Vitamin D and Calcium: Role in Prevention and Treatment of Fractures and Falls

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- 29 studies, 63897 participants
  - 92% women
  - age 67.8 ± 9.7 years
  - 17 reported fracture, 24 reported BMD
  - 13 trials calcium + vitamin D

Bone loss
- ↓ 0.54% (0.35 – 0.73) hip
- ↓ 1.19% (0.76 – 1.61) spine

Meta-analysis of calcium +/- vitamin D

<table>
<thead>
<tr>
<th>Study</th>
<th>Calcium alone vs. calcium + vitamin D</th>
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</thead>
<tbody>
<tr>
<td>Chapuy-1</td>
<td>0.75 (0.64-0.87)</td>
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<tr>
<td>Reid</td>
<td>0.40 (0.35-1.08)</td>
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<tr>
<td>Chevalley</td>
<td>0.96 (0.35-2.66)</td>
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<tr>
<td>Recker</td>
<td>0.85 (0.55-1.30)</td>
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<tr>
<td>Dawson-Hughes</td>
<td>0.46 (0.23-0.89)</td>
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<tr>
<td>Riggs</td>
<td>0.89 (0.51-1.87)</td>
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<tr>
<td>Peacock</td>
<td>0.81 (0.48-1.43)</td>
</tr>
<tr>
<td>Chapuy-2</td>
<td>0.85 (0.64-1.13)</td>
</tr>
<tr>
<td>Larsen</td>
<td>0.84 (0.72-0.98)</td>
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<tr>
<td>Harwood</td>
<td>0.49 (0.33-0.77)</td>
</tr>
<tr>
<td>Fujita</td>
<td>0.31 (0.07-1.30)</td>
</tr>
<tr>
<td>RECORD-1</td>
<td>0.94 (0.77-1.15)</td>
</tr>
<tr>
<td>Portius</td>
<td>0.98 (0.79-1.23)</td>
</tr>
<tr>
<td>RECORD-2</td>
<td>0.94 (0.77-1.15)</td>
</tr>
<tr>
<td>Jackson</td>
<td>0.97 (0.92-1.03)</td>
</tr>
<tr>
<td>Reid-2</td>
<td>0.92 (0.78-1.14)</td>
</tr>
<tr>
<td>Prince-1</td>
<td>0.87 (0.68-1.10)</td>
</tr>
<tr>
<td>Overall</td>
<td>0.88 (0.83-0.95)</td>
</tr>
</tbody>
</table>

12% reduction in fracture risk, p=0.0004

No differences in fracture reduction

- Type of fracture
- Calcium alone vs. calcium + vitamin D
- Gender

Factors associated with higher effect

• Baseline low 25-OH vitamin D (< 10 ng/mL)
• Baseline calcium intake < 700 mg/day
• Institutionalized vs. community dwellers
• Age > 70 years
• Higher adherence
• Calcium doses > 1200 mg
• Vitamin D doses > 800 IU

Calcium

• Current recommendations
  – up to age 50: 1000 mg/day
  – ages 51+: 1200-1500 mg/day
  – maximum: 2500 mg/day
• Threshold nutrient—↑17% kidney stones in WHI!
• Labels based on 1000 mg
  3% = 30 mg
  25% = 250 mg

Calcium

• Active and passive absorption throughout small intestine
• Max intake at once ~ 500 mg
• Diet w/no calcium rich foods = 250 mg calcium
• Interferes with iron, thyroid hormone absorption
• Caffeine  OK in moderation with adequate calcium intake
• Soda

Sources of Calcium

• Dairy foods
• Lactose intolerance: hard cheeses, lactase treated dairy products
• Fortified cereal, OJ, cereal bars, soy/rice milk
• Tofu
• Dark green leafy vegetables—broccoli, cabbage, brussel sprouts, mustard greens
• http://www.nal.usda.gov/fnic/foodcomp/search/
• http://www.dairycouncilofca.org  “Calcium Quiz”

Calcium Supplements

- Citrate vs. Carbonate
- Coral calcium = calcium carbonate
- USP verified
- Chewable — Viactiv, GNC, Tums
- Vitamin D
  - sufficient → calcium absorp = 30%
  - insufficient → calcium absorp = 10%

Vitamin D

- Prevalence of vitamin D deficiency
  - 50% elderly hip fx patients
  - 67% of inpatients > age 65
  - 42% premenopausal African American women
  - 4%-5% premenopausal Caucasian women
  - 57% interns/residents in Brazil

- Current recommendations:
  - up to age 50: 200 IU/day
  - ages 51-70: 400 IU/day
  - ages 71+: 600 IU/day
  - maximum: 2000 IU/day

Musculoskeletal effects

- Muscle has vitamin D receptors, binding alters intracellular calcium release
- Most trials show improvements in muscle performance, reduced falls
- May depend on dose, regimen, baseline vitamin D status, adherence
### Holick et al. J Clin Endocrinol Metab 93: 677-81, 2008

Regulated by PTH (parathyroid hormone)

- Cholecalciferol (vitamin D3)
- 7-Dehydrocholesterol
- Liver
- 25-hydroxyvitamin D3
- Ergocalciferol

**Sunlight**

**Skin**

**1,25-dihydroxyvitamin D3**

Maintains calcium balance in the body


**Short term: D2 vs. D3**

- Change in 25(OH) D (nmol/L)
- Time (days)

**Vitamin D Therapy**

- All osteoporosis therapeutic trials conducted with calcium/vitamin D
- Mixed results in literature
  - Lower doses
  - More replete populations
  - Poor adherence
- Target serum level = at least 32 ng/mL
- Probably need > 800 IU/day
- 10,000 IU/day no adverse effects, 25-OH D levels ~ 90 ng/mL
**Sources of vitamin D**

- Sunshine: 20 minutes/day, 6% body surface
- Food
  - Milk 100 IU/glass
  - Cod liver oil: 453 IU/teaspoon
  - Tuna in fish oil: 170 IU/1/2 cup
  - Egg: 26 IU/large egg
- Supplements
  - Multivitamin: 200-400 IU +
  - GNC—D3: 1,000, 2,000
    - liquid (100 IU/drop), gummy (1,000 IU)
    - D3: 1,000, 5,000 (2600 IU), 50,000 (30,000) IU

**Summary**

- Calcium: 1200 mg/day—diet + supplements
- Vitamin D: 1200 IU/day
- Be alert for conditions that might need more
  - malabsorption (gastric bypass)
  - healing osteomalacia
  - fracture healing
  - anabolic therapy
  - adolescence
  - post operative hyperparathyroid
  - hypoparathyroid