Protein’s Role in Bone Health: Does Protein Type and Amount Matter?

September 27, 2018

Moderator:
Katherine Tucker, PhD
University of Massachusetts Lowell
A Few Reminders

CPE Credit

• ASN designates this educational activity for a maximum of 1 CPEUs. Dietitians and Dietetic Technicians, Registered should only claim credit commensurate with the extent of their participation in the activity.

• To claim credit, please take the post webinar evaluation to be emailed after the webinar.
**Patient Education Handout**

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**How Can I Keep My Bones Strong?**

### The foods you eat can affect your bones.

- **Eating a healthy diet and being physically active helps keep bones strong.**

### Why are strong bones important?

- Each year, about one-third of people over age 65 fall. Many of these falls result in broken bones. As you get older, you lose some bone mass. Eating a healthy diet helps prevent bone loss and reduces your risk of fracture.

### What should I do to keep my bones strong?

- Eat a variety of foods. Include:
  - **Vegetables**
  - **Fruits**
  - Whole grains like whole wheat bread, oatmeal, and quinoa
  - Low- or non-fat dairy products such as milk and yogurt
  - Nuts and seeds
  - Eggs and tofu
  - Fish, chicken, and lean beef
  - Eat foods high in:
    - Calcium
    - Vitamin D
    - Magnesium
    - Protein
  - Do physical activities like:
    - Walking, yoga, dancing, basketball, soccer, karate, running, tennis
  - Avoid smoking

### FOOD SOURCES OF CALCIUM

- Low or non-fat milk
- Low or non-fat yogurt
- Cheese
- Tofu
- Sandwiches with hones
- Kale
- Collards
- Cabbage
- Broccoli
- Fortified juice
- Almonds

### FOOD SOURCES OF PROTEIN

- Low or non-fat milk
- Eggs
- Fish, chicken, and lean beef
- Nuts
- Tofu
- Beans

### MORE ABOUT BEANS

Beans contain many bone-healthy nutrients. But, they are also high in phytates. Phytates keep your body from absorbing calcium. To cut down on the phytates:

- Soak beans in water for a few hours
- Drain the beans
- Cook the beans in fresh water

### FOOD SOURCES OF VITAMIN D

- Low or non-fat milk, fortified
- Salmon
- Mackerel
- Sardines
- Mushrooms
- Cereal fortified
- Fortified juice

### FOOD SOURCES OF MAGNESIUM

- Whole grains
- Nuts and seeds
- Beans
- Avocado
- Eggs
- Tofu
- Sweet potato
- Tomatoes and tomato products
- Dark chocolate

### WHAT DOES FORTIFIED MEAN?

- Fortified means a food has extra vitamins and minerals added.
- Some foods have extra calcium or vitamin D added to them. These foods include cereal, fruit juice, and milk.

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**How Can I Keep My Bones Strong?**

### A note on supplements

It is best to get nutrients from food. If you eat a variety of foods, you should get nutrients from what you eat. If you're not getting enough nutrients, you may need a multivitamin and mineral supplement. Talk to your doctor to see if a supplement is right for you.

### Quick snack ideas for strong bones

- Cheese and apple
- Baby carrots with peanut butter
- Broccoli with yogurt dip
- Whole grain cereal and low or non-fat milk
- Bananas and almonds
- Yogurt and fruit
- Oatmeal with pumpkin seeds and fruit
- Whole wheat toast and avocado
- Lettuce wrap with cauliflower chicken
- Asparagus wraps with cheese and lean beef
- Hard-boiled egg and fortified orange juice
- Whole wheat crackers and tuna or salmon salad

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**USE THE FOOD LABEL TO COMPARE FOODS**

<table>
<thead>
<tr>
<th>Nutrition Facts</th>
<th>Number of Servings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serving size: 1 1/2 cup (26g)</td>
<td>One container may be more than one serving.</td>
</tr>
<tr>
<td>Calories</td>
<td>240</td>
</tr>
<tr>
<td>Serving Size: 1 1/2 cup (26g)</td>
<td>The information on the label is for this amount of food or beverage.</td>
</tr>
<tr>
<td></td>
<td>Choose foods with less sodium.</td>
</tr>
<tr>
<td></td>
<td>Choose foods with more calcium and vitamin D.</td>
</tr>
<tr>
<td></td>
<td>High sources are 20% or more.</td>
</tr>
</tbody>
</table>

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Questions & Answers

- Please use the “questions” box on your “Go To Meetings” screen to submit questions to our presenters.

- Please submit your questions at any time during today’s webinar.
Faculty

Wayne Campbell, PhD
Purdue University
– Dietary Protein and Food and Nutrition Guidance

Sue Shapses, PhD, RD
Rutgers University
– Dietary Protein Intake: Bone Acquisition, Maintenance and Risk of Fractures

Taylor C. Wallace, PhD
George Mason University
– Animal Versus Plant Protein and Adult Bone Density
Learning Objective

At the end of this program, attendees will be able to:

• Describe current dietary guidelines related to protein intake
• Discuss dietary protein with or without calcium and vitamin D on bone health outcomes in healthy individuals
• Assess whether animal versus plant proteins have different effects on bone health.
Dietary protein and food and nutrition guidance

Wayne W. Campbell, PhD
Department of Nutrition Science
Purdue University
Professional Disclosures
Wayne Campbell, PhD

- **Current Research, Speaking and/or Travel Funding Providers**
  - National Institutes of Health
  - National Pork Board (Pork Checkoff)
  - National Cattlemen’s Beef Association (Beef Checkoff)
  - National Dairy Council
  - North Dakota Beef Commission
  - American Egg Board – Egg Nutrition Center
  - Barilla Italy / Barilla America
A healthy eating pattern includes:

- A variety of vegetables
- Fruits, especially whole fruits
- Grains, at least half of which are whole grains
- Fat-free or low-fat dairy ... and/or fortified soy beverages
- A variety of protein foods, including seafood, lean meats* and poultry, eggs, legumes (beans and peas), and nuts, seeds, and soy products
- Oils
- Specified limits on saturated fats & trans fats, added sugars, and sodium

*unprocessed or processed
Protein Intake Declines With Age - NHANES, 2003-2004

Adapted from Fulgoni, VL. Am J Clin Nutr 2008
Protein Intake (% of calories) - NHANES, 2003-2004

Data Source: What We Eat in America, NHANES 2007-2008, individuals, day 1 dietary intake data, weighted. (Revised August 2010)
## Daily patterns of protein intake in younger and older adults

<table>
<thead>
<tr>
<th></th>
<th>Bkft</th>
<th>Lunch</th>
<th>Dinner</th>
<th>Snack</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Protein intake (g/d)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Younger</td>
<td>11.1</td>
<td>25.4</td>
<td>43.0</td>
<td>8.8</td>
<td>88.3</td>
</tr>
<tr>
<td>Older</td>
<td>13.3</td>
<td>20.2</td>
<td>35.8</td>
<td>7.2</td>
<td>76.5</td>
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<tr>
<td><strong>Protein intake (% of energy)</strong></td>
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<td></td>
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<tr>
<td>Younger</td>
<td>11.8</td>
<td>16.1</td>
<td>18.8</td>
<td>7.5</td>
<td>14.8</td>
</tr>
<tr>
<td>Older</td>
<td>13.1</td>
<td>16.8</td>
<td>18.7</td>
<td>8.1</td>
<td>15.3</td>
</tr>
<tr>
<td><strong>Energy intake (kcal/d)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Younger</td>
<td>377</td>
<td>631</td>
<td>914</td>
<td>469</td>
<td>2391</td>
</tr>
<tr>
<td>Older</td>
<td>405</td>
<td>479</td>
<td>766</td>
<td>355</td>
<td>2005</td>
</tr>
</tbody>
</table>

Adapted from Howarth, NC. Int J Obes 2007;31:675-684
## Sources of dietary protein in adults

<table>
<thead>
<tr>
<th>Protein source</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total animal</td>
<td>66 %</td>
<td>64 %</td>
</tr>
<tr>
<td>Flesh:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Beef</td>
<td>16 %</td>
<td>12 %</td>
</tr>
<tr>
<td>Pork</td>
<td>9 %</td>
<td>7 %</td>
</tr>
<tr>
<td>Poultry</td>
<td>10 %</td>
<td>14 %</td>
</tr>
<tr>
<td>Fish</td>
<td>5 %</td>
<td>6 %</td>
</tr>
<tr>
<td>Dairy:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Milk/yogurt</td>
<td>15 %</td>
<td>16 %</td>
</tr>
<tr>
<td>Cheese</td>
<td>5 %</td>
<td>5 %</td>
</tr>
<tr>
<td>Egg</td>
<td>5 %</td>
<td>4 %</td>
</tr>
<tr>
<td>Total plant</td>
<td>34 %</td>
<td>36 %</td>
</tr>
<tr>
<td>Grain</td>
<td>18 %</td>
<td>19 %</td>
</tr>
<tr>
<td>Fruits</td>
<td>2 %</td>
<td>3 %</td>
</tr>
<tr>
<td>Vegetables</td>
<td>8 %</td>
<td>9 %</td>
</tr>
<tr>
<td>Legumes/soy</td>
<td>2 %</td>
<td>2 %</td>
</tr>
<tr>
<td>Nuts/seeds</td>
<td>2 %</td>
<td>2 %</td>
</tr>
<tr>
<td>Other</td>
<td>&lt;2 %</td>
<td>1 %</td>
</tr>
</tbody>
</table>

Mean ± SEM

Adapted from Smit, E. J Am Diet Assoc 1999;99:813
Average HEI-2010 scores for Americans by age group

Food and Nutrient Intakes, and Health: Current Status and Trends
Average HEI-2010 scores for Americans by age group

What We Eat in America, NHANES 2007-10
### What counts as an ounce-equivalent in the Protein Foods Group?

<table>
<thead>
<tr>
<th>Protein source</th>
<th>1 ounce-equivalent</th>
<th>Common portions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meats</td>
<td>1 ounce cooked lean meat</td>
<td>1 small steak = 3.5-4 oz-eq&lt;br&gt;1 small hamburger = 2-3 oz-eq</td>
</tr>
<tr>
<td>Poultry</td>
<td>1 ounce cooked</td>
<td>1 small chicken breast half = 3 oz-eq&lt;br&gt;½ Cornish game hen = 4 oz-eq</td>
</tr>
<tr>
<td>Seafood</td>
<td>1 ounce cooked</td>
<td>1 can of tuna, drained = 3-4 oz-eq&lt;br&gt;1 salmon steak = 4-6 oz-eq</td>
</tr>
<tr>
<td>Eggs</td>
<td>1 large whole egg</td>
<td>3 egg white = 2 oz-eq&lt;br&gt;3 egg yolks = 1 oz-eq</td>
</tr>
<tr>
<td>Nuts and seeds</td>
<td>½ ounce whole or 1 Tbsp. nut butter</td>
<td>1 oz nuts or seeds = 2 oz-eq</td>
</tr>
<tr>
<td>Beans and peas</td>
<td>¼ cup cooked or 1 oz tempeh or 2 Tbsp. hummus</td>
<td>1 cup split pea soup = 2 oz-eq&lt;br&gt;1 cup lentil soup = 2 oz-eq&lt;br&gt;1 cup bean soup = 2 oz-eq&lt;br&gt;1 soy or bean burger patty = 2 oz-eq</td>
</tr>
</tbody>
</table>

*Dairy not included in the Protein Foods Group*
Protein ounce-equivalents from different sources are not nutritionally equivalent.

<table>
<thead>
<tr>
<th>Protein source</th>
<th>1 ounce-equivalent</th>
<th>Energy, kcal/oz-eq</th>
<th>Protein, g/oz-eq</th>
<th>Leucine, mg/oz-eq</th>
<th>PDCAAS</th>
<th>BV</th>
<th>PER</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lean pork</td>
<td>1 ounce cooked lean meat</td>
<td>36</td>
<td>7.4</td>
<td>598</td>
<td>~0.9</td>
<td>~80</td>
<td>~2.9</td>
</tr>
<tr>
<td>Whole eggs</td>
<td>1 large whole egg</td>
<td>73</td>
<td>6.3</td>
<td>538</td>
<td>~1.0</td>
<td>~100</td>
<td>~3.9</td>
</tr>
<tr>
<td>Almonds</td>
<td>½ ounce whole or 1 Tbsp. nut butter</td>
<td>80</td>
<td>3</td>
<td>208</td>
<td>~0.5</td>
<td>~43</td>
<td>~1.7</td>
</tr>
<tr>
<td>Black beans</td>
<td>¼ cup cooked</td>
<td>56</td>
<td>3.8</td>
<td>305</td>
<td>~0.7</td>
<td>~58</td>
<td>~1.6</td>
</tr>
</tbody>
</table>

PDCAAS: Protein digestibility-corrected amino acid score
BV: Biological value
PER: Protein efficiency ratio

Protein Foods Group

Dietary Guidance

• Protein foods group includes all foods made from meat, poultry, seafood, beans and peas, eggs, processed soy products, nuts, and seeds

• Select a variety of protein foods to improve nutrient intake and health benefits

• Meat and poultry choices should be lean or low-fat

• Most Americans eat enough food from this group, but need to make leaner and more varied selections of these foods

• Adolescent girls and older women are at greatest risk for inadequate protein intake

https://www.choosemyplate.gov/protein-foods
Thank you

Wayne Campbell, PhD
Professor, Department of Nutrition Science
ASN Webinar: Protein’s Role in Bone Health: Does Protein type and Amount Matter?

Protein: Bone acquisition, maintenance and risk of fractures

Sue Shapses, PhD, RDN
Professor, Nutritional Sciences
Rutgers, the State University
- NJ Obesity Group -

Protein: A nutrient for Bone
Too Much? Too Little?
Disclosure and Grant support

Disclosures: None

Research Support/Grants:
- USDA-NIFA, NJ-AES (0153866)
- International Life Sciences Foundation
- NIH (co-investigator or mentee)
- Veterans Health Administration
- OmniActive Technologies
Introduction to Bone

**Osteoporosis** - A skeletal disorder characterized by low BMD with compromised bone strength predisposing to an increased risk of fracture.

**Two separate Concerns to prevent fracture**
- Peak Bone Density
- Adult Bone loss (turnover unit ~4 mo)

**Definitions**
- BMD – Bone mineral density
- BMC – bone mineral content
- vBMD – volumetric BMD

**Measurement**
- (DXA)
- (DXA)
- (pQCT)
Bone Changes During Growth and Lifespan

Children: Level of evidence C was assigned for the benefit of protein on bone. Evidence based on findings from 4 prospective studies indicating positive findings and 1 null RCT.

Protein Intake and BMC in 223 Children

- Higher protein intake and exercise increase BMC
- Follow up Study: Boys maintained higher BMC and greater bone strength when followed up at 15 and 23 years.


~7 years of age
Dietary protein by FFQ

Physical Activity: Low
Protein Intake: Low

Physical Activity: High
Protein Intake: High

Children: RCT studies examining dietary protein are still needed
Low dietary protein or hypercatabolism: *not good for bone*

- Lower bone mass, microarchitecture and strength in rodent studies

- Protein Supplementation increases IGF-1 and BMD in the elderly with recent fracture

Low protein intake is associated with greater BMD loss

(Hannan M 2000)

<table>
<thead>
<tr>
<th>Changes (% baseline value)</th>
<th>Placebo</th>
<th>Protein supplementation</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prealbumin</td>
<td>+56±9</td>
<td>+86±14</td>
<td>0.07</td>
</tr>
<tr>
<td>IGF-I</td>
<td>+34±7</td>
<td>+86±15</td>
<td>0.01</td>
</tr>
<tr>
<td>IgM</td>
<td>+40±6</td>
<td>+66±9</td>
<td>0.02</td>
</tr>
<tr>
<td>Proximal femur (BMD)</td>
<td>-4.7±0.8</td>
<td>-2.3±0.7</td>
<td>0.03</td>
</tr>
</tbody>
</table>

Hypercatabolic ICU patients in negative N balance compared to “healthy” ICU patients and healthy controls

have high bone resorption, & negative Ca balance

Shapses SA 1997
High Protein Diet and Bone...*Bad*?

- Humans fed a high protein diet- hypercalciuria
- Female fracture rates derived from 16 countries is strongly associated with dietary animal protein intake (Abelow BJ 1992)
- Urinary calcium increased when doubling protein intake or ~1 mg urinary Ca/ 1 of dietary protein (Heaney 2007)
- Net endogenous non-carbonic acid production (NEAP) and potential renal acid load (PRAL) increase with higher protein intake and thereby may be detrimental to bone

Higher NEAP = lower bone quality at the spine (n=4672)  
DeJong E, Osteo Int 2017

![NEAP vs BMD graph](image)

Lower NEAP and higher BMD for 994 women  
lumbar spine femoral neck  
New et al. 2001
Dietary protein and bone... *Good*?

*It was assumed that the increase in urine calcium (Ca) that accompanies an increase in dietary protein was due to increased bone resorption. However, ....*

- **↑** Intestinal calcium absorption
  - *Kerstetter J, Insogna K – 10 day in-patient study*
    - *Intestinal transporters are increased*
  - **↑** Insulin like growth factor (IGF-1) + IGFBP-3
  - No rise in bone resorption
  - **↑** differentiation of the osteoblast
Protein and Calcium homeostatus ...in-patient study

Cao JJ et al. Calcium homeostasis and bone metabolic responses to high-protein diets during energy deficit in healthy young adults: a randomized controlled trial, AJCN 2014

• **Subjects and Methods**
  – Age: 21 y, BMI: 25 kg/m2, 32 men and 7 women
  – **Protein:** 0.8 (at RDA), 1.6 (2 x RDA), or 2.4 (3 x RDA)
  – **31 days in a metabolic unit**
  – Wt stable and 40% energy deficit – cross over
  – Ca intake - ~1000 mg/d (plus 160 suppl) + 400 IU vit D.

• **Results**
  – Regardless of energy intake, at higher protein (2-3 times RDA), there was lower urine pH, but no effect on urinary Ca excretion or retention.

• **Conclusion**
  – Higher protein is not detrimental to calcium homeostasis in a short term in-patient study
Dietary Protein and Bone

Randomized trial, whey protein or isocaloric maltodextrin supplement given to 208 older adults for 18 months did not negatively affect bone

Protein Supplement: 45g whey protein: Control: isocaloric drink
Both drinks contained 600 mg calcium
self-reported protein intake 0.6 to 1.0 g/kg/d

Total protein: 1.1 and ~1.4 g/kg/d in the maltodextrin and whey groups, respectively

Kerstetter JE et al. J Clin Endocrinol Metab 2015
**Effects of Lean Red Meat on Bone**

4-month RCT in Older Women: All Participants Completed Resistance Training 3/week

Protein intake increased from ~1.1 to 1.3 g/kg

High quality Lean Red Meat
160 g cooked (~45 g protein) of lean red meat for 6 days per week

Protein intake stable at ~1.1 g/kg

Carbohydrate (pasta, rice, bread)

High Protein Intake and Exercise

• **Population:** Individuals -50 years (BMI 25-35 kg/m²)

• **Design:** (0, 20, 40, or 60 g whey protein/d) along with their otherwise unrestricted diet (~ 1 g/kg/d) in a resistance and aerobic exercise (3 d/wk for 9 mo).

• **Conclusion:** Protein supplementation and total dietary protein intake did not negatively influence bone or benefit bone during a 9-mo exercise intervention.

Protein Intake and Bone

• Special conditions
  – Type of protein – next lecture
  – Rodent Studies and Amino Acids
  – During weight loss (model of bone loss)
Higher protein intake increases urinary Ca but improves Ca absorption and Ca balance. (Gaffney-Stromberg, 2010)

Gaffney-Stromberg, 2014
Both high protein and soy protein suppress PTH, and HP attenuates bone turnover and increases vBMD regardless of energy restriction in rats.
Is it total Protein or the individual amino acids that are important?

Tissues express the calcium-sensing receptor and that these receptors preferentially bind aromatic amino acids to serve as nutrient sensors (Conigrave AD et al Ann Rev Nutr, 2008).

Can amino acids select amino acids provide beneficial effects on bone mass in vivo?

Yes according to a new study in aged mice.

- 18- mo old mice - 2 mo diet intervention.
- A low-protein diet (8%) reduces BMD compared to 18% or 28% intake, partially due to an increase in osteoclastic activity.
- The decline in BMD on the low-protein diet is prevented by addition of aromatic AAs.

Ding KH, et al. Amino acids as signaling molecules modulating bone turnover. Bone. 2018
Weight Loss and Protein Intake

- Remains popular due to evidence of greater weight loss at 6 mo and at least as effective at 1 and 2 years (Dansinger ’05; Sacks FM ‘09)
- Enhances loss of fat mass & preservation of lean mass
- Satiety and adherence
- Insulin sensitivity (Hall & Chung 2018)
- Diet induced thermogenesis
- Prevent the decrease in serum IGF-1/IGFBP axis
- Effect on bone?

Wt loss, hunger, satiety and lipids were similar for all 4 diets after 2 yrs; only # sessions attended predicted wt loss. Sacks 2009
Goal: To compare the effects of weight loss with a high-protein (HP) diet to a normal protein (NP) diet on bone mass and quality in postmenopausal women over 1 year during caloric restriction

Sukumar et al, JBMR, 2011

**Screening**
- Telephone physicals, laboratory, bone density
- 1 month

**Baseline**
- Bone, Blood, urine, nutrient, Randomize to HP/NP diets
- 6 months wk-4,12 blood and urine

**Final**
- Bone, Blood, urine and nutrient intake
- 6 months Wk-38 blood and urine

**Pass Eligibility**
- Stabilized to 1.2g of ca and MV

**No exercise intervention, but encouraged**

**Bi-weekly dietary counseling, Compliance check, adverse symptoms, renal measures**

**Months 6 & 12 measurements**
Changes in BMD at various bone sites
1 Year weight loss (high or normal protein)

Bone mineral density (BMD) was attenuated due to: higher protein (HP) intake of 24% (1.1 g/kg/d) compared to 18% normal protein (NP; 0.8 g/kg/d) of total calories.

*Sukumar et al, JBMR, 2011*
Trabecular and cortical BMD (pQCT)
Higher protein intake (1 yr) reduced trabecular bone loss

Sukumar et al, JBMR, 2011
Conclusions

• Higher protein diet attenuates BMD loss at lumbar spine and radius and primarily influences trabecular bone as compared to a normal protein diet.

• Trend for a greater increase in the IGF-1 levels with higher protein.

Sukumar et al, JBMR, 2011
Support: NIH-NIA (AG12161) - Shapses Lab
Protein …study design matters


• Large 2-year well designed trial in 137 postmenopausal women (BMI =27 kg/m2) suggesting no beneficial effect of higher protein on BMD.

• Why do the results differ from Sukumar et al when wt loss was similar?

• The 2 levels of protein intake are high and are not very different from one another (77 g/d vs 90 g/d).

• The study was not powered to detect a BMD difference between groups with only 13 g difference between group. Or there is a threshold effect for protein on bone at about 1 g/kg/d.

• Conclusion based on both studies

Protein: at least 1 g/kg/d during weight loss
**Systematic Review and Meta analysis: Protein on adult bone**


16 RCTs and 20 prospective cohort studies

- Lumbar spine
  - **LS showed moderate evidence to increase BMD with higher protein intake, but not other sites.**
  - Limited or insufficient evidence did not support an effect of protein on fractures.

<table>
<thead>
<tr>
<th>Study</th>
<th>Population</th>
<th>Duration</th>
<th>Protein (g/d)</th>
<th>Change (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jasudion 2013 (34)</td>
<td>PM</td>
<td>2 y</td>
<td>69</td>
<td>0.50 (-1.01, 2.11)</td>
</tr>
<tr>
<td>Koenstetter 2015 (35)</td>
<td>Adults</td>
<td>1.5 y</td>
<td>105</td>
<td>0.01 (-3.56, 3.56)</td>
</tr>
<tr>
<td>Kukuljan 2009 (36)</td>
<td>Men</td>
<td>1 y</td>
<td>88</td>
<td>0.92 (0.08, 1.75)</td>
</tr>
<tr>
<td>Sukumar 2011 (38)</td>
<td>GWhibose, PM</td>
<td>1 y</td>
<td>26</td>
<td>1.60 (-4.42, 3.62)</td>
</tr>
<tr>
<td>Trinh 2015 (36)</td>
<td>Adults</td>
<td>2 y</td>
<td>210</td>
<td>0.25 (-2.55, 0.85)</td>
</tr>
</tbody>
</table>

Overall (I-squared = 0.0%, p = 0.579)

-0.52 (0.06, 0.97)

**Total Hip BMD**

<table>
<thead>
<tr>
<th>Study</th>
<th>Population</th>
<th>Time</th>
<th>Protein (g/d)</th>
<th>%Change (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jiaxiong 2013 (34)</td>
<td>PM</td>
<td>2 y</td>
<td>65</td>
<td>0.50 (-1.15, 2.15)</td>
</tr>
<tr>
<td>Jiaxiong 2013 (34)</td>
<td>PM</td>
<td>2 y</td>
<td>65</td>
<td>0.50 (-1.15, 2.15)</td>
</tr>
<tr>
<td>Koenstetter 2015 (35)</td>
<td>Adults</td>
<td>1.5 y</td>
<td>105</td>
<td>-1.23 (-4.04, 2.17)</td>
</tr>
<tr>
<td>Kukuljan 2009 (36)</td>
<td>Men</td>
<td>1 y</td>
<td>88</td>
<td>-0.36 (-1.85, 0.13)</td>
</tr>
<tr>
<td>Sukumar 2011 (38)</td>
<td>GWhibose, PM</td>
<td>1 y</td>
<td>26</td>
<td>0.60 (-4.45, 5.65)</td>
</tr>
<tr>
<td>Trinh 2015 (36)</td>
<td>Adults</td>
<td>2 y</td>
<td>210</td>
<td>-0.09 (-0.82, 0.64)</td>
</tr>
<tr>
<td>Zhu 2011 (37)</td>
<td>PM</td>
<td>2 y</td>
<td>81</td>
<td>-0.17 (-1.16, 0.85)</td>
</tr>
</tbody>
</table>

Overall (I-squared = 0.0%, p = 0.603)

-0.14 (0.00, 0.99)

**Femoral Neck BMD**

<table>
<thead>
<tr>
<th>Study</th>
<th>Population</th>
<th>Time</th>
<th>Protein (g/d)</th>
<th>%Change (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jiaxiong 2013 (34)</td>
<td>PM</td>
<td>2 y</td>
<td>65</td>
<td>0.50 (-1.15, 2.15)</td>
</tr>
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<td>PM</td>
<td>2 y</td>
<td>81</td>
<td>-0.17 (-1.16, 0.85)</td>
</tr>
</tbody>
</table>

Overall (I-squared = 0.0%, p = 0.603)

-0.14 (0.00, 0.99)
High Dietary Protein and Bone

**Known positive effects**

- Supplies amino acids for bone matrix collagen synthesis
- ↑ Serum IGF-1 → Increase bone formation
- ↓ Serum PTH → Decrease bone resorption and ↑ intestinal Ca absorption

**Known negative effects**

- Acid production from metabolism of sulfur amino acids
  - ↓ Renal reabsorb Ca
  - ↓ Osteoblast activity and ↑ Osteoclast activity
  - ↑ Urinary Ca excretion

- Ca homeostasis
- Improved muscle mass, strength
- Anabolic stress on bone and ↑ BMD

---

Modified Figure from Cao JJ. Curr Osteoporosis Rep. 2017

↑ Growth in children
↓ Falls and Fracture Risk
Summary: Protein-Bone 2018 Consensus Statement over the Lifespan

• Adequate dietary protein is required for optimal bone growth and maintenance.
• Variation in protein intakes within the "normal" range accounts for 2-4% of BMD variance in adults.
• There is no evidence that a diet-derived acid load is deleterious for bone.
• In older people with osteoporosis, higher protein intake (≥ 0.8-g/kg/d) has been associated with higher BMD, a slower rate of bone loss, and reduced risk of hip fracture, provided that dietary calcium is adequate.
• Protein supplements attenuates BMD decrease and reduces bone turnover in the aged population, together with an increase in IGF-I and a decrease in PTH. Evidence is stronger during weight loss diets. Generally improves muscle mass over shorter term periods, but unclear if this prevents falls.
• Insufficient dietary protein may be a more severe problem in the elderly than the need for protein excess.

Italics = added comments to the Consensus statement for this lecture.
Rizzoli R et al Benefits and safety of dietary protein for bone health-an expert consensus paper Osteoporosis Int. 2018
Thank you

Questions?
Animal vs. Plant Protein and Bone Health Across the Lifespan

Taylor C. Wallace, PhD, CFS, FACN
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](http://www.drtaylorwallace.com)
  – Adherence to ASN/ILSI North America guiding principles.
Featured, Food Safety, Food Technology, Nutrition / 09 Jan 2017

Industry Funded Science – Read This Before You Knock It!

About Dr. Taylor Wallace
I have always had a passion for food. When I was a kid, I basically lived in the kitchen with my grandmother (Manawa), a self-made homemaker, who taught me how to…

@DrTaylorWallace

www.drtaylorwallace.com
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:

\[ R-S \rightarrow CO_2 + Urea + H_2SO_4 \]

Human clinical trials where acid-base balance was pharmacologically manipulated with an alkaline source (e.g., potassium bicarbonate) showed a ↓ in bone resorption.

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.

\[\begin{align*}
\uparrow & \text{Bone resorption} \\
\downarrow & \text{BMD} \\
\uparrow & \text{Osteoporosis} \\
\uparrow & \text{Calcium excretion} \\
\downarrow & \text{Citrate excretion} \\
\uparrow & \text{Nephrolithiasis} \\
\uparrow & \text{Cortisol} \\
\uparrow & \text{Blood pressure} \\
\downarrow & \text{Lean body mass}
\end{align*}\]
In 25 studies, a positive linear relationship was found between urinary calcium excretion and net acid excretion.

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
J Bone Min Res. 2009;24:1835.
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.

### Fracture Risk (Calcium ≥ 525 mg/d)

<table>
<thead>
<tr>
<th>Diet Group</th>
<th>Men</th>
<th>Women</th>
<th>Men and Women</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>RR (95% CI)</td>
<td>N</td>
</tr>
<tr>
<td>Meat eater</td>
<td>172</td>
<td>1.00</td>
<td>851</td>
</tr>
<tr>
<td>Fish eater</td>
<td>34</td>
<td>0.90 (0.61-1.32)</td>
<td>214</td>
</tr>
<tr>
<td>Vegetarian</td>
<td>101</td>
<td>1.04 (0.79-1.38)</td>
<td>341</td>
</tr>
<tr>
<td>Vegan</td>
<td>11</td>
<td>0.80 (0.42-1.51)</td>
<td>20</td>
</tr>
</tbody>
</table>

2y RCT – Milk vs. Soy (25 g Protein)

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.

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

• 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.
• 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.
### Lumbar Spine BMD

<table>
<thead>
<tr>
<th>Study, Year (Ref)</th>
<th>Protein Dose</th>
<th>Follow-up</th>
<th>Plant</th>
<th>Animal</th>
<th>Net</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arjmandi 2005 (24)</td>
<td>25 g/d</td>
<td>1 y</td>
<td>35</td>
<td>27</td>
<td>$-0.21 (~7.29, 6.88)$</td>
</tr>
<tr>
<td>Kenny 2009 (23)</td>
<td>18 g/d</td>
<td>1 y</td>
<td>25</td>
<td>22</td>
<td>$-0.55 (~2.54, 1.45)$</td>
</tr>
<tr>
<td>Kreijkamp–Kaspers 2004 (25)</td>
<td>25.6 g/d</td>
<td>1 y</td>
<td>88</td>
<td>87</td>
<td>0.44 (~4.81, 5.70)</td>
</tr>
<tr>
<td>Vupadhyayula 2009 (27)</td>
<td>25 g/d</td>
<td>2 y</td>
<td>57</td>
<td>52</td>
<td>0.56 (~0.71, 1.83)</td>
</tr>
<tr>
<td>Overall (I-squared = 0.0%, p = 0.834)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.24 (~0.80, 1.28)</td>
</tr>
</tbody>
</table>

**NOTE:** Weights are from random effects analysis

(Favors Animal Protein) ↔ (Favors Soy Protein)

### Femoral Neck BMD

![Diagram showing the comparison between animal and soy protein on femoral neck bone mineral density (BMD).](image_url)

<table>
<thead>
<tr>
<th>Study, Year (Ref)</th>
<th>Protein Dose</th>
<th>Follow-up</th>
<th>Plant n</th>
<th>Animal n</th>
<th>Net %Change (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kenny 2009 (23)</td>
<td>18 g/d</td>
<td>1 y</td>
<td>25</td>
<td>22</td>
<td>0.50 (−1.79, 2.79)</td>
</tr>
<tr>
<td>Kreijkamp–Kaspers 2004 (25)</td>
<td>25.6 g/d</td>
<td>1 y</td>
<td>88</td>
<td>87</td>
<td>0.02 (−4.35, 4.39)</td>
</tr>
<tr>
<td>Vupadhyayula 2009 (27)</td>
<td>25 g/d</td>
<td>2 y</td>
<td>57</td>
<td>52</td>
<td>0.03 (−1.23, 1.29)</td>
</tr>
</tbody>
</table>

Overall (I-squared = 0.0%, p = 0.939)

- **(Favors Animal Protein) ⇐**
- **→ (Favors Soy Protein)**

*NOTE: Weights are from random effects analysis*

# Total Body BMD

<table>
<thead>
<tr>
<th>Study, Year (Ref)</th>
<th>Per Arm</th>
<th>Follow-up</th>
<th>Plant</th>
<th>Animal</th>
<th>Net</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arjmandi 2005 (24)</td>
<td>25 g/d</td>
<td>12 mo</td>
<td>35</td>
<td>27</td>
<td>0.00 (-5.03, 5.03)</td>
</tr>
<tr>
<td>Kenny 2009 (23)</td>
<td>18 g/d</td>
<td>12 mo</td>
<td>25</td>
<td>22</td>
<td>-0.17 (-1.06, 0.72)</td>
</tr>
<tr>
<td>Vupadhyayula 2009 (27)</td>
<td>25 g/d</td>
<td>24 mo</td>
<td>57</td>
<td>52</td>
<td>-0.29 (-1.03, 0.45)</td>
</tr>
<tr>
<td>Overall (I-squared = 0.0%, p = 0.976)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>-0.24 (-0.81, 0.33)</td>
</tr>
</tbody>
</table>

(Favors Animal Protein) ← → (Favors Soy Protein)

*NOTE: Weights are from random effects analysis*

# Shanghai Women’s Health Study

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

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

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

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

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

Taylor C. Wallace, PhD
Phone: (270) 839-1776
Email: taylor.wallace@me.com
Twitter: @drtaylorwallace
Facebook: /drtaylorwallace
www.drtaylorwallace.com
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