Animal vs. Plant Protein and Bone Health Across the Lifespan

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Disclosures

- **Research Grants**
  - National Dairy Council (NDC)
  - National Cattlemen's Beef Association (NCBA)
  - Other non-related industry research grants.
- **Scientific Consulting Fees**
  - Egg Nutrition Center
  - National Osteoporosis Foundation (NOF)
  - Other non-related scientific industry consulting fees.
- **Transparency**
  - All conflicts listed at www.drtaylorwallace.com
  - Adherence to ASN/ILSI North America guiding principles.

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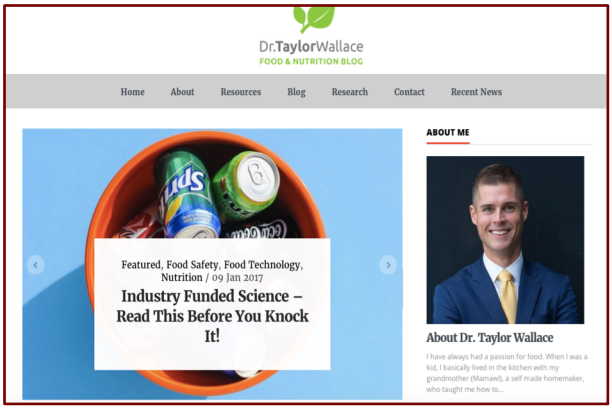

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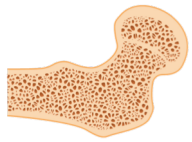
The Acid-Base Hypothesis

- Metabolism of animal proteins (comprised of **sulfur-containing amino acids**) leads to increased acid production.
- Sulfur-containing amino acids (R-S) are neutral but add to the body's acid load once metabolized. The reaction being:
  R-S → CO_2 + Urea + H_2SO_4
- Human clinical trials where acid-base balance was pharmacologically **manipulated with an alkaline source** (e.g., potassium bicarbonate) showed a **↓ in bone resorption**.

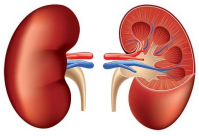
Br J Nutr. 2013;110:1168
Endocrinol Metab. 2009;94(1):96.

The Acid-Base Hypothesis

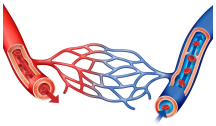
- The theory stemmed from studies of **CKD patients in the 1960's** where bone mineral mobilization served as a buffer system to acid accumulation.



↑ Bone resorption
↓ BMD
↑ Osteoporosis



↑ Calcium excretion
↓ Citrate excretion
↑ Nephrolithiasis

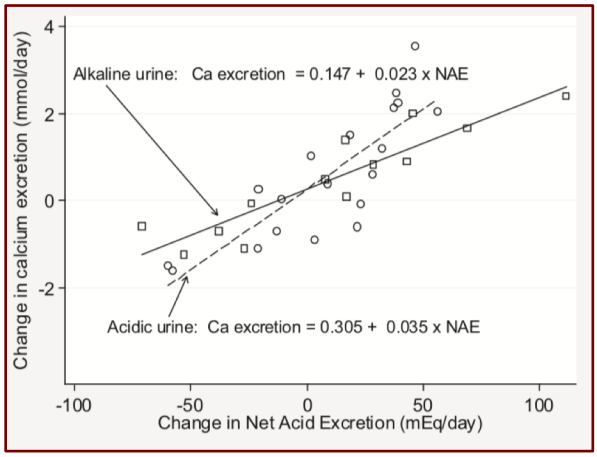


↑ Cortisol
↑ Blood pressure
↓ Lean body mass

Br J Nutr. 2013;110:1168
Clin Sci. 1969;36:517.

Fracture Risk (Calcium ≥ 525 mg/d)

- In 25 studies, a positive linear relationship was found between **urinary calcium excretion and net acid excretion.**



Am J Clin Nutr. 2008;88:1159.

The Caveat

- If the acid-base hypothesis were to hold true, we would expect over time **there to be a loss of BMD** due to chronic elevated bone resorption.
- Four systematic reviews of the acid-base hypothesis and one systematic review of animal vs. plant protein intake **do not support an association with adverse bone outcomes.**
- Higher protein intakes (diets were predominantly animal protein) **increase BMD and reduce fractures**.

Am J Clin Nutr. 2008;88:1159
Nutr J. 2009;8:41.
J Bone Min Res. 2009;24:1835.
Nutr J. 2011;10:41.
PLoS One. 2018;13(2):e0192459.
Am J Clin Nutr. 2017;105:1528.
J Am Coll Nutr. 2017;36:481.

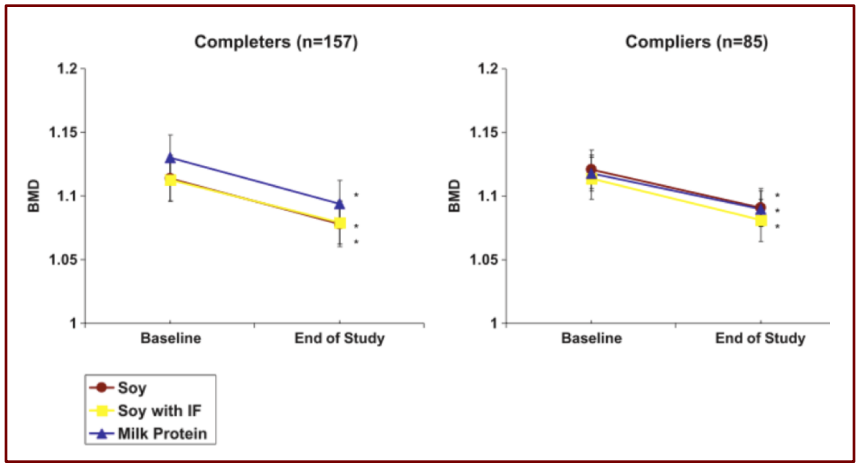
Fracture Risk (Calcium ≥ 525 mg/d)

- Among participants in the EPIC cohort, **fracture risk did not differ among those who consumed ≥ 525 mg/d of calcium**.
- Vegans with **low intake (< 525 mg/d) of calcium had a increased risk of total fractures** compared to meat eaters.

Diet Group	Men		Women		Men and Women	
	N	RR (95% CI)	N	RR (95% CI)	N	RR (95% CI)
Meat eater	172	1.00	851	1.00	1023	1.00
Fish eater	34	0.90 (0.61-1.32)	214	1.07 (0.91-1.25)	248	1.05 (0.90-1.21)
Vegetarian	101	1.04 (0.79-1.38)	341	0.98 (0.86-1.13)	442	1.02 (0.90-1.15)
Vegan	11	0.80 (0.42-1.51)	20	0.96 (0.61-1.51)	31	1.00 (0.69-1.44)

Eur J Clin Nutr. 2007;61:1400.

2y RCT – Milk vs. Soy (25 g Protein)



Menopause. 2009;16(2):320.

Osteoporotic Fractures in Men

- Higher protein intake (particularly high animal protein intake) **as a percentage of total energy intake** have a lower risk of osteoporotic fracture in a cohort of 5875 older men (mean age =74 y) followed for 15-years in the MrOS Study.

Fracture Type	N	Total Protein	Dairy	Non-Dairy Animal	Plant
Major OP	613	0.92 (0.84-1.00)	0.89 (0.78-1.01)	0.92 (0.84-1.01)	0.97 (0.83-1.13)
Low-trauma	806	0.92 (0.85-0.99)	0.89 (0.79-0.99)	1.07 (0.91-1.25)	0.95 (0.83-1.09)
Hip	270	0.84 (0.73-0.95)	0.80 (0.65-0.98)	0.84 (0.72-0.97)	0.99 (0.78-1.24)
Spine	193	1.06 (0.92-1.22)	1.05 (0.85-1.31)	1.09 (0.94-1.24)	1.02 (0.77-1.35)
Non-hip/ non-spine	919	0.94 (0.88-1.00)	0.87 (0.78-0.97)	0.96 (0.89-1.03)	0.95 (0.83-1.07)

J Bone Min Res. 2017;32(3):592.

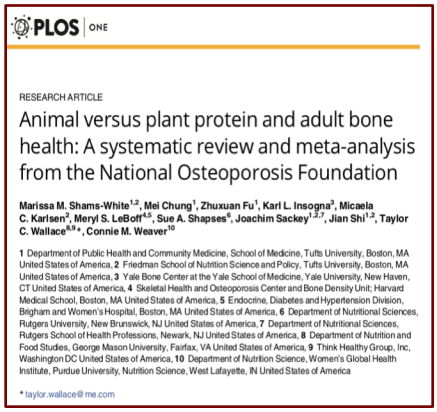
Dietary Considerations

- A strict vegetarian diet with protein derived from grains and legumes would **deliver as many millimoles of sulfur per gram of protein as would a purely meat-based diet.**
- It is **unlikely that bone is exposed to marked changes in extracellular pH** in relation to animal or plant protein consumption within limits of a balanced diet.
- A diet low in fruits and vegetables appears to be associated with higher fracture risk; however, **nutrient density of the diet seems to have a much stronger correlation.**

J Acad Nutr Diet. 1995;791.
Osteoporos Int. 2018 (doi: 10.1007/s00198-018-4534-5).
Am J Clin Nutr. 2011;93(1):192.

NOF Meta-Analysis

- Systematic review **does not support** consumption of soy protein is more advantageous (n=7 RCTs included).
- Data for bone health outcomes were **C-level or "limited"** at best.
- **Insufficient evidence** to draw conclusions regarding fractures and falls.


PLOS | ONE

RESEARCH ARTICLE

Animal versus plant protein and adult bone health: A systematic review and meta-analysis from the National Osteoporosis Foundation

Marissa M. Shams-White[1,2], Mei Chung[1], Zhuxuan Fu[1], Karl L. Insogna[3], Micaela C. Karlsen[2], Meryl S. LeBoff[4,5], Sue A. Shapses[6], Joachim Sackey[1,2,7], Jian Shi[1,2], Taylor C. Wallace[8,9]*, Connie M. Weaver[10]

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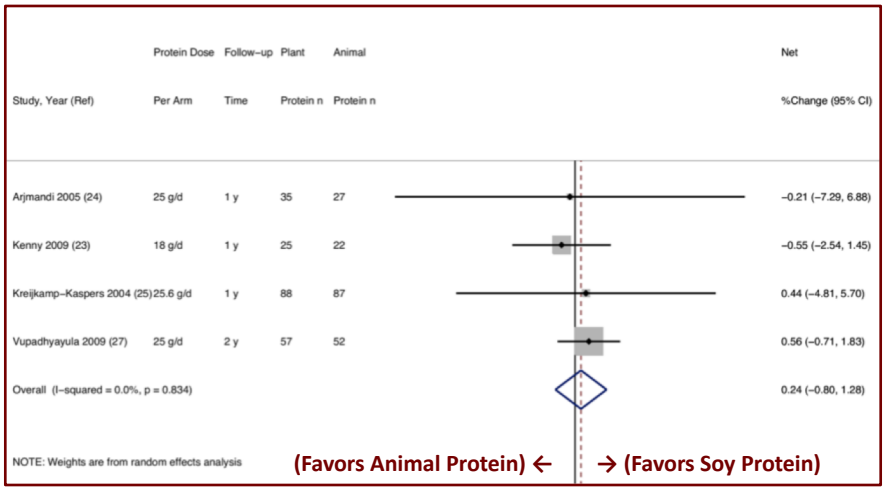
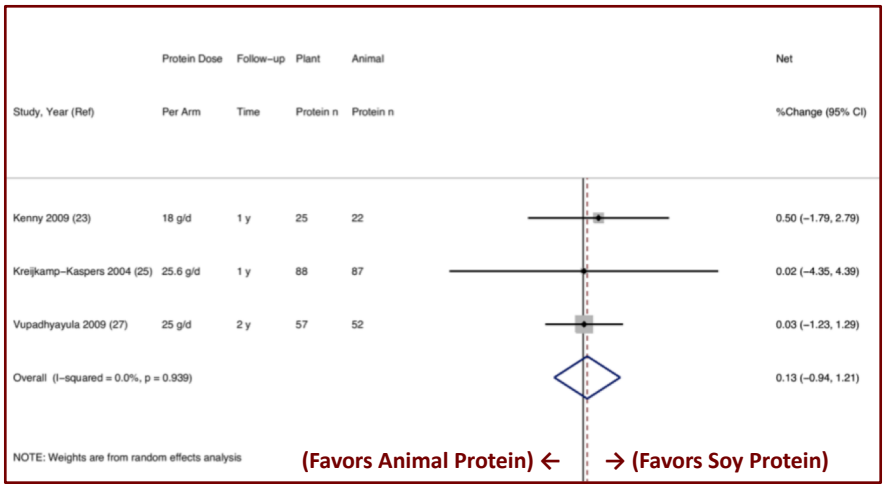
PLoS One. 2018;13(2):e0192459.

Lumbar Spine BMD



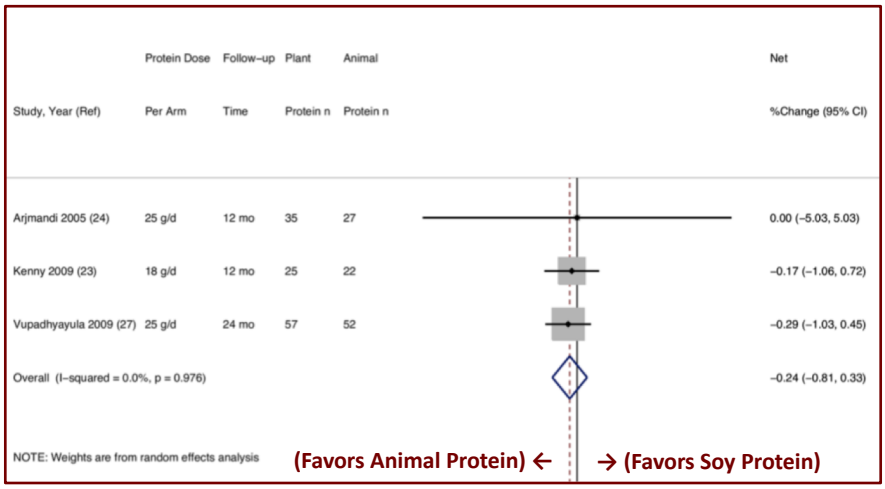
PLoS One. 2018;13(2):e0192459.

Femoral Neck BMD



PLoS One. 2018;13(2):e0192459.

Total Body BMD



PLoS One. 2018;13(2):e0192459.

Shanghai Women's Health Study

Table 2. Data for Fracture by Quintile of Soy Protein Intake

Variable	Quintile of Soy Protein Intake, g/d					*P* Value for Trend
	<4.98 (n = 4880)	4.98-7.32 (n = 4882)	7.33-9.77 (n = 4880)	9.78-13.26 (n = 4880)	≥13.27 (n = 4881)	
No. of follow-ups	9559	9610	9649	9662	9616	NA
Person-years	21 635	22 091	22 232	22 234	22 052	NA
No. of cases	459	332	329	317	333	NA
RR (95% CI)						
Age and calorie (energy) adjusted	1.00	0.69 (0.60-0.80)	0.67 (0.58-0.77)	0.63 (0.54-0.73)	0.63 (0.54-0.74)	<.001
Multivariate*	1.00	0.72 (0.62-0.83)	0.69 (0.59-0.80)	0.64 (0.55-0.76)	0.63 (0.53-0.76)	<.001

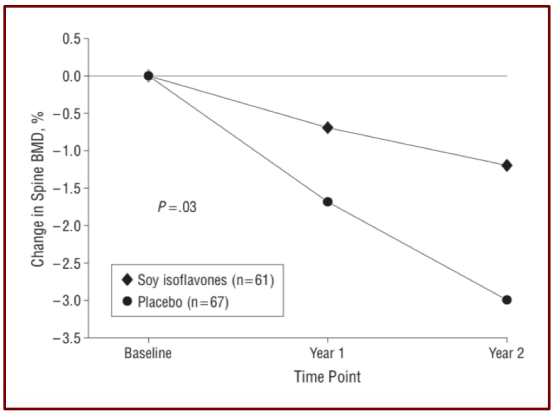
Table 3. Data for Fracture by Quintile of Soy Isoflavone Intake

Variable	Quintile of Soy Isoflavone Intake, mg/d					*P* Value for Trend
	<21.16 (n = 4881)	21.16-32.39 (n = 4881)	32.40-44.31 (n = 4880)	44.32-60.26 (n = 4880)	≥60.27 (n = 4881)	
No. of follow-ups	9564	9624	9648	9658	9602	NA
Person-years	21 654	22 147	22 288	22 136	22 018	NA
No. of cases	450	340	312	340	328	NA
RR (95% CI)						
Age and calorie (energy) adjusted	1.00	0.72 (0.63-0.83)	0.65 (0.56-0.75)	0.70 (0.60-0.81)	0.65 (0.56-0.76)	<.001
Multivariate*	1.00	0.75 (0.65-0.87)	0.67 (0.58-0.78)	0.72 (0.61-0.84)	0.65 (0.55-0.78)	<.001

Arch Intern Med. 2005;165(16):1890.

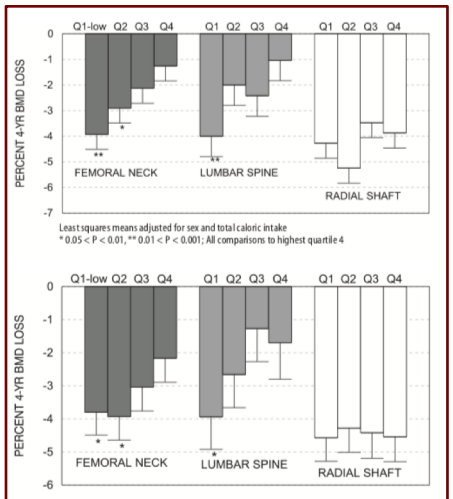
Purified Isoflavone and BMD

- A 2 year RCT of **purified soy isoflavones** suggests a beneficial impact on spine BMD, however the totality of evidence in regard to these dietary bioactive compounds is inconsistent.



Arch Intern Med. 2011;171(15):1363.

Framingham Osteoporosis Study



***Top**: total protein; **Bottom**: animal protein*

- The role of protein appears to be complex and is likely dependent on the presence of other nutrients available in a mixed diet.
  - e.g., minerals and fiber
- Adequate fruits, vegetables and protein appear to be critical.

J Bone Min Res. 2000;15:2504

Research Gaps

- Is there a synergistic effect of sufficient **protein + calcium/vitamin D** intakes on BMD and fracture risk?
- Does the type and amount of protein intake prior to, during and post-menopause transition have effects on bone health?
  - Most cohorts only assess during the postmenopausal state after a significant amount of BMD is lost.

Conclusion

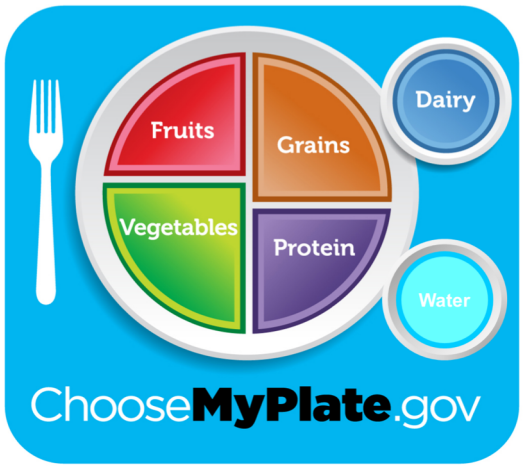
- **There currently no direct evidence of detriment** to BMD or fractures resulting from consumption of animal protein.
  - Evidence is limited due to low intake of plant protein across observational studies and interventions in relation to total protein intake.
- **The amount of total protein intake matters!**
  - New DRIs should consider the effects of dietary protein and its interactions with other nutrients on bone health across the lifespan.
- **Other minerals that co-occur with many food-based proteins also play an important role.**
  - e.g., calcium, magnesium, potassium, etc.

Two Last Thoughts…

- Diets high in plant-based foods are important for health and disease prevention. However, **we shouldn't underscore the importance of animal-derived foods** that contribute higher levels of protein (and certain micronutrients), particularly as we age and bone loss becomes more apparent.

- Its doubtful in my mind that the type of protein greatly influences body pH with respect to other components of the typical American diet (e.g., soda).

All About Balance!



http://choosemyplate.gov

Thank You!

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