects	67	0.7149	30.7405
21	Osteoporotic Fractures / epidemiology	53	0.5655	31.3060
22	Bone Remodeling / drug effects	51	0.5442	31.8502
23	Bone Density Conservation Agents / pharmacology	50	0.5335	32.3837
24	Osteoporosis / drug therapy	50	0.5335	32.9172
25	Bone and Bones / drug effects	48	0.5122	33.4294
26	Osteoporosis, Postmenopausal / pathology	47	0.5015	33.9309
27	Diphosphonates / administration & dosage	46	0.4908	34.4217
28	Osteoporosis, Postmenopausal / etiology	43	0.4588	34.8805
29	Bone Density / genetics	43	0.4588	35.3393
30	Osteoporotic Fractures / etiology	41	0.4375	35.7768
31	Dietary Supplements	40	0.4268	36.2036
32	Alendronate / therapeutic use	40	0.4268	36.6304
33	Diphosphonates / adverse effects	39	0.4161	37.0465
34	Postmenopause / physiology	37	0.3948	37.4413

35	Bone and Bones / metabolism	37	0.3948	37.8361
36	Teriparatide / therapeutic use	36	0.3841	38.2202

1

Table 3(on next page)

1

Highly frequent major MeSH a terms-source articles matrix (localized).

No.	Major MeSH terms/ MeSH subheadings	Pubmed Unique Identifiers of source articles				
		21631599	22057139	22302614	...	29782125
1	Osteoporosis, Postmenopausal / drug therapy	0	0	0	...	0
2	Bone Density Conservation Agents / therapeutic use	0	0	0	...	0
3	Osteoporosis, Postmenopausal / prevention & control	1	0	1	...	0
4	Bone Density / drug effects	0	0	1	...	0
...	...	...	...	...	...	...
35	Bone and Bones / metabolism	0	0	0	...	0
36	Teriparatide / therapeutic use	0	0	0	...	0

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ORIJINALLIK RAPORU

%31	%21	%22	%11
BENZERLIK ENDEKSI	İNTERNET KAYNAKLARI	YAYINLAR	ÖĞRENCI ÖDEVLERI

BIRINCIL KAYNAKLAR

1	www.jmir.org İnternet Kaynağı	%6
2	Submitted to Universiti Teknologi MARA Öğrenci Ödevi	%3
3	Richard Eastell, Terence W. O'Neill, Lorenz C. Hofbauer, Bente Langdahl, Ian R. Reid, Deborah T. Gold, Steven R. Cummings. "Postmenopausal osteoporosis", Nature Reviews Disease Primers, 2016 Yayın	%3
4	bmcophthalmol.biomedcentral.com İnternet Kaynağı	%3
5	www.ncbi.nlm.nih.gov İnternet Kaynağı	%2
6	link.springer.com İnternet Kaynağı	%1
7	journals.plos.org İnternet Kaynağı	%1

8	pubs.rsna.org İnternet Kaynağı	%1
9	Yue Ding, Jian-Cheng Zeng, Fei Yin, Chun-lin Zhang et al. "Multicenter Study on Observation of Acute-phase Responses After Infusion of Zoledronic Acid 5 mg in Chinese Women with Postmenopausal Osteoporosis", Orthopaedic Surgery, 2017 Yayın	%1
10	www.science.gov İnternet Kaynağı	%1
11	www.futuremedicine.com İnternet Kaynağı	%1
12	www.nature.com İnternet Kaynağı	%1
13	www.linknovate.com İnternet Kaynağı	<%1
14	S O'Donnell. "Strontium ranelate for preventing and treating postmenopausal osteoporosis", Cochrane Database of Systematic Reviews Reviews, 10/18/2006 Yayın	<%1
15	Submitted to University of Sheffield Öğrenci Ödevi	<%1
16	www.tandfonline.com	

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17	Muschitz, Christian, Roland Kocijan, Astrid Fahrleitner-Pammer, Imre Pavo, Judith Haschka, Wolfgang Schima, Stylianos Kapiotis, and Heinrich Resch. "Overlapping and Continued Alendronate or Raloxifene Administration in Patients on Teriparatide: Effects on Areal and Volumetric Bone Mineral Density The CONFORS Study", Journal of Bone and Mineral Research, 2014. Yayın	<%1
18	Michael Pazianas, Roger Smith. " Drug-Associated Atypical Femoral Fractures (DaAFFs): Balancing the Facts ", The Journal of Clinical Endocrinology & Metabolism, 2014 Yayın	<%1
19	linknovate.com İnternet Kaynağı	<%1
20	over50skifitness.blogspot.com İnternet Kaynağı	<%1
21	www.linguamedica.jp İnternet Kaynağı	<%1
22	www.jove.com İnternet Kaynağı	<%1

23	Bei Shi, Wenjuan Wei, Xin Qin, Fangkun Zhao, Yucen Duan, Weinan Sun, Da Li, Yu Cao. "Mapping theme trends and knowledge structure on adipose-derived stem cells: a bibliometric analysis from 2003 to 2017", Regenerative Medicine, 2019 Yayın	<%1
24	www.medsci.org İnternet Kaynağı	<%1
25	Submitted to University of Hong Kong Öğrenci Ödevi	<%1
26	L. H. R. Xu, B. Adams-Huet, J. R. Poindexter, N. M. Maalouf. "Determinants of change in bone mineral density and fracture risk during bisphosphonate holiday", Osteoporosis International, 2015 Yayın	<%1
27	Fangkun Zhao, Bei Shi, Ruixin Liu, Wenkai Zhou, Dong Shi, Jinsong Zhang. "Theme trends and knowledge structure on choroidal neovascularization: a quantitative and co-word analysis", BMC Ophthalmology, 2018 Yayın	<%1
28	Xiao Chen, Xin Zhi, Liehu Cao, Weizong Weng, Panpan Pan, Honggang Hu, Chao Liu, Qingjie Zhao, Qirong Zhou, Jin Cui, Jiacan Su. "Matrine	<%1

derivate MASM uncovers a novel function for ribosomal protein S5 in osteoclastogenesis and postmenopausal osteoporosis", Cell Death & Disease, 2017
Yayın

29	Submitted to Unviersidad de Granada Öğrenci Ödevi	<%1
30	epublications.uef.fi İnternet Kaynağı	<%1
31	K. Lippuner. "Remaining lifetime and absolute 10-year probabilities of osteoporotic fracture in Swiss men and women", Osteoporosis International, 10/31/2008 Yayın	<%1
32	stichtingiwo.nl İnternet Kaynağı	<%1
33	Kim, Hyo-Sang, Han Young Jung, Myeong-Ok Kim, Kyung-Lim Joa, Yeo Ju Kim, Su-Yeon Kwon, and Chang-Hwan Kim. "Successful Conservative Treatment : Multiple Atypical Fractures in Osteoporotic Patients After Bisphosphate Medication", Medicine, 2015. Yayın	<%1
34	Yi-Hsiang Hsu, Tianhua Niu, Henry A. Terwedow, Xin Xu et al. "Variation in genes involved in the RANKL/RANK/OPG bone	<%1

remodeling pathway are associated with bone mineral density at different skeletal sites in men", Human Genetics, 2005
Yayın

35	Submitted to University of Reading Öğrenci Ödevi	<%1
36	www.spandidos-publications.com İnternet Kaynağı	<%1
37	ieeecs-services.computer.org İnternet Kaynağı	<%1
38	Sabri Cavkaytar, Mehmet Murat Seval, Zeliha Atak, Rahime Bedir Findik, Sevgi Ture, Demet Kokanali. "Effect of reproductive history, lactation, first pregnancy age and dietary habits on bone mineral density in natural postmenopausal women", Aging Clinical and Experimental Research, 2015 Yayın	<%1
39	Jing Gan, Qianyun Cai, Peter Galer, Dan Ma, Xiaolu Chen, Jichong Huang, Shan Bao, Rong Luo. "Mapping the knowledge structure and trends of epilepsy genetics over the past decade", Medicine, 2019 Yayın	<%1
40	d-nb.info İnternet Kaynağı	<%1

41	bpspubs.pericles-prod.literatumonline.com İnternet Kaynağı	<%1
42	www.cambridge.org İnternet Kaynağı	<%1
43	www.mdpi.com İnternet Kaynağı	<%1
44	www.amato.com.br İnternet Kaynağı	<%1
45	Submitted to Leeds Metropolitan University Öğrenci Ödevi	<%1
46	"Abstracts At 28th Kansai Calcium Conference April 11, 1992 Restaurant Palace, New Hankyu Building, Osaka", Journal of Bone and Mineral Metabolism, 1993 Yayın	<%1
47	Elizabeth Shane, David Burr, Peter R Ebeling, Bo Abrahamsen et al. "Atypical subtrochanteric and diaphyseal femoral fractures: Report of a task force of the american society for bone and mineral Research", Journal of Bone and Mineral Research, 2010 Yayın	<%1
48	Mishaela R. Rubin, Hua Zhou, Natalie E. Cusano, Rukshana Majeed et al. "The Effects of Long-term Administration of rhPTH(1-84) in	<%1

Hypoparathyroidism by Bone Histomorphometry", Journal of Bone and Mineral Research, 2018
Yayın

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49 "Biomarkers in Bone Disease", Springer Nature, 2017 <%1
Yayın

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50 Elena Alacreu, David Moratal, Estanislao Arana. "Opportunistic screening for osteoporosis by routine CT in Southern Europe", Osteoporosis International, 2017 <%1
Yayın

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51 Akram Kharroubi, Elias Saba, Ibrahim Ghannam, Hisham Darwish. "Evaluation of the validity of osteoporosis and fracture risk assessment tools (IOF One Minute Test, SCORE, and FRAX) in postmenopausal Palestinian women", Archives of Osteoporosis, 2016 <%1
Yayın

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52 Fumito Yoshiki, Atsushi Nishikawa, Masanori Taketsuna, Kenta Kajimoto, Hiroyuki Enomoto. "Efficacy and safety of teriparatide in bisphosphonate-pretreated and treatment-naive patients with osteoporosis at high risk of fracture: Post hoc analysis of a prospective observational study", Journal of Orthopaedic <%1

Science, 2017
Yayın

53 Submitted to University of Ulster
Öğrenci Ödevi

<%1

Alıntıları çıkart	üzerinde	Eşleşmeleri çıkar	< 5 words
Bibliyografyayı Çıkart	üzerinde		