What is the Evidence for Supplement Use for Healthy Bones?
Osteoporotic Fractures in Women: Comparison With Other Diseases

Annual Incidence in the US x 1000

- **Osteoporotic Fractures**: 1,500,000
- **Heart Attack**: 500,000
- **Stroke**: 240,000
- **Breast Cancer**: 180,000

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# Risk Factors for Osteoporosis

<table>
<thead>
<tr>
<th>Lifestyle</th>
<th>Hormonal</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Poor diet</td>
<td>• Estrogen ↓</td>
</tr>
<tr>
<td>• Sedentary</td>
<td>• Thyroid ↑</td>
</tr>
<tr>
<td>• Thinness</td>
<td>• Glucocorticoids ↑</td>
</tr>
<tr>
<td>• Smoking</td>
<td></td>
</tr>
<tr>
<td>• Alcohol</td>
<td></td>
</tr>
<tr>
<td>• Prior fracture</td>
<td></td>
</tr>
</tbody>
</table>
Nutrients Related to Bone

- Protein
- Vitamin K
- Calcium
- Vitamin D
Bone Composition

- Mineral - 70%
- Protein - 22%
- Water - 8%
Protein
Protein Intake and Total Hip BMD in Caucasian Women (NHANES III)


* P < 0.01  † P < 0.05

Protein intake, g/day

Effects of Protein on Calcium Homeostasis

• Increases urine calcium losses
  (1 gm dietary protein → 1 mg urinary calcium loss)

• Stimulates production of IGF-1, a bone growth factor
Vitamin K
Vitamin K

- Vitamin K is required for the formation of osteocalcin
- Osteocalcin is the most abundant noncollagenous protein in bone matrix
- Osteocalcin acts as a regulator of bone mineralization
- In vitamin K deficiency, undercarboxylated osteocalcin is produced
- Undercarboxylated osteocalcin may not function normally
# Vitamin K Intake and Hip Fractures
Framingham Study 1988-1995
(888 subjects, 44 hip fractures)

<table>
<thead>
<tr>
<th>Q</th>
<th>Median vit K intake mcg/d</th>
<th>RR hip fracture</th>
<th>CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>56</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>105</td>
<td>0.53</td>
<td>0.22, 1.28</td>
</tr>
<tr>
<td>3</td>
<td>156</td>
<td>0.59</td>
<td>0.25, 1.39</td>
</tr>
<tr>
<td>4</td>
<td>254</td>
<td>0.35</td>
<td>0.13, 0.94</td>
</tr>
</tbody>
</table>

P for trend = 0.047

Calcium and Vitamin D
↓Calcium
↓Ca intake → absorption ← ↓ Vit D
↓
↓Circulating [Ca++]
↓
↑PTH
↓
↑Bone remodeling
↓
↑Bone loss → ↑ Fracture risk
Vitamin D Synthesis By Season and Latitude

What is the optimal 25(OH)D level?

The level that maximally suppresses PTH.
25OHD Level Needed to Maximally Suppress PTH

- 30 nmol/L – Lips
- 50 nmol/L – Malabanan and Holick
- 75 nmol/L – Peacock
- 80 nmol/L – Meunier
- 90 nmol/L – Krall and Dawson-Hughes
Intervention Studies

• Calcium

• Vitamin D

• Calcium + vitamin D
## Calcium Intake and Fracture Incidence - Intervention Studies

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>New Fracture Site</th>
<th>Significant reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chevalley ’94</td>
<td>18</td>
<td>vertebra</td>
<td>yes</td>
</tr>
<tr>
<td>Recker ’96</td>
<td>61</td>
<td>vertebra</td>
<td>yes*</td>
</tr>
<tr>
<td>Reid ’95</td>
<td>9</td>
<td>all sites</td>
<td>yes</td>
</tr>
<tr>
<td>Riggs ’98</td>
<td>40</td>
<td>all sites</td>
<td>no</td>
</tr>
</tbody>
</table>

* In subset with prior fracture
Vitamin D (400 IU/d) Does Not Alter Hip Fracture Rates

Intramuscular Vitamin D Lowers Clinical Fracture Rates

Effect of Calcium and Vitamin D on Fracture Rates in Very Elderly French Nursing Home Residents

Effect of Calcium and Vitamin D on Non-vertebral Fracture Rates in Healthy Men and Women

Stopping Calcium and Vitamin D Supplements – Effect on Femoral Neck BMD in Men

Effect of Estrogen ± Calcium on Change in BMD

<table>
<thead>
<tr>
<th>Age yrs</th>
<th>Calcium mg/d</th>
<th>Vitamin D UI/d</th>
</tr>
</thead>
<tbody>
<tr>
<td>30-50</td>
<td>1000</td>
<td>200</td>
</tr>
<tr>
<td>51-70</td>
<td>1200</td>
<td>400</td>
</tr>
<tr>
<td>71+</td>
<td>1200</td>
<td>600</td>
</tr>
<tr>
<td>Group</td>
<td>Age</td>
<td>% meeting Ca requirement</td>
</tr>
<tr>
<td>--------</td>
<td>-----------</td>
<td>--------------------------</td>
</tr>
<tr>
<td>Women</td>
<td>9 - 18</td>
<td>&lt;10</td>
</tr>
<tr>
<td></td>
<td>19 - 30</td>
<td>&lt;10</td>
</tr>
<tr>
<td></td>
<td>31 - 50.1</td>
<td>&lt;10</td>
</tr>
<tr>
<td></td>
<td>51 - 70</td>
<td>&lt;10</td>
</tr>
</tbody>
</table>
|        | 71+       | <1  
| Men    | 9 - 18    | 25                       |
|        | 19 - 30   | 50                       |
|        | 31 - 50.1 | 25                       |
|        | 51 - 70   | <10                      |
|        | 71+       | 5                        |

Estimates based on 1994 CSFII data
Conclusions

• Dietary protein and vitamin K
  - roles needs further definition
  - amounts > RDA may benefit bone
• Calcium and vitamin D
  - lower fracture rates in the elderly
  - dietary intakes are very low
  - supplements are needed