Vitamin D: Who is really at risk of deficiency?

Stephanie A Atkinson, PhD, DSc (Hon), FCAHS
Professor, Department of Pediatrics,
McMaster University
McMaster Children’s Hospital
Information Overload on Vitamin D

D-lemmas of D!
Five Vitamin D-lemmas

• Why do we need it?
• How much do we need?
• How to measure vitamin D status?
• Who is at risk of deficiency?
  o General Canadian population
  o Clinical disorders
• How do we optimize D status?
**Synthesis, Metabolism & Functions of Vitamin D**

**Vitamin D**

- Sunlight
- 7-dehydrocholesterol in skin
- Liver
- Dietary Sources
  - Foods containing D3

**25(OH)D**
- Major Circulating Metabolite

**1,25(OH)₂D**
- Active Metabolite

- Kidneys
- Pancreas
- Placenta
- Lungs, Colon, Skin, Prostate, Breast
- Macrophage

**Biological Effects**

- Impacts calcium homeostasis
- Aids blood pressure regulation
- Promotes bone formation
- Improves cardiovascular health
- Aids neurodevelopment
- Facilitates insulin secretion
- Influences fetal programming and placental development
- Supports placental calcium transfer for fetal bone mineral accrual
- Regulates cell cycle
- Inhibits cell proliferation
  - Apoptosis regulation
  - Angiogenesis inhibition
- Regulates auto-immune response
- Enhances innate immunity
- Immunomodulation

*Lockau & Atkinson 2017*
#2 Vitamin D-lemma

• How much do we need?
  
  o Dietary Reference Intakes (DRIs)

  o Other recommendations – why do they exist?
## DRI for Vitamin D

<table>
<thead>
<tr>
<th>Age Group</th>
<th>EAR (µg)/day</th>
<th>RDA, IU(µg)/day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infants to 1 yr</td>
<td>400</td>
<td>600 (15)</td>
</tr>
<tr>
<td>1-70 yr</td>
<td>400</td>
<td>600 (15)</td>
</tr>
<tr>
<td>&gt;70 yr</td>
<td>400</td>
<td>800* (20)</td>
</tr>
<tr>
<td>Pregnancy/lactation</td>
<td>400</td>
<td>600 (15)</td>
</tr>
</tbody>
</table>

* Higher due to greater variability in needs in older persons
How much is too much Vitamin D?

Upper Level - IU/d (µg)

Infants: 1000-1500 (25-38 µg)
1-3 yr: 2500 (63 µg)
4-8 yr: 3000 (75 µg)
9 yr+: 4000 (100 µg)

Basis

» Hypercalcemia of hypervitaminosis D
Dilemma.....

Why do different vitamin D recommendations exist from other agencies???
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>19-70</td>
<td>600</td>
<td>800-1000 (2000 &gt; 50 y)</td>
<td>1500-2000</td>
</tr>
<tr>
<td>&gt; 70</td>
<td>800</td>
<td>800-2000</td>
<td>1500-2000</td>
</tr>
<tr>
<td>Pregnancy Lactation</td>
<td>600</td>
<td>-</td>
<td>1500-2000</td>
</tr>
<tr>
<td>UL</td>
<td>&gt; 9 y 4000</td>
<td>-</td>
<td>1-18 y – 4000 &gt;19 y – 10,000</td>
</tr>
</tbody>
</table>
Rationale for Vitamin D Guidelines*

- DRIs for general **healthy** populations not therapeutic guidelines – systematic review

- Osteoporosis Canada – target is adults at **risk of osteoporosis** – systematic review

- US Endocrine Society – **not based on systematic review** – different targets for vitamin D status and deficiency criteria and populations at risk

  (Rosen LJ & IOM DRI committee. JCEM 2012)

* Citations for Guidelines on last slide
#3 Vitamin D-lemma

- Is vitamin D status easily measured?
  - What to assess?
  - What are normal values?
  - Who to assess?
  - Health authority regulations?
Measure of Vitamin D Status

- Vitamin D3
- 7-dehydrocholesterol (skin)
- Precholecalciferol
- Cholecalciferol (D3)
- Ergocalciferol (D2)
- 25(OH)D bound to DBP
  - 24,25(OH)2D (inactive)
  - 1,25(OH)2D (active hormone; acts on VDRs)

Wagner CL et al. Nutrients 2012 (Breastfeed Med 2008)
Definitions for Vitamin D Status by IOM

ADEQUATE

Severe Deficiency  EAR  RDA > 50 nM for bone health

Cut-off Values by IOM DRIs (2011)*

0  30  40  50  125

Serum 25OHD, nmol/L

*IOM. DRI for calcium and vitamin D. NAP, Washington. 2011
## “Other” Normal Values

<table>
<thead>
<tr>
<th>Vit D Status</th>
<th>DRI US/CAN 2010</th>
<th>US Endocrine Society 2010</th>
<th>Other (clinical labs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severely Deficient</td>
<td>&lt;30</td>
<td>&lt;25</td>
<td>&lt;30</td>
</tr>
<tr>
<td>Insufficient</td>
<td>30-40</td>
<td>50-75</td>
<td>&gt;30 &lt;75</td>
</tr>
<tr>
<td>Adequate/Sufficiency</td>
<td>&gt;50</td>
<td>&gt;75</td>
<td>&gt;75/80</td>
</tr>
<tr>
<td>Excess</td>
<td>&gt;150 for UL</td>
<td>&gt;250</td>
<td></td>
</tr>
</tbody>
</table>
Clinical Utility of Vitamin D Testing

Ontario Health Technology Advisory Committee (OHTAC)*

• Vitamin D tests in Ontario
  • mostly requested by patients → soared in 5 yr
  • 2004 - 30,000
  • 2008 - 400,000
  • 2009 - over 730,000

• COST
  • 2008 - $7.1M
  • 2009 - $66 M

Testing of Vitamin D Status

OHTAC – 2010 Recommendations

• No routine vitamin D testing in general population
  o Vitamin D intake/supplementation recommended by Health Canada through education

• OHIP (and other provinces) pay for testing only for:
  o osteoporosis, rickets, osteopenia, malabsorption syndromes, and renal disease or drugs that affect vitamin D metabolism.

Report at:
#3 Vitamin D–lemma

Is status easily measured? → YES

- Not necessary for most people, unless uncertain of intake
- May be costly if not clinically indicated
#4 Vitamin D-lemma

Are Canadians at risk of vitamin D deficiency?
Vitamin D Status of Canadians

Canadian Health Measures Survey

Cross sectional survey: 3 to 79 y
N= ~5600 subjects/cycle in 15-18 sites

Cycle 1: Mar 2007 to Feb 2009
Cycle 2: Sept 2009 to Dec 2011
Cycle 3: Jan 2012 to Dec 2013
Cycle 4: Jan 2014 to Dec 2015

Analysis of data across Cycles 1-3

SPJ Brooks et al. JAOAC Intern 2017
### Vitamin D Status in Canadians: 2012-13

**Chart 1**
Distribution of vitamin D levels in Canadians aged 3 to 79, by age group, household population, Canada, 2012 to 2013

<table>
<thead>
<tr>
<th>Age Group</th>
<th>&lt;30 nmol/L</th>
<th>30 to &lt;50 nmol/L</th>
<th>≥50 nmol/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>10%</td>
<td>20%</td>
<td>8%</td>
</tr>
<tr>
<td>3 to 11 years</td>
<td>6%</td>
<td>25%</td>
<td>27%</td>
</tr>
<tr>
<td>12 to 19 years</td>
<td>8%</td>
<td>30%</td>
<td>20%</td>
</tr>
<tr>
<td>20 to 59 years</td>
<td>12%</td>
<td>27%</td>
<td>6%</td>
</tr>
<tr>
<td>60 to 79 years</td>
<td>20%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Source:** Canadian Health Measures Survey, 2012 to 2013

http://www.statcan.gc.ca/pub/82-625-x/2014001/article/14125-eng.htm
Variables in vitamin D status*

- **Diet**
  - Servings milk/d
  - Servings fatty fish/d
  - Supplement use

- **Sun exposure**
  - UVB rays by season
  - Sunscreen SPF

- **Subject characteristics**
  - Age and sex
  - White/non-White
  - Serum cholesterol
  - BMI

*Significant in multiple regression model. SPJ Brooks et al. JAOAC Intern 2017*

80-90% of Canadians had vit D intakes <EAR

Since deficient status occurs in only 10%; sun exposure must be a major contributor

http://www.hc-sc.gc.ca/fn-an/surveill/nutrition/commun/art-nutr-adol-eng.php#a331
Vitamin D Status by Milk Consumption

Chart 2
Average vitamin D blood levels, by milk consumption, by age group

nmol/L

<table>
<thead>
<tr>
<th>Age group</th>
<th>Had milk once or more a day</th>
<th>Had milk less than once a day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>68</td>
<td>59</td>
</tr>
<tr>
<td>3 to 5</td>
<td>75</td>
<td>60</td>
</tr>
<tr>
<td>6 to 11</td>
<td>68</td>
<td>60</td>
</tr>
<tr>
<td>12 to 19</td>
<td>67</td>
<td>57</td>
</tr>
<tr>
<td>20 to 39</td>
<td>63</td>
<td>58</td>
</tr>
<tr>
<td>40 to 59</td>
<td>68</td>
<td>58</td>
</tr>
<tr>
<td>60 to 79</td>
<td>75</td>
<td>64</td>
</tr>
</tbody>
</table>

Note: 1. Data are from Cycle 2 of the Canadian Health Measures Survey, collected from August 2009 to November 2011.
Source: Statistics Canada, Canadian Health Measures Survey.
Vitamin D Supplements Alter Status

CHMS Cycle 2007-13

In ~21% subjects taking D-supplements:
- s25OHD changes by season (#3 is summer) similar to non-sup users;
- s25OHD higher by 11 nmol/L

Note: D-supplement use rose from 2004 to 2015, especially > 31 yr (StatsCan, 6/17)

~ 11 nmol/L

SPJ Brooks et al. JAOAC Intern 2017

Figure 5. 25(OH)D concentrations as a function of the quarter of the year and supplement consumption. Symbols represent LSM ± SE (n = 500 bootstrap determinations; obtained from the regression analysis) for participants consuming vitamin D-containing supplements (filled circles) and participants who did not consume supplements (open circles).
Vitamin D & Population Diversity
Vitamin D Status by Skin Colour

Chart 2
Distribution of vitamin D levels of Canadians aged 3 to 79, by racial background, household population, Canada, 2012 to 2013

% Vitamin D Deficient or Insufficient

<table>
<thead>
<tr>
<th>Racial Background</th>
<th>Vitamin D Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>White</td>
<td></td>
</tr>
<tr>
<td>6%</td>
<td></td>
</tr>
<tr>
<td>21%</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td></td>
</tr>
<tr>
<td>20%</td>
<td></td>
</tr>
<tr>
<td>38%</td>
<td></td>
</tr>
</tbody>
</table>

Source: Canadian Health Measures Survey, 2012 to 2013

http://www.statcan.gc.ca/pub/82-625-x/2014001/article/14125-eng.htm
Multi-ancestry Canadians  
~ 21 yr old university students

Gozdzik et al. BMC Public Health 2008 8:336
Vitamin D Status at 3-17 years by BMI

Overweight/obese: 31% children

Chart 3
Percentage of children and youth aged 3 to 17, by vitamin D level and body mass index,\(^1\) household population, Canada, 2012 to 2013

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E use with caution (data with a coefficient of variation (CV) from 16.6% to 33.3%)

F too unreliable to be published (data with a coefficient of variation (CV) greater than 33.3%; suppressed due to extreme sampling variability)

\(^1\) Body mass index (BMI) classification based on de Onis M et al. (2007). For 3 and 4 year olds, "overweight" also includes those who are considered to be "at risk for overweight".

Source: Canadian Health Measures Survey, 2012 to 2013

http://www.statcan.gc.ca/pub/82-625-x/2014001/article/14125-eng.htm
Vitamin D Status & BMI

- s25OHD ↓ with ↑ BMI
- Varies by racial grouping

SPJ Brooks et al. JAOAC Intern 2017
Summary: Vitamin D Status (2007-13)

Adequate (serum 25OHD > 50 nmol/L)
- a level sufficient for healthy bones for most people

• ~68% of all Canadians; most children 3 to 5 yr
• Adequacy more prevalent in:
  o White vs non-White
  o Vitamin D supplement users
  o Normal weight vs obese
  o Summer vs winter
  o Milk and fish consumers

Deficient (< 30 nmol/L) ~ 10% Canadians
  ~ 20% non-White
#5 Vitamin D-lemma

Who is risk of sub-optimal D status?

- Low sun exposure
  - Skin pigment
  - Full-coverage clothing
  - Live/work/play indoors
- Non-milk and non-fish eaters
- Non-supplement users
- Obese due to sequestration of vitamin D in adipose tissue
- Breast-fed without D supplements

NO SURPRISES here!!!!!!!!!!
Clinical Risks of Vitamin D Deficiency
Vitamin D Deficiency Rickets in Children: A national travesty

- 2002-4 - Canadian Pediatric Surveillance Program (CPSP); n=2400 pediatricians
  - N= 104 cases of rickets
    - Radiographic rickets in 93% cases at mean age of 1.4 y
    - Vit D deficiency in 75%: 25OHD=15 nmol/L (6 ng/ml)
  - Demographics: 93% term infants
    - 10% Caucasian; 24% Inuit/First Nations; 33% black
    - 96% breast-fed (mean 14 wk)
    - 86% NO vitamin D supplements
2015: Rickets still striking Canadian kids

• 2014-15 – one-time survey of 671 pediatricians

• N= 149 cases reported by 58 MDs
  • 48 radiographic rickets - ~67% 0-2 yr; 23% 3-8 yr
  • 101 severe symptomatic vit D deficiency but no rickets - ~26% 0-2 yr; ~26% 3-8 yr; 48% > 9 yr

• Symptoms: hypotonia/weakness; delayed milestones; fractures; poor dentition; cardiomyopathy; respiratory distress; seizures

• Demographics: intermediate/dark skin; exclusive breast feeding; no vit D supplement

Prevention of Rickets in Kids

- **Pregnancy**
  - Ensure dietary sources & vitamin D supplement (600 IU/d)

- **Infants** – Breast-fed±formula 0-2 y
  - Vitamin D drops supplement @ 400 IU/d

- **Toddlers and children**
  - D-fortified beverage – milk, soy, other plant-based
  - Or supplement @ 600 IU/d
Clinical Disorders of Vitamin D Deficiency

- Kidney disease
- Malabsorption syndromes
- Severe liver disease
- Drug interactions: anticonvulsants, cimetidine, thiazides, corticosteroids
- Drugs that decrease absorption: mineral oil, laxatives orlistat, cholestyramine etc.
Clinical Disorders – Malabsorption of vitamin D

- celiac disease
- cystic fibrosis
- inflammatory bowel diseases, Crohn’s > ulcerative colitis
- short bowel syndrome
- autoimmune hepatitis
- small intestinal bacterial overgrowth
- lactose intolerance

Therapy include high dose vitamin D supplements > RDA and possibly UV tanning beds or moderate sun exposure
Approaches to Ensure Optimal Vitamin D Status in Canadians
Vitamin D in Fortified Food

**Fortification IU/100g**

**Mandatory**
Cow milk (42)
Margarine (530)

**Optional**
Cereals (350)
Grains/pasta (90)
Fruit juice (40)
Plant milks (42)
Health Canada recognizes that it is challenging for Canadians to consume the recommended amounts of vitamin D through the current food supply.

**GOAL**

To address insufficient vitamin D in the food supply to allow Canadians to meet intake recommendations & reduce current vitamin D inadequacy (20%) & deficiency (8%)

Health Canada to Increase D-Fortification

New vitamin D fortification strategy

• **Phase 1** - Double vitamin D in cow and goat milk (2 µg/100 mL) & margarine (26 µg/100g) by amendment to Food and Drugs Regulations – may take to 2022 to implement
  • Permit vitamin D fortification of yogurt and fortified plant-based beverages equal to milk

• **Phase 2** – permit addition of vitamin D to other vehicles based on popularity of consumption in subpopulations at risk of vitamin D deficiency and inadequacy (dark skin & obese).

Vitamin D–lemmas: Current status

**Issues**: Well documented with CHMS data

**Resolutions**:
- Target risk groups with education & food sources
  - Breast-fed infants to 2 yr
  - Non-white – especially very dark skin
  - Low sun exposure – living indoors, clothing coverage
  - Overweight due to sequestration of vit D in adipose
  - Non-milk/non-fatty fish eaters

- Improved vitamin D availability in food supply - FDR

- Need implementation strategies in community
  - Health Canada
  - Public health initiatives
  - School Boards
Options to Increase Intake of Vitamin D

The body itself makes vitamin D when it is exposed to the sun.

Cheese, butter, margarine, fortified milk, fish, and fortified cereals are food sources of vitamin D.

- D₃
- D₂
- Fish oil
- Vegan
- Organic
- Gluten-free

- Capsule
- Gel cap
- Drop
- Liquid
- Flavoured
- Chewable
D'end of D-lemmas!

THANK YOU!
Key References

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