Vitamin D – perspectives in human health

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DSM Nutrition Science & Advocacy
Content

• Introduction: Vitamin D is essential
• Status and how much do we need
• Biological functions and benefits
• Intake recommendations, health claims and safety
• Summary: the optimal status provides benefits for long term health
Vitamin D3 is naturally occurring in humans and animals

Vitamin D3: Cholecalciferol
- Formed by action of ultraviolet light on vitamin D precursors in skin
- Present in certain foods
- Precursor for biologically active hormone

Vitamin D2: Ergocalciferol
- Obtained by irradiation of plants or foods
- Vitamin D2 seems to be less potent than vitamin D3
Dietary sources are low in vitamin D

- Fortified Milk (240 mL): 50 IU
- Margarine (2 tea sp): 40 IU
- Salmon (115 g): 80 IU
- Eggs (2 pc): 32 IU
- Shitake Mushrooms (100 g): 1200 IU

[Mason R. Climacteric 2010; DOI: 10.3109/13697137.2010.514366]
Vitamin D content in human milk is low (aprox. 25 IU /L -0.62 µg/L)
To achieve the IOM recommendation 2011 of 600 IU vitamin D/d = 15 µg per person ....

.... this requires an intake of

- 24 l human milk or
- 3 l fortified milk or
- 37 eggs or
- 870 g salmon or
- 30 tea spoons margarine or
- 50 g shitake mushrooms
Therefore:

Neither exclusive breastfeeding nor a balanced diet can provide enough Vitamin D to meet the dietary recommendations.
A short excursion: cod liver oil changed the world

- Cod liver oil is rich in vitamin D3, A, K and omega-3
- Cod has been an important economic commodity since the Viking period (~800 AD)
- Cod liver oil was valued like gold
- Market lasted for more than 1000 years, enduring Black Death, wars and other crises
- In the 21st century fishing off severely depleted stocks and resulted in restricted catches
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Vitamin D comes from different sources

Food → Sun → Supplements

7-Dehydrocholesterol → Vitamin D

Liver → 25(OH)D (Major circulating form)

Kidney → 1,25(OH)₂D (Active form)

25(OH)D serum level is the relevant indicator of Vitamin D status (IOM 1997)

< 25 nmol/L (deficient)
25 - 50 nmol/L (insufficient)
50 - 75 nmol/L (adequate)
> 75 nmol/L (desirable)

< 10 ng/ml
10 - 20 ng/ml
20 - 30 ng/ml
> 30 ng/ml

SunFood Supplements
7-Dehydrocholesterol
Vitamin D
Liver
25(OH)D
Kidney
1,25(OH)₂D
Active form

DSM
Bright Science. Brighter Living.
Vitamin D

Factor in Sun Exposure

- Clothing
- Altitude
- Latitude
- Time-of-day outdoors
- Duration of time outdoors
- Skin pigmentation
- Aging of the skin
Paradox of sunny countries …..

**High Prevalence of Vitamin D Deficiency in Cambodian Women: A Common Deficiency in a Sunny Country**

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Sunny country unleashed ....


Postulate

• The human species was designed to obtain the majority of its vitamin D from sun-exposure – not from the diet.

• While most populations averted overt rickets, It is probable that marginal and insufficient vitamin D status has been the norm throughout human evolution.

• Since life expectancy was only about 35 years until the 20th Century, humans tolerated the consequences of vitamin D deficiency for three decades and escaped the consequences for later life. [There was very little “later life”]
A systematic review of vitamin D status in populations worldwide

Mean 25(OH)D levels:
- 6.7% below 25 nmol/l
- 37.3% below 50 nmol/l
- 88.1% below 75 nmol/l

Reference:
Actions derived from these findings

- Promote a wider understanding of the essentiality and newly-appreciated functions of vitamin D.
- Promote a wider understanding of the role of vitamin D in disease prevention.
- Eliminate the MYTH of vitamin D sufficiency because a country is sunny and tropical.
- Establish evidence, preferably through representative national sampling, of the prevalence of insufficient and deficient vitamin D status in all countries – sunny or gray.
Finland acted and implemented milk fortification

Simulation of Vitamin D intake via the different carriers

Source: THL, Helsinki, 2009
Vitamin D status in Finish population after implementation of fortification

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
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</tr>
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<tbody>
<tr>
<td>Mean</td>
<td>75.9</td>
</tr>
<tr>
<td>SD</td>
<td>22.2</td>
</tr>
<tr>
<td>Median</td>
<td>74.0</td>
</tr>
<tr>
<td>% &lt;25 nmol/L</td>
<td>0.1</td>
</tr>
<tr>
<td>% &lt;50 nmol/L</td>
<td>8.9</td>
</tr>
<tr>
<td>% &lt;75 nmol/L</td>
<td>51.6</td>
</tr>
</tbody>
</table>

Finland may act as a role model for a successful implementation of food fortification with vitamin D3
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• Summary: the optimal status provides benefits for long term health
Vitamin D: the inadequate status impacts a number of body functions

Classical role of vitamin D: bone health
- Improves bone mineral density through calcium absorption and deposition
- Necessary to prevent rickets & osteomalacia

Emerging health benefits of vitamin D
- Muscle - Reduces risk of falling by improving muscle strength
- Immunity - Strengthens the immune system
  - Reduces risk of multiple sclerosis and diabetes type I and II
- Cardiovascular - Lowers blood pressure
- Cancer - Inhibits cell proliferation
One in three women and one in five men over the age of 50 years will sustain an osteoporotic fracture
In women, the incidence of fractures is higher than the total incidence of cancer, heart infarction, stroke or diabetes.
Germany: Health care cost impact of low vitamin D status

Hip and vertebral fractures have the most „cost-intense“ medical implications
- Number osteoporosis patients: 8-10 mio (2010)*
- Number of hip and vertebral fractures p.a.: 150,000*

Optimized vitamin-D status reduces number of fractures by 20 %
- Reduction of 5,478 hip fractures and 18,420 less vertebral fractures (in osteoporosis-diagnosed population)

Net socio-economic benefit ranges from* : 585 mio €
Including medical and therapeutic costs for prevention, treatment and supplementation costs vitamin D up to 778 mio € Including societal perspective, e.g. family care, reha costs

Costs of vit D supplementation for women > 55 with low vit D status: 180 - 200 mio EUR

Source: * Sproll 2011
US: Potential cost savings by vitamin D supplementation

By vitamin D supplementation among all women over 55 years with osteoporosis, up to USD 1.5 billion savings per year could be realized.

Health Care Expenditures in B USD

- Optimal vitamin D status yields:
  - 20% relative risk reduction
  - An average of 151,053 avoided events per year

Source: US Health Care Costs
Magnitude of vitamin D considering additional health benefits

<table>
<thead>
<tr>
<th>Condition</th>
<th>Reduction (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bone fractures</td>
<td>20%</td>
</tr>
<tr>
<td>Cardio Vascular Diseases</td>
<td>20%</td>
</tr>
<tr>
<td>Multiple Sclerosis</td>
<td>50%</td>
</tr>
<tr>
<td>Diabetes</td>
<td>25%</td>
</tr>
<tr>
<td>Cancer and others</td>
<td>25%</td>
</tr>
</tbody>
</table>

Source: Grant et al 2009
Vitamin D reduces risk for respiratory tract infections

Upper respiratory tract infections (URTI; %) in 18,883 subjects according to 25(OH)D levels (ng/mL)

- Strong inverse association between URTI and 25(OH)D levels
- Subjects with 25(OH)D below 75nmol/L show significantly higher risk for URTI

Conversion: ng/ml x 2.49 = nmol/l

Source: Ginde, Arch Intern Med 2009
Vitamin D has an effect on cancer risk

US colon cancer geography
Sorenson, 2006

Cancer Mortality Rates by State Economic Area
Colon: White Males, 1970-94

Increased cancer incidence towards North

Prevalence of all cancers in post-menopausal women given 1100 IU Vit D day
Lappe, AJCN 2007

Survival after 4 years of vitamin D and Ca supplementation is significantly higher than placebo group

Consistent evidence for inverse association 25(OH)D and colorectal cancer

WHO-IARC 2008 report ‘Vitamin D and Cancer’
Vitamin D status is related to risk reduction for CVD

Mean age 55 years at study

- Inverse association between 25(OH)D levels and CVD
- higher 25(OH)D levels are associated with lower risk of CVD

Wang, 2008
Vitamin D and risk of cause specific death: systematic review and meta-analysis of observational cohort and randomised intervention studies

<table>
<thead>
<tr>
<th></th>
<th>No of studies</th>
<th>No of participants</th>
<th>No of deaths</th>
<th>Relative risk (95% CI)* for cause specific mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cardiovascular death</strong></td>
<td></td>
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<td></td>
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<tr>
<td>Primary prevention cohorts</td>
<td>19</td>
<td>80 662</td>
<td>6416</td>
<td>1.35 (1.13 to 1.61)</td>
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<tr>
<td>Secondary prevention cohorts</td>
<td>10</td>
<td>20 987</td>
<td>3787</td>
<td>1.60 (1.32 to 1.94)</td>
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<tr>
<td>All cohorts</td>
<td>29</td>
<td>101 649</td>
<td>10 203</td>
<td>1.43 (1.25 to 1.64)</td>
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<tr>
<td><strong>Cancer death</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary prevention cohorts</td>
<td>12</td>
<td>104 353</td>
<td>5903</td>
<td>1.14 (1.01 to 1.29)</td>
</tr>
<tr>
<td>Secondary prevention cohorts</td>
<td>5</td>
<td>16 382</td>
<td>1617</td>
<td>1.59 (1.17 to 2.16)</td>
</tr>
<tr>
<td>All cohorts</td>
<td>17</td>
<td>120 733</td>
<td>6620</td>
<td>1.25 (1.10 to 1.43)</td>
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<tr>
<td><strong>Non-cardiovascular, non-cancer death</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary prevention cohorts</td>
<td>7</td>
<td>38 526</td>
<td>1444</td>
<td>1.30 (1.07 to 1.59)</td>
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<tr>
<td>Secondary prevention cohorts</td>
<td>3</td>
<td>13 035</td>
<td>1121</td>
<td>1.49 (0.94 to 2.35)</td>
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<tr>
<td>All cohorts</td>
<td>10</td>
<td>51 561</td>
<td>2565</td>
<td>1.34 (1.13 to 1.60)</td>
</tr>
<tr>
<td><strong>All cause mortality</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary prevention cohorts</td>
<td>27</td>
<td>780 990</td>
<td>48 488</td>
<td>1.35 (1.22 to 1.49)</td>
</tr>
<tr>
<td>Secondary prevention cohorts</td>
<td>41</td>
<td>59 918</td>
<td>16 148</td>
<td>1.50 (1.36 to 1.65)</td>
</tr>
<tr>
<td>All cohorts</td>
<td>68</td>
<td>840 908</td>
<td>64 636</td>
<td>1.44 (1.34 to 1.55)</td>
</tr>
</tbody>
</table>

73 cohort studies and 22 randomized trials show benefit of 25OH-D in reducing risk for CVD, cancer and all-cause mortality

Chowdhury R, et al. BMJ 2014;348:g1903
25-Hydroxyvitamin D Levels and the Risk of Stroke
A Prospective Study and Meta-analysis

Qi Sun, MD, ScD; An Pan, PhD; Frank B. Hu, MD, PhD;
JoAnn E. Manson, MD, DrPH; Kathryn M. Rexrode, MD, MPH

Study                  | Relative risk (95% CI)
----------------------|------------------------
Marniemi et al.       | 1.00 (0.51, 1.96)      
Pilz et al.            | 1.94 (0.78, 4.80)      
Küikkinen et al.       | 2.08 (1.33, 3.23)      
Bolland et al.         | 1.40 (0.80, 2.50)      
Drechsler et al.       | 2.58 (0.74, 8.98)      
Anderson et al.        | 1.78 (1.20, 2.66)      
Nurses' Health Study   | 1.48 (1.01, 2.18)      
Overall (I-squared = 0.0%, P = 0.63) | 1.52 (1.20, 1.85)      

Low vitamin D levels are associated with risk of stroke
RR 1.52
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• Summary: the optimal status provides benefits for long term health
Vitamin D status important for various health outcomes

Optimum plasma level is above 75nmol/L

Daily intake of 800 IU (20mcg) will bring 50% of population up to 80nmol/L

Adapted from Bischoff-Ferrari: Optimal Serum 25-Hydroxyvitamin D levels for multiple health outcomes
A number of professional and national health organizations advocate for optimal recommendations.

- Recommended 400 IU/d for infants during 1st year and north of 55° latitude increase to 800 IU/d from Oct-Apr.

<50 y should consume 400-800 IU/d
>50 y should consume 800-1,000 IU/d
To maintain optimal bone health, maintain ≥ 75 nmol/L (30
EFSA has evaluated the strength of evidence for health benefits of vitamin D: Positive Scientific Opinions

Calcium and Vitamin D
- “…are needed for the maintenance of normal bone.”

Childrens’ Growth & Development
- “…Vitamin D is needed for normal growth and development of bone in children.”
- “…Calcium and vitamin D are needed for normal growth and development of bone in children.”

Disease Risk Reduction
- “…Calcium and vitamin D may reduce the loss of bone mineral density in post-menopausal women. Low bone mineral density is a risk factor in the development of osteoporotic fractures.”
- “…Vitamin D may reduce the risk of falling. Falling is a risk factor for bone fractures.”
Safety of vitamin D: The safe upper limit was raised to 4000 IU/day

Benefit/Risk assessment based on clinical studies

2010 Institute of Medicine (IOM) recommendations
Safe upper intake 4000 IU / day

Bischoff-Ferrari HA, Shao A, Dawson-Hughes B, Giovannucci E, Willett WC; Benefit-Risk Assessment of Vitamin D; OP International 2010
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A call to act

Communicate and advocate role of Vitamin D for health and well being

Install food fortification for the general population

Support supplementation for risk groups
Large intervention studies are currently going on

<table>
<thead>
<tr>
<th>NAME</th>
<th>PLACE</th>
<th>PARTICIPANTS</th>
<th>DOSE</th>
<th>MAIN OUTCOMES</th>
<th>CURRENT STATE</th>
<th>RESULTS EXPECTED</th>
</tr>
</thead>
<tbody>
<tr>
<td>VITAL</td>
<td>U.S.</td>
<td>20,000, men: 50+, women: 55+</td>
<td>2000 IU D₃ daily</td>
<td>Cancer, Cardiovascular disease</td>
<td>Recruitment to finish end of 2012</td>
<td>2017</td>
</tr>
<tr>
<td>FIND</td>
<td>Finland</td>
<td>18,000 men: 60+, women: 65+</td>
<td>1800 IU D₃ daily or 3200 IU D₃ daily</td>
<td>Cancer, Cardiovascular disease, Diabetes</td>
<td>Recruitment started in spring, supplementation to start in autumn</td>
<td>2020</td>
</tr>
<tr>
<td>ViDA</td>
<td>New Zealand</td>
<td>5100, 50+</td>
<td>100,000 IU D₃ a month (200,000 IU in June)</td>
<td>Cardiovascular disease, Respiratory disease, Fractures</td>
<td>Recruitment to finish this year</td>
<td>2017</td>
</tr>
<tr>
<td>DOHealth</td>
<td>8 European cities</td>
<td>2150, 70+</td>
<td>2000 IU D₃ daily</td>
<td>Infections, Fractures, Blood pressure, Cognitive function, Lower extremity function</td>
<td>Recruiting</td>
<td>2017</td>
</tr>
<tr>
<td>VIDAL</td>
<td>U.K.</td>
<td>20,000, 65–84</td>
<td>60,000 IU monthly</td>
<td>Longevity and others</td>
<td>Planned 2-year feasibility study on 1600 patients (if main study gets go-ahead)</td>
<td>2020</td>
</tr>
</tbody>
</table>

DHEALTH  Australia  25000, 65-84  60,000 IU monthly  CVD, cancer, others  Recruiting  2021
Measuring status for individual feedback is the next step

- in-home vitamin D test kit
- convenient and easy to complete
- finger prick and a few drops of blood
- can be used in both adults and children
- spot card to be mailed using the return envelope
- results available online

www.vitamindcouncil.org
Take care for yourself!

1. EVALUATE your personal Vitamin D status
2. ENRICH your diet with foods fortified in Vitamin D
3. ENHANCE your diet by a Vitamin D supplementation
Who has health has hope, who has hope has everything

Thank you!

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