Beyond the Break
Role of Vitamin D in Nutrition, Bone health and Osteoporosis Clinical: updates & practical considerations

Presenter: Hope Weiler, RD(CDO), PhD
Date: March 4, 2016
Disclosures

• OC Consultant 2013- ; OC Knowledge Transfer Committee 2013-2015
• Research funding CIHR, NSERC, CFI, Canada Research Chair 2005-2015, ESAC DFC
• Participated in systematic reviews for IOM:
  – Cranney et al 2007, Evid Rep Technol Assess (Full Rep) as co-author
  – Chung et al 2009, Evid Rep Technol Assess (Full Rep) as content reviewer
• Euro-pharm International Canada Inc., has provided in-kind product (Gallo et al, JAMA 2013)
Learning Objectives

By attending this workshop, physicians and health care professionals will have a strong understanding of:

- Epidemiology of osteoporosis, falls and fractures in Canada
- Practice guidelines in Canada for prevention and management of osteoporosis
- The physiology of vitamin D
- Measurement of vitamin D status and definitions
- Evidence behind recommendations – focus on vitamin D
- New concepts in vitamin D nutrition
  - falls and fracture prevention, lean body mass
Community residents

- **Risk factors:** female, aboriginal, income below 5th quintile, underweight.
  
  **Source:** 2009 Canadian Community Health Survey—Healthy Aging.

- **Men > 50 y overall - may be under-diagnosed - 6.6%**
  
  **Garriguet, Health Reports 2011;22:3.**

  **Tenenhouse et al, Osteoporos Int 2000.**
Canadians are living longer

Life expectancy continues to increase

<table>
<thead>
<tr>
<th>Year</th>
<th>Men (y)</th>
<th>Women (y)</th>
<th>Year</th>
<th>% ≥65 y</th>
<th>% ≥ 80 y</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000-02¹</td>
<td>77</td>
<td>82</td>
<td>2013</td>
<td>15.3</td>
<td>4.1</td>
</tr>
<tr>
<td>2007-09¹</td>
<td>79</td>
<td>83</td>
<td>2026</td>
<td>5.3</td>
<td></td>
</tr>
<tr>
<td>2041²</td>
<td>81</td>
<td>86</td>
<td>2030-45</td>
<td>22.8</td>
<td>9.6</td>
</tr>
</tbody>
</table>

Life expectancy at birth
¹Statistics Canada, CANSIM, table 102-0512 and Catalogue no. 84-537-XIE.
²Canada’s Aging Population, Health Canada, 2002, p. 5-6
³The Daily, Statistics Canada, Sept 17, 2014 (based on medium growth)
Osteoporosis/Fracture

- 57,413 osteoporosis-related fractures 2007/-8
  - 14.5 d mean hospital stay
  - Hip fractures accounted for half of the hospitalized d
- 112,740 emergency visits,
  - 85% wrist fx
- 3433 same day surgeries
  - 30% wrist
  - 23% hip
  - 30% other fractures
- $1.2 billion
  - Highest cost for multiple fractures and hip fractures ($20,163/hospitalization)
  - 53% of total costs hip fractures
- Continuing care
  - 91 additional days
  - Estimated $245 million in home care
    - 41% hip fractures

Tarride et al, Osteoporos Int, 2012
Injuries and Falls → Fracture

• Those 85 y or over
  – 70% more likely to have an injury
  – 60% more common in women
  – Falls are the main cause

• Falls
  – 65% of all injuries
  – 84% of injury-related admissions
  – 58% of injury-related deaths
  – Annual health care costs due to falls
    • $1.2 billion (50% due to hip fractures)

CCHS community surveillance

Falls and Osteoporosis in Canada

CANSIM Database 2008-2009 Statistics Canada
Prevention & management of osteoporosis – lifestyle including diet, supplements and exercise

☑ Exercise resistance &/or weight bearing activity
  • Improves physical function, pain, strength and balance

☑ Nutrition to build or preserve mineral mass

Before age 50 y:
  • High risk 800 to 2000 IU vitamin D/d

Over age 50 y:
  • Calcium 1200 mg/d total
  • Vitamin D 400-1000 IU/d; 800-1000 IU/d if high risk

Papaioannou et al, CMAJ 2010
Diagnosis of Osteoporosis: > 50 y

T-score below -2.5 = osteoporosis

Papaioannou et al, CMAJ 2010
Vitamin D + Ca for preventing fractures

Avenell et al, Cochrane Database of Systematic Reviews; 14 APR 2014 DOI: 10.1002/14651858.
### SUMMARY OF FINDINGS FOR THE MAIN COMPARISON

**Vitamin D (D2, D3 or 25(OH)D) plus calcium compared with control or placebo for preventing fractures in older people**

**Patient or population:** post-menopausal women and older people at risk of osteoporotic fractures  
**Settings:** community or institutional  
**Intervention:** vitamin D (D2, D3 or 25(OH)D) plus calcium  
**Comparison:** control or placebo

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Illustrative comparative risks* (95% CI)</th>
<th>Relative effect (95% CI)</th>
<th>No of Participants (studies)</th>
<th>Quality of the evidence (GRADE)</th>
<th>Comments Notes on assessment of the quality</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>Assumed risk</strong></td>
<td></td>
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<td></td>
<td><strong>Corresponding risk</strong></td>
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<tr>
<td>No vitamin D plus calcium</td>
<td>8 per 1000 (6 to 8)</td>
<td><strong>RR 0.84 (0.74 to 0.96)</strong></td>
<td>49,853 participants (9 trials)</td>
<td>☮️.ManyToManyField High</td>
<td></td>
</tr>
<tr>
<td>Vitamin D plus calcium</td>
<td>7 per 1000</td>
<td></td>
<td></td>
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<tr>
<td>Persons sustaining new hip fracture (1 year estimate)</td>
<td>Lower risk population²</td>
<td>54 per 1000 (40 to 52)</td>
<td><strong>RR 0.86 (0.78 to 0.96)</strong></td>
<td>10,380 participants (8 trials)</td>
<td>☮️河流域 High</td>
</tr>
<tr>
<td></td>
<td>High risk population³</td>
<td>45 per 1000 (40 to 52)</td>
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<tr>
<td>Persons sustaining new non-vertebral fracture (1 year estimate)</td>
<td>Overall population⁴</td>
<td>39 per 1000 (30 to 37)</td>
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</tbody>
</table>

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*Illustrative comparative risks are derived from the review authors. GRADE: Grading of Recommendations Assessment, Development and Evaluation.
Terminology
• Cholecalciferol or vitamin D₃
• Ergocalciferol or vitamin D₂
• Vitamin D
  – 1 μg = 40 IU vitamin D
• 25-hydroxyvitamin D or calcidiol
  – 1 ng/ml =~ 2.5 nmol/L
• 1,25(OH)₂D or calcitriol
Vitamin D

Dietary Sources

UVB

7-Dehydrocholesterol (present in the skin)

[25(OH)D] = status indicator

Sun, diet and supplements
50 nmol/L Health Canada/IOM
75 nmol/L Osteoporosis Canada

Modified from Norman, A. W
Am J Clin Nutr 2008;88:1455-1456
<table>
<thead>
<tr>
<th>Age</th>
<th>Vitamin D RDA</th>
<th>Vitamin D UL</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>µg (IU)</td>
<td>µg (IU)</td>
</tr>
<tr>
<td>0 - 6 mo</td>
<td>(AI: 400 IU)</td>
<td>1000</td>
</tr>
<tr>
<td>7 - 12 mo</td>
<td>(AI: 400 IU)</td>
<td>1500</td>
</tr>
<tr>
<td>1 - 3 y</td>
<td>600</td>
<td>2500</td>
</tr>
<tr>
<td>4 - 8 y</td>
<td>600</td>
<td>3000</td>
</tr>
<tr>
<td>9 - 18 y</td>
<td>600</td>
<td>4000</td>
</tr>
<tr>
<td>19 - 50 y</td>
<td>600</td>
<td>4000</td>
</tr>
<tr>
<td>50 - 70 y</td>
<td>600</td>
<td>4000</td>
</tr>
<tr>
<td>&gt; 70 y</td>
<td>800</td>
<td>4000</td>
</tr>
</tbody>
</table>
Chart 1
Distribution of vitamin D levels in Canadians aged 3 to 79, by age group, household population, Canada, 2012 to 2013

Source: Canadian Health Measures Survey, 2012 to 2013

www.statcan.gc.ca 2014-12-16.
Serum 25-hydroxyvitamin D and risk of major osteoporotic fractures in older U.S. adults

Looker et al, 2013 JBMR

Journal of Bone and Mineral Research
http://onlinelibrary.wiley.com/doi/10.1002/jbmr.1828/full#fig1
Tests are now indicated only for individuals with specific conditions:

- Osteoporosis, rickets, osteomalacia, malabsorption syndromes, renal disease and if taking medications that may affect vitamin D status

https://www.cadth.ca/media/pdf/htis/jan-2015/RC0626%20Vitamin%20D%20Testing%20Final.pdf
Endogenous Synthesis

- Moderately fair-skinned 6 to 7 min/d mid-morning to mid-afternoon on most days to maintain vitamin D status
- Risk of low status:
  - Housebound, community-dwelling older people
  - Disabled people
  - Residential care
  - Dark-skinned people
  - Clothing coverage
  - Regular avoidance of sun
  - Indoor workers

Exogenous Intakes

- In countries with no fortification policy, most adults are likely to achieve 5 to 10% of needs by food
- If sun exposure is minimal
  - 600 IU/d people < 70 y
  - 800 IU/d people > 70 y
  - High risk may require higher dosages

“Vitamin D and health in adults in Australia and New Zealand: a position statement”
Nowson et al, 2014 MJA
Potential contribution to dietary vitamin D intake

- Fluid milk (~100 IU or 2.5 μg/250 ml)
  - 19-50 y: 2 servings ~200 IU or 5 μg/d
  - 51+ y: 3 servings ~300 IU or 7.5 μg/d
  - > 50 y: 3 servings + 400 IU/10 μg supplement

= 700 IU or >15 μg/d
Dietary Patterns:

- It is possible to achieve intakes mostly from food as long as compliance to food and supplements is high.

<table>
<thead>
<tr>
<th>Food</th>
<th>Vitamin D (IU)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Milk 3 cups/d</td>
<td>300 (or 2 enriched)</td>
</tr>
<tr>
<td>Orange juice 0.5 cup/d</td>
<td>50</td>
</tr>
<tr>
<td>Egg whole/d</td>
<td>25</td>
</tr>
<tr>
<td>Pink Salmon 7 oz/wk</td>
<td>171</td>
</tr>
<tr>
<td>Yoghurt 175 g made with fortified milk</td>
<td>44</td>
</tr>
<tr>
<td>Margarine 4 tsp/d</td>
<td>100</td>
</tr>
<tr>
<td>Supplement</td>
<td>400 Total=1090 IU</td>
</tr>
</tbody>
</table>

May be feasible at most ages from childhood to aging
### Vitamin D Intakes of Canadians from Food (CCHS; mean μg/d)

<table>
<thead>
<tr>
<th>Age (y)</th>
<th>Males and Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-3</td>
<td>6.5</td>
</tr>
<tr>
<td>4-8</td>
<td>6.0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Age (y)</th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>9-13</td>
<td>7.0</td>
<td>5.7</td>
</tr>
<tr>
<td>14-18</td>
<td>7.6</td>
<td>5.0</td>
</tr>
<tr>
<td>19-30</td>
<td>5.9</td>
<td>4.7 (188 IU)</td>
</tr>
<tr>
<td>31-50</td>
<td>5.8</td>
<td>5.2 (208 IU)</td>
</tr>
<tr>
<td>51-70</td>
<td>7.1 (284 IU)</td>
<td>5.0 (200 IU)</td>
</tr>
<tr>
<td>&gt;70</td>
<td>6.3 (252 IU)</td>
<td>5.3 (212 IU)</td>
</tr>
</tbody>
</table>

- 5 μg = 200 IU
- 10 μg = 400 IU
- 15 μg = 600 IU

#### Milk products intake
- 51-70 y: <1.4 servings
- >70 y: <1.4 servings

#### Canadian seniors on average meet less than ¼ of the recommended servings of milk products.
Milk Intakes by Canadians

Percentage below recommended minimum number of servings of milk products, by age group and sex, household population ages 4 or older, Canada excluding territories, 2004.

49% of vitamin D intake from food is derived from milk
Response of 25(OH)D to 1 µg or 40 IU:
• Supplementation: elevates by 1.4 nmol/L
• Food: elevates by 3.1 nmol/L
• Summer: 14 nmol/L higher

Barake et al, J Nutr 2010
Random-effects meta-analysis comparing the effects of daily and bolus supplementation of D3 with that of D2 on net changes in serum 25(OH)D concentrations.

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>D3</th>
<th>D2</th>
<th>Mean Difference IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biancuzzo 2010-1 (7)</td>
<td>23.3</td>
<td>27</td>
<td>-3.70 [-14.35, 6.95]</td>
</tr>
<tr>
<td>Biancuzzo 2010-2 (7)</td>
<td>32</td>
<td>26.5</td>
<td>5.50 [-8.99, 19.99]</td>
</tr>
<tr>
<td>Binkley 2011-1 (15)</td>
<td>23</td>
<td>15.3</td>
<td>7.70 [-10.73, 26.13]</td>
</tr>
<tr>
<td>Binkley 2011-2 (15)</td>
<td>22.3</td>
<td>9</td>
<td>13.30 [1.69, 24.91]</td>
</tr>
<tr>
<td>Glendenning 2009 (16)</td>
<td>40</td>
<td>26</td>
<td>14.00 [1.27, 26.73]</td>
</tr>
<tr>
<td>Heaney 2011 (17)</td>
<td>98.4</td>
<td>57.4</td>
<td>41.00 [23.46, 58.54]</td>
</tr>
<tr>
<td>Holick 2008 (6)</td>
<td>23.3</td>
<td>24.8</td>
<td>-1.50 [-10.23, 7.23]</td>
</tr>
<tr>
<td>Romagnoli 2008-1 (5)</td>
<td>70.2</td>
<td>25.5</td>
<td>44.70 [26.13, 63.27]</td>
</tr>
<tr>
<td>Romagnoli 2008-2 (5)</td>
<td>65.4</td>
<td>23.1</td>
<td>42.30 [19.23, 65.37]</td>
</tr>
<tr>
<td>Trang 1998 (4)</td>
<td>23.3</td>
<td>13.7</td>
<td>9.60 [2.77, 16.43]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>194</td>
<td>150</td>
<td>15.23 [6.12, 24.34]</td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 162.74; Chi² = 47.10, df = 9 (P < 0.00001); I² = 81%
Test for overall effect: Z = 3.28 (P = 0.001)

mean difference D₃ over D₂: 15.23; 95% CI: 6.12, 24.34; P = 0.001

Taking the same vitamin D with the largest meal improves absorption and higher serum levels of 25-hydroxyvitamin D

Meal conditions affect absorption of vitamin D₃ but not status response

50,000 IU tablet every 3 mo.

Like letters indicate different P≤0.04
VITAMIN D ENDOCRINE SYSTEM

VITAMIN D₃

DIETARY SOURCES

25(OH)D₃

BLOOD

LIVER

24-HYDOXYLASE

KIDNEY

25(OH)D₃

1-25(OH)D₃

1α,25(OH)₂D₃

PARATHYROID HORMONE

ENDOCRINE MODULATORS

ESTROGEN

CALCIUM IN GROWTH HORMONE

PRLACTIN

INSULIN

GLUCOCORTICOIDS

PARATHYROID HORMONE

SHORT FEEDBACK LOOP

LONG FEEDBACK LOOP

VITAMIN D₃

7-DEHYDOCHOLESTEROL

(SUNLIGHT)

37 CHEMICALLY CHARACTERIZED METABOLITES

DIETARY SOURCES

BLOOD

LIVER

DIETARY SOURCES

BLOOD

VDR PRESENT IN 37 TISSUES

Genomic and/or Rapid Responses

SELECTED BIOLOGICAL RESPONSES

AWN 2008

• **Muscle strength**
  – Standardized mean difference 0.17 (P=0.02).
  – >65 y standardized mean difference of 0.25 (0.01 to 0.48) vs younger 0.03 (-0.08 to 0.14)

• **Muscle Mass**
  – NS

• **Muscle Power**
  – NS

Beaudart et al 2014
Falls in community – Vitamin D supplementation helps if low status

Rate of falls: RaR 0.57 (0.37-0.89); Risk of falls: RR 0.70 (0.56-0.87)

“Overall vitamin D did not reduce rate of falls or risk of falling; but may do so in people with lower vitamin D levels before treatment”

Gillespie et al 2012
Vitamin D and Falls

Review: Interventions for preventing falls in older people in care facilities and hospitals
Comparison: Vitamin D supplementation vs no vitamin D supplementation (care facilities)
Outcome: Rate of falls

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Vitamin D</th>
<th>N</th>
<th>No vitamin D</th>
<th>N</th>
<th>log [Rate ratio] (SE)</th>
<th>Rate ratio IV,Random,95% CI</th>
<th>Weight</th>
<th>Rate ratio IV,Random,95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Vitamin D3 + calcium vs calcium</td>
<td>Bischoff 2003</td>
<td>62</td>
<td>60</td>
<td>-0.67 (0.41)</td>
<td>10.9 %</td>
<td>0.51 [0.23, 1.14]</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Flicker 2005</td>
<td>313</td>
<td>312</td>
<td>-0.31 (0.13)</td>
<td>29.9 %</td>
<td>0.73 [0.57, 0.95]</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>40.8 %</td>
<td>0.71 [0.56, 0.90]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: Tau² = 0.0; Chi² = 7.0; df = 1 (P = 0.40); I² =0.0%</td>
<td>Test for overall effect: Z = 2.77 (P = 0.0057)</td>
<td></td>
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<tr>
<td>2 Vitamin D2 vs usual care or placebo</td>
<td>Broe 2007 (1)</td>
<td>23</td>
<td>25</td>
<td>-1.27 (0.51)</td>
<td>7.9 %</td>
<td>0.28 [0.10, 0.76]</td>
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<tr>
<td></td>
<td>Lavv 2006</td>
<td>1762</td>
<td>1955</td>
<td>-0.14 (0.04)</td>
<td>36.2 %</td>
<td>0.87 [0.80, 0.94]</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>44.1 %</td>
<td>0.55 [0.39, 0.74]</td>
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<tr>
<td>Heterogeneity: Tau² = 0.51; Chi² = 4.88; df = 1 (P = 0.03); I² =80%</td>
<td>Test for overall effect: Z = 1.07 (P = 0.29)</td>
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<tr>
<td>3 Multivitamins (including vitamin D3 + calcium) vs placebo</td>
<td>Grieger 2009</td>
<td>48</td>
<td>43</td>
<td>-0.97 (0.32)</td>
<td>15.1 %</td>
<td>0.38 [0.20, 0.71]</td>
<td></td>
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</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>15.1 %</td>
<td>0.38 [0.20, 0.71]</td>
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<tr>
<td>Heterogeneity: not applicable</td>
<td>Test for overall effect: Z = 3.03 (P = 0.0024)</td>
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<tr>
<td><strong>Total (95% CI)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>100.0 %</td>
<td>0.63 [0.46, 0.86]</td>
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<tr>
<td>Heterogeneity: Tau² = 0.07; Chi² = 14.08; df = 4 (P = 0.01); I² =72%</td>
<td>Test for overall effect: Z = 2.87 (P = 0.0041)</td>
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<tr>
<td>Test for subgroup differences: Chi² = 3.43, df = 2 (P = 0.18), I² =42%</td>
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</tbody>
</table>

(1) 800 IU vitamin D group only vs placebo

Cameron et al, 2012
Vitamin D in Skeletal Muscle

Skeletal Muscle Cell (Myocyte)

**Gene transcription:**
- IGF-1
- VDR
- calmodulin
- type 2 muscle CSA

**Non-genomic effects**

**Mitochondria**

**CYP27B1**

**Blood vessel**

**25(OH)D**

**1,25(OH)\(_2\)D**

**VDR**

**RXR**

**VDRE**
C2C12 muscle cell 1α-hydroxylase

With authors’ permission; Girgis et al, Endocrinology 2014
Skeletal Muscle Cell Vitamin D Metabolism

C2C12 muscle cell - functional 1α-hydroxylase - less proliferation and greater myotube diameter

With authors’ permission; Girgis et al, Endocrinology 2014
Vitamin D supplementation elevates VDR in muscle biopsies

$1,25(OH)_2 D$ dose-dependently elevates VDR mRNA expression ($\uparrow 36\%$) in human primary myoblasts from healthy young adults

Pojednic et al, Calcif Tissue Int, 2014
Vitamin D supplementation elevates VDR in muscle biopsies

- 16 wk trial of 4000 IU/D vs placebo in 8 older men and 12 women elevates VDR gene expression in muscle biopsies.
- VDR protein higher if vitamin D sufficient $p=0.02$, regardless of trial group.

Pojednic et al, Calcif Tissue Int, 2014
Vitamin D supplementation elevates muscle VDR and fibre size

- 4 mo trial
- Women > 65 y
- 4000 IU vitamin D vs placebo
- 25(OH)D 43.6 to 80.0 nmol/L in treatment group; NS change in placebo.

Ceglia et al, JCEM 2013
Vitamin D supplementation trial after stroke

- 2-y trial of 1000 IU vitamin D$_2$ vs placebo
- Women (n=96) after stroke
- Baseline 25(OH)D < 25 nmol/L
- Treatment:
  - ↑ relative number and size of type II muscle fibres
  - Improved muscle strength
  - 59% reduction in falls (95% CI, 28-81, p=0.03)
  - Fewer hip fractures (4/48 vs 0/48, p=0.049)

Sato et al Cerebrovasc Dis 2005
From: Exercise and Vitamin D in Fall Prevention Among Older Women: A Randomized Clinical Trial


- 2-y double blind RCT 800 IU/d with and without exercise vs placebo
- Women 70-80 y, home-dwelling, Finland
- \(25(\text{OH})\text{D} > 65 \text{nmol/L}\) at baseline
- Primary outcome: falls
- Vitamin D maintained femoral neck BMD and increased tibial trabecular BMD, but did not alter muscle strength or balance.

Figure Legend:
Hazard Ratios (95% CIs) for Fallers, Injured Fallers, and Multiple Fallers Using the Placebo Without Exercise Group as the Reference
Cumulative hazard is presented for the injured fallers.\(^a\)P < .05 compared with the placebo without exercise group.
• Osteoporosis and falls are similarly common in Canadian women > 65 y; dx in men is less common
• Osteoporosis Canada recommends calcium, vitamin D and activity in the prevention and management of osteoporosis
• Most Canadians have good vitamin D status
• For those with low vitamin D status
  – Benefits of achieving good vitamin D status may realized as improved:
    • musculoskeletal health, bone density, muscle mass, falls prevention
Acknowledgements

CRC Tier I, Nutrition and Health Across the Lifespan

McGill

Canada Research Chairs
Vitamin D Food Policy in Canada

• Mandated fortification
  – Milk ~100 IU/cup
  – Margarine ~25 IU/tsp

• Food label panels
  **Nutritional Facts**
  – 1983 recommendations
    • 200 IU/d RNI vs
  – 2011 recommendations
    • 600 to 800 IU/d RDA