Dietary protein and bone health: an update on clinical research

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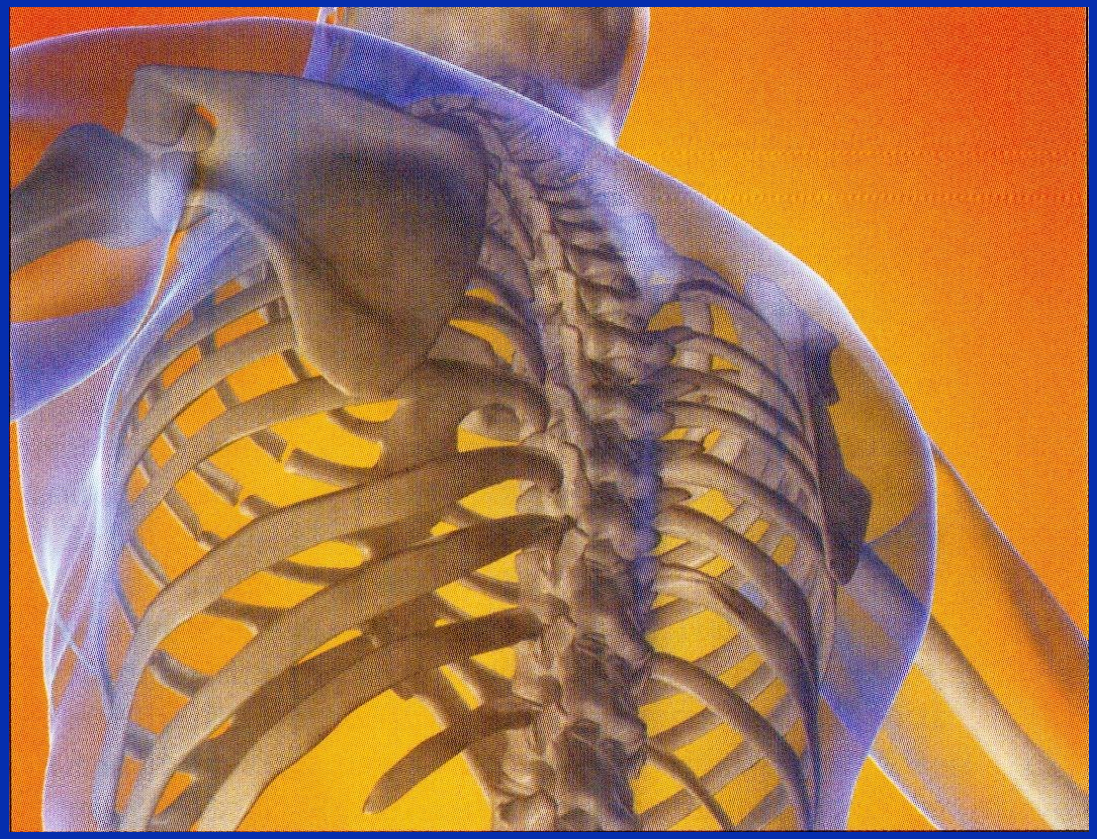
Our Skeleton

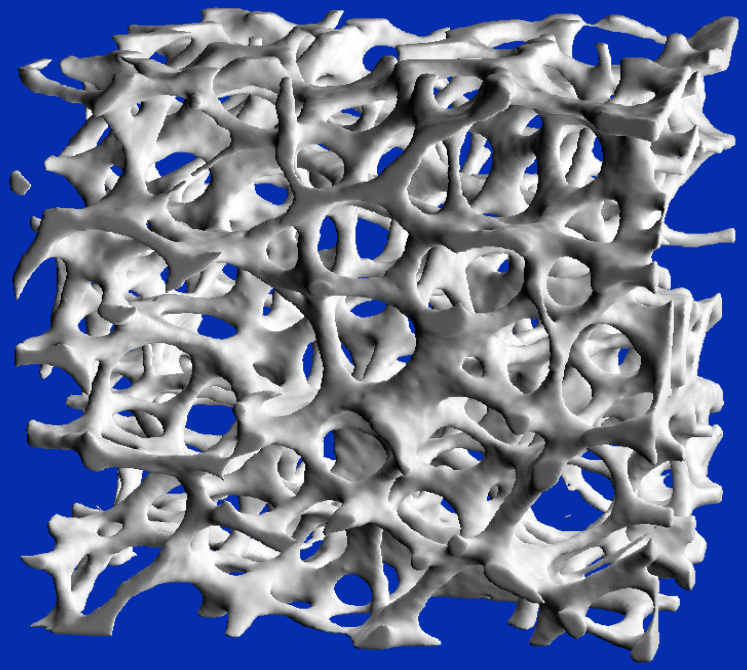


Functions:

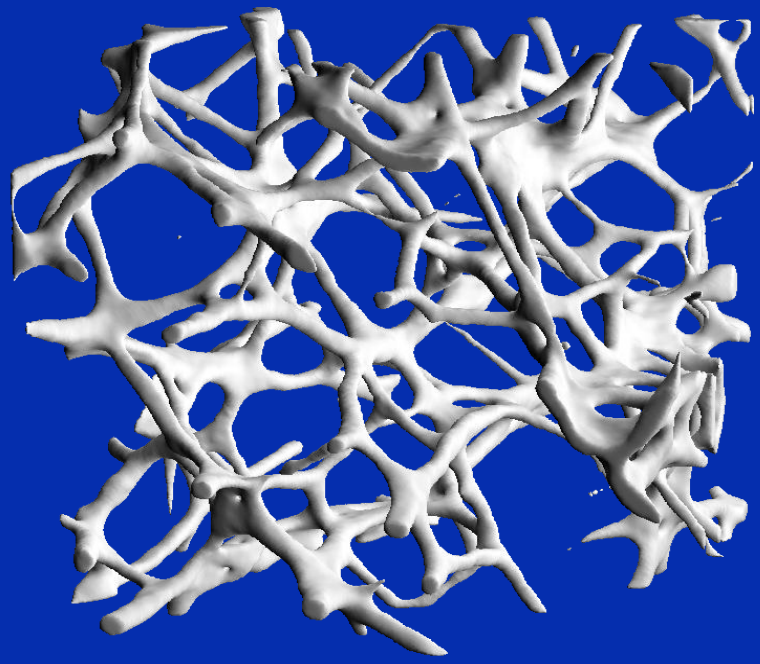
- Support
- Protection
- Mobility
- Reservoir for essential minerals such as calcium & phosphorus

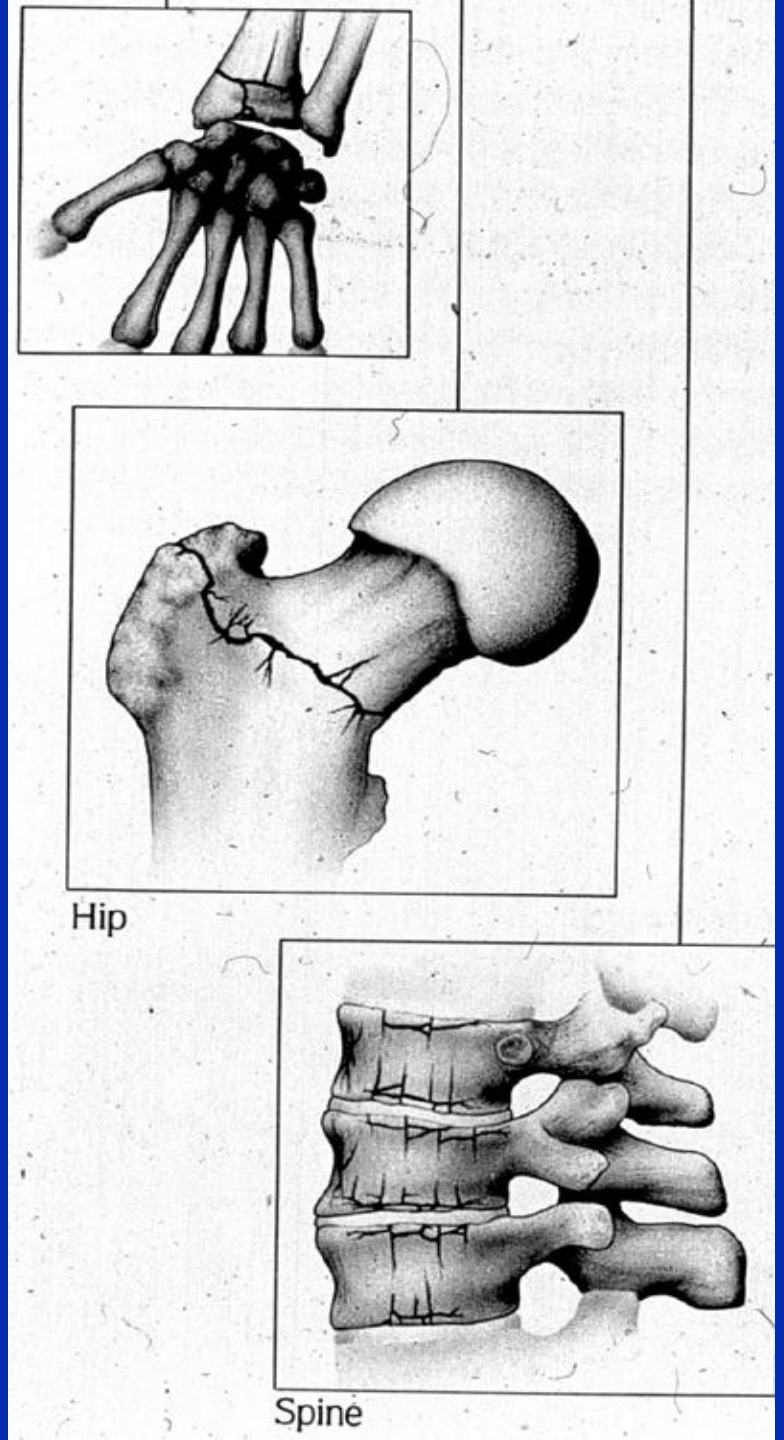
Osteoporosis is a disease of low bone mass and structural deterioration, leading to bone fragility and an increased susceptibility to fractures.

Young normal



Elderly



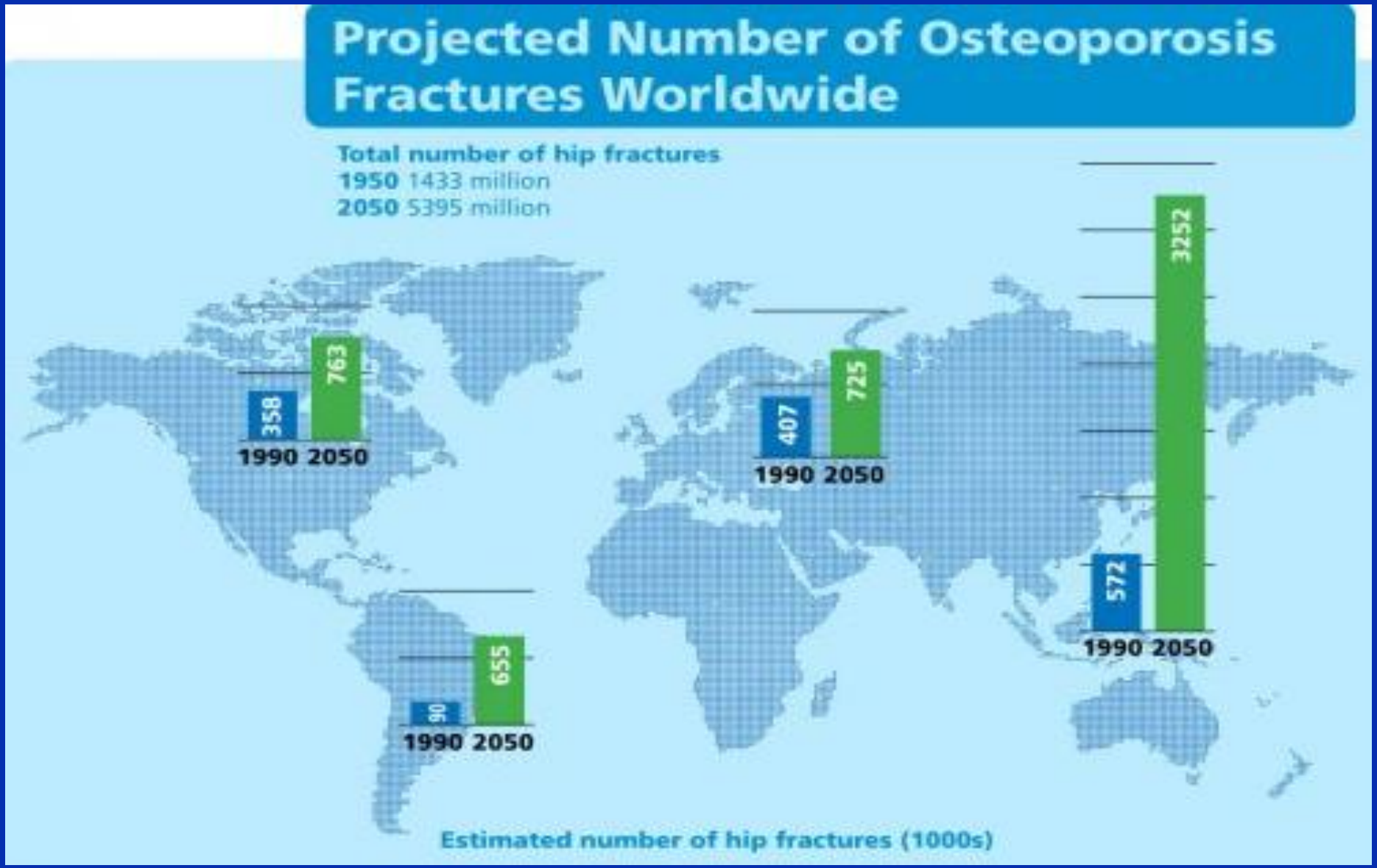


Osteoporosis is a Global problem

According to the WHO: Osteoporosis is second to cardiovascular disease as a global health care problem

50 yo woman has a similar lifetime risk of dying from a hip fracture as from breast cancer

By 2050, the worldwide incidence of hip fracture is projected to increase by 240% in women and 310% in men.



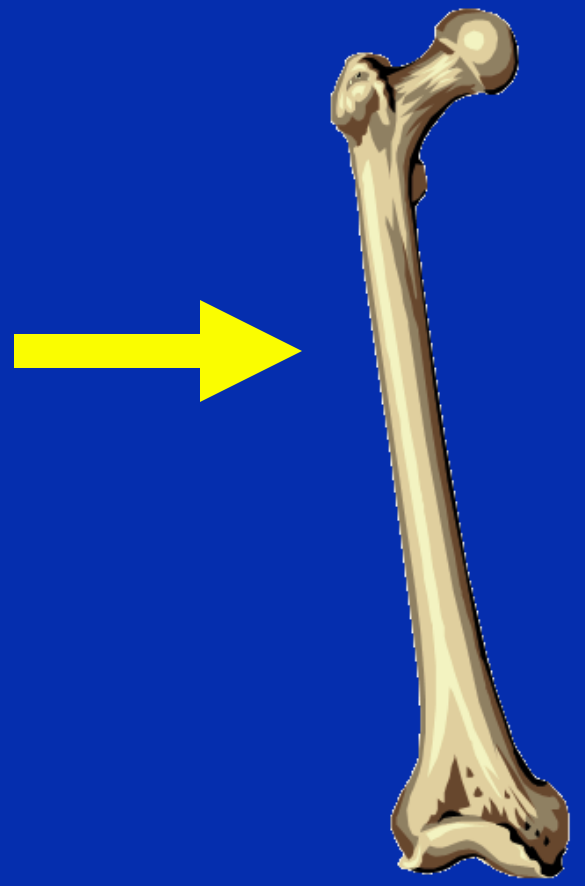
Risk factors for osteoporosis

- Sex
- Age
- Race
- Disease/Medications
- Lifestyle factors
- **DIET**

Nutrition and Bone Health

Calcium, Vitamin D,

Energy, Protein, Carbohydrates,
Amino Acids, Fatty Acids,
Vitamins A, Folate, Vitamin B_6,
Vitamin B_{12}, Vitamin C, Vitamin K
Phosphorus, Copper, Magnesium,
Zinc, Boron, Fluoride, Iron,
Sodium, Alcohol, Homocysteine,
Caffeine, Acid-Alkaline Ash,
Phytoestrogens, Soy, Herbals-
Botanicals, Fiber, Oxalates



These nutrients do not work independently

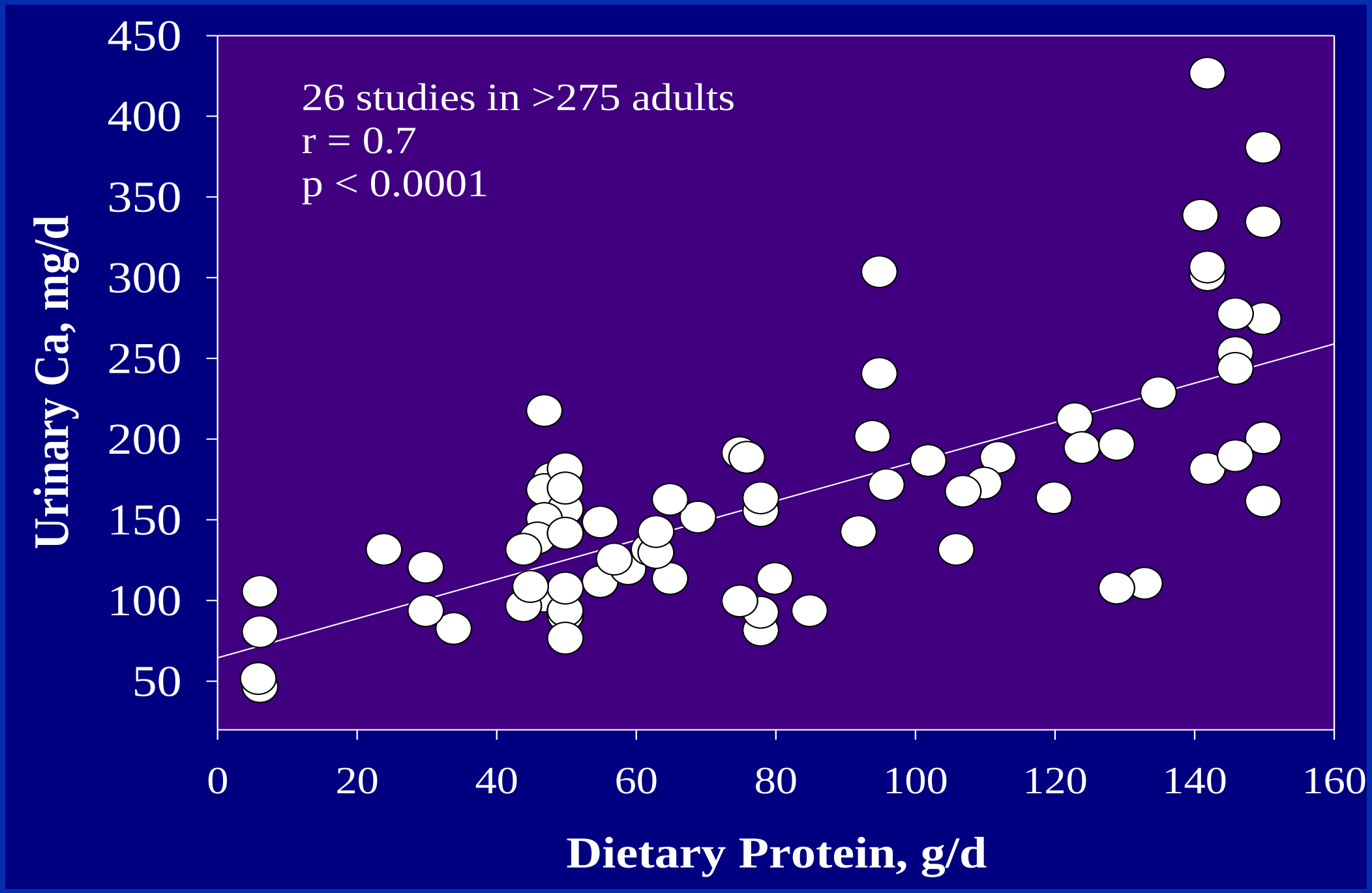
Dietary Protein

↓

Interaction with other nutrients

↓

Bone Health


26 studies in >275 adults
r = 0.7
p < 0.0001
Urinary Ca, mg/d
450
400
350
300
250
200
150
100
50
0
20
40
60
80
100
120
140
160
Dietary Protein, g/d

What is the source of the extra urinary Ca?

Traditional hypothesis

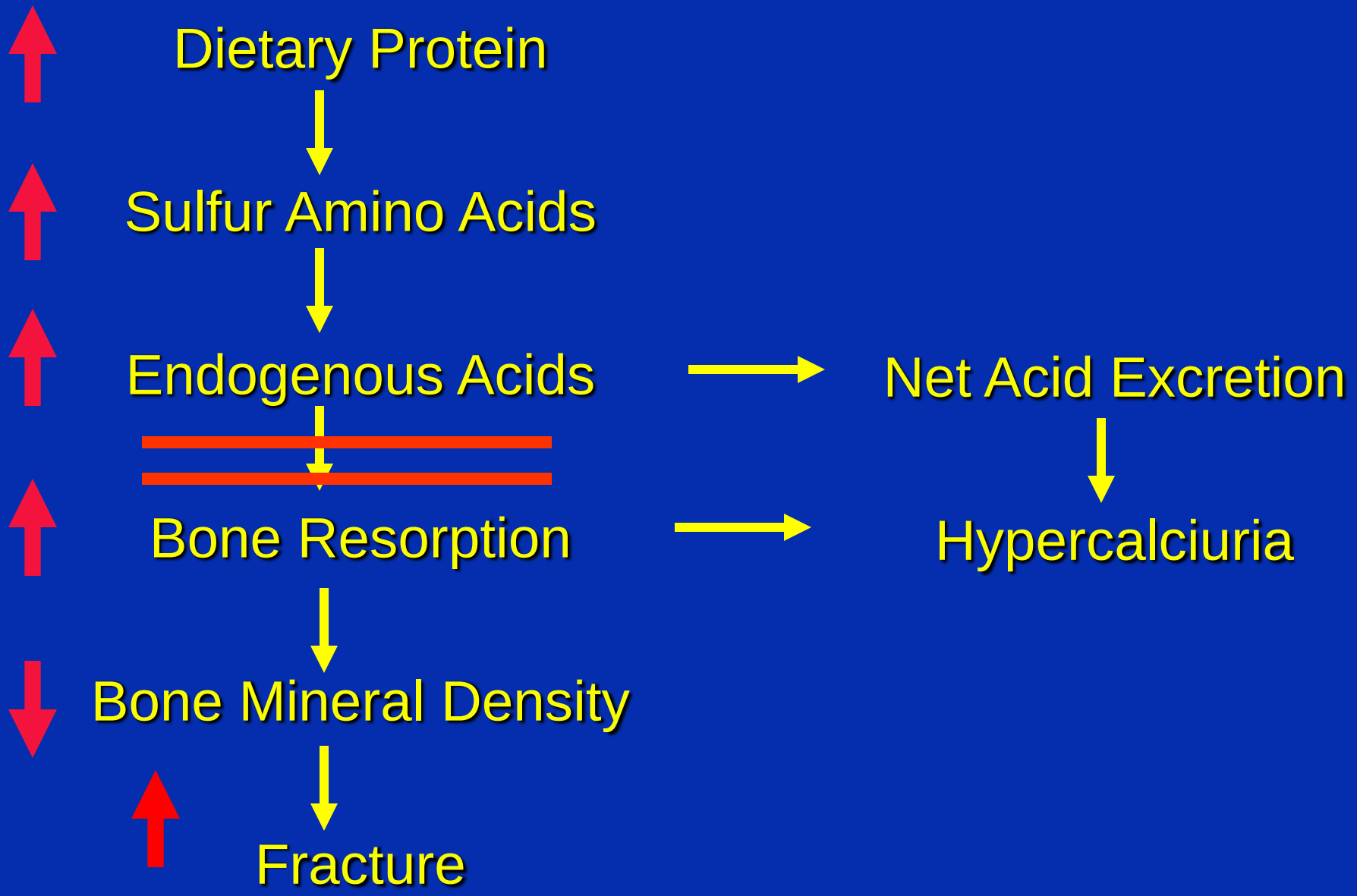
1. Increased bone resorption?

Recent hypotheses

2. Increased calcium absorption?

3. A combination of the two?

The Acid-base (traditional) hypothesis



The acid-base hypothesis is not supported by population level data

- Endogenous acid load, estimated by dietary intake, is not linked with bone mineral density among older adults
  - National Health and Nutrition Examination Survey 2005-2008 (Mangano, 2014)
  - Framingham Osteoporosis Study (McLean, 2011)

What happens biologically with increased protein?

~ 1 Week Diet Controlled Intervention Trials

(at 800 mg Ca + no vit D supplementation)

Low Protein Diets < 0.8 g/kg	Medium Protein Diets 0.8 – 1.2 g/kg	High Protein Diets > 1.2 g/kg
Decrease Intestinal Ca Absorption Rise in Parathyroid Hormone (PTH) Decreased Urinary Ca	**Nothing bad ever happens**	Increased Intestinal Ca Absorption Suppressed PTH Increased Urinary Ca

While calcium absorption is interesting, it is bone that really matters!

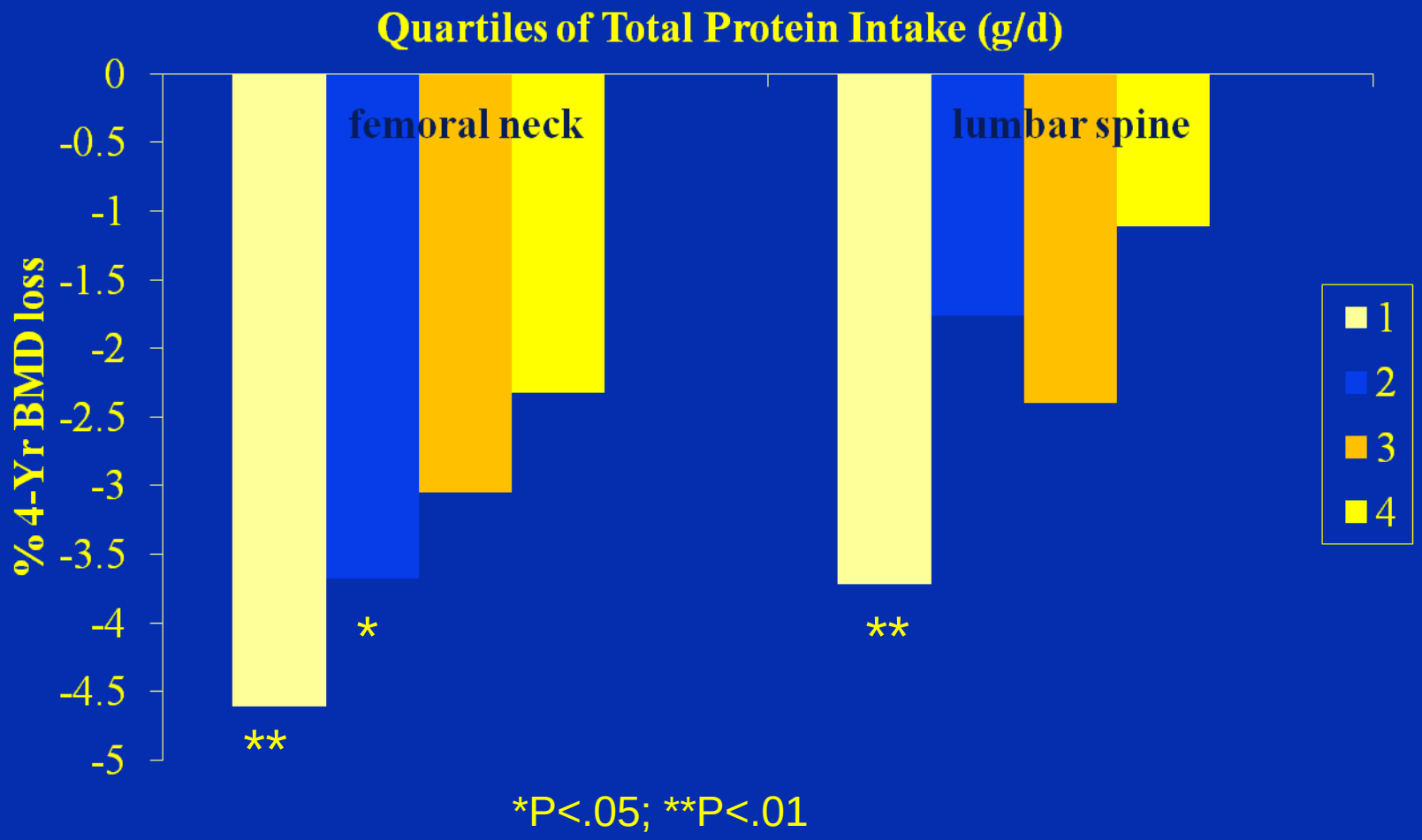
JOURNAL OF BONE AND MINERAL RESEARCH
Volume 15, Number 12, 2000

Effect of Dietary Protein on Bone Loss in Elderly Men and Women: The Framingham Osteoporosis Study*

MARIAN T. HANNAN,[1,2] KATHERINE L. TUCKER,[3] BESS DAWSON-HUGHES,[3]
L. ADRIENNE CUPPLES,[2] DAVID T. FELSON,[2,4] and DOUGLAS P. KIEL[1]

Research question: is dietary protein associated with bone loss over time in older adults?

Adjusted 4-year Bone Loss (%) by Quartiles of Total Protein Intake



*P<.05; **P<.01

Hannan, MT J Bone Minr Res 2001; 15:2504-2512

Protein & bone: the evidence

Study	Study Sample	Exposure	Outcome
Kerstetter et al. 2000 NHANES III	–n=1822 –women –Age≥50 y	Total protein intake	↑ BMD
Munger et al. 1999 Iowa Women's Health Study	–n=41,837 –women –Age=55-69 y	Total protein intake Animal protein intake	↓ Hip fracture
Dawson-Hughes et al. 2002 Randomized controlled trial	–n=342 –men & women –Age≥ 65 y	Total protein intake in calcium supplemented group	↑ BMD

ORIGINAL ARTICLE

JBMR

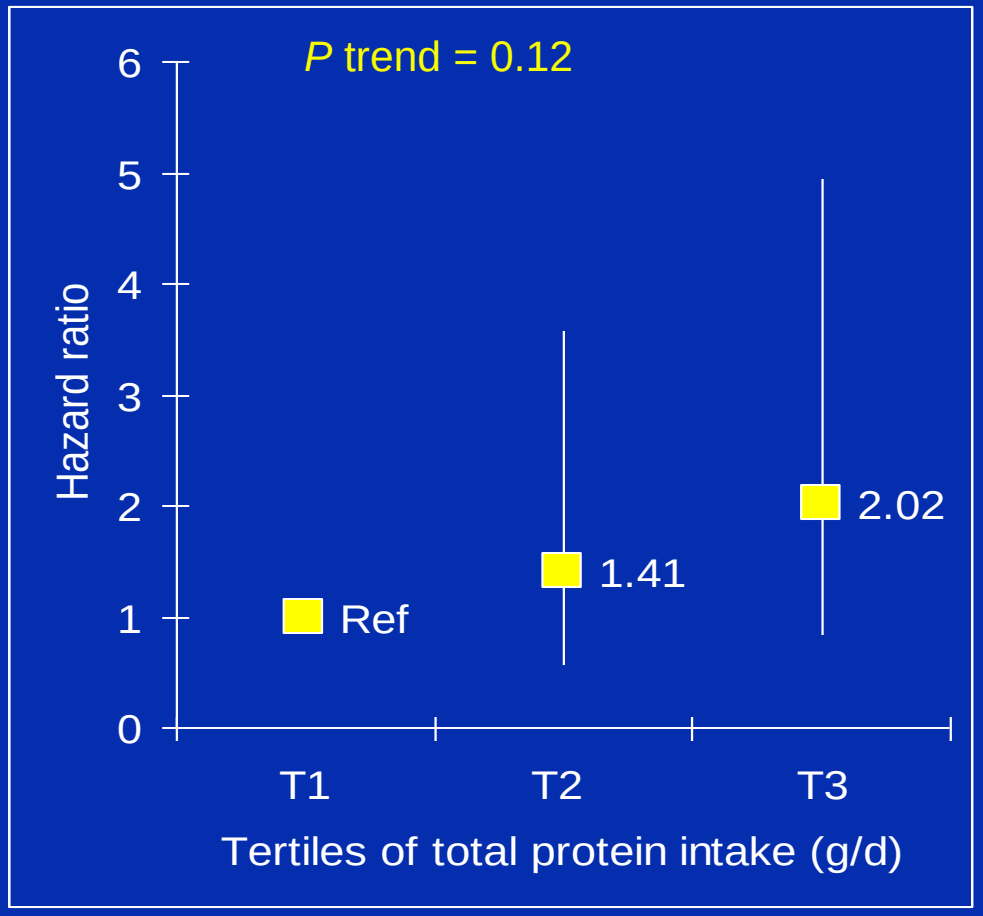
Protective Effect of High Protein and Calcium Intake on the Risk of Hip Fracture in the Framingham Offspring Cohort

Shivani Sahni,[1] L Adrienne Cupples,[2] Robert R Mclean,[1] Katherine L Tucker,[3] Kerry E Broe,[1] Douglas P Kiel,[1] and Marian T Hannan[1]

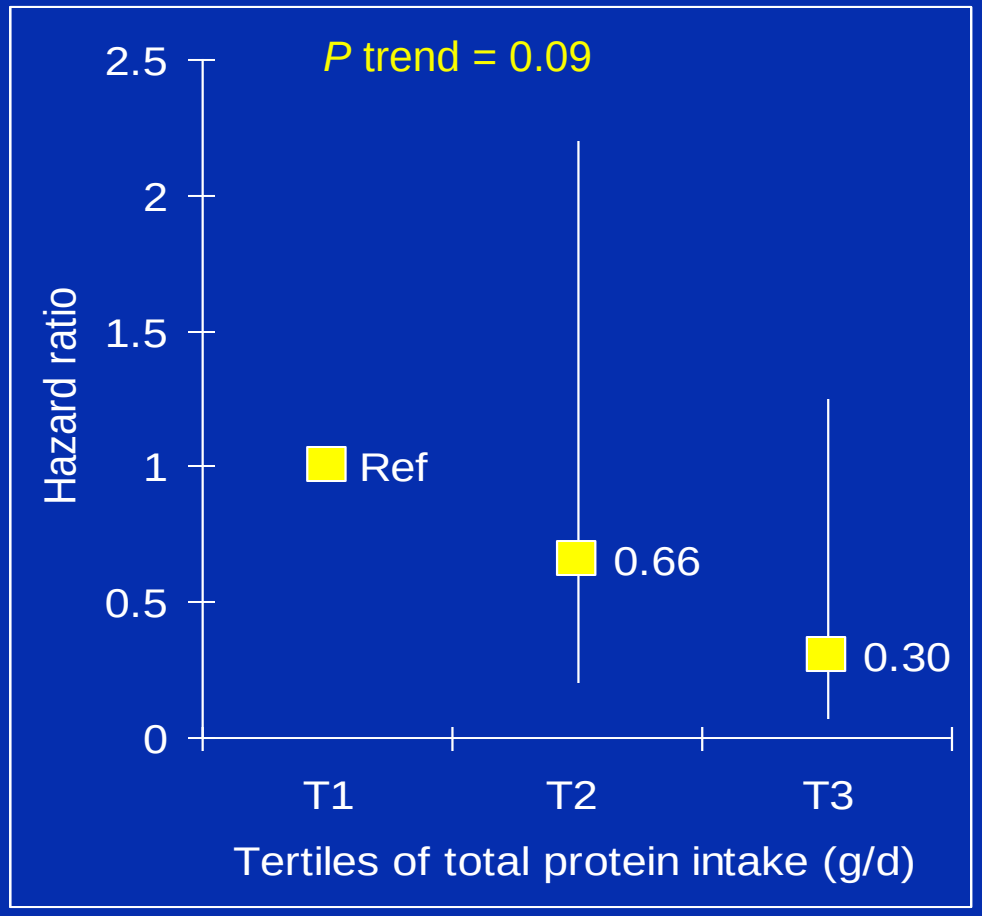
Research question: does calcium intake modify the association between dietary protein and bone health in adults?

Total Protein Intake & Risk of Hip Fracture

Total Calcium <800mg/d



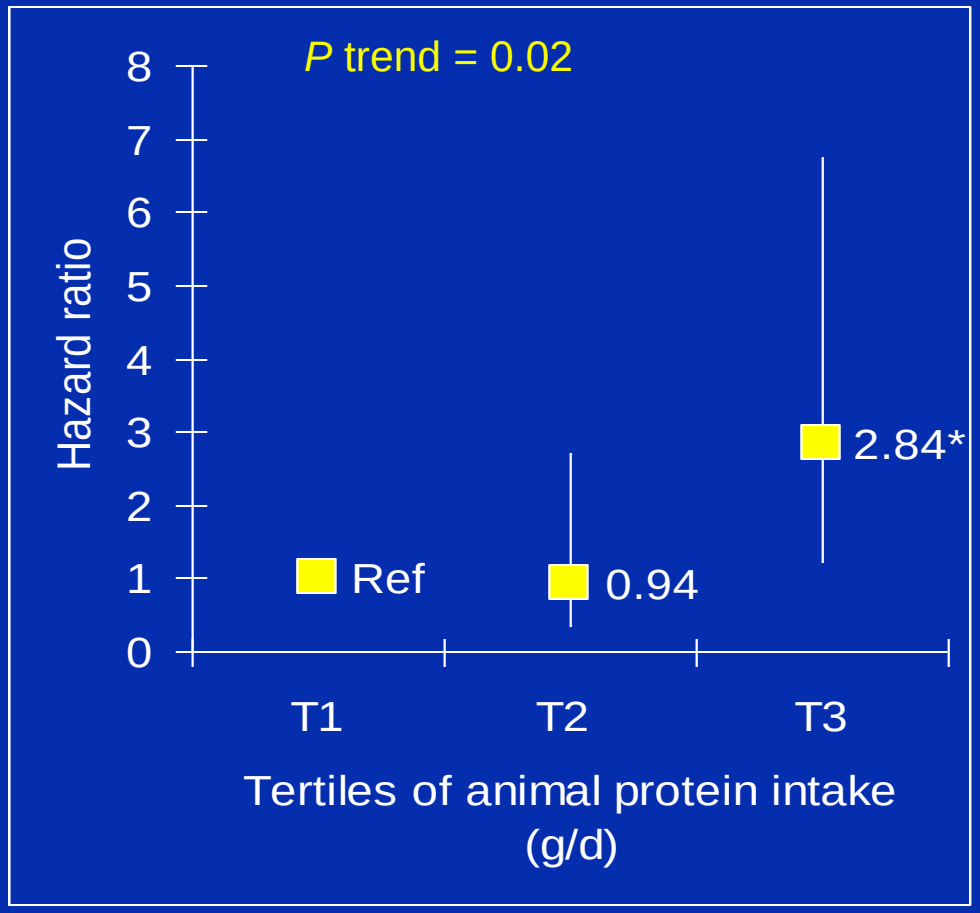
Total Calcium ≥ 800mg/d



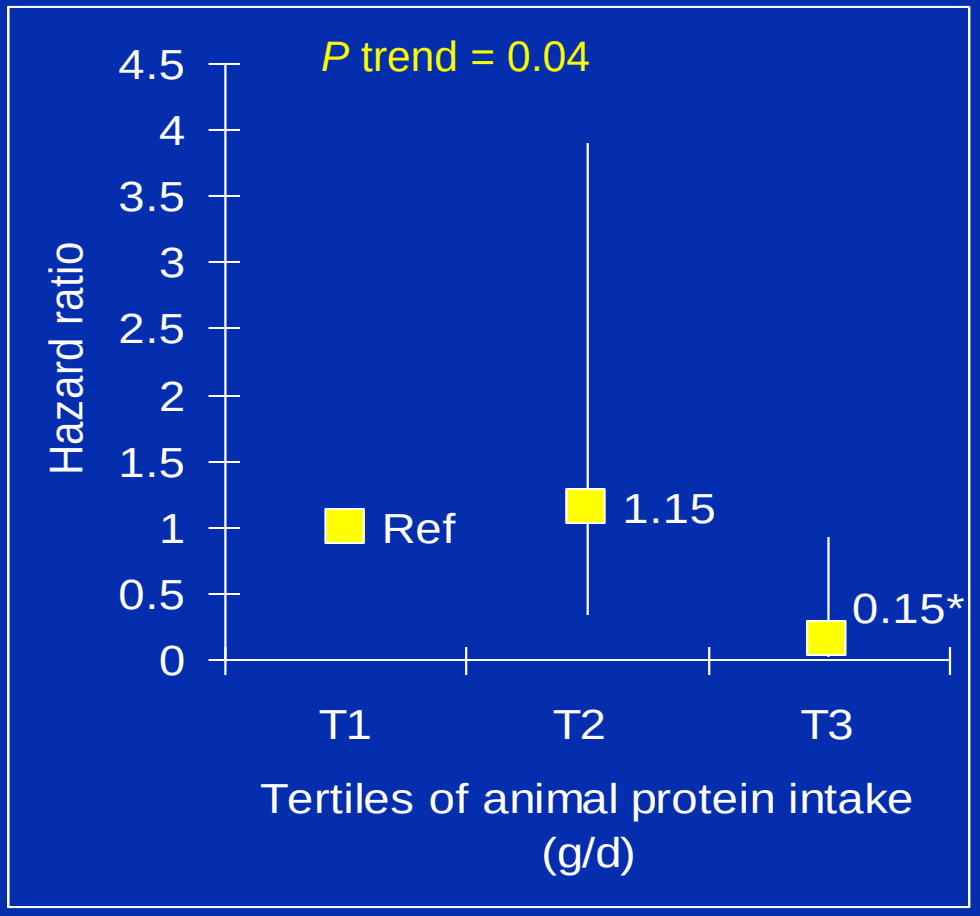
Sahni, 2010

Animal Protein Intake & Risk of Hip Fracture

Total Calcium <800mg/d

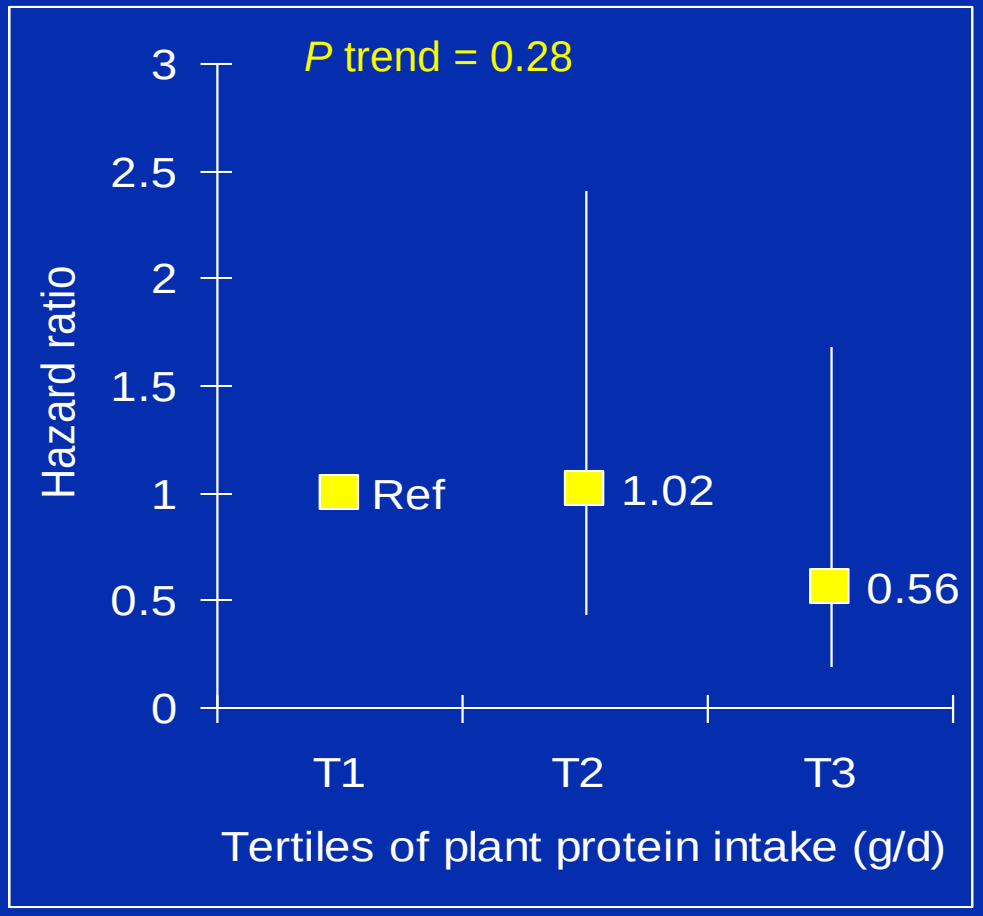


Total Calcium ≥ 800mg/d

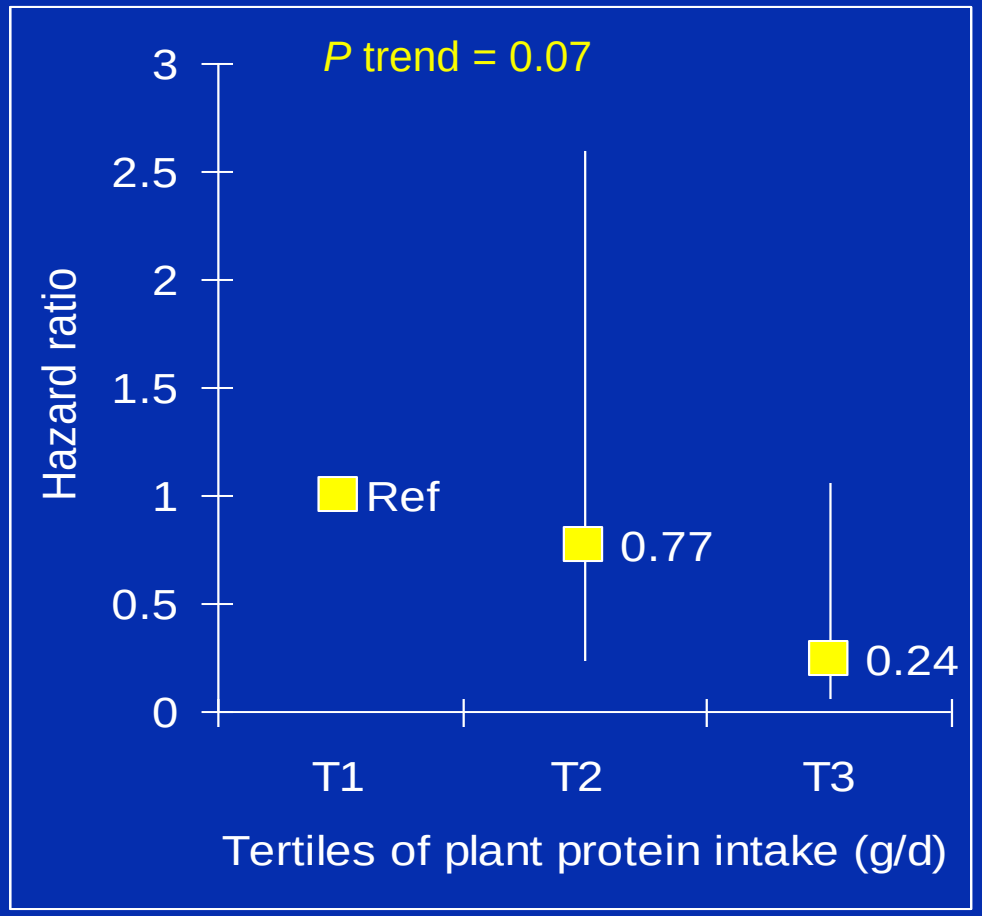


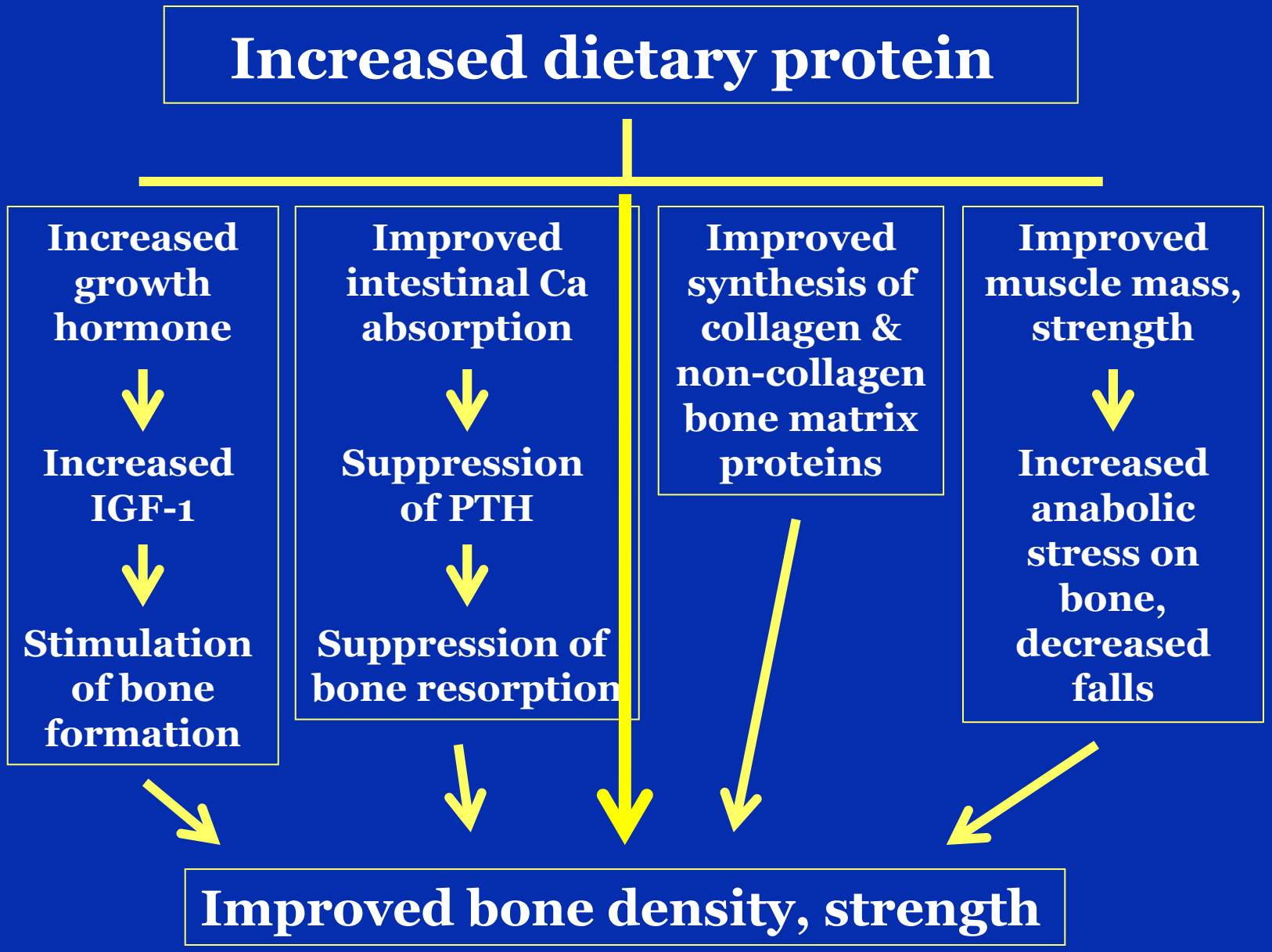
Plant Protein Intake & Risk of Hip Fracture

Total Calcium <800mg/d



Total Calcium ≥ 800mg/d




Increased dietary protein
Increased growth hormone
Increased IGF-1
Stimulation of bone formation
Improved intestinal Ca absorption
Suppression of PTH
Suppression of bone resorption
Improved synthesis of collagen & non-collagen bone matrix proteins
Improved muscle mass, strength
Increased anabolic stress on bone, decreased falls
Improved bone density, strength

What do we know so far?

Greater dietary protein is associated with greater BMD and less bone loss over time in adults

This is may be due to increased calcium absorption, circulating levels of IGF-1 and suppression of PTH

There appears to be an interaction with calcium intake, possibly due to dietary protein's ability to increase calcium absorption

Population level studies are important, but what happens to bone when we supplement protein intake?

ORIGINAL ARTICLE

JBMR

Areal and Volumetric Bone Mineral Density and Geometry at Two Levels of Protein Intake During Caloric Restriction: A Randomized, Controlled Trial

Deeptha Sukumar,[1] Hasina Ambia-Sobhan,[1] Robert Zurfluh,[1] Yvette Schlussel,[1] Theodore J Stahl,[2] Chris L Gordon,[3] and Sue A Shapses[1]

Journal of Bone and Mineral Research, Vol. 26, No. 6, June 2011, pp 1339–1348

Research Problem: Weight loss causes bone loss

Research Question: Under weight loss conditions, can we prevent bone loss simply by adding more protein to the diet?

Approach

60 women (age: 58y) enrolled in a lifestyle behavior modification weight loss program for 1 year.

Randomized to a diet of:

High Protein (HP) 30% of total calories

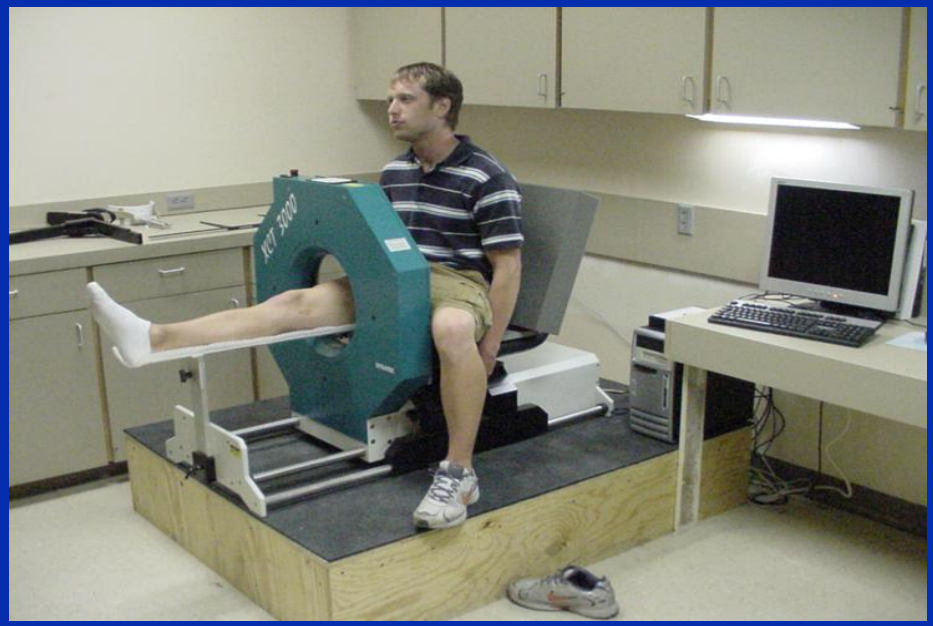
Normal Protein (NP) 18% of total calories

Bone measures:

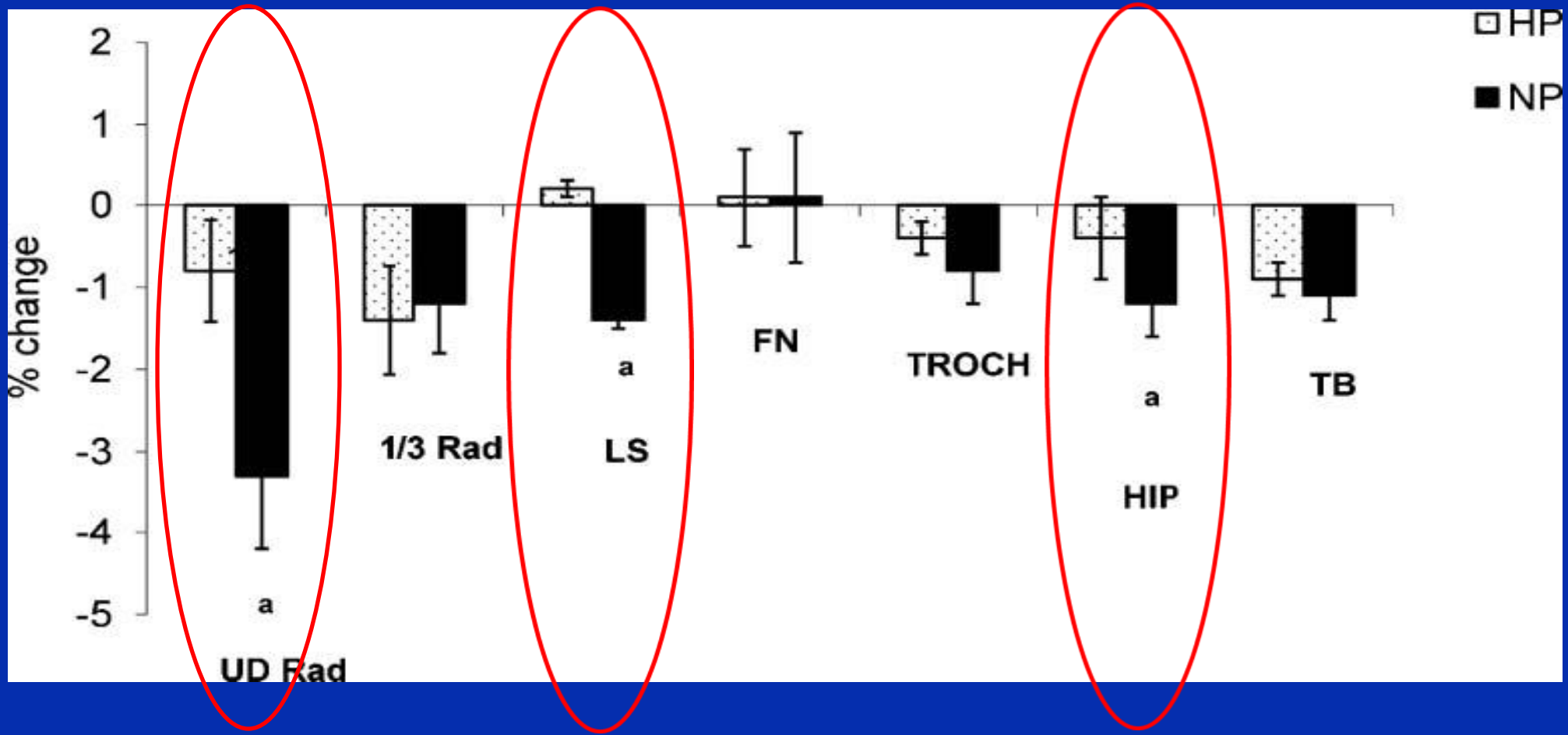
Peripheral quantitative computed tomography (pQCT).

Measures volumetric BMD, bone geometry, bone mineral content and bone strength indices.

Generates a 3-D image of the object from a large series of 3- D X-ray images.



The HP lost less BMD at these 3 sites



In Summary:

Both groups lost equivalent weight (6-7%)

However, more protein in the diet . . .

Stimulated IGF 1 (anabolic for bone)

Attenuated trabecular bone loss (density, content) at the distal tibia (as measured with pQCT) and at the ultradistal radius, hip and spine (as measured with standard DXA)

These observations occurred despite

- relatively high dietary calcium intakes (1200 mg/d)
- relatively small difference in dietary protein intake (18 vs. 24% kcal)

CLINICAL TRIALS

JBMR

The Effects of a Two-Year Randomized, Controlled Trial of Whey Protein Supplementation on Bone Structure, IGF-1, and Urinary Calcium Excretion in Older Postmenopausal Women

Kun Zhu,[1,2] Xingqiong Meng,[3] Deborah A Kerr,[3] Amanda Devine,[4] Vicky Solah,[3] Colin W Binns,[3] and Richard L Prince[1,2]

Journal of Bone and Mineral Research, Vol. 26, No. 9, September 2011, pp 2298-2306

Research problem: can we see similar results in older adults during weight maintenance; longer duration study

Research Question: Can protein supplementation alter bone density and strength over 2y?

Approach

219 women (70-80y) enrolled for 2 years.

Randomized to:

Table 1. Nutritional Composition of the Test Drink (per 250 mL)

	Protein drink	Placebo drink
Energy (kJ)	809.5	819.5
Protein (g)	30.1	2.1
Fat (g)	2.3	2.0
Cholesterol (mg)	8.6	8.6
Carbohydrate (g)	13.2	42.3
Calcium (mg)	602.7	600.1
Sodium (mg)	47.9	33.0

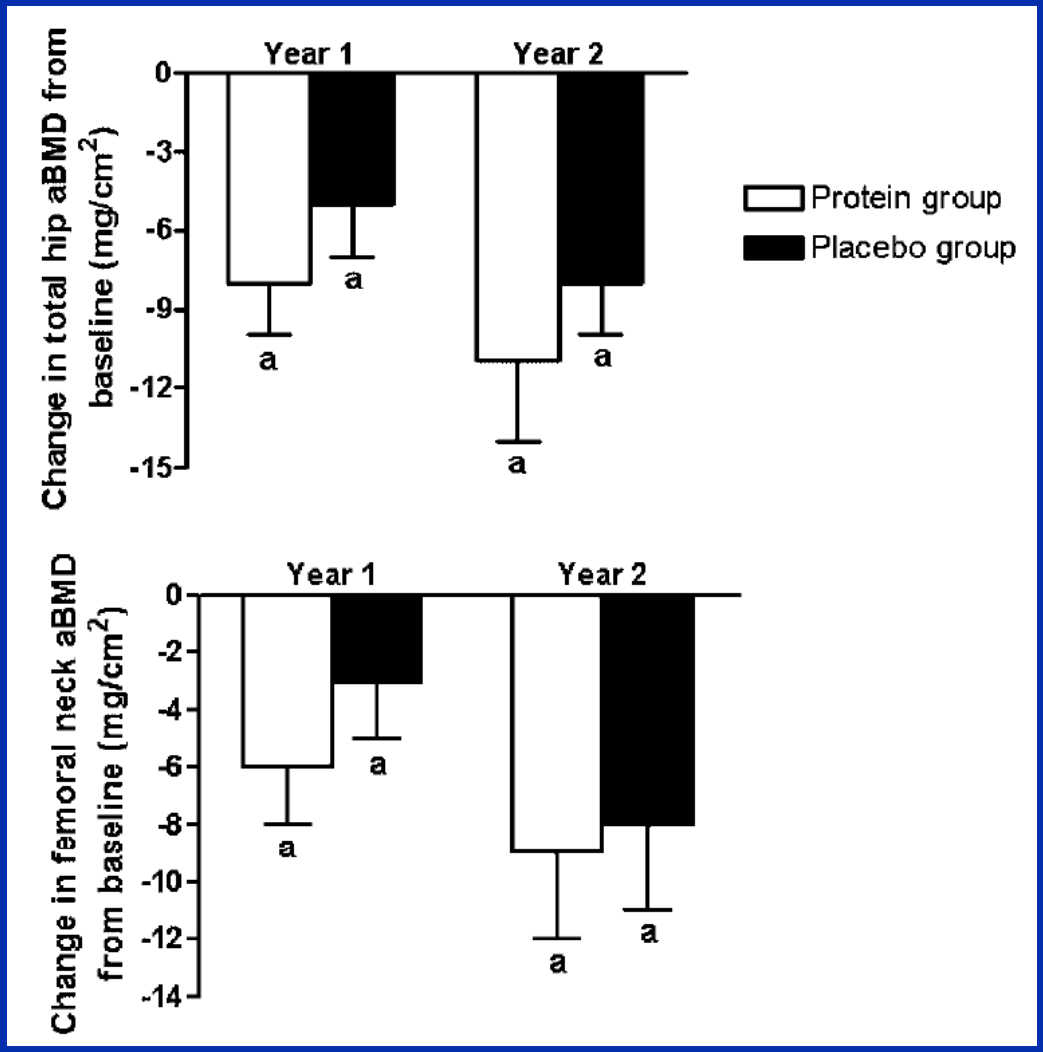
Bone measures:

Total hip BMD by dual-energy X-ray absorptiometry

QCT of the hip as a secondary outcome

Serum IGF-1

No effect of protein supplementation on bone density or strength



- No significant differences in hip BMD between protein and placebo groups
- No detectable changes in QCT measures of the femoral neck

Why do the outcomes of these intervention trials differ?

- Different population groups
  - average age 58y during weight loss, vs. 74y protein replete older women
- Similar increase in protein intake, but differing protein sources
- Does source protein food source matter? What about other components of the diet?

Protein food source probably matters

- Protein-rich foods differ:
  - amino acid composition
  - digestibility
  - synergy with other nutrients

- Higher animal:plant protein ratios associated with 62% lower risk of fracture (Martinez-Ramirez, 2012)
- High animal protein intake associated with greater BMD (Promislow, 2002) and decreased risk of fracture (Munger, 1999; Sahni 2010) where plant protein was not

Dairy Foods and Bone

Dairy foods:

- complex source of protein, calcium, phosphorus, vitamin D, magnesium
- the most dense source of these bone beneficial nutrients per calorie

Dairy Foods & Bone Health

- Dairy foods are positively related to bone mineral density
- The association with fracture is less clear
  - Meta-analysis, 9 prospective cohort studies concluded none in women, more research needed in men *(Bischoff-Ferrari, 2011)*
- Not all dairy foods are equally beneficial for bone
  - Milk, fluid dairy (milk + yogurt) and total dairy (milk + yogurt + cheese) were positively associated with hip BMD (*Sahni, 2013*)
  - 40% lower risk of hip fracture among individuals with milk intake >1serv/wk; similar results for milk+yogurt, but not with other dairy *(Sahni, in press)*

Effect of dairy intake on bone mineral density is only beneficial with higher vitamin D intake

The Framingham Original Cohort

(The FASEB Journal. 2013;27:106.5)

Shivani Sahni, Katherine L. Tucker, Douglas P. Kiel,
Lien Quach, Virginia A. Casey, Marian T. Hannan

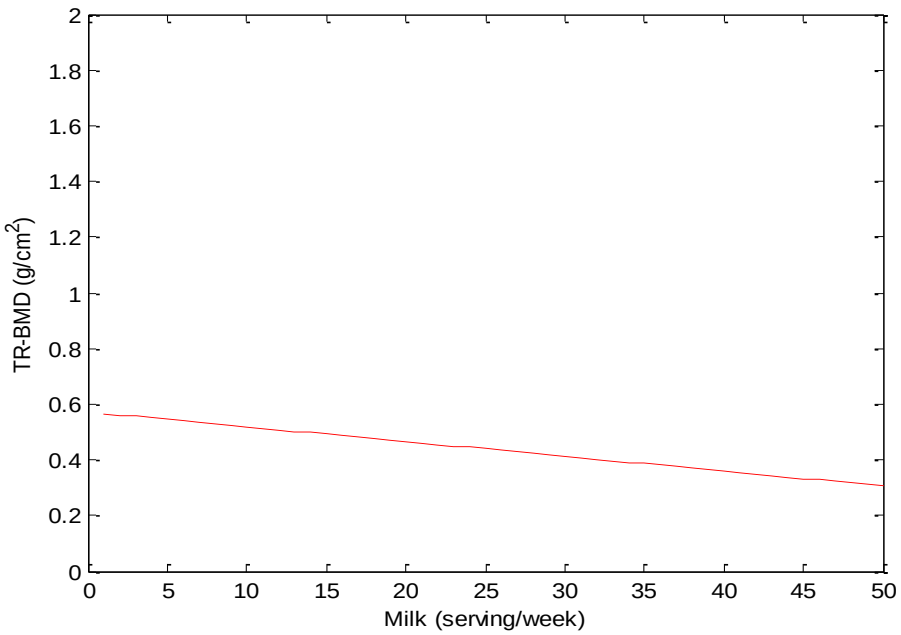
Institute for Aging Research
Hebrew SeniorLife
Harvard Medical School
Northeastern University

Boston, MA, USA

Milk Intake & 4-y % △TR-BMD

Low Vit. D intake <474 IU/d:

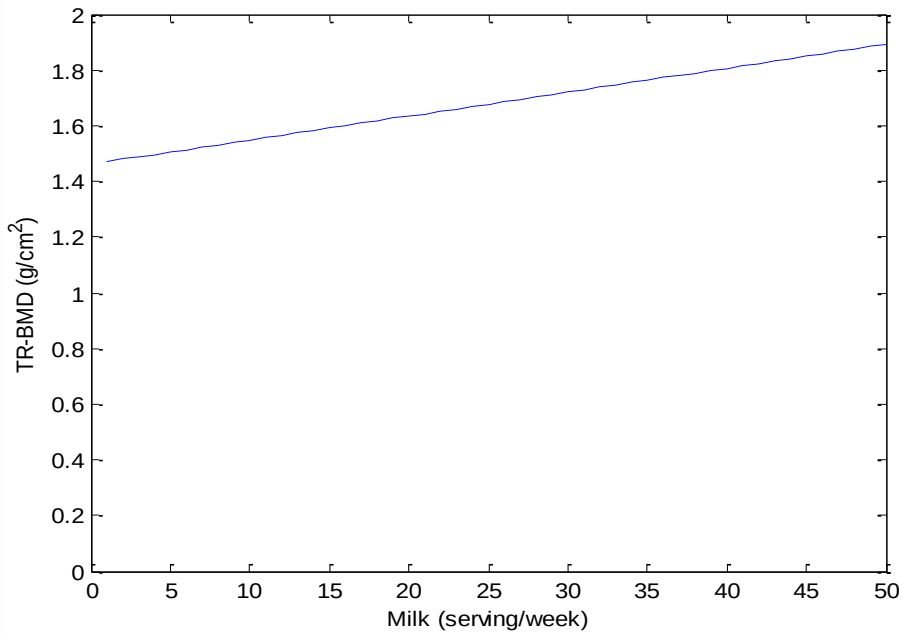
β= -0.0053 ± 0.004, *P*=0.14



n=449

High Vit. D intake ≥474 IU/d:

β= 0.0086 ± 0.003, *P*=0.02

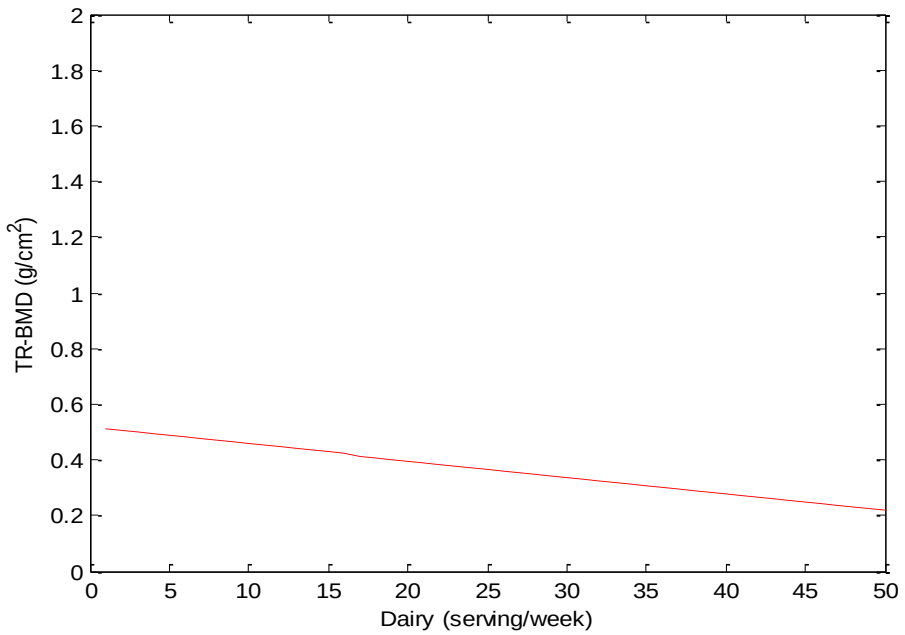


n=148

Total Dairy Intake & 4-y % △TR-BMD

Low Vit. D intake <474 IU/d:

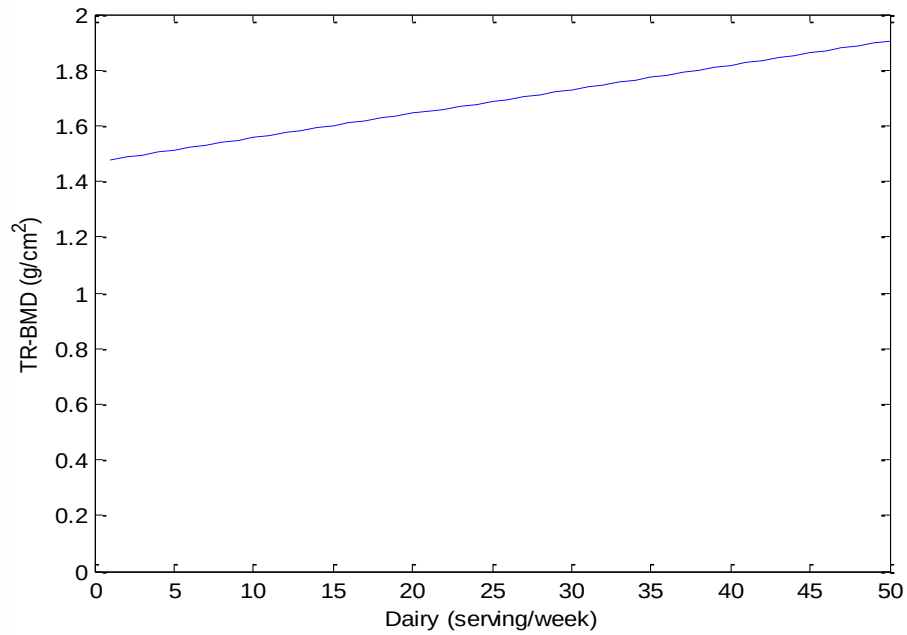
β= -0.0060 ± 0.003, *P*=0.06



n=449

High Vit. D intake ≥474 IU/d:

β= 0.0087 ± 0.003, *P*=0.01



n=148

Conclusions: Dairy & Bone

- Greater dairy intake is associated with greater BMD
- Association of dairy intake with BMD may be dependent on vitamin D intake
  - Vitamin D plays a role in the absorption of calcium from dairy products
- More evidence needed on the role of dairy intake in fracture prevention

Take Home Message

- Usual dietary protein is beneficial to bone health
- The positive impact of dietary protein on bone health may be most beneficial under conditions of adequate calcium intake
- Dairy products contain many bone benefiting nutrients, including protein and may be protective of bone loss

Where is the field moving?

Future research: protein & bone health

- Sources of protein
  - in context of the whole diet (diet patterns)
  - amino acid groups & supplements
- More vulnerable populations
  - Older age groups
  - Lower usual protein intakes
- Mechanisms
  - At the bone
  - Intestinal calcium absorption