

A Systematic Review and Meta Analysis of Dietary Interventions in Prevention and Management of Osteoporosis among Adults

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Abstract

Objectives: To identify evidence based dietary patterns in preventing osteoporosis and fracture risk among both post menopause women and elderly men

Design: Systematic review and meta-analysis.

Participants: healthy postmenopausal women and elderly men with age range 39-80 years

Measurements: PubMed, Google scholar databases were searched for relevant studies. Data extracted for all studies include study identification details, country of study conducted, subject baseline demographics, diet intervention details, duration of intervention details, dietary details of control and treatment groups, data details (included number of control and treatment subjects), exposure assessment method and outcome

Results: Systematic review findings have found that vitamin D3 and calcium-fortified dairy product improves vitamin D status and reduces accelerated bone resorption. Dietary Intervention reporting C-terminal telopeptide (CTX) and P1NP (Procollagen Type 1N-Terminal Propeptide) outcomes were included in Meta analysis. Standardized mean differences, standard deviations, p values computed for 6 studies to undergo meta-analysis. Heterogeneity was significantly present for both CTX and P1NP, variance across the studies shown significance, positive association found between diet interventions and effect on bone biomarkers.

Conclusion: A significant association found between fortified dairy and fortified orange juice with vitamin D and calcium in reducing risk of fracture among postmenopausal women and elderly men. A Med-Diet in combination with virgin olive oil or Nuts found to improvement in bone health among both adult and elderly men and women and a diet rich in vegetable, fruit, nuts, milk, high fibre bread, legumes found to low BMD levels and processed diet found to have low serum calcium levels causing bone resorption.

Keywords Postmenopause, Bone Mineral Density, Osteoporosis, CTX, IGF-1, P1NP, PTH, TRAP-5b

Introduction

Osteoporosis condition has witnessed severity not just among postmenopausal women and also among adults with early stages of bone loss studies have determined an improved bone regulation based on life style modifications like dietary habits and physical activities with regard to dietary patterns a balanced diet rich in nutrients like proteins unsaturated fatty acids minerals and probiotics has shown to reduce bone loss and help in prevention as well as management of osteoporosis this review study thus provides a detailed perspective on available

dietary variations and food groups in bone regulation¹

Osteoporosis prevention among adults maintained by suitable dietary interventions² bone mass of an individual at growth amount stage has an effect in bone and maintenance at adult and elderly stages among women bone loss related fractures starts after menopause and ovarian cessation^{4,5,6} nutritional intake in recent times has observed to have impact on bone concepts like BMD bone matrix mineralisation metabolism growth and loss⁷ though many suggestions on bone loss management through nutrition are observational there comes need for understanding experimental works providing scientific evidence of diet on bone regulation.

Randomised controll trails are effective to identify effect of food or nutrition on fracture risk or prevention or management. Since RCTs are time taking and expensive only few nutrients have been studied based on the baseline intake and the resulting effects.⁸ Consumption of fruits and vegetables on a regular and adequate intake shown to reduce risk of osteoporosis.^{9,10}

Evidence based recommended diets like dash in decreasing high blood pressure and Meddiet focusing in promoting healthy heart are included in recommended dietary intakes similarly in case of osteoporosis traditional diets like Chinese and Nordic diets have impact on improving bone strength but yet there requires a scientific dietetic guidelines for avoiding risk of osteoporosis the present review is focused to identify evidence based diets in preventing osteoporosis by reviewing out results through studies on randomised and observation on regulation of bone induced diets also analyse the levels of bone markers

Materials and Methods

This systematic review and meta-analyses are followed thoroughly as per prisma guidelines databases includes original research works in pubmed as well as books related to clinical nutrition the searches were implemented through 1st january 2010 to 16 february 2025 and research articles identified only in english and the studies included based on diet interventions in human.

Table 1: Literature Search Strategy

Database	Search Strategy
Pubmed	"Osteoporosis, diet therapy"[Mesh]) AND ("Osteoporosis, Postmenopausal"[Mesh])) OR "Bone Remodeling"[Mesh]) AND "Cancellous Bone"[Mesh]
	"Osteoporotic Fractures/diet therapy" [Mesh]
	("Osteoporosis/diet therapy"[Mesh]) AND "Osteoporosis, Postmenopausal"[Mesh]) AND "Bone Diseases, Metabolic/diet therapy"[Mesh])
Google Scholar	Cohort study on effect of bone health through dietary intake among adults

Study Eligibility Criteria

Prospective Cohort studies, Randomised Control Trail, Intervention studies, Observational studies which examined relationship between dietary intervention on bone health among healthy postmenopausal women and elderly men with age range 39-80 years. Adults, healthy or obese; with past or current fractures but no other existing conditions; adults with cardiovascular disease but no other clear disease and not on any supplements included in definition of healthy adults.

Study Ineligibility Criteria

Animal models used in study, studies based on testing drug safety or efficacy, clinical trials

Study Selection Process

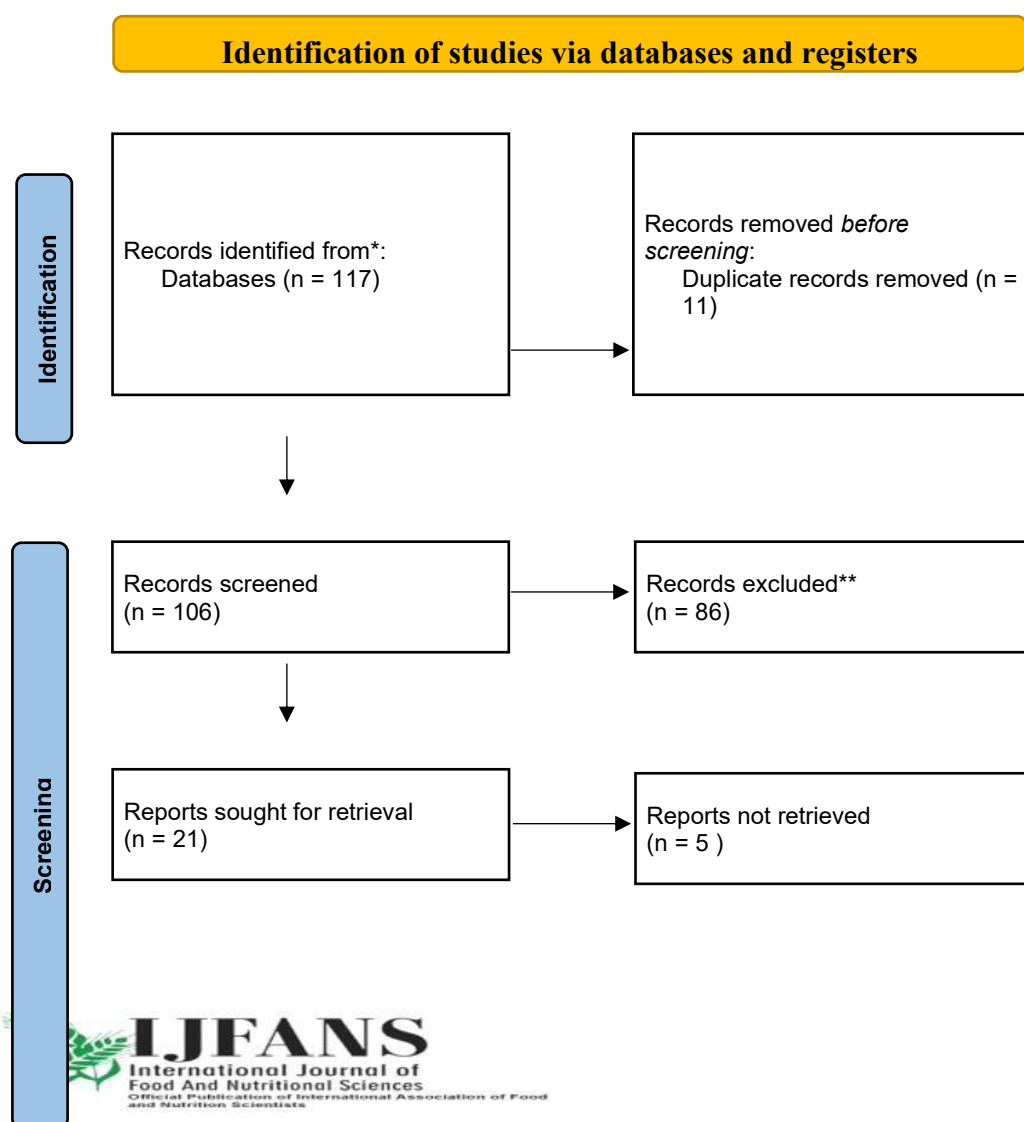
Mendeley free reference manager pdf organizer opted to collect studies as per required database and from all the collected references repeated articles were removed followed by studying of summary and topics of articles to include or exclude eligible or ineligible data finally screened articles reviewed for data analysis

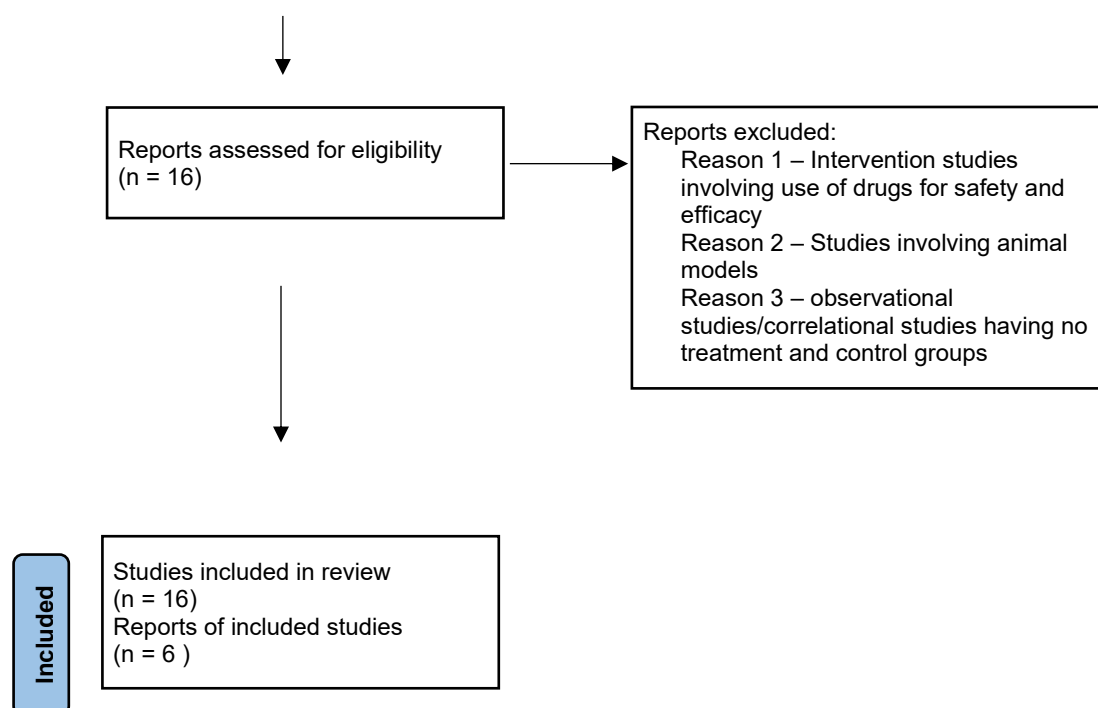
Data Extraction

A data extraction sheet was created in word to capture all data of interest from RCTs, Cohort, Case Control, Observational studies. Data extracted for all studies and validated by mentor. The items extracted include (1) study identification details; country of study conducted (2) subject baseline demographics; (3) diet intervention details; duration of intervention details; (4) dietary details of control and treatment groups (5) data details (included number of control and treatment subjects); (6) Exposure assessment method; (7) Outcome

Results and Findings

Figure 1: PRISMA 2020 (Preferred Reporting Items for Systematic Reviews and Meta-Analysis flow diagram to illustrate search results)



**Table 2: Characteristics of 16 RCT/Cohort/Observational/Case Control Studies**

Cohort	Participants	Baseline Mean Age or Age range (years)	Dietary Intervention	Follow up period (years)	Exposure Assessment	Outcome	Reference
1. PRODIGIA Research organization, Jakarta Metro, Manila	60 postmenopausal women 60 postmenopausal women	Women of 55 years of age, postmenopause for at least 5 years, body mass index (BMI) between 17 and 30 kg/m ² .	High Calcium Milk drink with added vitamin D, Magnesium and Zinc versus a placebo drink supplementat ion	4 months	On Serum Parathyroid Hormone (PTH), 25OHD and Blood Mineral Levels as well as Markers of Bone (CTX levels, Osteocalcin, PINP) BMI, Waist and Hip Circumference	Improved Vit D status, lowered PTH levels, reduced Bone Turnover	11
2. Community dwelling women, France	Postmenopausal women 71	50-65 yrs Menopause for >3yrs; BMI 18-27kg/m ²	Vitamin D and Ca fortifies dairy product(Two servings 2*100g) of skimmed milk, soft plain cheese	6 weeks	Markers of bone CTX and TRAP 5b and Serum changes of IGF-I, 25OHD, PTH, OC, 25OHD	Reduced Serum concentration of TRAP 5b and increase in IGF-I	4
3. Community dwelli	127 men	55-80 yrs diagnosed with type 2 diabetes or having hypertension/dyslipi	MedDiet plus supplementat ion with virgin olive	2 years	OC, PINP,CTX, serum phosphate,	Increase d serum osteocalcin and	5

ng men, PREDIMED study center		demia/overweight/family history of premature CVD with normal renal function	oil; MedDiet plus supplementat ion with mixed nuts vs low-fat diet		serum calcium, age, BMI, LDL, HDL cholesterol, Fasting glucose, insulin, SBP, DBP	PINP, decrease d CTX levels in MedDiet enriched Med Diet and olive oil - Increase in serum levels of bone markers Osteocal cin, PINP and decrease in CTX levels; MedDiet, nuts and low fat diet - decrease in serum calcium, increase beta cell function	
4. Institut ionalis ed wome n in French nursin g homes	60 elderly women	Women aged 68-99 years years with low vitamin D status, moderately elevated PTH level, no sun exposure and mini nutritional assessment score >20	Vitamin D and Calcium fortified yogurt vs nonfortified control yogurt	56 days	25 OHD, PTH, IGF 1, BAP, Markers of Bone Resorption (CTX levels, TRAP5b, PINP), Age, BMI, ca, inorganic phosphate, albumin, prealbumin	Increase in serum 25 OHD levels, decrease PTH levels, TRAP5b levels and CTX levels, reduced serum expressio n of secondar y hyperthy roidism	6
5. Nursin g home in Iasi, Roma nia	45 patients (28 women;17m en)	58-89 years	Bread buns fortified with vitamin D3	1 year	Bone Mineral Density, Serum calcium, PTH, 25(OH)D	Increase in Serum 25(OH) D, PTH during trail. 36 th month follow up after	12

						clinical trails 25(OH) D, PTH reached to baseline value	
6. Volunteers, California	160 women	Osteopenic postmenopausal women	Dried plum or dried apple along with Ca and Vitamin D supplements	1 year	Serum levels of RANKL, OPG, Sclerostin, BMD, BMI, TRAP 5b, OC, P, Ca	Dried plum intake - increase in BMD of Ulna and Spine; Increase in serum levels of RANKL and OPG and decrease in serum levels of Sclerostin	13
7. Winthrop University Hospital, New York	76 women	50-70 years Healthy postmenopausal women	Vitamin D3, Ca fortified orange juice	8 weeks	Calcium absorption, 25(OH)D, 1,25(OH) ₂ D, PTH, CTX, PINP	Increase Calcium absorption and	14
8. Participants from European Prospective Investigation in to cancer, Norfolk	Cross-sectional ultrasound study – 4000 (1759 men; 2241 women) and case cohort fracture 5319	39-79 years	Vitamin C foods like Kiwi and supplements	7 days	Vitamin C intake estimation through 7-d diet diary (7dDD), vitamin C concentration in blood samples impact on bone fractures	Reduced fracture risk of hip and spine in men with higher plasma vitamin C concentrations, Both in men and women vitamin C intake found to promote bone health	15
9. EPIC	Cross sectional	40-79 years	Dietary magnesium	13.4 years	Bone density status for	Reduced hip	16

Norfolk cohort, United Kingdom	analyses for bone density among 1958 men; 2755 women; case-cohort longitudinal analysis for fracture among 968 men; 1360 women with fracture cases		and potassium		fracture risk and osteoporosis	fracture risk in both men and women	
10. Community, San Diego, California	48 osteopenic women	65-79 years	Dried plum in 3 treatment groups : 50g, 100g, 0g control	6 months	Total body, hip, lumbar bone mineral density, blood biomarkers BAP, TRAP-5b, hs-CRP, IGF-1 and sclerostin, OPG, RANKL, calcium, phosphorous and vitamin D	Prevented bone loss among older osteopenic women	17
11. Hongqi Community Health Center	210 postmenopausal women	50-65 years	high calcium, low fat milk powder with calcium contents 300, 600 and 900mg for A,B,C groups and 800 IU of vitamin D	2 years	Bone Mineral Density of femoral neck, greater trochanter, lumbar spine and ward's triangle along with food frequency	600 and 900mg/d ay of calcium reduced bone loss in lumbar spine and greater trochanter, and 900mg/d ay reduced bone loss in greater trochanter	18
12. North West Adelaide Health Study, Australia	545 men; 637 women	50 years and above	Prudent pattern – fruit, vegetable, fish, nut based milk, high fibre bread, legumes; western pattern – processed	12 months	Dietary data through FFQ, BMD	Inverse association between prudent pattern and low BMD and positive association	19

			and red meat, fast foods, soft drinks, white bread, high fat dairy			between western pattern low Ca and high levels of energy content and P, low serum Calcium causing bone resorption and high energy intake reduced BMD	
13. Local community, Indianapolis	14 postmenopausal women >4y postnatural menopause or hysterectomy	39-79 years	Multivitamin – 200mg Calcium/day and 400 IU vitamin D/day to maintain calcium levels, doses of 0, 10 and 20g fiber from soluble corn fibre for 50days	6months	Medical history, diet assessment, physical activity evaluation, 4-d diet record, bone turnover markers- N-terminal telopeptide and osteocalcin, bone formation marker bone-specific alkaline phosphate	Increased bone calcium retention and improved bone calcium balance	20
14. Women's Antioxidant and Folic Acid Cardiovascular Study	300 women with Pre-existing cardiovascular diseases or 3 or more coronary risk factors		Vitamin b, folic acid, vitamin B6, vitamin B12	7.3 years	Non-spine fracture risk, bone turnover markers- C-terminal cross-linking telopeptide of type 1 collagen (CTX) and intact type 1 procollagen N-propeptide (PINP)	No effect on reduced fracture risk and on bone metabolism	21
15. Participants of	870 adults with high risk of CVD	Men: 55-80 years Women: 60-80 years	MedDiet with extra virgin olive oil – 50g or	8.9 years	FFQ on dietary habits and olive oil consumption	Reduced risk of osteoporosis	22

PRED IMED			more per day; MedDiet with mixed nuts – 30g per day; low fat diet		on fracture risk	related fracture	
16.	160 Postmenopa usal women with amenorrhea >12 months	50-65	Vitamin D	9 months	PTH, Alkaline Phosphate, CTX, P1NP, 25(OH)D	Increase in 25(OH) D, decrease in PTH and CTX levels,	23

Systematic Review Findings

Lowered levels of PTH on consumption of fortified milk

Kruger et al. [2] studied effect of fortified milk supplementation along with added vitamin D, magnesium and zinc on bone biomarkers for a 16-week period in a cohort of postmenopausal women from Jakarta and Manila. The study found out, lower levels of PTH, improved vitamin d levels and reduced bone turnover.¹¹

Vitamin D3- and calcium-fortified dairy product improves vitamin D status and reduces accelerated bone resorption

Bonjour et.al. found that yogurt fortification with vitamin D and calcium found to address issues of osteoporosis in elderly women along with preventive care in developing hyperparathyroidism, deficiency of vitamin D and increased bone resorption.

The study involved dietary intervention of vitamin D and calcium fortified yogurt and non-fortified yogurt in randomized double-blind controlled-trial among 60 institutionalized women aged 68-99 years. It was observed the levels of serum 25OHD were increased and decrease in levels of serum PTH, TRAP5b, and CTX in intervention group.⁶

Nutrition-induced reduction in postmenopausal bone loss rate

Bonjour et al. found decrease in TRAP 5b and increase in IGF-I through vitamin D and Calcium fortified dairy product in a 6-week prospective control study conducted on 71 postmenopausal community dwelling women aged 50-65 years in France. The study showed that the regular consumption of fortified soft white cheese by healthy, community-dwelling women shown increase in protein intake, increase in IGF-I and decrease in TRAP 5b in treatment group.⁴

Improved levels of calcium absorption and bone biomarkers among postmenopausal women with vitamin D3 supplementation

Aloia, J.F. et.al identified calcium absorption increases when supplemented with vitamin D3. The study was conducted on 76 healthy postmenopausal women in 50-60 years of age. The study also concluded an increase in serum calcitriol and serum CTX, while decrease in PTH levels.¹⁴

Bone loss prevention through supplementation by 600 and 900 mg/day of calcium

Chen, Y., et.al, conducted randomized controlled double-blind trial for 2years on 210 postmenopausal Chinese women aged 50-65 years by providing them with 300, 600 and 900 mg of calcium contents added in milk powder. The study observed significant reduction in bone loss in the lumber spine and greater trochanter.¹⁸

Vitamin C intake promotes bone remodeling and bone collagen synthesis

Finck et.al identified that on consumption of high vitamin C reduces risk of hip and spine fractures. The study was based on Norfolk men and women were heel ultrasound observations found higher BUA and VOS values indicating vitamin C role in bone density and stiffness.¹⁵

Effect of magnesium and potassium in diet in preventing osteoporosis

Hayhoe, R. P., et.al, studied the effect of dietary intake of magnesium and potassium on bone density and fracture risk among Norfolk cohort of both men and women aged about 40-79 years for a mean 13-year period. The study found out reduced risk of hip fracture in both women and men and reduced risk of risk of hip, spine, or wrist in men.¹⁶

Mediterranean diet with virgin olive oil supports bone health

Fernández-Real et.al. conducted a randomised diet intervention study for 2 years in 127 elderly men with high cardiovascular risk. The elderly men were randomised with intervention diets namely, low fat diet, a mediterranean diet with nuts and a mediterranean diet with virgin olive oil and observed its effect on bone biomarkers. The study found out that, consumption of a MedDiet enriched with olive oil has a significant increase of total osteocalcin concentrations, serum P1NP and decreased CTX levels.⁵

Olive oil effective for minimising bone fracture risk

García-Gavilán, J. F., et.al, observed for osteoporosis risk on a cohort of men for about 8.9 years who were at risk of cvd. A diet based on Mediterranean food pattern with use of only extra virgin olive oil showed effective in lowering risk of fractures related to osteoporosis.²²

High intakes of fruits, vegetables, medium-fat dairy products and fish promotes higher bone mineral density

Melaku, Y. A., studied the effect on prudent and western dietary patterns on bone mineral density among a cohort of adults in Australia. It was observed that adults who consumed prudent diet rich in fruits, vegetables, milk and high fibre had better BMD levels as compared with ones who had western diet rich in processed foods.¹⁹

Soluble corn fiber consumption helps in maintaining strong bones and prevent bone loss

Jakeman, S. A., et.al, conducted a randomised study on 14 postmenopausal women for finding dose response effect of soluble corn fiber in maintaining bone calcium and found a significant increase in bone calcium retention among participants.²⁰

Reversing bone loss through dried plum consumption

Hooshmand, S. et.al observed effect of dried plum for 1 year in 160 women within age range of being below 10 years to post menopause stage and having osteopenia receiving 500mg Ca plus and 10mg vitamin D per day. The study found dried plum consumption effective in increasing the levels of bone mineral density in ulna and spine region and in reversing bone loss positive by suppressing RANKL production, inhibiting sclerotin and promoting OPG.¹³

Dried plums intake show results of bone resorption inhibition

Hooshmand, S., et.al, studied effect of consumption of dried plums in preventing bone loss among 48 osteopenic postmenopausal women aged 65-79 years. The study included dried plum consumption in two groups with 50g and 100g and observed changes in 3 months and 6 months. Bone biomarkers like TRAP-5b decreased at 3 months and further in 6 months. The study identified dried plum as an effective diet in preventing loss of bone mineral density.¹⁷

High intakes of fruits, vegetables, medium-fat dairy products and fish promotes higher bone mineral density

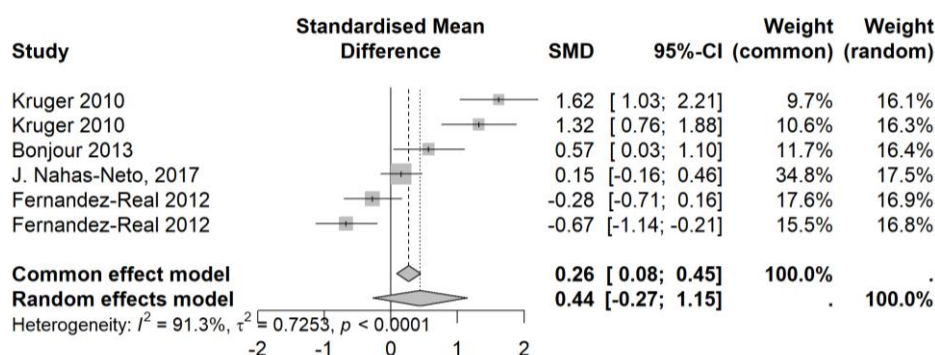
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Figure 2: Association of Biochemical Markers of Bone Resorption and Bone Formation – Relative Changes through Dietary Intervention

CTX



CTX (C-terminal telopeptide of type I collagen)

Interpretation:

Overall effect: SMD = 0.44 (95% CI: -0.27 to 1.15),

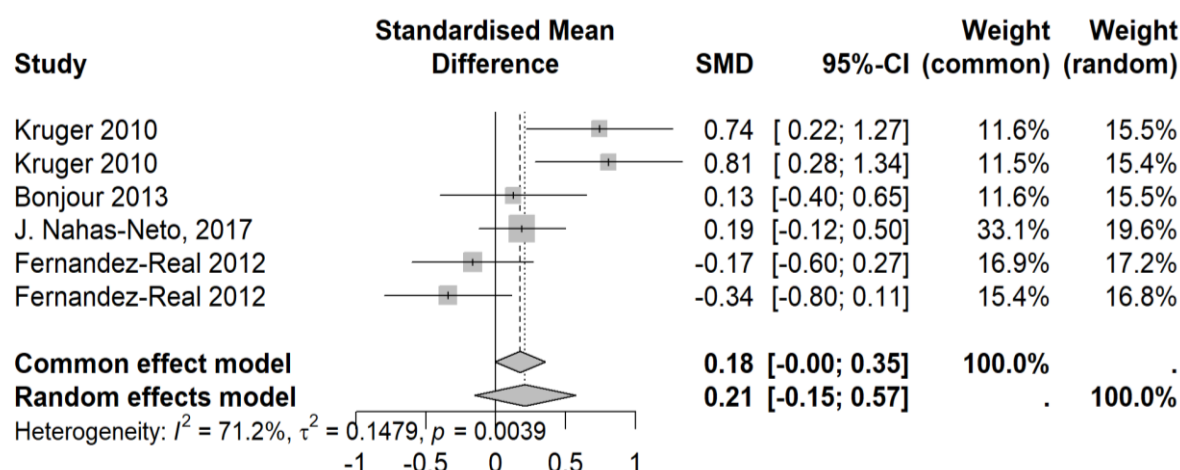
$p < 0.001$ suggests a statistically significant heterogeneity is there

$\tau^2 = 0.72 \rightarrow$ Estimates variance across studies.

$I^2 = 91.3\% \rightarrow$ High heterogeneity

Conclusion: Positive association between healthy dietary patterns and reducing levels of CTX biochemical marker of bone resorption.

P1NP



P1NP (Procollagen Type 1N-Terminal Propeptide)

Interpretation:

Overall effect: SMD = 0.21 (95% CI: -0.15 to 0.57),

$p < 0.001$ suggests a statistically significant heterogeneity is there

$\tau^2 = 0.1479 \rightarrow$ Estimates variance across studies.

$I^2 = 71.2\% \rightarrow$ High heterogeneity

Conclusion: Positive association between healthy dietary patterns and improved levels of P1NP biochemical marker of bone formation.

Meta-analysis Findings

Dietary Intervention reporting C-terminal telopeptide (CTX) and P1NP (Procollagen Type 1N-Terminal Propeptide) outcomes were included. Other outcome measures that were evaluated in some studies had too few studies to evaluate (<4 studies) included calcium absorption, calcium balance, calcium retention, plasma or serum insulin-like growth factor-1 (IGF-1), serum insulin-like growth factor binding protein-3 (IGFBP-3), and serum osteocalcin. Serum PTH ($n = 5$ studies) and serum calcium ($n = 8$ studies) had more studies but are not believed to be sufficiently robust measures of bone turnover and were not included in the meta-analyses. Intervention studies on BMC and BMD not included for evaluation as the results were based on shorter duration of the studies. Prospective cohort studies on fractures were included. There were 6 unique studies with information about dietary interventions effect on bone biomarkers. Standard deviations were calculated from standard errors as provided in studies and the values were evaluated from the results obtained in experimental and control groups.

Standardized mean differences, standard deviations, p values computed for 6 studies to undergo meta-analysis. Heterogeneity was significantly present for both CTX and P1NP,

variance across the studies showed significance, positive association found between diet interventions and effect on bone biomarkers.

Discussion

Nutrients like calcium, dietary protein and vitamin D plays key role in bone growth and maintenance. In this systematic review across 117 studies were screened and confounded to review dietary intervention effects on control and treatment groups assessing biochemical markers of bone in 17 studies and finding association through 6 studies on diet impact in bone health among adults. This systematic review covers studies on BMD testing and bone turnover markers which are generally used to assess treatment therapy in bone loss or identify risk of fracture. BMD testing is done in every 1 to 2 years to either identify fracture risk or detect bone loss.²⁴ Biomarkers of bones were measured based on the metabolites released during bone resorption and bone formation process.²⁵

Biomarkers of bone resorption, serum CTX and bone formation marker, serum procollagen type I N propeptide used as reference markers in the current review based on observational and intervention studies. Parameters like age, gender, physical activity, disease condition, post menopause status referred for accurate analysis.

Fractures are the most important outcome from a clinical and health care cost savings perspective.²⁶ An observational study on fracture outcomes among postmenopausal women from WHI (Women health Initiative) identified decrease in risk of forearm fractures among patients who consumed 20% higher calibrated protein.²⁷ Dietary magnesium and potassium has shown significant effect in reducing hip fracture risk in both men and women.¹⁶

Inverse association between dietary food including fruit, vegetables, nuts, milk, high fiber bread, legumes to that of low BMD levels and positive association found in dietary intake of processed foods. One study showed low serum calcium in processed foods causing bone resorption and high energy intake leading to reduced BMD.¹⁹ Improved BMD in Ulna and Spine on consumption of dried plums. It was also observed that dried plums promote bone regeneration and regulation.⁶ Dried plum also shown significance in preventing bone loss among osteopenic women.¹⁷

MedDiet supplemented with virgin olive oil shown effective bone regulation than other intervention diet including nuts and low-fat diet in elderly men.⁵ Fortified dairy with calcium, vitamin D and fortified orange juice with calcium has shown changes in bone biomarkers like CTX, P1NP, PTH, OC levels suggesting fortified diets improve bone health and prolong life without disability among adults and elderly population.

Our study shown improved vitamin D status, lowered PTH levels and bone turnover among postmenopausal women who consumed fortified milk with Calcium and other minerals for 4 months. The effect was found evident in blood mineral levels as well as bone markers.¹¹ Similar study among postmenopausal women found on fortified dairy products of daily two servings for 6 weeks where levels of TRAP 5b and IGF-I reduced which play key role in bone remodeling.⁴ Similar study and results found in fortified vitamin D3 bread buns.¹²

Conclusion

Our systematic review and meta-analysis suggest significant association between fortified dairy and fortified orange juice with vitamin D and calcium in reducing risk of fracture among postmenopausal women and elderly men.

Med-Diet in combination with virgin olive oil or Nuts found to improvement in bone health among both adult and elderly men and women.

Diet rich in potassium and magnesium has shown significance in preventing fracture risk in elderly.

Dried plum intake about 5 pieces a day has shown improvement in BMD, Ulna and Spine thereby promoting bone regeneration and regulation and in preventing bone loss among osteopenic women.

A diet rich in vegetable, fruit, nuts, milk, high fibre bread, legumes found to low BMD levels and processed diet found to have low serum calcium levels causing bone resorption.

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