

# Alternative Treatments for Osteoporosis in Postmenopausal Women: A Systematic Review

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## Introduction

Osteoporosis-related fractures pose a significant burden to postmenopausal women in regards to morbidity, mortality, and cost to society. The age-related decline of bone health is apparent as the body becomes less responsive to the hormones that control calcium homeostasis, less efficient at extracting necessary vitamins and minerals from the diet, and more sensitive to any deficiencies that were present earlier in life.

Many postmenopausal women desire non-pharmaceutical alternatives to bisphosphonates for the treatment of osteoporosis and prevention strategies against osteoporosis. Although highly effective in the treatment of osteoporosis, bisphosphonates have a serious side effect profile. These side effects limit the use and duration of bisphosphonates for the treatment of osteoporosis, thus revealing the need for alternative therapies for osteoporosis.

## Research Question

The research question posed was: In postmenopausal women (P), are non-pharmaceutical treatments such as vitamins and supplements (I) effective in increasing bone mineral density (O) as compared to no treatment with non-pharmaceutical agents (C)?

The proposed hypothesis is that vitamins and supplements are effective in increasing bone mineral density (BMD) as compared to no treatment.

## Materials and Methods

The systematic review was conducted by searching the electronic database of PubMed/MEDLINE using the MeSH terms “postmenopausal osteoporosis” and “vitamins” from January 1961 to April 2019. Only English language publications were selected for review. The review included randomized controlled trials that studied the effects of vitamin supplementation on bone turnover markers and bone mineral density in postmenopausal women with or without osteoporosis. The articles selected for use in this review were assessed for quality using an assessing instrument developed by Jadad et al.

The following data were extracted from the randomized controlled trials: the number of participants, the intervention and study design, the duration of treatment, and outcomes, including differences in bone turnover markers, and bone mineral density of the lumbar spine, total hip, and femoral neck before and after the proposed treatment.

## Results

Twelve articles were included in the final systematic review. These studies showed that multispecies probiotic supplements, folic acid, phylloquinone, calcium, and a combination of phytochemicals, vitamin D and vitamin K decreased the measured markers of bone turnover in studies with a treatment period ranging from 84 days to 48 months.

It is important to take into consideration the widely positive increase in bone mineral density as shown in the study evaluating the effects of denosumab with vitamin D, which is an outlier compared to the other articles in this review. However, another study involving calcium supplementation for 12 months also found improvement in femoral neck bone mineral density.

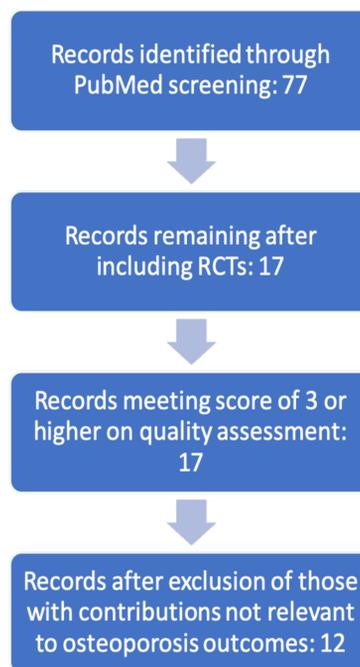


Figure 1. Flowcharts of records included in systematic review.

Studied intervention	Number	Duration	BTM	LS BMD	TH BMD	FN BMD
Calcium, vitamin D, vitamin K2	210	18 months	0	0	n/a	0
Multispecies probiotic supplement	50	6 months	-	0	0	n/a
Denosumab with active vitamin D or native vitamin D	56	12 months	n/a	+	+	+
Folic acid	40	6 months	-	n/a	n/a	n/a
Vitamin D and calcium	279	24 months	0	n/a	n/a	n/a
Soy isoflavones	70	6 months	+	n/a	n/a	0
Phytochemicals, vitamin D and vitamin K	51	14 weeks	-	n/a	n/a	n/a
Vitamin K	440	48 months	0	0	0	n/a
Calcium and vitamin D with and without clodronic acid	79	36 months	0	-	n/a	-
Vitamin K2	325	36 months	n/a	0	n/a	n/a
Phylloquinone	21	84 days	-	n/a	n/a	n/a
Calcium (chicken eggshell powder)	85	12 months	-	0	n/a	+

Table 1: Overview of results of records included in systematic review. Abbreviations: BTM – bone turnover markers, LS BMD – lumbar spine bone mineral density, TH BMD – total hip bone mineral density, FN BMD – femoral neck bone mineral density. Number – number of study participants. N/a – not recorded or not available in original study. Minus sign (-) – decrease in measured values. Plus sign (+) – increase in measured values. Zero (0) – no change in measured values.

## Conclusion

Supplementation with probiotic supplements, folic acid, vitamin K, calcium, and phytochemicals with vitamins D and K are shown to be beneficial to bone health with evidence that bone turnover markers are decreased in these treatment groups. In regards to vitamin K, dietary phylloquinone must be taken at levels up to five times the recommended vitamin K AI level to result in a statistically significant decrease in serum N-telopeptides of collagen cross-links. In regards to probiotic supplements, bone resorption and turnover are suppressed when treated with multispecies probiotics for six months, and calcium supplements alone at a level of 500mg twice daily suppress markers of bone turnover. These findings demonstrate that vitamin or probiotic supplementation are not effective in increasing bone mineral density, as bisphosphonates are effective in doing, but that these dietary supplements significantly decrease various bone turnover markers. This appears to be the main effect of vitamins on bone health.

Weaknesses of this systematic include outcome measures as patient-related outcomes, such as fractures, should be the primary outcome that is recorded. Methodological weaknesses include the possible presence of publication bias, as only published randomized-controlled trials in English were selected for use in this systematic review. It is important to note that no two studies used the same treatment agents. Also, the scope of studies could be expanded to include more than one database to ensure that the systematic review includes as many relevant studies as possible. Finally, there were many differences in the types of bone turnover markers that were measured in the studies included.

## Summary

Supplementation with probiotic supplements, folic acid, vitamin K, calcium, and phytochemicals with vitamins D and K are shown to be beneficial to bone health with evidence that bone turnover markers are decreased in these treatment groups, although these findings demonstrate that vitamin or probiotic supplementation are not effective in increasing bone mineral density.

## Acknowledgements

I wish to thank my mentor Dr. David Beyda and my scholarly project advisor, Dr. Joseph Stapczynski, for their assistance and guidance in this project. I would also like to thank Dr. Matthew McEchron for encouraging an evidence-based approach to the practice of medicine.