AVAILABILITY OF VITAMIN D FOR CONSUMERS AND PATIENTS

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Overview

- **Why** is the availability of vitamin D important to patients and consumers?
  - Sources of vitamin D // how many are deficient?
  - Scientific Evidence
  - Safety
  - Public Health Potential
  - Economic Considerations
Background: How come whole nations are vitamin D deficient?

1. Main Source of Vitamin D

- We expose less than 5% of our skin to the sun + we wear sunscreen
- Very little vitamin D production from November to May in all of Europe
- Vitamin D production in the skin decreases 4 times with age
- Seniors avoid the sun: lowest levels in the Mediterranean (SENeca study)

2. Nutritional sources of vitamin D are limited

- not enough in the sea

How many are deficient?

Adult European Population

<table>
<thead>
<tr>
<th>Threshold for 25-hydroxyvitamin D serum concentration in nmol/l</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>less than 30</td>
<td>0</td>
</tr>
<tr>
<td>less than 50</td>
<td>30</td>
</tr>
<tr>
<td>less than 75</td>
<td>60</td>
</tr>
</tbody>
</table>

How many are deficient?

Hip Fracture Patients (mean age 84 years)

- At risk for osteomalacia
- Below minimal target range
- Below optimal target range

Threshold for 25-hydroxyvitamin D serum concentration in nmol/l

Bischoff-Ferrari HA, Staehelin HB, Theiler R et al.; Severe Vitamin D Deficiency in Swiss Hip Fracture Patients; Bone 2008
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WE HAVE EVIDENCE TODAY

Vitamin D

Benefit on Bone

Benefit on Muscle

Fracture
EVIDENCE: two 2009 Meta-analyses of double-blinded Trials

Effect was dose-dependent increasing with dose and vitamin D level

18% Reduction  20% Reduction (33% 65-74 yrs)  19% Reduction

Hip fractures  Any non-vertebral fracture  Falls

Received dose (treatment dose*adherence) of > 480 IU vitamin D/d

Treatment dose of 700 to 1000 IU vitamin D/d

Optimal Vitamin D Levels for Fall and Fracture prevention from Clinical Trials

Bischoff-Ferrari, Staehelin HB et al.; Archives of Internal Medicine 2009; Bischoff-Ferrari, Dawson-Hughes et al.; British Medical Journal 2009
Bischoff-Ferrari HA, Shao A, Dawson-Hughes B, Giovannucci E, Willett WC; Benefit-Risk Assessment of Vitamin D; OP International 2009
Additional public health potential

Vitamin D

Fracture and Fall Prevention

General Health
Small clinical trials, mechanistic and large cohort studies suggest benefit of vitamin D on cardio-vascular health

Large clinical trials needed to confirm such benefits

Mouse without the VDR: has hypertension and dies from heart failure

Small clinical trials in humans: UVB-irradiation or 800 IU vitamin D reduces blood pressure by about 6 mmHG

Large cohort studies: vitamin D levels of at least 75 nmol/l compared to levels below 36 nmol/l 6-fold lower risk of hypertension among men 3-fold lower risk among women 2.5-fold lower risk of myocardial infarction

Large Cohort Studies: Optimal Vitamin D Levels for cardio-vascular health

Incident hypertension: Forman JP et al. (NHS + HP); Hypertension 2007.

Bischoff-Ferrari HA, Shao A, Dawson-Hughes B, Giovannucci E, Willett WC; Benefit-Risk Assessment of Vitamin D; Osteoporosis International 2009
One small clinical trial, mechanistic studies and large cohort studies suggest a benefit of vitamin D on cancer prevention.

Large clinical trials needed to confirm such benefits.

Vitamin D inhibits cell proliferation: Shown for fibroblasts, colo-rectal, breast and prostate cancer cells.

Clinical trial in humans: Among 1179 women age 55+ 1100 IU vitamin D + calcium compared to placebo reduced cancer risk by 60% in 4 yrs.

Large cohort studies: Higher vitamin D levels associated with lower cancer risk, and less mortality from cancer, strongest data for colo-rectal cancer.

Large Cohort Studies: Optimal Vitamin D Levels for colorectal cancer

**Colorectal cancer: Goreham ED (a quantitative meta-analysis of 5 studies; Am J Prev. Med. 2007)**

Bischoff-Ferrari HA, Shao A, Dawson-Hughes B, Giovannucci E, Willett WC; Benefit-Risk Assessment of Vitamin D; Osteoporosis International 2009
Multivariable* RR for a 25 nmol/l increment in vitamin D status in men (1986-2000)

- Total Cancer Incidence: -17%
- Total Cancer Mortality: -29%
- Digestive Organ Cancer Incidence: -43%

age, smoking, height, alcohol, calories, red meat, calcium, retinol, fruits and vegetables

Giovannucci E. et al., JNCI 2006
Additional public health potential

Vitamin D

Fracture and Fall Prevention

General Health

↓ Type 1 diabetes
↓ Multiple Sclerosis
↓ Infections
↓ Asthma

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Safety based on Trials with Vitamin D // dose

- 25 RCTs
- 10,000-14,000 IU in 20 minutes
- 8 RCTs – falls
- 12 RCTs - fractures

Bischoff-Ferrari HA, Shao A, Dawson-Hughes B, Giovannucci E, Willett WC; Benefit-Risk Assessment of Vitamin D; OP International 2009
Safety based on Trials with Vitamin D levels

Bischoff-Ferrari HA, Shao A, Dawson-Hughes B, Giovannucci E, Willett WC; Benefit-Risk Assessment of Vitamin D; OP International 2009
Summary safety

- Vitamin D intakes of 800 to 1000 IU vitamin D per day or vitamin D levels of about 75 to 110 nmol/l provide optimal benefits for fall and fracture prevention without increasing health risks (Evidence-based).

- Vitamin D levels of about 75 to 110 nmol/l also provide optimal benefits on cardiovascular health and cancer prevention without increasing health risks (Epidemiologic data).

- 800 to 1000 IU vitamin D per day, will bring about 50% to 75 - 110 nmol/l -- Higher intakes are needed to bring all adults to 75 to 100 nmol/l (1800 to 4000 IU per day based on benefit risk assessment – not tested for important endpoints)

Bischoff-Ferrari HA, Shao A, Dawson-Hughes B, Giovannucci E, Willett WC; Benefit-Risk Assessment of Vitamin D; OP International 2009
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Public Health Potential based on Fall and Fracture Prevention with Vitamin D – we have **EVIDENCE**

- **Hip fractures are the most frequent fracture at age 75+**
  - In the first 12 months after hip fracture
    - 50% of seniors are less mobile
    - 30% of seniors lose their independence
    - 10% of seniors fracture their other hip
    - 30-50% of seniors are re-admitted to acute care for any reason
    - 15 to 25% die

- **30% of seniors age 65 and 50% of seniors age 80 fall each year**
  - Falls are the primary cause of hip fracture
  - Falls are independent predictors of functional decline
  - 9% of emergency room visits are due to a fall
  - 5% of falls lead to a fracture
  - 40% of nursing home admissions are due to a fall

*With 800 to 1000 IU vitamin D per day we could reduce these events and their serious consequences by about 20%*
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Economic Considerations

- Economic benefits of having all Europeans reach a desirable 25-hydroxyvitamin D threshold of 100nmol/l (40ng/ml) were estimated by Grant et al. based on epidemiological data on the expected reduction of chronic disease.

- For a daily dose between 2000–3000 IU of vitamin D3, the reduction in health care expenditures was estimated to be 187,000 million Euro per year (2007 €), while the estimated cost of 2000–3000 IU of vitamin D3 per day along with costs for education and testing was estimated to be 10,000 million Euro per year.

- As epidemiologic estimates often appear inflated due to artificially defined control populations, more clarity on health economic savings will be achieved from a large-scale clinical trial of the health benefits and health resource savings associated with vitamin D.

- Ongoing cost-efficacy analysis for fracture and fall prevention by Dawson-Hughes, Wong and Bischoff-Ferrari

We have evidence today that in seniors 800 to 1000 IU Vitamin D could reduce 20% of hip fractures, any non-vertebral fractures and falls.

Potential additional benefit on general health.

Yet, 50% to 70% of the adult population is vitamin D deficient.

**Action at a public health level:**
1. recommend 800 to 1000 IU vitamin D to all seniors age 60 – 65 +
2. to all adults?
3. large trial to confirm additional health benefits