Revista de Osteoporosis
y Metabolismo Mineral

Eficacia de las terapias combinadas con teriparatida sobre la densidad mineral ósea en la osteoporosis posmenopáusica: un metanálisis en red

Efficacy of teriparatide combination therapies on bone mineral density in postmenopausal osteoporosis – A network meta-analysis

10.20960/RevOsteoporosMetabMiner.00115

04/08/2026

00115

Efficacy of teriparatide combination therapies on bone mineral density in postmenopausal osteoporosis – A network meta-analysis

Heri Nugroho[1], Steven Alvianto[2], Olivia Wangidjaja[2], Imelda Beatric[2]

[1]Division of Diabetes, Endocrine, and Metabolism. Department of Internal Medicine. Faculty of Medicine. Diponegoro University. Semarang, Indonesia. [2]School of Medicine and Health Sciences. Atma Jaya Catholic University of Indonesia. Jakarta, Indonesia

Received: 20/01/2026

Accepted: 22/03/2026

Correspondence: Heri Nugroho. Division of Diabetes, Endocrine, and Metabolism. Department of Internal Medicine. Faculty of Medicine. Diponegoro University. Prof. Mr. Sunario Street. Diponegoro University Campus. Central Java, Indonesia. 50275 Semarang, Indonesia

Authors' contribution: H. N.: conceptualization, methodology, software, investigation, validation, formal analysis, funding acquisition, visualization, project administration, resources, supervision, writing-original draft, writing-review and editing. S. A.: conceptualization, methodology, software, investigation, validation, formal analysis, funding acquisition, visualization, project administration, resources, supervision, writing - original draft, writing-review and editing. O. W.: conceptualization, methodology, investigation, writing-original draft, writing-review and editing. I. M.: conceptualization, methodology, investigation, writing-original draft, writing-review and editing.

Statement of authorship: All authors certified fulfilment of ICMJE authorship criteria.

Data availability statement: Datasets generated and analyzed are included in the published article.

Conflict of interest: The authors declare no conflict of interest.

Artificial intelligence: The authors declare that no generative artificial intelligence (AI) or AI-assisted technologies were used in the writing or preparation of this manuscript.

ABSTRACT

Introduction: teriparatide (TPTD) is an effective anabolic agent for osteoporosis; however, its comparative efficacy when combined with antiresorptive drugs or other interventions remains uncertain. This network meta-analysis (NMA) aimed to compare the effects of various TPTD combination therapies and monotherapies on bone mineral density (BMD) in patients with postmenopausal osteoporosis.

Methods: a Bayesian random-effects models were used. Primary endpoints were Mean Differences (MD) in BMD percentage change at the lumbar spine, femoral neck, and total hip. We estimated MDs with 95 % credible intervals (CrIs) and ranked treatments using SUCRA probabilities.

Results: a total of 10 studies were included in this analysis. No combination therapy demonstrated statistically significant improvements in mean BMD across skeletal sites. At the lumbar spine, Denosumab (DEN) +TPTD showed the largest estimated effect (MD 3.12; 95 % CrI -1.65 to 7.83). For the total hip, Zoledronic acid (ZOL) +TPTD yielded the highest estimated mean change (MD 6.75; 95 % CrI -1.65 to 15.10). At the femoral neck, DEN+TPTD had the greatest estimated effect (MD 3.71; 95 % CrI -3.08 to 10.5). SUCRA rankings indicated DEN+TPTD as most effective for lumbar spine (79.32) and femoral neck (76.45), while ZOL+TPTD ranked highest for total hip (83.77).

Conclusion: this NMA indicates that TPTD combination therapies may offer potential benefits in improving BMD, with DEN+TPTD and ZOL+TPTD

ranking highest across different skeletal sites. However, the absence of statistically significant differences underscores the need for further studies.

Keywords: Combination. Osteoporosis. Teriparatide. Postmenopausal.

INTRODUCTION

Postmenopausal osteoporosis (PMO) clinically expressed as low bone mineral density (BMD), microarchitectural deterioration, and heightened fragility-fracture susceptibility due to estrogen deficiency (1). It remains a major global health burden as postmenopausal women (PMW) experience a 15.17-fold higher mortality, a 5.84-fold higher burden in disability-adjusted life years (DALYs), and a 6.29-fold higher burden in years lived with disability (YLDs) compared with premenopausal populations, underscoring the urgent need for more effective therapeutic strategies (2). Although antiresorptive agents remain widely used as first-line therapies, their predominant suppression of bone resorption may be insufficient to rapidly restore skeletal mass and strength in women at very high fracture risk, prompting greater reliance on bone-forming approaches and optimized treatment sequencing (3). Teriparatide (TPTD), a recombinant human parathyroid hormone 1-34, is a prototypical anabolic agent with well-established antifracture efficacy in severe PMO, including significant reductions in vertebral and non-vertebral fractures (4). This is the first FDA-approved as bone antimetabolic therapy (5).

An ideal anti-osteoporosis agent would theoretically both suppress bone resorption and stimulate new bone formation, yet neither current antiresorptive nor parathyroid hormone (PTH) analogs achieve this dual action. As a result, combining anabolic and antiresorptive therapies has been proposed as a practical substitute, with the rationale that stimulating bone formation while simultaneously inhibiting resorption could yield greater gains in bone mass and strength than either approach alone (6,7). However, the American Association of Clinical Endocrinologists and

American College of Endocrinology 2020 guidelines state that until the effect of combination therapy on fracture risk is better understood, concomitant use of multiple osteoporosis agents is generally not recommended for treatment of osteoporosis[8]. Moreover, when anabolic agents are used, current guideline recommend transitioning to sequential therapy with an antiresorptive agent, such as a bisphosphonate or denosumab, after discontinuation of the anabolic course to preserve gains in BMD and reduce the risk of subsequent fractures (8,9).

Therefore, due to limited data and the lack of comprehensive head-to-head comparisons among TPTD combination therapy and other interventions, a network meta-analysis (NMA) is necessary to rank therapeutic strategies according to BMD efficacy, while also emphasizing the importance of generating more evidence on the clinical effectiveness of TPTD combination approaches.

METHODS

This systematic review and NMA was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement. The study protocol was prospectively registered in the International Prospective Register of Systematic Reviews (PROSPERO; CRDxx) on 10 November 2025.

Search Strategy

A comprehensive literature search was undertaken across multiple electronic databases, including Cochrane, MEDLINE, and ClinicalTrials.gov. The search was independently performed by HN, SA, and OW using predefined keywords and Medical Subject Headings (MeSH), namely “Teriparatide,” “Parathyroid Hormone,” “Combination therapy,” “Osteoporosis,” and “Postmenopausal Osteoporosis” (Supplementary material). The search strategy was developed in accordance with the PICOTS-SD framework as follows:

- Population: Adults (≥ 18 years) with PMO.
- Intervention: TPTD-based combination therapy.

- Comparator: TPTD monotherapy, other active monotherapies, or alternative TPTD-containing combination regimens.
- Outcomes: Mean change in BMD at the lumbar spine, total hip, and femoral neck.
- Time: No restrictions applied.
- Setting: All relevant clinical settings.
- Study Design: Randomized controlled trials (RCTs).

Eligibility criteria

Type of studies

Only RCTs were eligible for inclusion. Observational studies, case series, case reports, narrative or systematic reviews, book chapters, editorials or commentaries, as well as in vitro and in silico studies, were excluded.

Outcome of interest

The primary objective of this study was to compare and rank the efficacy of TPTD-based combination therapies relative to TPTD monotherapy and other treatment strategies in improving BMD at the femoral neck, total hip, and lumbar spine.

Study selection

Studies were identified through a structured screening process. After duplicates were removed using Zotero (version 7.0.15; Corporation for Digital Scholarship, Virginia, USA) on 10 November 2025, HN, SA, OW independently screened titles and abstracts for relevance. Full texts of potentially eligible articles were then assessed against predefined inclusion criteria. Reference lists of included studies were manually reviewed to identify additional eligible reports. Final inclusion was determined by reviewer consensus.

Data collection process

Data were extracted using a standardized form by two reviewers (HN and SA). Extracted variables included study characteristics, sample size, participant age, intervention details, daily treatment regimens, and follow-up duration.

Summary measures

Changes in BMD were analyzed as continuous outcomes using mean differences (MDs) as the summary effect measure.

Risk of bias assessment

Two reviewers (OW and IB) independently evaluated study quality using the Cochrane Risk of Bias tool, version 2 (RoB 2) (10). Disagreements were resolved through consensus.

Synthesis of results and statistical analysis

For studies reporting outcomes only in graphical form, numerical values were extracted using WebPlotDigitizer (version 4.8; Autometris LLC; https://apps.automeris.io/wpd4/). A Bayesian NMA was conducted using the MetaInsight platform (version 6.4.0; NIHR Complex Reviews Support Unit; https://crsu.shinyapps.io/MetaInsight/) accessed on 20 November 2025 (11). Results were summarized using forest plots, with between-study heterogeneity addressed through a random-effects model. Inconsistency and sensitivity analysis were also conducted. Treatment rankings were generated using the surface under the cumulative ranking curve (SUCRA), with higher values indicating greater efficacy. Sensitivity analyses were conducted. Studies identified as having a high risk of bias, as well as poorly fitting studies based on leverage plots falling outside the threshold line at c = 3, were excluded when present. Inconsistency was further assessed using the node-splitting model.

RESULTS

Selection of study

The study selection process is summarized in figure 1. Following an initial retrieval of 717 records from the database search, screening based on predefined criteria resulted in 35 articles undergoing full-text assessment.

Of these, exclusions were made for mismatched interventions (*n* = 13), inappropriate comparators (*n* = 8), and outcomes not aligned with the study objectives (*n* = 4). Consequently, 10 studies fulfilled all inclusion criteria and were incorporated into the NMA for data synthesis.

Characteristics of the included studies

A total of 1459 participants from 10 RCTs were included. The studies enrolled PMW with osteoporosis from United States, Europe, China, and multinational cohorts. Sample sizes ranged from 33 to over 412 participants, with mean ages predominantly in the sixth to seventh decades of life. All trials evaluated TPTD-based combination therapies versus TPTD monotherapy, with some including additional active comparators such as alendronate (ALD), raloxifene (RAL), zoledronic acid (ZOL), denosumab (DEN), or nonpharmacological interventions (pulsed electromagnetic fields [PEMFs] or whole-body vibrations [WBV]). TPTD (20-100 µg/day) was most frequently combined with antiresorptive agents, and calcium and vitamin D supplementation was routinely provided. Follow-up periods ranged from 6 to 30 months, most commonly 12 months. Overall, study quality was acceptable, with several trials at low risk of bias and the remainder showing some concerns. Further details were shown in table I.

Network meta-analysis results

Figure 2 and figure 3 illustrate the network plots and forest plots for BMD changes at the lumbar spine, total hip, and femoral neck. No intervention showed a statistically significant difference in mean BMD change across these skeletal sites. At the lumbar spine, the largest estimated effect was observed with DEN + TPTD (MD 3.12; 95 % CrI -1.65 to 7.83), followed by PEMF + TPTD (MD 2.48; 95 % CrI -3.83 to 8.72). For the total hip, ZOL + TPTD demonstrated the highest estimated mean change (MD 6.75; 95 % CrI -1.65 to 15.1), with DEN + TPTD ranking second (MD 4.27; 95 % CrI -4.32 to 12.7). At the femoral neck, DEN + TPTD showed the greatest estimated effect (MD 3.71; 95 % CrI -3.08 to 10.5), followed by

ZOL + TPTD (MD 3.17; 95 % CrI -3.56 to 9.92). SUCRA-based ranking indicated that DEN+TPTD had the highest probability of being the most effective intervention for lumbar spine BMD (SUCRA 79.32) and femoral neck BMD (SUCRA76.45), whereas ZOL + TPTD ranked highest for total hip BMD (SUCRA 83.77). Detailed SUCRA rankings are presented in table II and figure 4.

Sensitivity analysis and inconsistency analysis

No studies were identified as having a high risk of bias or as poorly fitting according to the leverage plots. Inconsistency assessments using node-splitting analyses likewise revealed no significant findings, except at the femoral neck. A significant local inconsistency emerged between RAL + TPTD and ALD + TPTD (p = 0.0043). While direct evidence indicated a significant benefit of RAL + TPTD, indirect evidence pointed the opposite direction. This discrepancy resulted in a non-significant overall network estimate in femoral neck. Further details are provided in the **supplementary material**.

Publication bias

Publication bias was evaluated qualitatively using funnel plots and quantitatively using Egger's regression test. In this analysis, lumbar spine, hip, and femoral neck plots appeared asymmetrical, yet Egger's regression test showed no significant bias, with p-values of 0.2121, 0.9783, and 0.4635 for the lumbar spine, total hip, and femoral neck, respectively, as illustrated in **supplementary material**. Such discrepancies may reflect small-study effects, heterogeneity, particularly given the limited number of studies. As funnel plots are less reliable with small samples, the observed asymmetry is more likely due to heterogeneity.

DISCUSSION

The main strength of this study is that it represents the first comprehensive NMA comparing the effectiveness of various TPTD combination therapies, including both pharmacological and non-pharmacological interventions, in PMO patients. Although the comparative analysis revealed no statistically significant differences in increasing BMD across the interventions, this study demonstrated that several combination therapies involving combination of TPTD consistently showed larger estimated mean changes in BMD in PMO compared with other interventions.

In particular, the combination of DEN + TPTD demonstrated the greatest estimated effects at the lumbar spine and femoral neck, while ranking second at the total hip. The direction of effect observed in this study is consistent with a meta-analysis by Sun et al. (2022), which reported that combination therapy with TPTD + DEN in PMO was associated with greater BMD than monotherapy, including statistically significant mean percentage increases of approximately 2.91 % at the lumbar spine and 3.19 % at the hip (12). The overall beneficial effect may be attributed to DEN's ability to fully inhibit the pro-resorptive effects of TPTD through suppression of the RANKL pathway, while still allowing TPTD-induced stimulation of bone formation via activation of parathyroid hormone receptors. This combination thus establishes a dynamic balance (13).

At the total hip, the combination of ZOL + TPTD produced the greatest estimated improvement in BMD. While TPTD exerts a distinctive adverse effect on cortical bone by increasing cortical porosity, the addition of ZOL appears to mitigate this remodelling process by reinforcing cortical structure, thereby enhancing hip BMD. Nevertheless, in the clinical trial, the absence of sustained BMD gains during the final six months may reflect renewed cortical remodelling and rising cortical porosity as the antiresorptive effect of ZOL diminishes (14).

Furthermore, combining TPTD with non-pharmacological therapies (PEMF/WBV) was also shown to improve lumbar vertebra and femoral neck BMD, with outcomes comparable to those of TPTD combined with anti-resorptive agents. However, no improvement was observed in hip BMD. WBV delivered through a platform transmits mechanical signals across the skeletal muscle system via centrifugal conduction from the lower limbs.

This stimulation triggers widespread neuromuscular activation and plays a role in regulating bone metabolism. Its benefits appear even greater when paired with pharmacological treatments such as TPTD, where synergistic effects have been observed (15). A meta-analysis also found that using PEMF together with standard medications led to a significant increase in BMD the lumbar spine and femur (16). PEMFs enhance osteoblast activity, inhibit osteoclast formation, and modulate BMSCs and osteocytes, thereby preserving bone mass and strength (17).

Emerging evidence from previous meta-analyses suggests potential benefits of combination therapy. A meta-analysis by Lou et al. (2019) demonstrated that combination regimens were superior to monotherapy, while more recent data from Jin et al. (2025) indicated that the DEN + TPTD combination clinically preferable for BMD enhancement (6,13). Consistent with these findings, our NMA identified a trend favoring combination therapy for BMD improvement, with the highest rank probabilities observed for DEN + TPTD and ZOL + TPTD.

A key limitation of this study is that, although several TPTD-based combination strategies achieved the high SUCRA rankings, the corresponding credible intervals were wide and consistently crossed the null effect. This reflects substantial uncertainty in the estimated treatment effects and indicates that these rankings should be interpreted cautiously. The observed imprecision is likely attributable to small sample sizes, limited number of included studies, heterogeneity in intervention and follow-up duration, and the reliance on indirect comparisons inherent to the NMA framework. A local inconsistency in the femoral neck was also noted, indicates that the rankings should be interpreted with caution. Consequently, although relative treatment rankings provide insight into potential comparative performance, the absence of statistically significant differences highlights the need for larger, well-powered RCTs to more precisely define the effects of combination therapies on site-specific BMD outcomes.

This study focused exclusively on TPTD-based combination strategies, without addressing other anabolic agents such as abaloparatide (ABL) or romosozumab (ROMO). Evidence regarding ROMO in combination therapy for PMO remains limited. Meta-analyses have suggested that ROMO demonstrated superior efficacy than TPTD (18). This monoclonal antibody targets sclerostin and acts through a dual mechanism, promoting bone formation while simultaneously reducing bone resorption (19). Observational data indicate that the addition of ROMO to ongoing DEN produced significant gains in lumbar spine BMD (20). Preliminary analyses further suggest that ROMO combined with DEN led to greater improvements in BMD and required fewer injections compared with DEN plus TPTD (21). Meta-analysis on ABL has demonstrated beneficial effects on BMD and lower risk of adverse events compared to TPTD (22). However, clinical trials investigating ABL in combination therapy remain limited and are still ongoing, such as NCT04467983 (23). Future studies that comprehensively compare combination therapies for PMO are warranted to better define optimal treatment strategies. Comparisons between TPTD sequential therapy and combination therapy have not yet been evaluated, highlighting the necessity of future trials with direct head-to-head evaluations.

CONCLUSION

This NMA highlights the trend of TPTD combination therapies in improving BMD, with DEN + TPTD and ZOL + TPTD emerging as leading candidates in relative rankings. The absence of statistically significant differences underscores the need for larger, well-powered trials.

REFERENCES

1. Charde SH, Joshi A, Raut J, Charde SH, Joshi A, Raut J. A Comprehensive Review on Postmenopausal Osteoporosis in Women. Cureus 2023 Nov 9;15(11):e48582. DOI: 10.7759/cureus.48582
2. Liang H, Chen S, Shi M, Xu J, Zhao C, Yang B, et al. Global epidemiology and burden of osteoporosis among postmenopausal women: insights

from the Global Burden of Disease Study 2021. NPJ Aging 2025 Sep 1;11(1):78. DOI: 10.1038/s41514-025-00269-2
3. Clinical Review. In: Romosozumab (Evenity): CADTH Reimbursement Review: Therapeutic area: Osteoporosis [Internet]. Canadian Agency for Drugs and Technologies in Health; 2022 [cited 2026 Jan 13]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK595381/
4. Neer RM, Arnaud CD, Zanchetta JR, Prince R, Gaich GA, Reginster JY, et al. Effect of Parathyroid Hormone (1-34) on Fractures and Bone Mineral Density in Postmenopausal Women with Osteoporosis. N Engl J Med 2001 May 10;344(19):1434-41. DOI: 10.1056/NEJM200105103441904
5. Chen YJ, Jia LH, Han TH, Zhao ZH, Yang J, Xiao JP, et al. Osteoporosis treatment: current drugs and future developments. Front Pharmacol 2024 Aug 12;15:1456796. DOI: 10.3389/fphar.2024.1456796
6. Lou S, Lv H, Yin P, Li Z, Tang P, Wang Y. Combination therapy with parathyroid hormone analogs and antiresorptive agents for osteoporosis: a systematic review and meta-analysis of randomized controlled trials. Osteoporos Int 2019 Jan;30(1):59-70. DOI: 10.1007/s00198-018-4790-4
7. McClung MR. Using Osteoporosis Therapies in Combination. Curr Osteoporos Rep 2017 Aug;15(4):343-52. DOI: 10.1007/s11914-017-0376-x
8. Camacho PM, Petak SM, Binkley N, Diab DL, Eldeiry LS, Farooki A, et al. American Association of Clinical Endocrinologists/American College of Endocrinology Clinical Practice Guidelines for the Diagnosis and Treatment of Postmenopausal Osteoporosis-2020 Update. Endocr Pract 2020;26(Suppl 1):1-46. DOI: 10.4158/GL-2020-0524SUPPL
9. Veronese N, Briot K, Guañabens N, Albergaria BH, Alokail M, Al-Daghri N, et al. Recommendations for the optimal use of bone forming agents in osteoporosis. Aging Clin Exp Res 2024;36(1):167. DOI: 10.1007/s40520-024-02826-3
10. Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. BMJ. 2019 Aug 28;366:l4898. DOI: 10.1136/bmj.l4898

11. Owen RK, Bradbury N, Xin Y, Cooper N, Sutton A. MetaInsight: An interactive web-based tool for analyzing, interrogating, and visualizing network meta-analyses using R-shiny and netmeta. Res Synth Methods 2019;10(4):569-81. DOI: 10.1002/jrsm.1373
12. Sun Y, Li Y, Li J, Xie X, Gu F, Sui Z, et al. Efficacy of the Combination of Teriparatide and Denosumab in the Treatment of Postmenopausal Osteoporosis: A Meta-Analysis. Front Pharmacol 2022 May 24;13:888208. DOI: 10.3389/fphar.2022.888208
13. Jin H, Huang C, Zhang Y, Dong Y, Xiong Q, Wang D, et al. Comparative efficacy of teriparatide and bisphosphonates or denosumab vs. teriparatide monotherapy in osteoporosis: a meta-analysis. Front Pharmacol 2025 May 21;16:1605279. DOI: 10.3389/fphar.2025.1605279
14. Cosman F, Eriksen EF, Recknor C, Miller PD, Guañabens N, Kasperk C, et al. Effects of intravenous zoledronic acid plus subcutaneous teriparatide [rhPTH(1-34)] in postmenopausal osteoporosis. J Bone Miner Res 2011 Mar;26(3):503-11. DOI: 10.1002/jbmr.238
15. Lu X, Duan H. Advances in vibration therapy for the treatment of osteoporosis. Front Endocrinol 2025 Aug 18;16:1611677. DOI: 10.3389/fendo.2025.1611677
16. Lang S, Ma J, Gong S, Wang Y, Dong B, Ma X. Pulse Electromagnetic Field for Treating Postmenopausal Osteoporosis: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Bioelectromagnetics 2022 Sep;43(6):381-93. DOI: 10.1002/bem.22419
17. Wang T, Yang L, Jiang J, Liu Y, Fan Z, Zhong C, et al. Pulsed electromagnetic fields: promising treatment for osteoporosis. Osteoporos Int 2019 Feb 1;30(2):267-76. DOI: 10.1007/s00198-018-04822-6
18. Tian A, Jia H, Zhu S, Lu B, Li Y, Ma J, et al. Romosozumab versus Teriparatide for the Treatment of Postmenopausal Osteoporosis: A Systematic Review and Meta-analysis through a Grade Analysis of Evidence. Orthop Surg 2021 Oct;13(7):1941-50. DOI: 10.1111/os.13136

19. Mäkinen VN, Sølling AS, McClung M, Langdahl BL. Romosozumab for the treatment of osteoporosis – a systematic review. J Endocrinol Invest 2025 Mar 1;48(3):547-72. DOI: 10.1007/s40618-024-02469-1
20. Adami G, Pedrollo E, Rossini M, Fassio A, Braga V, Pasetto E, et al. Romosozumab added to ongoing denosumab in postmenopausal osteoporosis, a prospective observational study. JBMR Plus 2024 Feb 7;8(4):ziae016. DOI: 10.1093/jbmrpl/ziae016
21. Chiang MH, Fan TS, Lee CC, Tseng TH, Yen HK, Hung CC, et al. Preliminary analysis of combined romosozumab and denosumab versus teriparatide and denosumab on bone mineral density. Osteoporos Sarcopenia. 2025 Dec;11(4):137-44. DOI: 10.1016/j.afos.2025.11.002
22. Hong P, Liu R, Rai S, Liu J, Zhou Y, Zheng Y, et al. Is abaloparatide more efficacious on increasing bone mineral density than teriparatide for women with postmenopausal osteoporosis? An updated meta-analysis. J Orthop Surg Res 2023 Feb 17;18:116. DOI: 10.1186/s13018-023-03595-x
23. Lane J. Abaloparatide Added to Ongoing Denosumab vs Continued Denosumab Alone [Clinical trial registration] [Internet]. clinicaltrials.gov; 2025 Apr [cited 2026 Mar 2]. Report No.: NCT04467983. Available from: https://clinicaltrials.gov/study/NCT04467983
24. Deal C, Omizo M, Schwartz EN, Eriksen EF, Cantor P, Wang J, et al. Combination teriparatide and raloxifene therapy for postmenopausal osteoporosis: results from a 6-month double-blind placebo-controlled trial. J Bone Miner Res 2005 Nov;20(11):1905-11. DOI: 10.1359/JBMR.050714
25. Finkelstein JS, Wyland JJ, Lee H, Neer RM. Effects of teriparatide, alendronate, or both in women with postmenopausal osteoporosis. J Clin Endocrinol Metab 2010 Apr;95(4):1838-45. DOI: 10.1210/jc.2009-1703
26. Muschitz C, Kocijan R, Fahrleitner-Pammer A, Lung S, Resch H. Antiresorptives overlapping ongoing teriparatide treatment result in

additional increases in bone mineral density. J Bone Miner Res 2013 Jan;28(1):196-205. DOI: 10.1002/jbmr.1716

27. Tsai JN, Uihlein AV, Lee H, Kumbhani R, Siwila-Sackman E, McKay EA, et al. Teriparatide and denosumab, alone or combined, in women with postmenopausal osteoporosis: the DATA study randomised trial. Lancet 2013 Jul 6;382(9886):50-6. DOI: 10.1016/S0140-6736(13)60856-9

28. Muschitz C, Kocijan R, Fahrleitner-Pammer A, Pavo I, Haschka J, Schima W, et al. Overlapping and continued alendronate or raloxifene administration in patients on teriparatide: effects on areal and volumetric bone mineral density-the CONFORS Study. J Bone Miner Res 2014 Aug;29(8):1777-85. DOI: 10.1002/jbmr.2216

29. Leder BZ, Tsai JN, Uihlein AV, Burnett-Bowie SAM, Zhu Y, Foley K, et al. Two years of Denosumab and teriparatide administration in postmenopausal women with osteoporosis (The DATA Extension Study): a randomized controlled trial. J Clin Endocrinol Metab 2014 May;99(5):1694-700. DOI: 10.1210/jc.2013-4440

30. Xuan M, Wang B, Bi W, Li Y, Song L, Xie Z, et al. (V) Treatment of postmenopausal osteoporosis with recombinant human parathyroid hormone and electromagnetic field. Aging Clin Exp Res 2025 Feb 22;37(1):44. DOI: 10.1007/s40520-025-02932-w

31. Jepsen DB, Ryg J, Hansen S, Jørgensen NR, Gram J, Masud T. The combined effect of Parathyroid hormone (1-34) and whole-body Vibration exercise in the treatment of postmenopausal OSteoporosis (PaVOS study): a randomized controlled trial. Osteoporos Int 2019 Sep;30(9):1827-36. DOI: 10.1007/s00198-019-05029-z

32. Wei K, Qu Y, Gao Y, Ma Y. Comparison of Efficacy of Teriparatide (Parathyroid Hormone 1-34) Alone and in Combination with Zoledronic Acid for Osteoporosis in Postmenopausal Women. J Coll Physicians Surg Pak 2021 Feb;31(2):240-2. DOI: 10.29271/jcpsp.2021.02.240

FIGURES

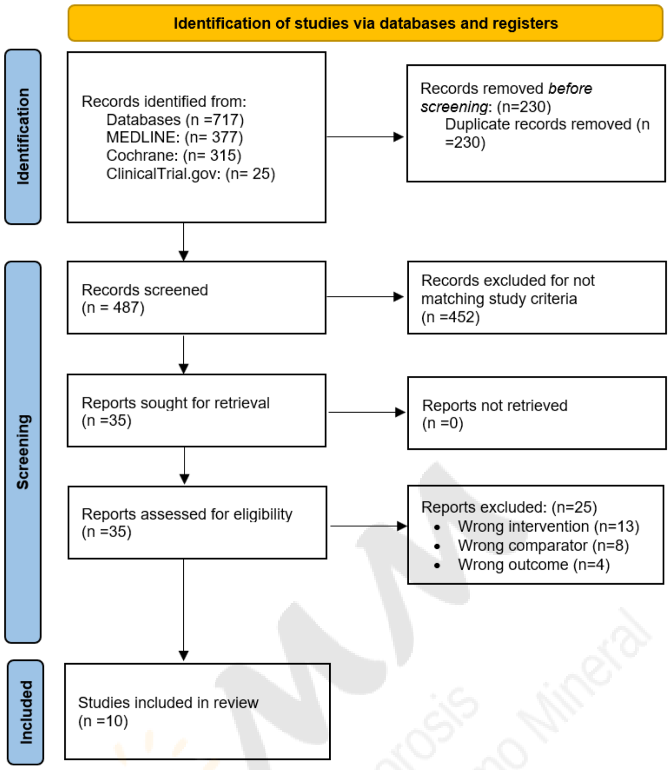

Figure 1. PRISMA flowchart diagram.

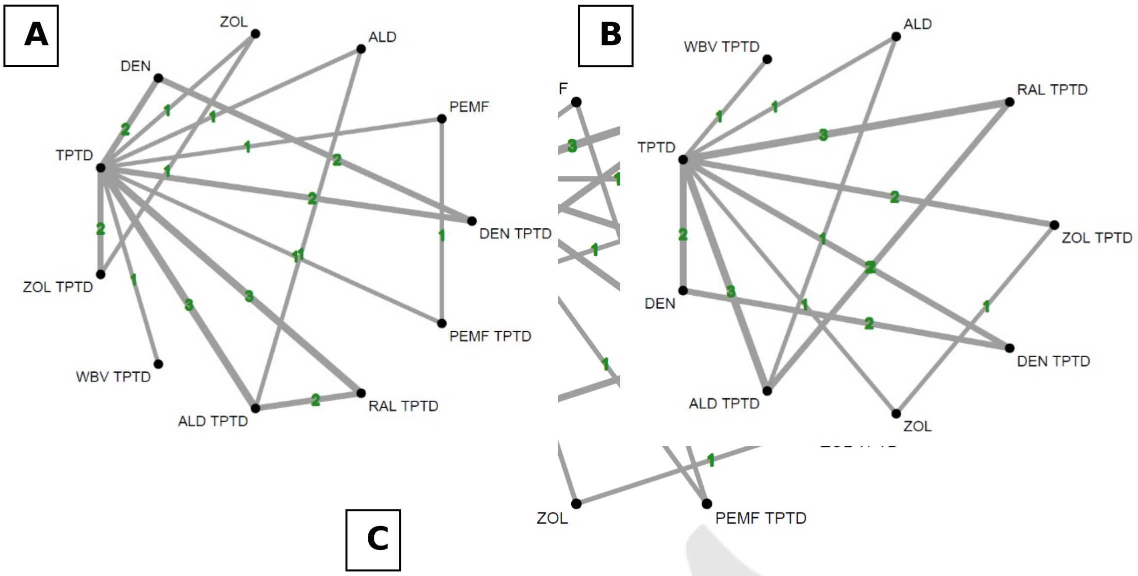

Figure 2. Network plot for BMD of: (A) lumbar spine; (B) total hip; (C) femoral neck.

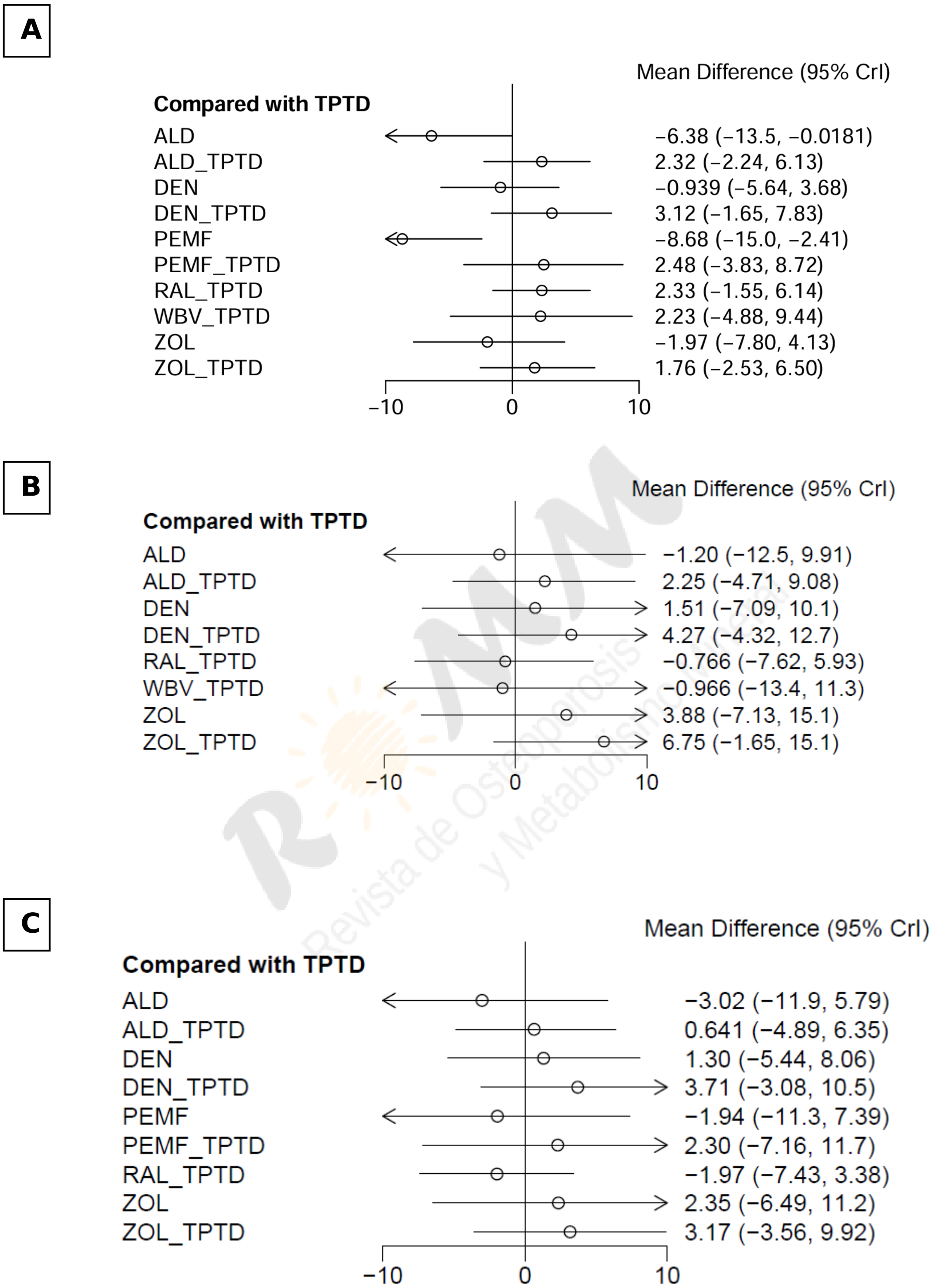

Figure 3. Forest plot of NMA: (A) lumbar spine; (B) total hip; (C) femoral neck.

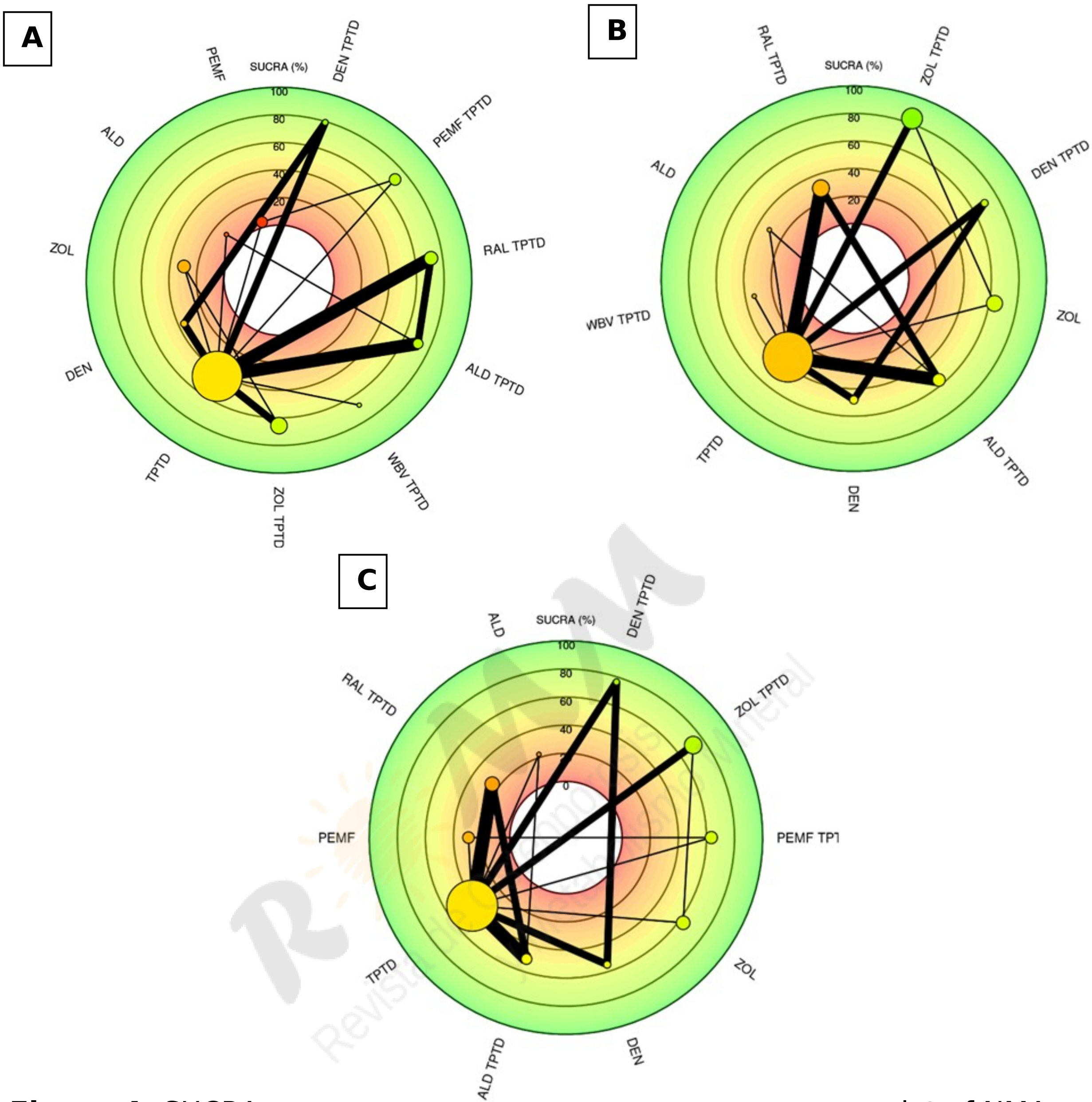

Figure 4. SUCRA plot of NMA: (A) lumbar spine; (B) total hip; (C) femoral neck.

TABLES

Table I. Study characteristics

No	Study ID	Participants *(n)*		Age		Intervention		Basic treatment/ day	Follow up (month)	RoB2
		I	C	I	C	I	C			
1	Deal 2005, (24)	RAL + TPTD: 69	TPTD: 68	66.6 ± 7.5	66.1 ± 7.8	RAL 60 mg/day, oral + TPTD 20 µg/day, IM	TPTD 20 µg/day, IM	Calcium 1000 mg Vitamin D 400-800 IU/ day	6	Low
2	Finkelstein 2010 (25)	ALD + TPTD: 20	TPTD: 20 ALD: 29	62 ± 7	65 ± 7 64 ± 6	ALD 10 mg/day, oral + TPTD 100 µg/day, IM	TPTD 56.5 µg/day, IM ALD 10 mg/day oral	Calcium 1000-1200 Vit. D 400 IU	30	Some concerns
3	Cosman 2011, (14)	ZOL + TPTD: 137	TPTD: 138 ZOL: 137	65 ± 8.8	63.8 ± 9.1 66.1 ±9.0	ZOL 5 mg/year IVdrip + TPTD 20 µg/day, IM	TPTD 20 µg/day, IM ZOL 5 mg/year IVdrip	Calcium 1000-1200 mg Vit D 400-800 IU	12	Some concerns
4	Muschitz 2013 (26)	ALD + TPTD: 41 RAL + TPTD: 37	TPTD: 47	71.6 ± 8.5	71.7 ± 9.3	ALD 70 mg/week oral + TPTD 20 µg/day, IM RAL 60 mg/day + TPTD 20 µg/day, IM	TPTD 20 µg/day, IM	Calcium 1000 mg Vit D 800 IU	18	Some concerns
5	Tsai 2013 (27)	DEN + TPTD: 30	TPTD: 29 DEN: 33	65.9	65.5 ± 7.9	DEN 60 mg/6 months + Teriparatide 20 µg/day, IM	TPTD 20 µg/day, IM	Calcium 1200 mg Vit D 400 IU	12	Low
6	Muschitz 2014, (The CONFORS Study) (28)	ALD + TPTD: 41 RAL + TPTD: 37	TPTD: 47	72.4 ± 9.1 70.5 ± 8.4	72.8±8.9	ALD 70 mg/week oral + TPTD 20 µg/day, IM RAL 60 mg/day + TPTD 20 µg/day, IM	TPTD 20 µg/day, IM	Calcium Vit D	12	Some concerns
7	Leder 2014 (The DATA Extension Study) (29)	DEN + TPTD: 24	TPTD: 28 DEN: 31	65.9 ± 9.0	65.5 ± 7.9 66.3 ± 8.3	Denosumab 60 mg/6 months + TPTD 20 µg/day, IM	TPTD 20 µg/day, IM DEN 60 mg/6 months	Calcium 1200 mg Vit D 20 ng/ml	24	Some concerns
8	Xuan 2025 (30)	PEMF + TPTD: 15	TPTD: 113 PEMFs: 108	65.04 ± 7.10	65.23 ± 7.07 65.37 ± 7.38	PEMF 5 month then initiated 1 month later + TPTD 20 µg/day, IM	TPTD 20 µg/day, IM PEMF monotherapy	Calcium 600 mg Vitamin D 125 U	18	Some concerns

9	Jepsen 2019, (PaVOS study) (31)	WBV+TPTD: 15	TPTD: 18	69 ± 5	69 ± 8	WBV training protocol consisted of twelve minutes training with the WBV: rest ratio 1:1 min, including six minutes of vibration, three days a week with one day pause in between + TPTD 20 µg/day, IM	TPTD 20 µg/day, IM	Calcium 800 mg Vitamin D 400-800 mg	12	Some concerns
10	Wei 2021 (32)	ZOL + TPTD : 48	TPTD:48	64.31 ± 2.56		ZOL 5 mg/day, IV + TPTD 20 µg/day, IM	TPTD 20 µg/day, IM	Calcium carbonate 600 mg Vitamin D 125 IU	6	Some concerns

ALD: alendronate; PEMFs: pulsed electromagnetic fields; RAL: raloxifene; RID: risedronate; TPTD: teriparatide; WBV: whole body vibrations.

Table II. SUCRA rank

Treatment	Lumbar spine	Total HIP	Femoral neck
ALD	10.57	30.85	22.27
ALD + TPTD	70.97	56.13	50.89
DEN	35.85	48.08	55.05
DEN + TPTD	79.32	69.70	76.45
PEMF	3.98	N/A	29.41
PEMF + TPTD	71.59	N/A	63.47
RAL + TPTD	71.56	29.83	24.88
TPTD	42.97	34.34	42.46
WBV + TPTD	67.81	33.50	N/A
ZOL	29.75	63.81	63.14
ZOL + TPTD	65.61	83.77	71.97