Protein & Vitamin K:
"Other" Nutrients for Bone Health

Wendy E. Ward
Professor & Canada Research Chair
Faculty of Applied Health Sciences

Protein

- **Current RDA versus suggested intake**
- **Intakes above RDA & bone health**
- **High vs. low intakes & bone health: BMD, Fracture**
  - ***Calcium as a modifier***
  - ***Protein source***

Recommended Dietary Allowance (RDA)

RDA (for all ages!)

0.8 g protein/kg body weight/day

Higher Protein Intakes?

RDA (for all ages!)

0.8 g protein/kg body weight/day

But….likely higher need due to aging

- **Sarcopenia: loss of muscle mass & function**
- **Anabolic resistance due to compromised:**
  - **-protein digestion**
  - **-AA absorption & uptake into muscle**
  - **-insulin-mediated muscle tissue perfusion**

-Position paper from the PROT-AGE Study Group. JAMDA. 2013:14:542-559
-Recommendations from the ESPEN Expert Group. Clin Nutr. 2014;33:929-936
-Consensus statement of ESCEO. Maturitas. 2014;79:122-132

Higher Protein Intakes?

RDA (for all ages!)

0.8 g protein/kg body weight/day

Maintain Muscle in Healthy Older Adults:

1.0-1.2 g protein/kg bw/day

20-25 g, 25-30 g protein/meal
2.5-2.8 g leucine

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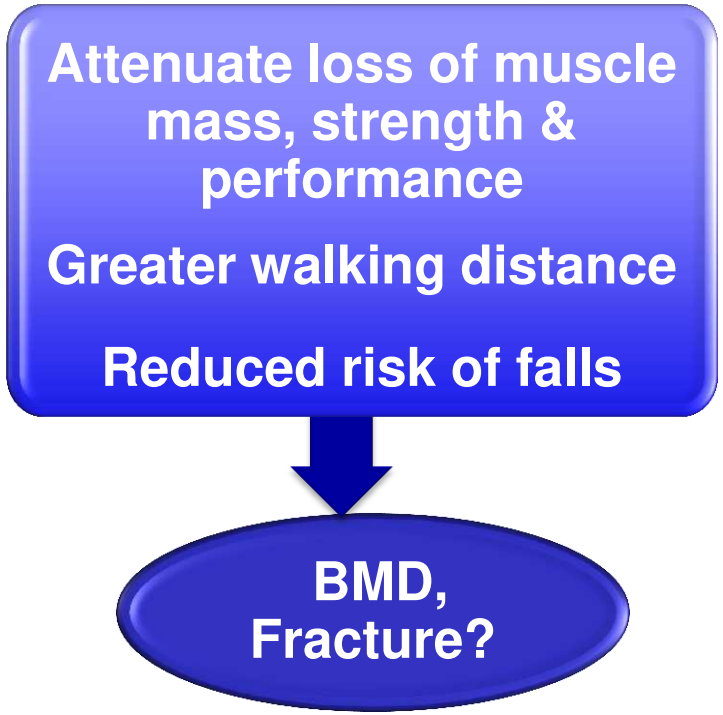

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Is higher protein harmful to bone?

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↑ dietary protein

↓

↑ urinary Ca excretion

↓

↓ bone mineral

↑ risk of fracture

***Assuming* Ca is from bone….or is it?**

Is higher protein harmful to bone?

↑ dietary protein

↓ ↑ Ca absorption

↑ urinary Ca excretion

↓ ?

? bone mineral

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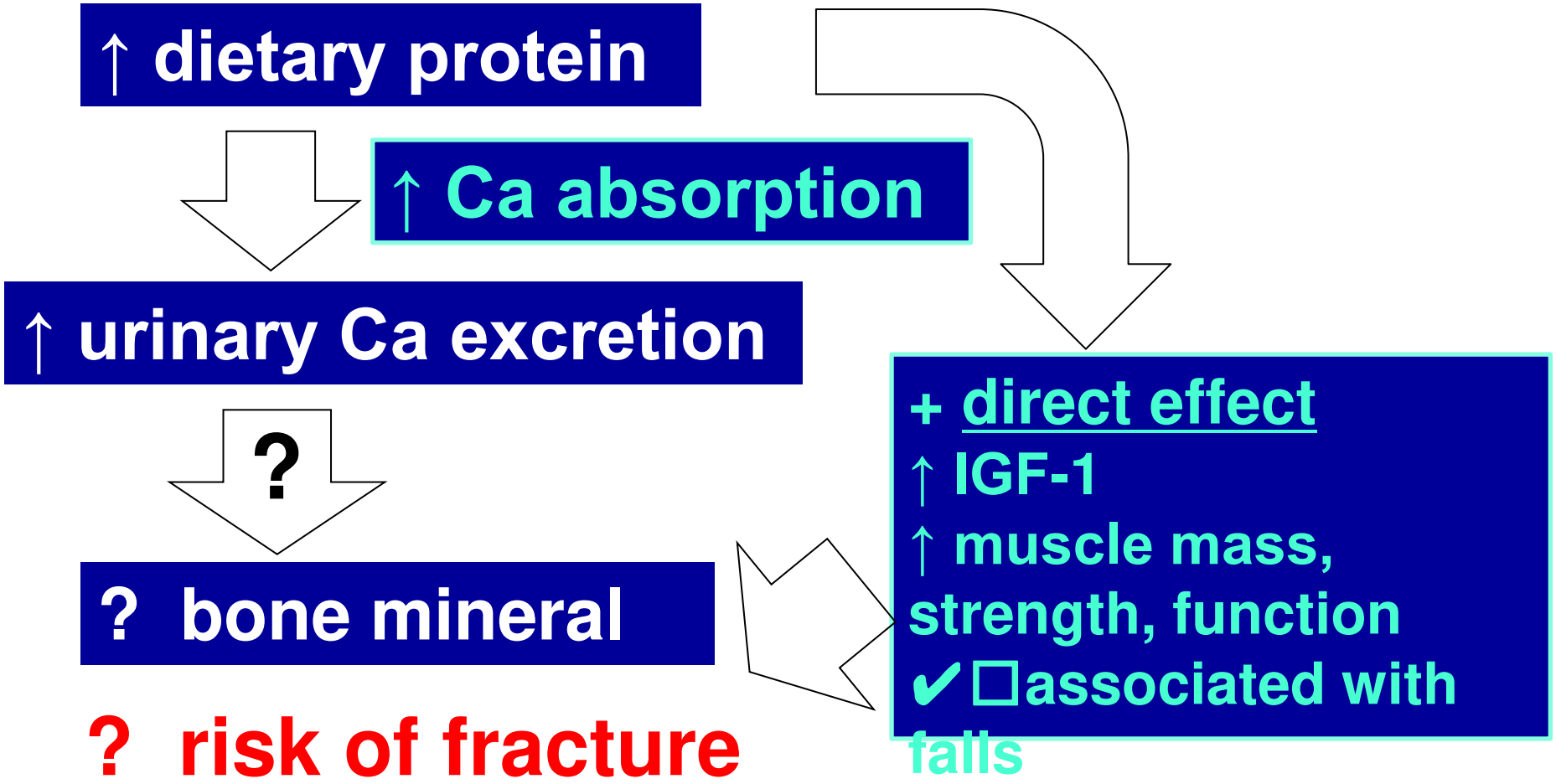
Is higher protein harmful to bone?



High *Dietary* Protein & Calcium Excretion

Healthy older men & women, ≥ 50 y, n=32
≤0.85 g protein/kg or less, <700 mg Ca

low vs. high dietary protein (meat), 0.75 vs.1.6 g/kg
9 week intervention

- ***No increase in calcium excretion or adverse effect on biochemical markers of bone turnover***
- ***Some favourable effects:***
  - ↑ ***IGF-1***
  - ↓ ***N-telopeptide***

(Dawson-Hughes et al. JCEM. 2004;89:1169)

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Journal of the American College of Nutrition **2017**

Dietary Protein Intake above the Current RDA and Bone Health: A Systematic Review and Meta-Analysis

Taylor C. Wallace & Cara L. Frankenfeld

- **Protein intakes 0.66 to 2.5 g/kg body weight/day**
- **Males, Females (16 RCTs, 13 prospective studies)**
- **No weight loss or HRT use**
- **Main outcomes: BMD, Fracture**

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CONCLUSIONS:

-no adverse effects up to 2.5 g protein/kg bw/day
-protein intakes above RDA *may* have some beneficial role in preventing hip fractures and BMD loss

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Taylor C. W...

Caution…
Limited number of studies for individual outcomes

- Prot… /day
- Male… udies)
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The American Journal of Clinical Nutrition 2017

Dietary protein and bone health: a systematic review and meta-analysis from the National Osteoporosis Foundation[1,2]

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***Two research questions*:**

- **Effect of high versus low protein intake**
- **Synergistic effect of dietary protein with Ca+Vit D**

16 RCTs, 20 prospective cohorts

- **Various outcomes: BMD, fracture, markers**
- **Different skeletal sites**

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***FINDINGS*:**

1. High vs. low intakes:

- ✓ **Positive trends for high vs. low protein intakes to benefit BMD**
  - **-spine but not total hip or body, femur neck**
- ✓ **No adverse effects on BMD**

2. Synergy with Ca, Vit D:

- **Evidence not strong, heterogeneity, study design**

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Conclusion:

"Existing data are too heterogeneous and the SOE is not enough to warrant a clinical guideline to recommend an increase in protein intake as standard care protocol"

FINDI

1

✓ **es to**

neck

✓ **adverse effects on BMD**

2. Synergy with Ca, Vit D:

- **Evidence not strong, heterogeneity, study design**

Prospective Study: Protein & Fracture *& Ca*

Framingham Offspring Cohort

- **n=1752 m, n=1972 f**
- **mean age=75 years**
- **44 hip fracture over 12 years (10 m, 34 f)**
- **Baseline ffq**

***** interaction between Ca and Protein *****

(Sahni et al. JBMR. 2010;25:2770)

Prospective Study: Protein & Fracture *& Ca*

CALCIUM MODULATES EFFECT OF PROTEIN!

Ca intakes <800 mg/d

Animal protein (median 60 vs. 34 g/day)

- **highest vs. lowest tertile of protein intake, *higher* risk of hip fracture**

(Sahni et al. JBMR. 2010;25:2770)

Prospective Study: Protein & Fracture *& Ca*

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Ca intakes <800 mg/d

Animal protein (median 60 vs. 34 g/day)

- **highest vs. lowest tertile of protein intake, *higher* risk of hip fracture**

Ca intakes >800 mg/d

Animal protein (median 76 vs. 48 g/day)

- **highest vs. lowest tertile of protein intake, *lower* risk of hip fracture**

(Sahni et al. JBMR. 2010;25:2770)

Prospective Studies: Protein & BMD *& Ca*

DIETARY CALCIUM MATTERS!

3 year RCT studying effect of supplementation:
500 mg Ca, 700 IU Vit D, (healthy m,f, age≥65 y)

Mean protein=79 g/d

9.64-15.49% 15.53-18.15% 18.16-29.14%

- ***Higher protein associated with a more favourable 3 year change in total and hip BMD in supplemented group only (met RDA for Ca)***
- ***No change in IGF-1, PTH, bone markers***

(Dawson-Hughes et al. 2002)

Protein Source & Bone Health

ANIMAL
dairy, chicken, pork, beef, fish

PLANT
legumes (soy), peas, beans, lentils, quinoa

Protein:Energy, Fiber, Fat profile, Bioactives

RESEARCH ARTICLE 2018

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Equal amounts of dietary protein from animal vs. plant sources

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Equal amounts of dietary protein from animal vs. plant sources

***Outcomes*:**

- **1 year: BMD (total body, hip, spine)**
- **6 months: bone formation or resorption markers**

7 RCTs

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Equal amounts of dietary protein from animal vs. plant sources

Outcomes:

- 1 year: BMD (total body, hip, spine)
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7 RCTs

Conclusion: No advantage of either soy or animal protein (BMD, bone markers)

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[illegible]aylor

CONSIDERATIONS:

- **Quality of evidence low**
- **Soy as supplement, not whole food**
- **Low levels of plant protein**

Future study: other plant & animal sources (legumes, beans, quinoa, pea, egg)

- **[illegible] of resorption markers**
- **7 RCTs**

<u>Conclusion</u>: No advantage of either soy or animal protein (BMD, bone markers)

Protein Source & Bone Health

ANIMAL
chicken, fish
pork, beef,

PLANT
Legumes (soy),
beans, peas,
lentils, quinoa

Protein:Energy, Fiber, Fat profile, Bioactives

Summary: Protein

- ✓ **No strong evidence for adverse effect of protein on bone health during aging**
  - **-levels beyond RDA, up to 2.5 g/kg bw/d**
- ▪ **Protein intakes proposed to support muscle during aging *may* benefit BMD**
- ✓ **Ca is a positive modifier**
- ▪ **Protein source – further study required**

Vitamin K

- Current recommendation
- Sources
- Mechanism
- Effect on bone: BMD, fractures

Adequate Intake (AI) & Sources

Men 120 µg/d, Women 90 µg/d

Adequate Intake (AI) & Sources

Men 120 µg/d, Women 90 µg/d

Naturally Occurring Forms of Vitamin K

Phylloquinone (K_1)
(primary form in diet)

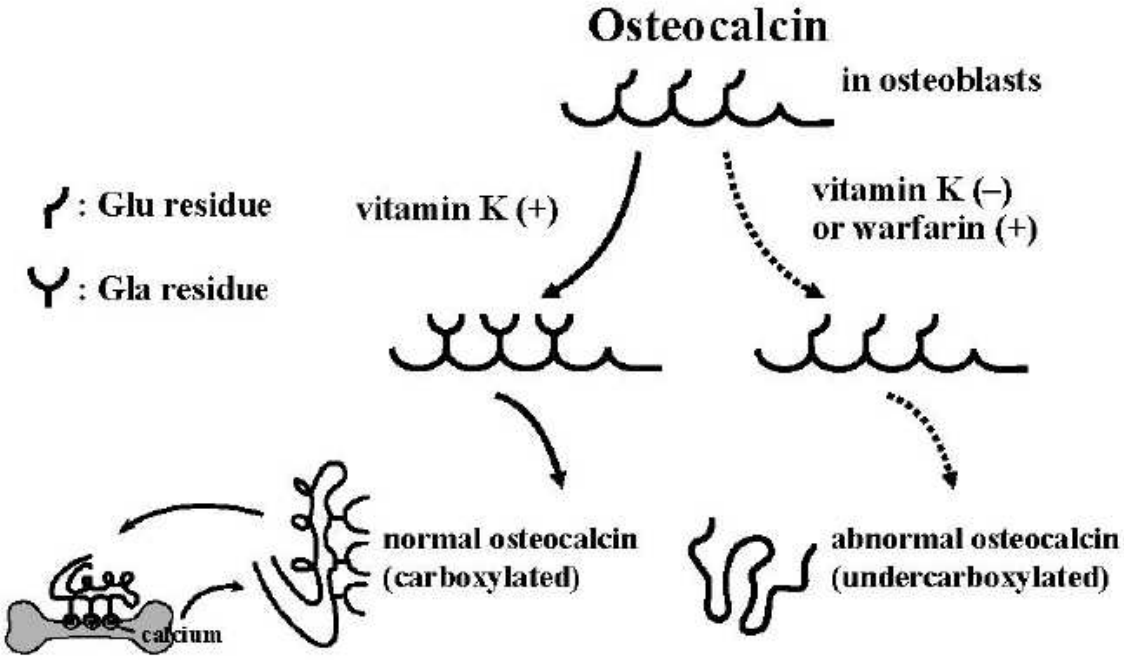
- **green leafy vegetables**
- carrots, kiwi, tomatoes
- soybean & olive oil

Menaquinone (K_2)

- fish oils, meats,
- fermented foods
- synthesized by intestinal bacteria

- **Menatetrenone (synthetic)**

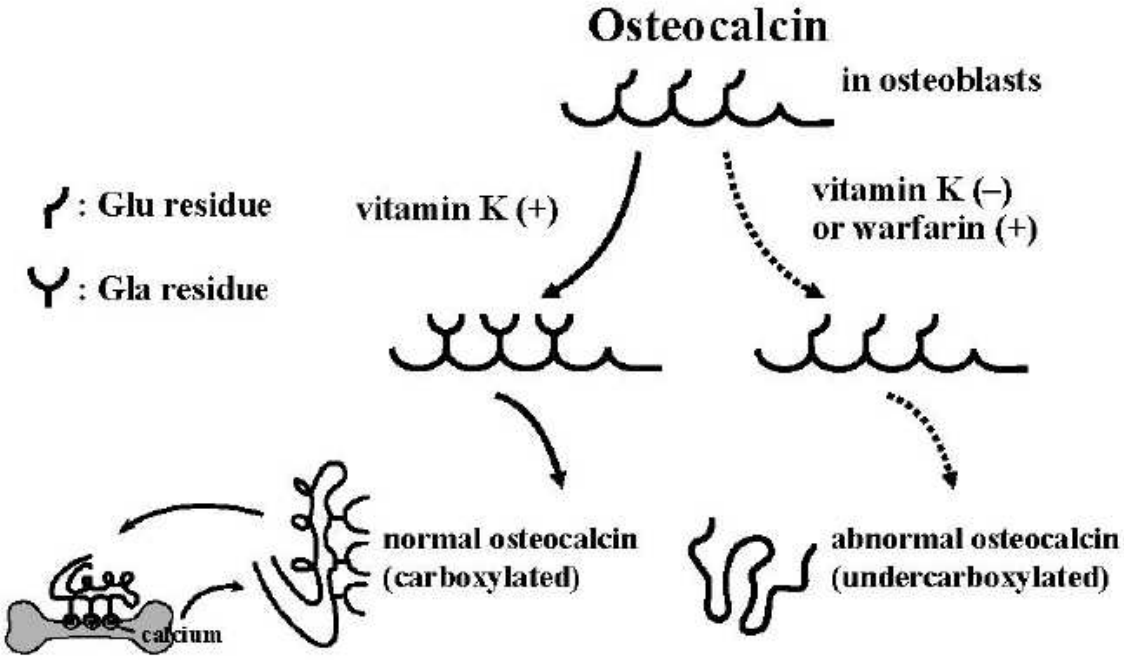
Mechanism: Vit K & Bone



- Vit K required cofactor for gamma carboxylation of three glutamic acid residues on osteocalcin, a bone matrix protein.
- Osteocalcin binds hydroxyapatite (mineralization)
- "carboxylation" status of osteocalcin: used experimentally as a marker of bone health.

Iwamoto J. Vitamin K_2 therapy for postmenopausal osteoporosis. Nutrients. 2014;6:1971-1980.

Mechanism: Vit K & Bone



Supplementation with K_1 or K_2

↓ undercarboxylated osteocalcin

Undercarboxylated osteocalcin as a marker of poor bone status?

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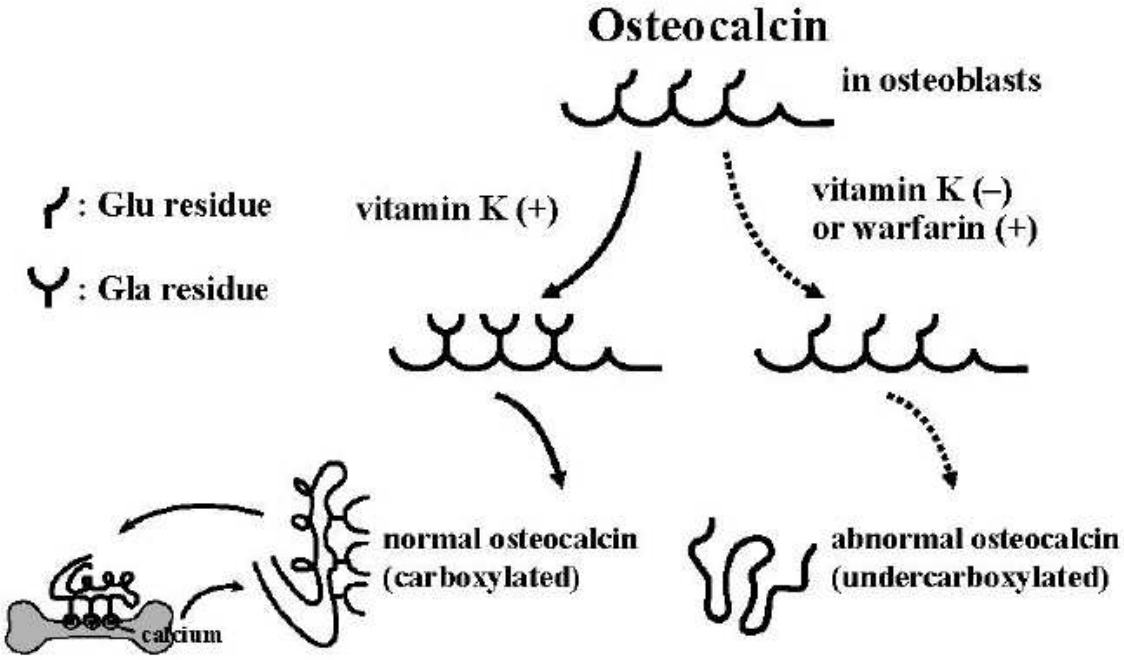
Mechanism: Vit K & Bone



Supplementation with K_1 or K_2

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Undercarboxylated osteocalcin as a marker of poor bone status?

No clear relationship of Vit K supplementation with BMD, fracture

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Findings

Vitamin K_1

- 440 PM women, osteopenia
- 2 years: 5 mg or placebo
- Primary outcomes:
  no benefit to BMD at hip, spine
- ↑ serum vit K
- ↓ undercarboxylated OC
- fewer clinical fractures but
  not powered for this outcome
- *agreement with other studies at lower doses*
  -some studies in women without osteoporosis

(Cheung et al. 2008 PLoS Med)

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Vitamin K_2 (synthetic)

- Menatetronone: RCTs with small sample sizes (mostly Japan)
- ↓ undercarboxylated osteocalcin
- mixed findings:
  -may depend on bone health
- heterogeneity of studies is challenging
  -Ca, vit D, meds
  -health status

(Guralp & Erel. 2014 Maturitas; Huang et al. 2015 Osteoporos Int; Binkley et al. 2009 JBMR)

Protein & Vitamin K:
"Other" Nutrients for Bone Health

Thank you for watching.

wward@brocku.ca

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