ILSI Workshop New Delhi

A Global Assessment of Vitamin D Status in Healthy Populations

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DSM Nutritional Products

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Scientific evidence supports vitamin D benefits in different segments

- ~3500 publications in 2011
- More than 250 human studies ongoing
- Indications well beyond bone health

**Vitamin D**

- **Bone** (14,605 publications)
  - Colon cancer (459 publications)
  - Muscle (1,583 publications)
  - Multiple sclerosis (260 publications)
  - Diabetes type I & II (1,287 publications)
  - Brain & cognition (1,123 publications)

- **Immunity** (1,001 publications)
- **Blood pressure & CVD** (2,721 publications)
- **Tuberculosis** (493 publications)

**PubMed Hits**

- Pubmed Hits Vitamin D in Title / Abstract

**Year** (1961-2011)

- 1971: 500
- 1981: 1000
- 1991: 1500
- 2001: 2000
- 2011: 3500

**Brain & cognition** (1,123 publications)
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
Vitamin D comes from different sources

Food
- 7-Dehydrocholesterol
- Vitamin D
- 25(OH)D
- 1,25(OH)₂D

Sun

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

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

- nmol/L
  - < 25: deficient
  - 25 - 50: insufficient
  - 50 - 75: inadequate
  - > 75: desirable

- ng/ml
  - < 10: deficient
  - 10 - 20: insufficient
  - 20 - 30: inadequate
  - > 30: desirable
Traditionally living populations have a mean serum 25-OH D concentration of 115 nmol/l.

Luxwolda MF, Kuipers RS, Kema IP, Janneke Dijck-Brouwer DA, Muskiet FA.
Laboratory Medicine, University Medical Center Groningen (UMCG), PO Box 30.001, 9700 RB, Groningen, NL

Cutaneous synthesis of vitamin D by exposure to UVB is the principal source of vitamin D in the human body. Our current clothing habits and reduced time spent outdoors put us at risk of many insufficiency-related diseases that are associated with calcaemic and non-calcaemic functions of vitamin D. Populations with traditional lifestyles having lifelong, year-round exposure to tropical sunlight might provide us with information on optimal vitamin D status from an evolutionary perspective.

We measured the sum of serum 25-hydroxyvitamin D2 and D3 (25(OH)D) concentrations of 35 pastoral Maasai (34 (sd 10) years, 43 % male) and 25 Hadzabe hunter-gatherers (35 (sd 12) years, 84 % male) living in Tanzania.

The mean serum 25(OH)D concentrations of Maasai and Hadzabe were 119 (range 58-167) and 109 (range 71-171) nmol/l, respectively. These concentrations were not related to age, sex or BMI.

People with traditional lifestyles, living in the cradle of mankind, have a mean circulating 25(OH)D concentration of 115 nmol/l.

Whether this concentration is optimal under the conditions of the current Western lifestyle is uncertain, and should as a possible target be investigated with concomitant appreciation of other important factors in Ca homeostasis that we have changed since the agricultural revolution.
Why a global assessment on vitamin D?

• Provide a global overview on the vitamin D status in the general population.

• Understand the situation by regions, countries and by sub-groups.

• Generate awareness for the role of vitamin D for health.

• Advocate for actions to improve vitamin D levels in populations/groups at risk for low status.
Approach taken

- **Systematic review according to PRISMA**
  (Preferred Reporting Items for Systematic reviews and Meta-Analyses)
  - Collaboration with the Mannheim Institute of Public Health, Germany

- **Visualizing the outcome (Global Map)**
  - Co-created with the International Osteoporosis Foundation (IOF)
Approach taken for systematic review

Search for relevant studies in relevant data bases

Exclusion of not relevant publications
- No outcome measures vitamin D
- Patient populations
- Duplicates
- Reviews
- Others

Taken into account
Studies fulfilling the following criteria were selected

- Randomly selected persons from the general population in countries worldwide
- Mean or median 25(OH)D serum levels reported
- Population-based cohorts
- Only English publications
- Published between Jan 1st 1990 to Feb 28th 2011

.... an update of the map is planned for 2014
Global Vitamin D status in children & adolescents

http://www.iofbonehealth.org/facts-and-statistics/vitamin-d-studies-map

Ref: Wahl DA et al, Archives of Osteoporosis 2012
Global Vitamin D status in adults

http://www.iofbonehealth.org/facts-and-statistics/vitamin-d-studies-map

Ref: Wahl DA et al, Archives of Osteoporosis 2012
Main findings (1)

- Data coming mostly from Europe (48%), followed by North America (27%) and Asia Pacific region (16.5%)
- Insufficiencies affect both developing world and industrialized countries
- Women have lower status compared to men
Main findings (2)

In children and adolescents, predominant colour is orange (25-49 nmol/L), which means that levels are in the insufficient range.

Gaps in data:
Central America, much of South America, most of Africa, much of Europe, in Australia
Main findings (3)

In adults, predominant colour code is orange (25-49 nmol/L) and yellow (50-74 nmol/L)

Gaps in data:
Central America, South America (with the exception of Brazil), much of Africa
Inadequate vitamin D status is a global issue

.... if we extrapolate the data, it means globally are

88.1 % below 75 nmo/l = est. 6.2 bio
37.3 % below 50 nmol/l = est. 2.6 bio
6.7 % below 25 nmol/l = est. 500 mio
Limitations of the Map

- Variability in the measurement of vitamin D
- Seasonality of vitamin D levels
- Adequate information not always available, e.g.:
  - small study in a limited region of a country and a too narrow age range
  - small regions within large countries with diverse latitudes
- Information on clothing habits and skin pigmentation not always available
Even in ‘sunny’ countries vitamin D status is frequently low!

Vitamin D serum levels from n=46 studies in ASIA

Australia (N=8)  China (N=6)  Fiji Islands (N=1)  India (N=3)  Indonesia (N=2)  Japan (N=5)  Malaysia (N=1)  Mongolia (N=1)  New Zealand (N=11)  South Korea (N=2)  Thailand (N=5)  Vietnam (N=1)

0  25  50  75  100  125
25(OH)D [nmol/L]

< 25  25 - 50  50 - 75  > 75  nmol/L

deficient  insufficient  inadequate  desirable
Vitamin D Insufficiency is prevalent in the general adult population in Thailand

Vitamin D: striking deficiency in SEA

Vitamin D deficiency with different cut off values

Serious problem!

British Journal of Nutrition (in press), 2013
Vitamin D insufficiency

Vitamin D deficiency based on 25 (OH) D < 50 nmol/l
### Vitamin status in Chinese children

<table>
<thead>
<tr>
<th>Publication</th>
<th>Age</th>
<th>Number</th>
<th>Site</th>
<th>Latitude (north)</th>
<th>Season</th>
<th>D Use</th>
<th>25-OH-D nmol/L</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>&lt;25</td>
<td>&lt;25 &lt;50 &lt;75 &lt;80</td>
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<tr>
<td><strong>World J Pediatr 2010</strong></td>
<td>Newborn</td>
<td>77 (MF)</td>
<td>Chengdu</td>
<td>30</td>
<td>Sept</td>
<td>Unknown</td>
<td>40.98±18.9</td>
<td>96.1</td>
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<tr>
<td><strong>Public Health Nutr 2012</strong></td>
<td>Newborn</td>
<td>58 (MF)</td>
<td>Beijing</td>
<td>40</td>
<td>Apr-May</td>
<td>No</td>
<td>27.9±1.6</td>
<td>46.6 93.2 100</td>
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<tr>
<td><strong>BMC Public Health 2012</strong></td>
<td>6-11 yrs</td>
<td>1440 (MF)</td>
<td>Hangzhou</td>
<td>30</td>
<td>All</td>
<td>Unknown</td>
<td>56.1±19.9</td>
<td>2.0 40.3 88.3</td>
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<tr>
<td></td>
<td>12-16 yrs</td>
<td>183 (MF)</td>
<td>Hangzhou</td>
<td>30</td>
<td>All</td>
<td>Unknown</td>
<td>52.1±17.0</td>
<td>3.3 46.4 89.6</td>
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<tr>
<td><strong>J Orthop Surg 2002</strong></td>
<td>12.2 yrs</td>
<td>16 (MF)</td>
<td>Beijing</td>
<td>40</td>
<td>Dec</td>
<td>No</td>
<td>34.3±12.0</td>
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<tr>
<td><strong>Am J Clin Nutr 2001</strong></td>
<td>12.7 yrs</td>
<td>108 (F)</td>
<td>Beijing</td>
<td>40</td>
<td>Jan</td>
<td>Unknown</td>
<td>13.9±9.6</td>
<td>42.5</td>
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<tr>
<td></td>
<td>13.0 yrs</td>
<td>57 (F)</td>
<td>Beijing</td>
<td>40</td>
<td>Jan</td>
<td>Unknown</td>
<td>12.7±5.9</td>
<td>49.6</td>
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<tr>
<td></td>
<td>13.2 yrs</td>
<td>64 (F)</td>
<td>Beijing</td>
<td>40</td>
<td>Jan</td>
<td>Unknown</td>
<td>12.8±6.7</td>
<td>45.1</td>
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<tr>
<td><strong>Osteoporos Int 2009</strong></td>
<td>15.0 yrs</td>
<td>301(F)</td>
<td>Beijing</td>
<td>40</td>
<td>Mar-Apr</td>
<td>No</td>
<td>34.0</td>
<td>32.8 89.2</td>
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<tr>
<td><strong>J Clin Endocrinol Metab 2009</strong></td>
<td>16.4 yrs</td>
<td>226 (FM)</td>
<td>Anqing</td>
<td>33.5</td>
<td>All</td>
<td>Unknown</td>
<td>45.0±23.5</td>
<td>90.3</td>
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</tbody>
</table>

Vitamin D status was poorer in the north
Vitamin D status was poorer in winter-spring
Vitamin D levels were largely below 50 nmol/l
### Vitamin status in Chinese adults

<table>
<thead>
<tr>
<th>Publication</th>
<th>Age (yrs)</th>
<th>Number</th>
<th>Site</th>
<th>Latitude (north)</th>
<th>Season</th>
<th>D Use</th>
<th>25-OH-D (nmol/L)</th>
<th>Prevalence</th>
<th>&lt;25</th>
<th>&lt;50</th>
<th>&lt;75</th>
<th>&gt;75</th>
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<tr>
<td>Bri J Nutr 2008</td>
<td>26.9</td>
<td>220 (F)</td>
<td>Beijing</td>
<td>40</td>
<td>Feb-May</td>
<td>No</td>
<td><strong>29</strong></td>
<td>40*</td>
<td>94</td>
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<tr>
<td>World J Pediatr 2010</td>
<td>27.9</td>
<td>221 (F)</td>
<td>Hong Kong</td>
<td>22</td>
<td>Feb-May</td>
<td>No</td>
<td><strong>34</strong></td>
<td>18*</td>
<td>92</td>
<td>92</td>
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<tr>
<td>Acta Paediatr 2012</td>
<td>27.4</td>
<td>78 (F)</td>
<td>Nanjing</td>
<td>32</td>
<td>Winter</td>
<td>No</td>
<td><strong>22.6±12.7</strong></td>
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<tr>
<td>J Matern Fetal Neonatal Med 2012</td>
<td>28.1</td>
<td>1695 (F)</td>
<td>Shanghai</td>
<td>31</td>
<td>All</td>
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<td><strong>43.9±28.6</strong></td>
<td>69.0</td>
<td>91.0</td>
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<td>Int J Androl 2012</td>
<td>29.4</td>
<td>41 (M)</td>
<td>Xian</td>
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<td>70 (F)</td>
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<td>40</td>
<td>Apr-May</td>
<td>No</td>
<td><strong>28.6±1.4</strong></td>
<td>54.3</td>
<td>90.2</td>
<td>100</td>
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<tr>
<td>Int J Androl. 2012</td>
<td>30.3</td>
<td>314 (M)</td>
<td>Xian</td>
<td>34</td>
<td>All</td>
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<td><strong>53.3±14.5</strong></td>
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<td>Eur J Clin Nutr 2000</td>
<td>30.5</td>
<td>195 (M)</td>
<td>Xian</td>
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<td>Plos One 2012</td>
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<td>Shenyang</td>
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<td>31.1</td>
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<td>Mar-May</td>
<td>No</td>
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<td></td>
<td>43.0</td>
<td>2588 (M+F)</td>
<td>Shanghai</td>
<td>31</td>
<td>All</td>
<td>No</td>
<td><strong>52.2</strong></td>
<td></td>
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</tr>
</tbody>
</table>
Vitamin D status in Latin America and Caribbean

[Map and data representation on the page]

Deficiency (25 OHD)
- < 20 nmol/L
- < 23 nmol/L
- < 25 nmol/L

Insufficiency (25 OHD)
- Between 25 and 50 nmol/L
- < 38 nmol/L
- < 40 nmol/L
- < 43 nmol/L
- < 50 nmol/L

Inadequacy (25 OHD)
- Between 50 and 75 nmol/L
- Between 38 and 75 nmol/L
- Between 51 and 73 nmol/L
- < 75 nmol/L
- Between 50 and 100 nmol/L

* 25 OHD = 25-hydroxyvitamin D

Countries
- National representative samples
- Data from individual studies
- No data

(DSM logo at the bottom)
Ways of Increasing Vitamin D Intake

1. Increase exposure to limited daily sunlight

2. Improving nutrition: consume foods that are high in vitamin D (fatty fish, eggs, fortified products)

3. Supplementation should be considered for people who are vitamin D insufficient or at risk
How to achieve adequate Vitamin D level

Randomized Clinical Trials with vitamin D less than 10‘000 IU per day and duration of at least 4 weeks

Conclusion
- Optimal 25(OH)D range between 75 - 110nmol/L
- These levels can be obtained with oral doses in the range of 800 IU – 2000 IU
- Benefit is clearly dose dependent

Bischoff-Ferrari, 2009 Osteoporos Int
Who is most at risk of vitamin D deficiency?

- People over 65 years of age
- People who avoid sun exposure such as institutionalized or housebound or who cover their skin for cultural reasons
- Pregnant and breastfeeding women and their newborns
- Obese individuals
- People with darker skin, because they are not able to produce much vitamin D in their skin, especially if they immigrate to Northern countries
- In some regions, such as South Asia and Middle East, vitamin D deficiency is very common in all age groups, from infants to the elderly (despite ample sunshine)
New recommendations for higher vitamin D intake

As a concern to the widespread vitamin D deficiency and the beneficial effect of vitamin D on bone health

government documents, position statements and clinical practical guidelines

have recently been published with higher recommendations for daily vitamin D intake.
Experts in the U.S. double recommended daily vitamin D intake for children to 400 IU in 2008

The American Academy of Pediatrics (AAP) has doubled the recommended intake of vitamin D to 400 IU per day for infants, children and adolescents!

http://pediatrics.aappublications.org/content/122/5/1142.full.html
The IOM has reviewed the latest data on bone health.

This review has resulted in new Dietary reference intakes (DRIs) in the US:

- tripled to 600 IU/day for general population age 1-70 years
- to 800 IU/day for elderly > age 70 years

... and many other countries followed.

http://www.iom.edu/Reports/2010/Dietary-Reference-Intakes-for-Calcium-and-Vitamin-D.aspx
EFSA confirms DSM Health Claim Article 14 in 2011

Health claim
Vitamin D may reduce the risk of falling.
Falling is a risk factor for bone fractures

The Conditions of use:
In order to obtain the claimed effect, 800 I.U. (20 µg) of vitamin D from all sources should be consumed daily. The target population is men and women 60 years of age and older.

Conclusion

• Vitamin D deficiency is a global issue affecting developing and developed countries

• Specific groups like pregnant women, infants, elderly can be even more at risk

• Especially, in the Middle East, Asia and Southern Europe vitamin D deficiency is widespread

• Vitamin D deficiency and inadequacy has detrimental health effect

• Ensuring desirable Vitamin D levels is a cost effective approach for a healthy and productive life

The scientific evidence calls for action by a joint approach of the key stakeholders
Back up
Vitamin D nutritional status through the ages

Sources, include Cosman, Osteoporosis Int 2000; Fuleihan NEJM 1999; Scharla Osteoporosis Int 1998; Vieth AJCN 1999, 2000
Vitamin D added to calcium osteoporosis health claim

Food and Drug Administration (FDA) on January 5, 2007

FDA Updates Health Claim for Calcium and Osteoporosis
Proposal Would Give Consumers More Information to Make Healthy Food Choices

Amendments in the published final rule include:
• Add a claim for calcium and vitamin D together and a reduced risk of osteoporosis.

Shorten the claim language by:
• Dropping the reference to sex, race, and age since the benefits apply to both sexes at all ages and race categories.
• Dropping the need to identify the mechanism by which calcium reduces the risk of osteoporosis.
• Dropping the requirement that the claim state that there are limits to benefit of calcium intakes above 200% of the Daily Value.

www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/2007/ucm108824.htm#.T0NmHNdLZHM.email
Europe: Vitamin D insufficiency in adolescents distribution according to geographic location

Vitamin D levels in 1006 adolescents: aged 12 to 17 years, from ten cities in nine European countries

- The highest levels of 25-OH-D were observed in Rome, Athens, Vienna and Zaragoza
- Lowest levels were obtained in Dortmund, Gent, Lille Heraklion.
- Average concentrations did not reach the 75 nmol/l cut-off in any of the cities.
- Deficiency/insufficiency influenced by age, sex, body weight, and geographical location.

IOF interactive map

http://www.iofbonehealth.org/facts-and-statistics/vitamin-d-studies-map
The Interactive Map

HTTP://WWW.IOFBONEHEALTH.ORG/FACTS-AND-STATISTICS/VITAMIN-D-STUDIES-MAP
In Germany
Country Colour: Orange
Population Group: Adults
Country Colour Rationale: Representative of the entire country, population-based, and based on a weighted average

DETAILS
Age: 18-79
Gender: Men
Vitamin D Levels (nmol/L): 45.2
Number of participants: 1763
Study Colour: Orange

URL: http://www.ncbi.nlm.nih.gov/pubmed/17538533

<table>
<thead>
<tr>
<th>Studies Gender</th>
<th>Vitamin D Levels (nmol/L)</th>
<th>Number of participants</th>
<th>Season</th>
<th>Study Colour</th>
<th>References</th>
<th>URL</th>
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</thead>
<tbody>
<tr>
<td>18-79</td>
<td>Women</td>
<td>44.7</td>
<td>No information</td>
<td>Orange</td>
<td>Hintzpeter B et al (2008)</td>
<td>View</td>
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<tr>
<td>50-80</td>
<td>Men &amp; Women</td>
<td>42.5</td>
<td>Mixed</td>
<td>Orange</td>
<td>Scharla SH et al (1995)</td>
<td>View</td>
</tr>
</tbody>
</table>

25-hydroxyvitamin D is lower serum
**Example Germany: Cost impact of low vitamin D status on fractures**

**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)

<table>
<thead>
<tr>
<th>Net socio-economic benefit ranges from* :</th>
<th>585 mio €</th>
</tr>
</thead>
<tbody>
<tr>
<td>Including medical and therapeutic costs for prevention, treatment and supplementation costs vitamin D</td>
<td></td>
</tr>
<tr>
<td>up to</td>
<td></td>
</tr>
<tr>
<td>Including societal perspective, e.g. family care, reha costs</td>
<td></td>
</tr>
<tr>
<td>778 mio €</td>
<td></td>
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</table>

Source: * Sproll 2011
Magnitude of vitamin D considering additional health benefits

<table>
<thead>
<tr>
<th>Condition</th>
<th>Reduction</th>
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<tbody>
<tr>
<td>Bone fractures</td>
<td>20 %</td>
</tr>
<tr>
<td>Cardiovascular 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
Large health care cost savings could be achieved with adequate vitamin D status

<table>
<thead>
<tr>
<th>Source</th>
<th>Year</th>
<th>Location</th>
<th>Estimated Savings</th>
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</thead>
<tbody>
<tr>
<td>Zittermann</td>
<td>2010</td>
<td>Germany: overall perspective, including direct and indirect costs and implications</td>
<td>€ 37.5 bio/y</td>
</tr>
<tr>
<td>Grant et al</td>
<td>2009</td>
<td>17 countries in Europe: direct and indirect cost savings (= 16.7% of total health care costs)</td>
<td>€ 187 bio/y</td>
</tr>
</tbody>
</table>

Adequate levels can be achieved with voluntary food fortification and/or supplementation for risk groups with costs of only 20-30 EUR/person per year.
A call to act on vitamin D deficiency

- 88% of the healthy population is below the optimal vitamin D status of 75 nmol/l 25 (OH)D
- 37% below 50 nmol/l
- Specific groups like pregnant women, infants, elderly can be even more at risk

Regulatory bodies act
- US RDA tripled
- Europe 4-fold increase proposed
- India evaluation ongoing
- China evaluation ongoing
- Thailand ?
- …

Nutritional solutions required
- Communication
- Food fortification
- Supplementation

Scientists, International Osteoporosis Foundation, Endocrine Society and others engage to fight vitamin D deficiency
Broad variation of studies: example Vitamin D levels in Switzerland

Vitamin D levels are critical in institutionalized people compared to free-living elderly
Seasonal variations in representative samples in Switzerland & Germany

Switzerland

[Graph showing seasonal variations for Switzerland]

Burnand et al, 1992

Germany

[Graph showing seasonal variations for Germany]

Hintzpeter et al, 2008
Vitamin D Status of migrants and non-migrants children and adolescent in Germany

Infants achieve a higher vitamin D status due to recommended supplementation during the first year of life

Hintzpeter, 2009
Vitamin D status in hospitalized elderly is critical (Theiler et al, 1999)
Building a map on global vitamin D status

• The challenge:
  Quality and quantity of data differs between the countries

• Assigning a color code to a specific country was based on hierarchical selection criteria:
  1. Representative of the entire country
  2. Representative of a region/city of the country
  3. Based on a weighted mean of multiple studies
  4. Based on a single study
## Vitamin status in Chinese elderly

<table>
<thead>
<tr>
<th>Publication</th>
<th>Age</th>
<th>Number</th>
<th>Latitude (north)</th>
<th>Site</th>
<th>Season</th>
<th>25-OH-D nmol/L</th>
<th>D Use</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eur J Clin Nutr 2000</td>
<td>66.9 yrs</td>
<td>48 (F)</td>
<td>42</td>
<td>Shenyang</td>
<td>Apr-May</td>
<td>42.9±21.2</td>
<td>No</td>
<td>15.0</td>
</tr>
<tr>
<td></td>
<td>68.9 yrs</td>
<td>50 (M)</td>
<td>42</td>
<td>Shenyang</td>
<td>Mar-May</td>
<td>28.4±12.5</td>
<td>No</td>
<td>48.0</td>
</tr>
<tr>
<td>Diabetes Care 2009</td>
<td>50-70 yrs</td>
<td>3262 (M+F)</td>
<td>31 40</td>
<td>Shanghai+Beijing</td>
<td>Apr-Jun</td>
<td>40.4 Unknown</td>
<td></td>
<td>69.2</td>
</tr>
<tr>
<td>Bri J Nutr 2012</td>
<td>61 yrs</td>
<td>1460 (M+F)</td>
<td>31</td>
<td>Shanghai</td>
<td>All</td>
<td>34.7 Unknown</td>
<td>Unknown</td>
<td>96.1</td>
</tr>
<tr>
<td>Menopause 2011</td>
<td>64.1 yrs</td>
<td>1724 (F)</td>
<td>40</td>
<td>Beijing</td>
<td>Unknown</td>
<td>33.0±13.5</td>
<td>Unknown</td>
<td>89.7 99.4</td>
</tr>
<tr>
<td>Bone 2003</td>
<td>65.2 yrs</td>
<td>110 (F)</td>
<td>42</td>
<td>Shenyang</td>
<td>Feb-Apr</td>
<td>30.9±13.5</td>
<td>14.5%</td>
<td>39.1</td>
</tr>
<tr>
<td></td>
<td>67.9 yrs</td>
<td>108 (M)</td>
<td>42</td>
<td>Shenyang</td>
<td>Feb-Apr</td>
<td>27.1±11.5</td>
<td>9.3%</td>
<td>52.8</td>
</tr>
</tbody>
</table>
Tab 4. Vitamin status can be improved: Hangzhou and Nanjing

Vitamin D deficiency in China: present & widespread

East of Hu’s line: <40 % land, >90 % population since 1930s
Broad variation of studies: example Vitamin D levels throughout Europe

High variations within one country and between countries