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Bibliometric Analysis

Bibliometric analysis reveals lagging research progress on vitamin D and osteoporosis in Southeast Asia compared to global trends

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Abstract

Osteoporosis, a widespread global health concern, is strongly linked to vitamin D deficiency, which affects calcium absorption and bone metabolism. Understanding the interplay between vitamin D and osteoporosis is crucial, yet disparities in research output between global and Southeast Asia (SEA) contexts may highlight gaps in regional knowledge and healthcare strategies. The aim of this study was to assess and compare the research landscape on vitamin D and osteoporosis between global and SEA datasets, identifying disparities and areas that require further research focus. A bibliometric analysis was performed using Scopus data as of August 12, 2024. Two datasets were analyzed: a global dataset with 24,829 publications and a SEA dataset with 345 publications. Bibliometrix and VOSviewer software were employed to analyze publication trends, thematic evolution, and co-occurrence networks. The global dataset showed an exponential increase in research publications starting in the 1980s, with a recent trend toward saturation. In contrast, the SEA dataset is experiencing growth but remains significantly behind the global output, with SEA countries contributing a relatively small number of publications. The SEA dataset had a higher proportion of original research (69.6%) compared to the global dataset (59.4%). Thematic analysis revealed that SEA research predominantly focuses on well-established topics, lacking the diversification and specialization observed globally. The research on vitamin D and osteoporosis in SEA is lagging behind global trends, with fewer publications and less thematic specialization. We recommend intensifying research in the SEA region, aligning local guidelines with international standards, and increasing international and interdisciplinary collaborations.

Keywords: Bibliometric analysis, cholecalciferol, low bone mineral density, vitamin D, osteoporosis

Introduction

According to a meta-analysis published in 2022 which used World Health Organization criteria, the prevalence of osteoporosis across countries has reached 19.7% [1]. The prevalence was reported to be higher in developing countries (22.1%), as opposed to developed countries (14.5%) [1]. In the global burden of disease study, the mortality attributed to low bone mineral density

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disease worldwide has increased up to 111.16% from 1990 to 2019 [2]. On the other hand, vitamin D has been suggested to play an essential role in calcium absorption and bone metabolism [3, 4]. Deficiency in vitamin D is widespread, particularly in regions with limited sunlight exposure or poor dietary intake, and it is strongly associated with the development of osteoporosis [3, 4]. Among Asian countries, including those in Southeast Asia (SEA), a meta-analysis reported that the prevalence of hypovitaminosis D could reach up to 20.93% [5]. Given the increased prevalence of osteoporosis, understanding the relationship between vitamin D and osteoporosis is of urgent matter. Moreover, the effects of this fat-soluble vitamin are varied across populations, suggesting the importance of observing the research progress in multiple regions, including in SEA.

To assess the existing body of evidence on the interplay of vitamin D and osteoporosis, bibliometric analysis was used to provide a structured approach to evaluating the scope and impact of research in the field. By analyzing trends in publication output, citation networks, and the evolution of key research themes, bibliometric studies can reveal the most influential research, identify gaps in the literature, and highlight emerging areas of interest [6, 7]. In previous research, the analysis was employed to observe the impact of a pandemic on certain research topics, such as essential oils and systematic reviews of medical subjects [8, 9]. Herein, we assessed both global and SEA datasets to understand not only the overall research landscape but also to identify regional disparities in research focus and output. By comparing these datasets, we aimed to determine whether SEA countries are keeping pace with global research trends and to highlight areas where further research investment is needed. This dual focus ensures a comprehensive understanding of the field and helps guide strategic decisions to address potential gaps, particularly in regions that may be underrepresented in the global discourse on vitamin D and osteoporosis.

Methods

Search strategy

The study used two datasets (global and SEA datasets) to compare the global research trend with that in the SEA region. The bibliography information was identified through Scopus database as of August 12, 2024. The combination of keywords was designed by employing Boolean operators (AND and OR) to selectively obtain the bibliography information relevant to vitamin D and osteoporosis research. The combination of keywords used for each dataset is presented in **Table 1**. No restrictions on document type, language, or date of publication were applied in the search protocol. The .csv file of each dataset was downloaded with all bibliography information selected.

Table 1. Keyword combinations used in the Scopus database

Dataset	Search field	Keywords	Hits
Global	Title, abstract, and keywords	Osteoporosis AND ("Vitamin D" OR "25-hydroxyvitamin D" OR "25-OH vitamin" OR "Calciferol" OR "Cholecalciferol" OR "Ergocalciferol" OR "1, 25-dihydroxyvitamin D")	24,829
Southeast Asia	Title, abstract, and keywords	Osteoporosis AND ("Vitamin D" OR "25-hydroxyvitamin D" OR "25-OH vitamin" OR "Calciferol" OR "Cholecalciferol" OR "Ergocalciferol" OR "1, 25-dihydroxyvitamin D")	345
	Affiliation country	Indonesia OR Malaysia OR Laos OR Vietnam OR Cambodia OR Myanmar OR Thailand OR Brunei OR Singapore OR Philippines OR Timor	

Bibliometric analysis

Distributions of the published articles based on publication year, types of documents, and countries were retrieved from the Scopus page. The acquired .csv files from the Scopus database were analyzed using Bibliometrix and VOSviewer, according to the suggestion from previous studies [8, 10-12]. Bibliometrix software was used to obtain thematic plots, thematic evolution, and collaboration maps. As for the VOSviewer, the software was employed to generate co-occurrence network of the author's network. All analysis was performed on global and SEA datasets, respectively.

Results

Number of publications

This study found 24,829 and 345 publications in global and SEA datasets, respectively. The numbers of annual publications of vitamin D and osteoporosis research are presented in **Figure 1**. Both the worldwide (adjusted R^2= 0.949) and SEA datasets (adjusted R^2=0.736) fit well with the polynomial regression (orders: 6 and 2, respectively). The exponential increase of vitamin D and osteoporosis research based on the global dataset occurred in the 1980s. However, after 2005, the trend was likely to be stagnant, and may potentially decrease in the coming years. This suggests the saturation of the research trend, where the intersection between vitamin D and osteoporosis is mostly understood. However, the exponential growth of publications is being experienced by SEA countries. Higher proportion of original research is observable in SEA dataset (n=240, 69.6%) as compared with the global dataset (n=14752, 59.4%). Reviews take up 24.9% (n=6185) and 22.3% (n=77) of the total documents in global and SEA datasets, respectively. Taken altogether, the publication trends suggest that research on vitamin D and osteoporosis is lagging in SEA, necessitating further studies.

Globally, the United States is leading the publication trends with a total publication reaching 6,686, leaving other countries, including the United Kingdom (n=2,005), Italy (n=1,686), and Germany (n=1,371) far behind (**Figure 2**). As for the SEA region, the publication trends are led by Thailand (n=135), and followed by Malaysia (n=91), Singapore (n=89), Indonesia (n=27), and Brunei (n=1). Other SEA countries, such as Myanmar, Vietnam, Lao, Cambodia, and East Timor, did not have a single publication in the Scopus database (**Figure 2**).

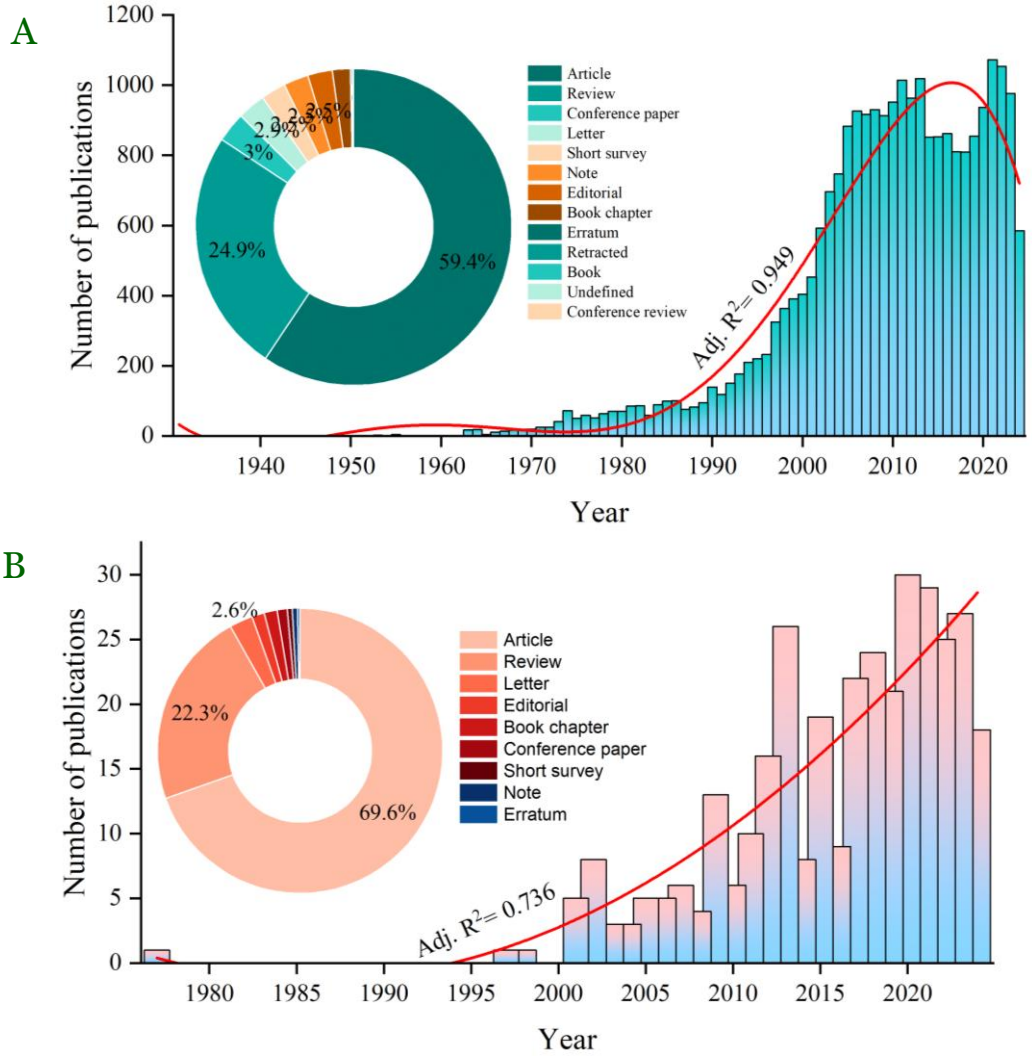


Figure 1. Number and types of publications for studies involving vitamin D and osteoporosis published by authors from all countries (A) and Southeast Asia only (B).

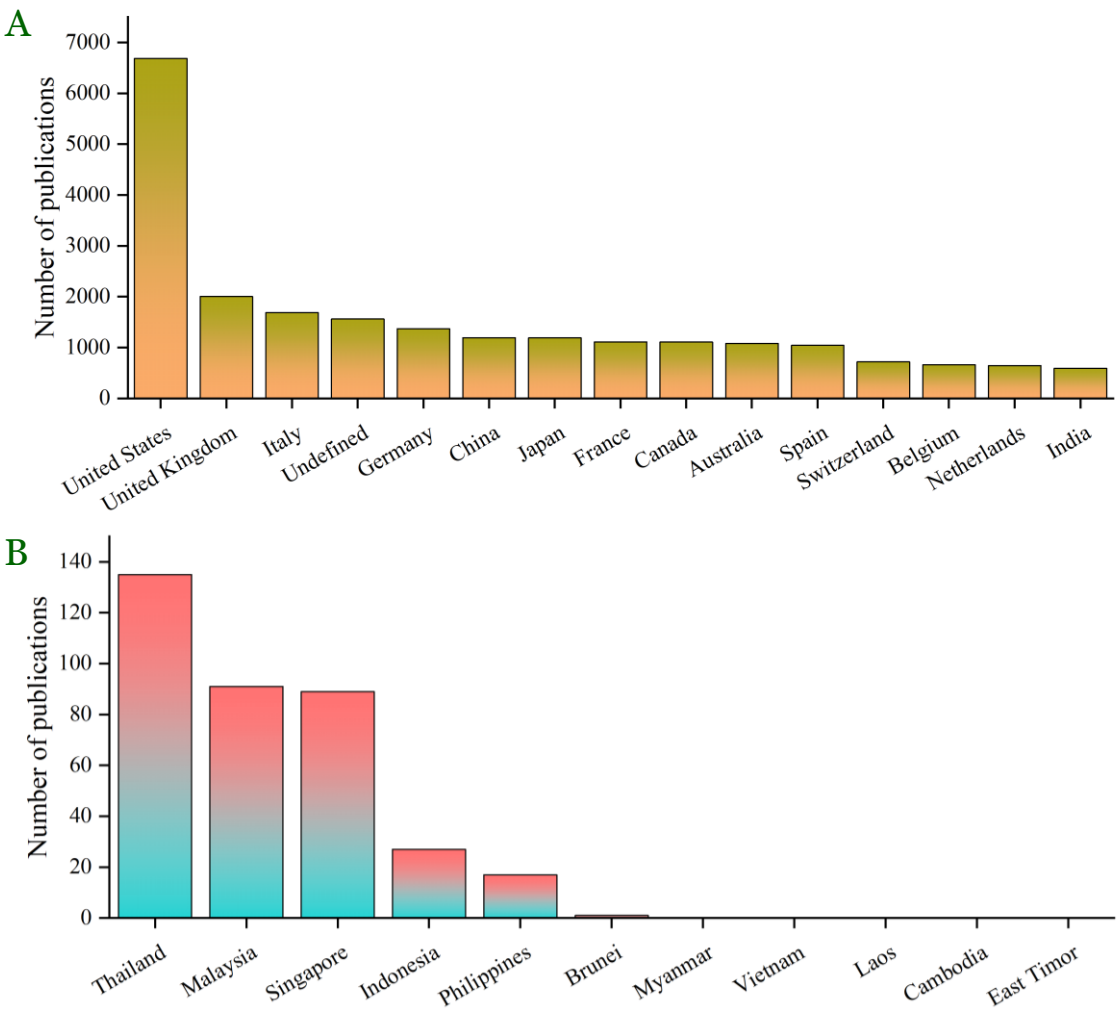


Figure 2. Number of publications of each country: worldwide (A) and Southeast Asia (B).

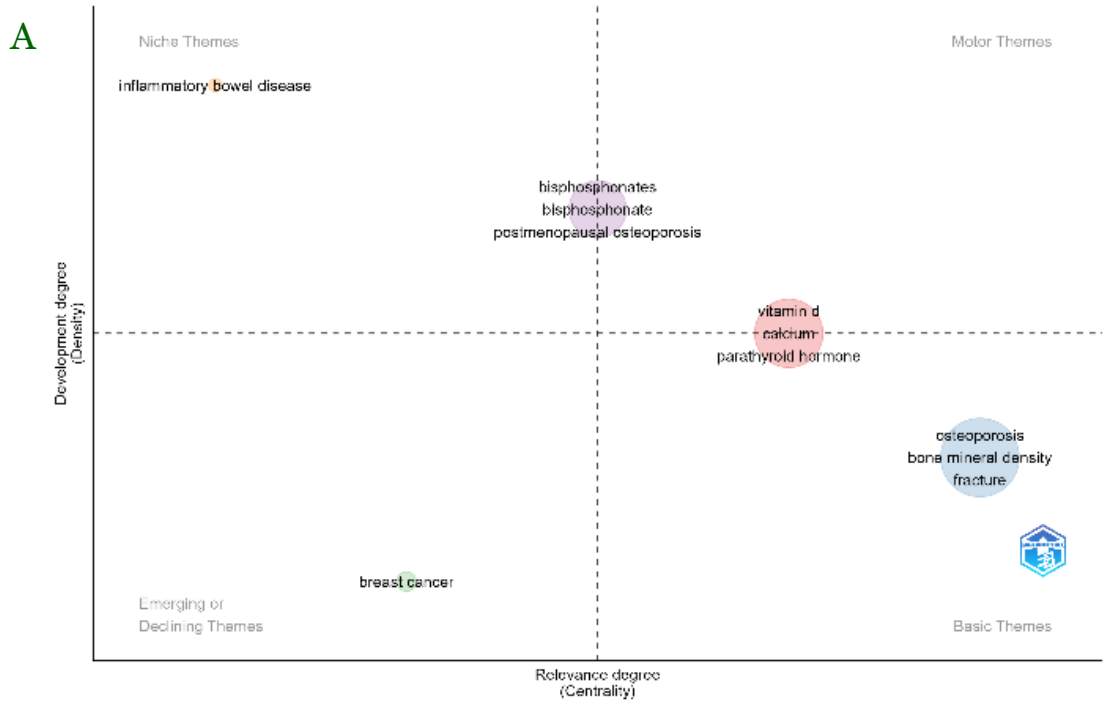
Research focus

The developed research themes related to vitamin D and osteoporosis and their evolutions are presented in **Figure 3**. The thematic suggests the evolution of research themes in the context of vitamin D and osteoporosis topics over two different time slices (1931–2014 and 2015–2024). In the 1931–2014 time slice, the inflammatory bowel disease theme is located in the "niche theme" quadrant, indicating that while it may be a well-developed topic, it is not significantly related to vitamin D and osteoporosis research. "Osteoporosis, bone mineral density, and fracture" and "vitamin D and parathyroid hormones" themes are observed as "basic themes" suggesting that both are significantly correlated with the topic of interest. "Bisphosphonates and postmenopausal osteoporosis" theme is located near the center, suggesting their moderate relevance and development within 1931–2014 time frame. The thematic plot of the time frame suggests that "breast cancer" theme is potentially gaining relevance to the vitamin D and osteoporosis research, though its prominence is declining. No clear motor themes are present, indicating no topics have achieved both high centrality and development.

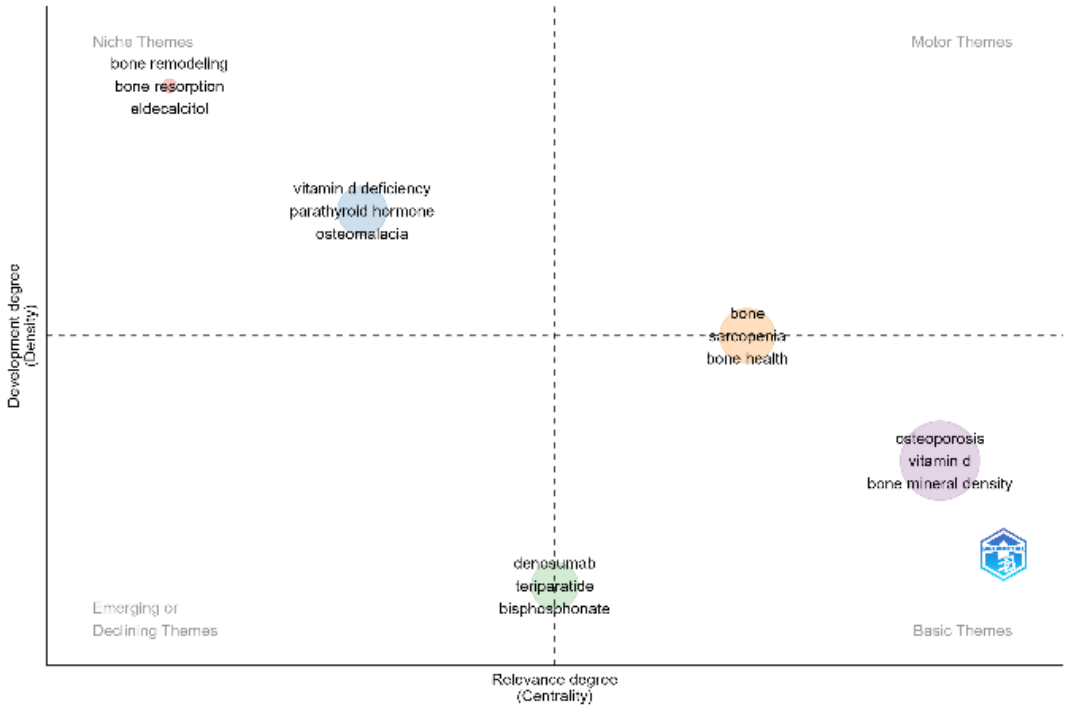
As for the 2015–2024 time frame, "bone remodeling, bone resorption, and eldecalcitol" theme is found to be more specialized and mature, but it does not necessarily influence the overall vitamin D and osteoporosis research. In the motor themes, "bone, sarcopenia, and bone health" themes are located, indicating its well-developed nature and strong influence in the discourse of vitamin D and osteoporosis intersection. "Osteoporosis, vitamin D, bone mineral density" appears to be consistently important, where the themes remain central and continue to be key components of the research landscape. "denosumab, teriparatide, and bisphosphonate" themes are located in the emerging and declining quadrant, suggesting the significance of new findings or shifting interest.

In the SEA region, vitamin D and osteoporosis research is highly influenced by studies investigating the impacts of vitamin D on osteoporosis. Gaining or declining interest in obesity in the discourse of vitamin D and osteoporosis was observed. Further, we observed the absence of niche themes, suggesting a lack of highly specialized, well-developed research areas. Studies on vitamin D and osteoporosis are intertwined with zoledronic acid, which is in line with that present in the global dataset, where resorptive agent is a consistently important topic. However, in the global dataset, the interest in bisphosphonates is shifted to resorptive monoclonal antibodies, such as denosumab. Vitamin D and osteoporosis research in the SEA region are mainly driven by the topic that has been well-established decades ago in the global setting. Taken altogether, these findings support the suggestion that the research is not well carried out in the SEA region.

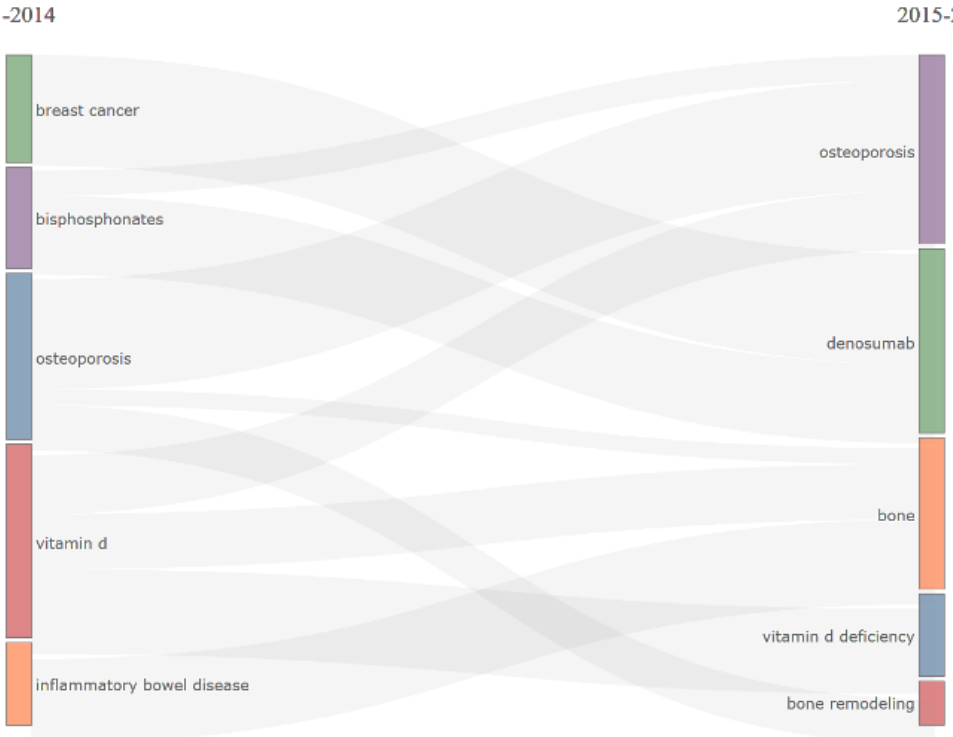
The co-occurrence network of author's keywords for global dataset is presented in **Figure 4**. The research trend is mainly related to the correlation between vitamin D and osteoporosis. Other topics, such as those related to bone health, bisphosphonates (antiresorptive), and calcium are strongly relevant to the research. As for the SEA dataset, the visualization of co-occurrence network of the author's keywords is presented in **Figure 5**. The co-occurrence network suggests that, in SEA regions, the research is primarily driven by the vitamin D effect on bone health, where most of the connected keywords are related to osteoporosis. Comparison of the co-occurrence network between the global and SEA databases revealed that the global dataset has more specialized topics (indicated by the formation of multiple clusters), while they are minimal in the SEA dataset. Collectively, the analysis suggests lack of vitamin D and osteoporosis research in SEA regions.



B


Niche Themes
bone remodeling
bone resorption
aldecalcitol
Motor Themes
vitamin d deficiency
parathyroid hormone
osteomalacia
bone
sarcopenia
bone health
osteoporosis
vitamin d
bone mineral density
denosumab
teriparatide
bisphosphonate
Emerging or
Declining Themes
Basic Themes
Development degree
(Density)
Relevance degree
(Centrality)

C


1931-2014
2015-2024
breast cancer
bisphosphonates
osteoporosis
vitamin d
inflammatory bowel disease
osteoporosis
denosumab
bone
vitamin d deficiency
bone remodeling

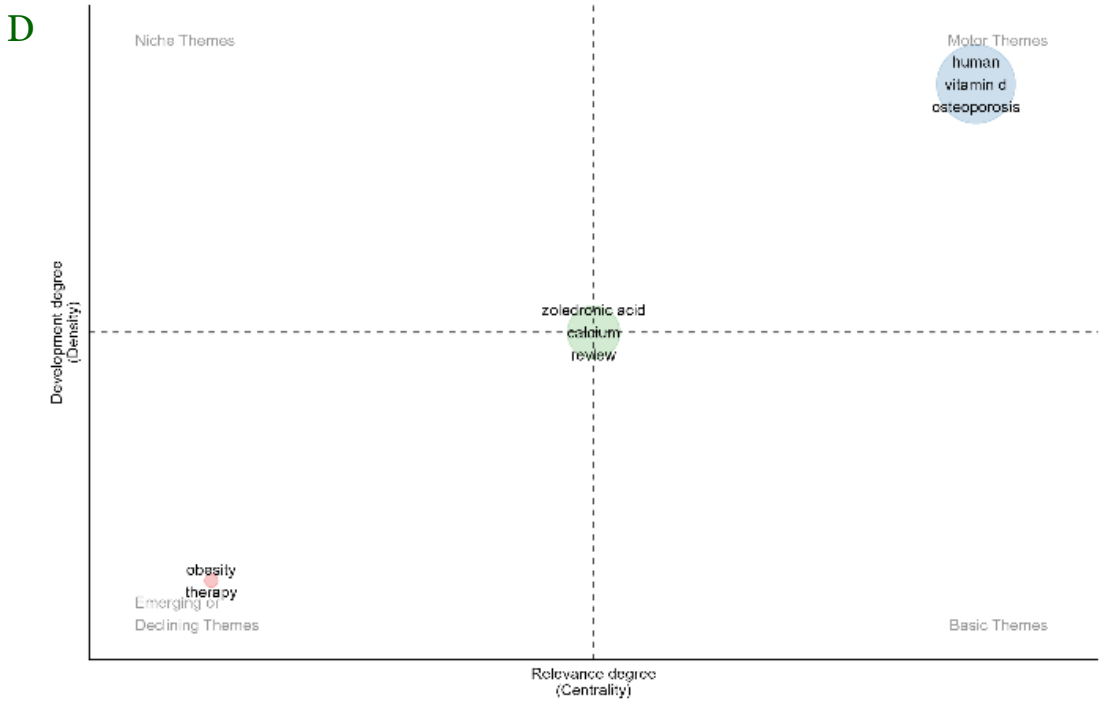
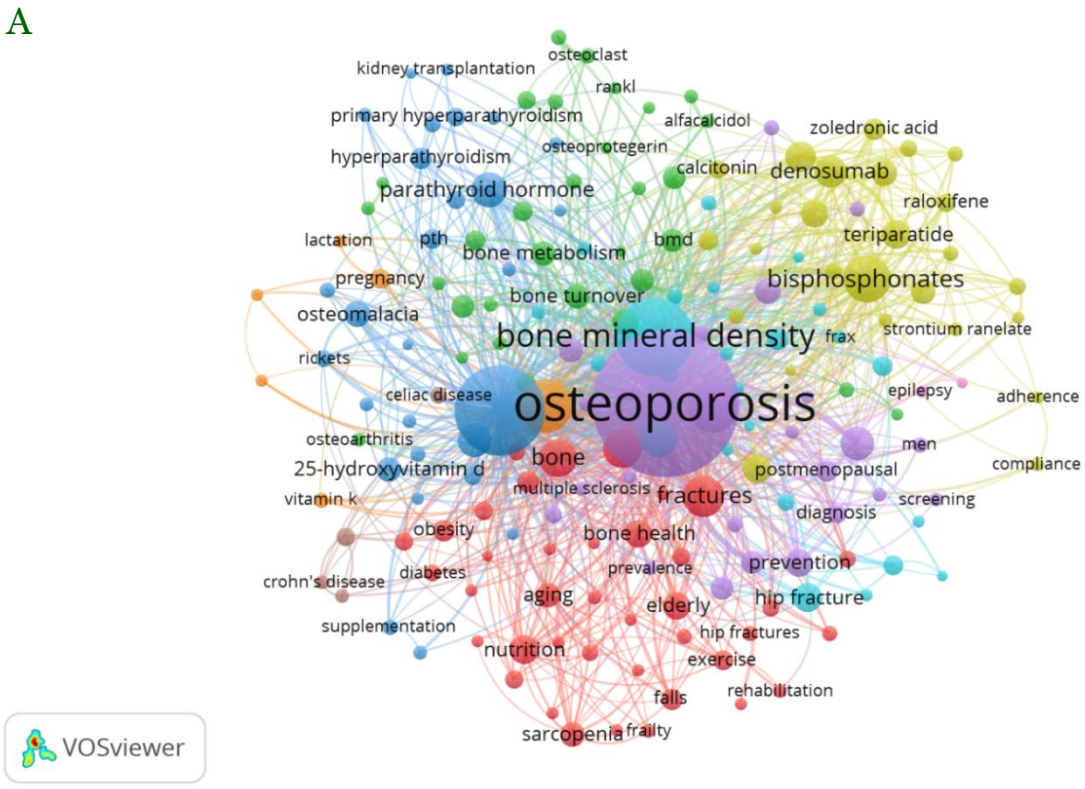


Figure 3. Thematic plots for global trends of vitamin D and osteoporosis research in 1931–2014 (A) and 2015–2024 timelines (B). Sankey diagram for the changes in research themes related to vitamin D and osteoporosis (C). Thematic plots for vitamin D and osteoporosis research in Southeast Asia between 1977 and 2014 (D).



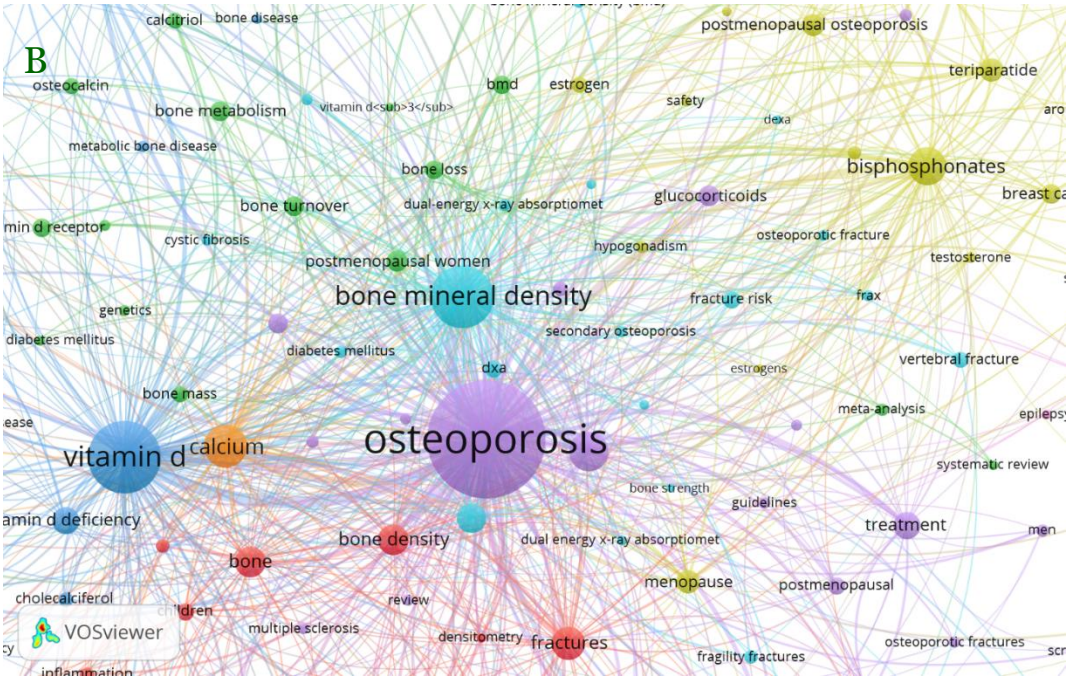


Figure 4. Co-occurrence network analysis on authors' keywords depicting the global landscape of vitamin D and osteoporosis research (minimal occurrence, n=50).

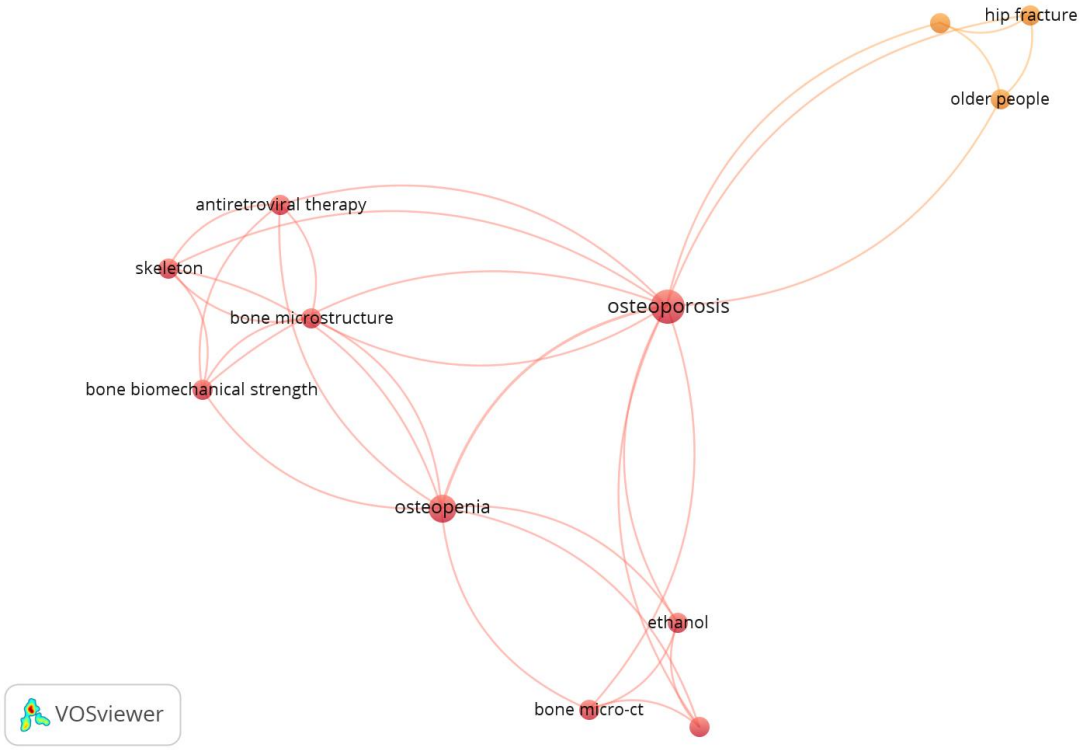


Figure 5. Co-occurrence network analysis on authors' keywords depicting the landscape of vitamin D and osteoporosis research in Southeast Asia (minimal occurrence, n=1).

Collaboration patterns

Maps illustrating the international collaborations between authors of studies in the global and SEA datasets are presented in **Figure 6**. In the global dataset, the international collaboration was observed to be intense, where the United States and European countries acted as the centers of collaboration. The United States, European countries, Canada, and Australia have formed

strong collaborations in investigating the interplay between osteoporosis and vitamin D. In the SEA dataset, the international collaborations were observed to be intense in Malaysia, Singapore, and Indonesia. Prominent non-SEA partners in this research area include the United States, the United Kingdom, and Italy.

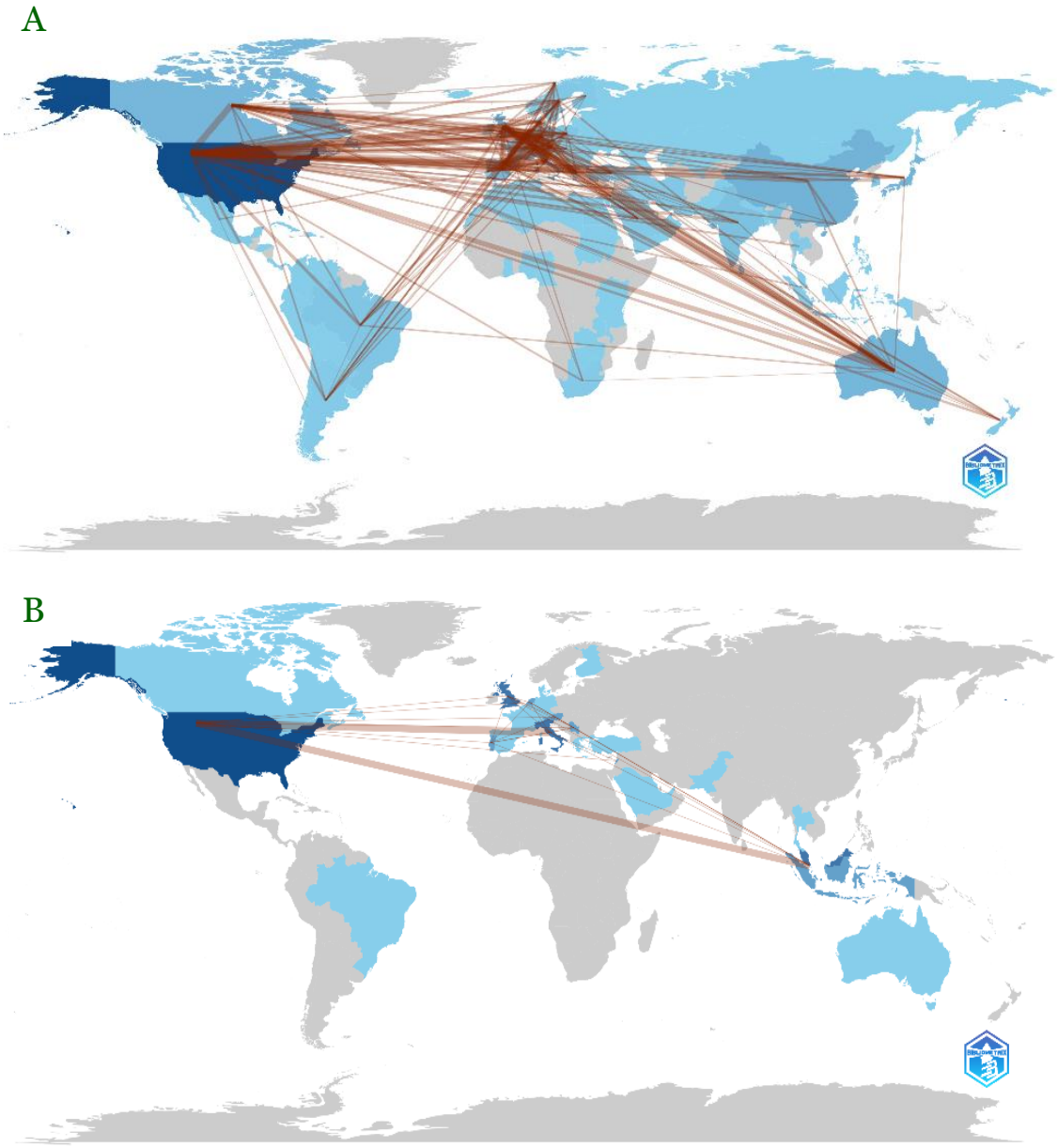


Figure 6. Collaboration maps of vitamin D and osteoporosis research for global (A) and SEA datasets (B).

Discussion

The thematic evolution of vitamin D research revealed the shifted trends, with some themes becoming more central and others more developed. This reflects the dynamic nature of research and how treatments and scientific understanding evolve. The consistent presence of osteoporosis and bone mineral density highlights the ongoing importance of these areas in the intersection of vitamin D and osteoporosis research. The movement of treatments like denosumab from emerging themes to more central ones may indicate new research findings or clinical practices emphasizing these therapies.

The thematic analysis of SEA dataset reveals that the research is mainly investigating the direct consequence of vitamin D on osteoporosis, with minimum presence of specialized topics. Zoledronic acid, a key bisphosphonate in treating osteoporosis and bone metastases, is positioned centrally, suggesting its significance and potential for further exploration. The emergence of

obesity and therapy as themes indicate new research directions, particularly in integrating obesity management into bone health strategies. Vitamin D deficiency is closely linked to the development of osteosarcopenic obesity, a condition characterized by reduced bone and muscle mass in obese individuals [13-15]. This deficiency exacerbates insulin resistance, further worsening the interplay between obesity, muscle deterioration, and bone health [14, 16]. Low vitamin D levels impair bone mineralization and muscle function, leading to a higher risk of osteoporosis and physical frailty [14]. Additionally, the chronic inflammation associated with obesity is intensified by vitamin D deficiency, which could consequently impair both bone and muscle health [17]. While vitamin D supplementation is suggested to have potential benefits, its effectiveness in improving musculoskeletal health in osteosarcopenic obesity remains inconclusive [18].

In the global dataset, there is a shift from bisphosphonates to denosumab, indicating the shifting of interest, probably driven by the change in clinical guidelines. In contrast, bisphosphonates are still gaining interest in SEA regions. The correction of serum vitamin D levels before and during denosumab therapy has been recommended by various guidelines, including those issued by the Japanese Ministry of Health [19], Endocrine Society [20], and American Association of Clinical Endocrinologists [21]. As for bisphosphonates therapy, guidelines from various organizations in the United States and Canada recommend achieving and maintaining serum 25-hydroxyvitamin D levels of at least 30 ng/mL during the therapy [20, 22, 23]. However, among SEA countries, guidelines for denosumab and bisphosphate therapies do not specifically recommend the correction or maintenance of 25-hydroxyvitamin D levels. It is worth noting that despite the absence of national guidelines, healthcare providers might adopt the international guideline to employ 25-hydroxyvitamin D correction before the initiation of the therapies. Indeed, guidelines for osteoporosis management in some Southeast Asian countries, such as Indonesia, Malaysia, and Thailand, have expressed concern over 25-hydroxyvitamin D levels but not specific to the antiresorptive therapies [24]. In previous studies, vitamin D supplementation during the management using antiresorptive agents has shown efficacy in mitigating the adverse effects, where the findings have been summarized in **Table 2**.

Table 2. Scientific evidence on vitamin D in improving the efficacy and mitigating the adverse effect of antiresorptive agents

Author, year [ref]	Study design	Subjects	Antiresorptive agents	Vitamin D supplementation	Outcome
Demiray *et al.*, 2021 [25]	Retrospective cohort	PO (n=31 vs. 27)	Denosumab	Oral cholecalciferol (200 IU) + Ca (762.5 mg) Mg (59.2 mg) BID	↑ Zinc ↑ L-BMD ↑ H-BMD
Nakamura *et al.*, 2017 [26]	Randomized clinical trial	PO (n=23 vs. 18)	Denosumab	Oral cholecalciferol (200 IU) + Ca (762.5 mg) + Mg (59.2 mg) BID	↑ BMD
Sakai, *et al.*, 2015 [27]	Randomized clinical trial	OP (n=110 vs. 109)	Alendronate	Oral vitamin D (400 IU) + Ca (610 mg) QD	↓ BTMs ↑ FN-BMD
Suzuki, *et al.*, 2018 [28]	Retrospective cohort	PO + RA (n=31 vs. n=27)	Denosumab	Oral cholecalciferol (200 IU) + Ca (762.5 mg) + Mg (59.2 mg) TID	↑ Zinc ↑ L-BMD ↑ H-BMD
Nakamura *et al.*, 2017 [19]	Retrospective cohort	OP + RA (n=22 vs. n=21)	Denosumab	Oral cholecalciferol (200 IU) + Ca (762.5 mg) + Mg (59.2 mg) TID	↑ H-BMD
Mukaiyama *et al.*, 2015 [29]	Retrospective cohort	OP (n=20)	Bisphosphonate	Oral eldecalcitol (0.75 µg) QD	↓ BTMs ↑ L-BMD
Merlotti *et al.*, 2020 [30]	Retrospective and prospective cohort	PDB (n=66)	Bisphosphonate	Intravenous cholecalciferol (50,000 IU) weekly	↓ APR ↓ HCA
Songpatanasilp T *et al.*, 2018 [31]	Non-randomized clinical trial	OP (n=198)	Alendronate	Oral cholecalciferol (5600 IU) weekly	↓ β-CTx

Author, year [ref]	Study design	Subjects	Antiresorptive agents	Vitamin D supplementation	Outcome
Mochizuki T, *et al.*, 2022 [32]	Randomized, open-label clinical trial	OP (n=51 vs. 47)	Zoledronic acid	Oral eldecalcitol (0.5–0.75 μg) QD	↑ LS-BMD ↑ TH-BMD ↑ FN-BMD ↓ BTMs
Yoo *et al.*, 2017 [33]	Prospective cohort	OP (n=691)	Alendronate	Oral calcitriol (0.5 μg) QD	↑ LS-BMD

β-CTx: beta-crosslaps; APR: acute phase reaction; BMD: bone mineral density; BTMs: bone turnover markers; FN: femoral neck; HCA: hypocalcemia; OP: osteoporosis; PDB: Paget's disease of bone; PO: postmenopausal osteoporosis; RA: rheumatoid arthritis

The analysis of publication trends and research focus reveals that the SEA region is lagging in vitamin D and osteoporosis research compared to the global landscape. While global research experienced an exponential increase in the 1980s, the SEA region is only now beginning to see significant growth. Despite some progress, SEA countries still contribute a minimal number of publications, with many nations in the region not producing any research at all. Furthermore, the thematic evolution in SEA is heavily influenced by established global topics, with a noticeable absence of niche or specialized themes. The co-occurrence network analysis further reveals that research in SEA is less specialized and primarily focused on well-established topics like the effects of vitamin D on bone health. These findings collectively indicate that the research in SEA is not keeping pace with global developments, highlighting the need for more focused and specialized studies in the region. Moreover, vitamin D and osteoporosis research suggest the significance of an interdisciplinary approach involving experts and clinicians from orthopedics, endocrinology, nutrition, and pharmacology.

Conclusion

The analysis demonstrates that research on vitamin D and osteoporosis in SEA is significantly lagging behind global trends. While the global research landscape on this topic has experienced substantial growth and diversification over the decades, SEA has only recently begun to show an increase in publication output. However, this growth is not on par with global advancements, and the research in SEA remains largely centered on established topics without significant exploration of niche or specialized areas. The lack of specialized themes and the minimal contribution of several SEA countries further underscore the region's underrepresentation in this crucial area of study. To bridge the research gap, SEA countries should invest in collaborative initiatives, enhance funding, and encourage exploration of specialized themes in vitamin D and osteoporosis, thereby aligning regional studies with global advancements.

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All authors have nothing to declare.

Competing interests

The authors declare no conflicts of interest.

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Underlying data

All underlying data have been presented in this article.

Declaration of artificial intelligence use

We hereby confirm that no artificial intelligence (AI) tools or methodologies were utilized at any stage of this study, including during data collection, analysis, visualization, or manuscript

preparation. All work presented in this study was conducted manually by the authors without the assistance of AI-based tools or systems.

How to cite

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