# FROM SCIENCE TO ECONOMICS

# THE POTENTIAL VALUE OF SUPPLEMENTATION

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International Alliance of Dietary/
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# Micronutrient challenges and opportunities: Where do we stand?

Manfred Eggersdorfer, PhD
Professor for Healthy Ageing

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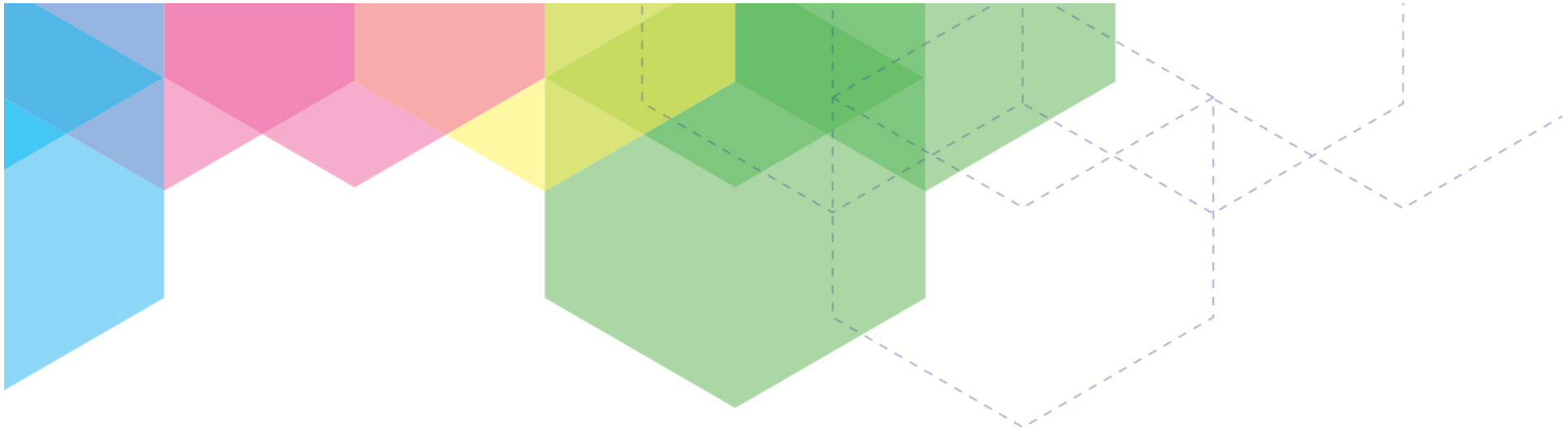
# Micronutrient challenges and opportunities: Where do we stand?

- Inadequate micronutrient intake is a global issue
- Opportunities: Case studies
  - Vitamin D
  - Vitamin C
  - Omega-3
- Challenges in micronutrients
- Summary and outlook



# Do we need nutritional ingredients?

# Do we need supplements?

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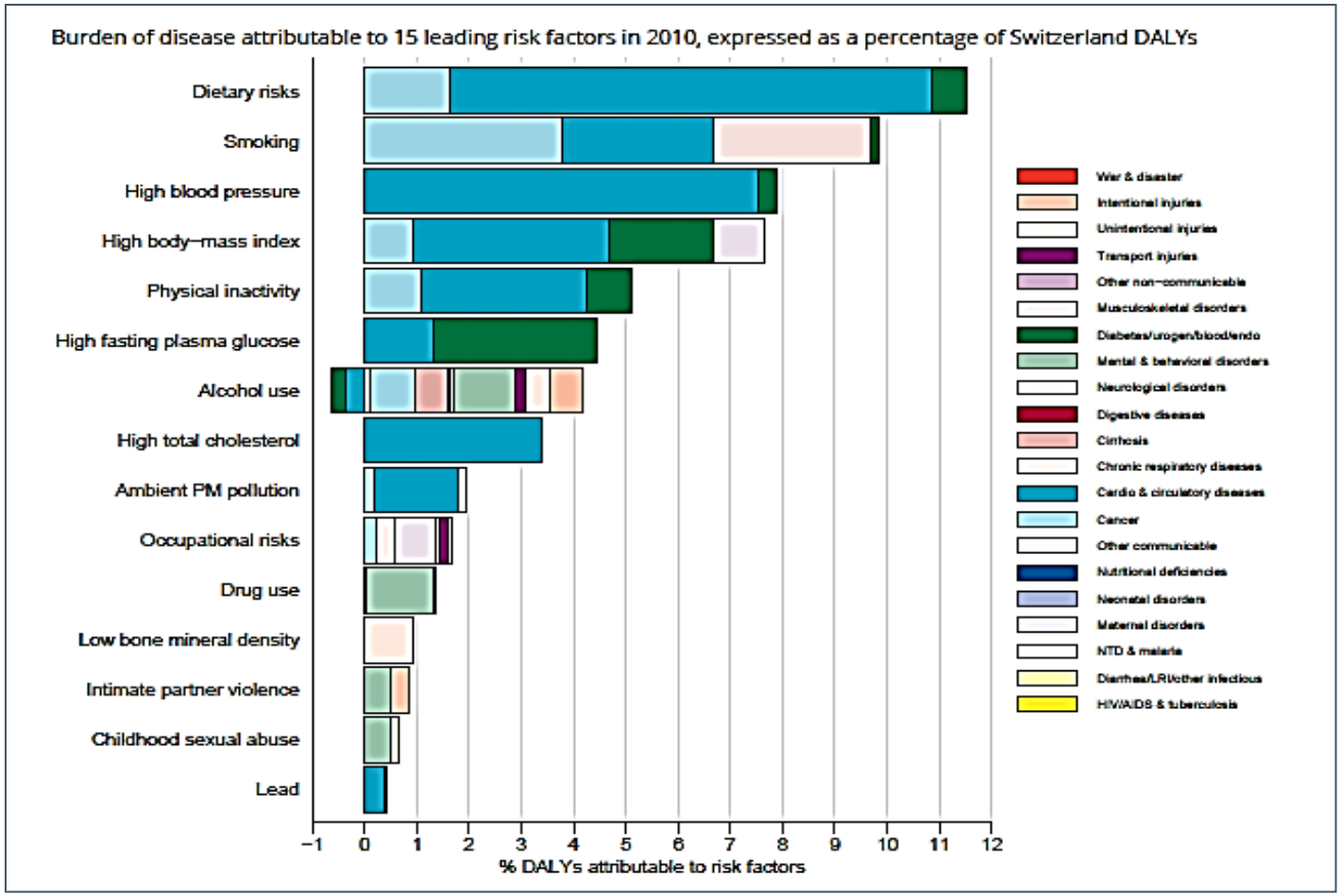
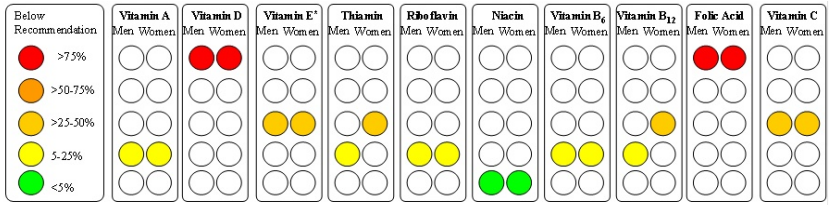
# Dietary risks are the key risk factor for mortality

*Example Switzerland*

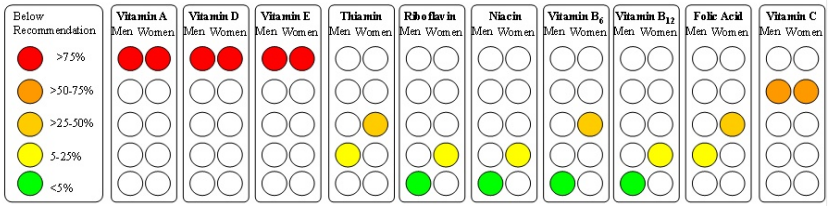


# Adequate micronutrient intake is an issue in Western countries

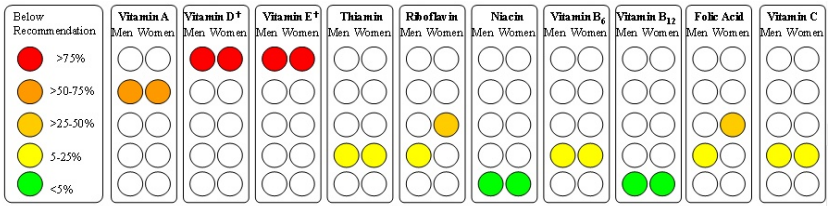

Germany



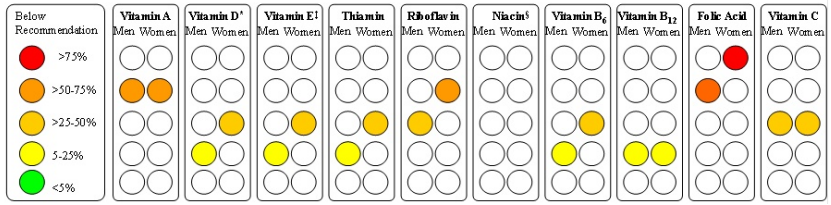

United States




United Kingdom

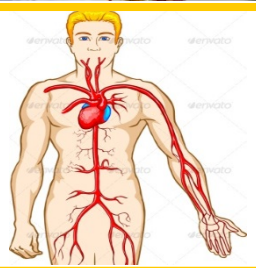
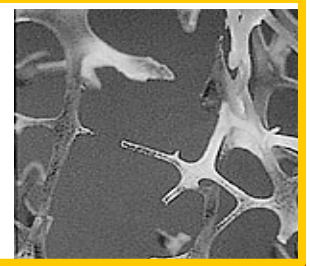
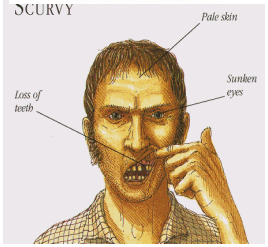
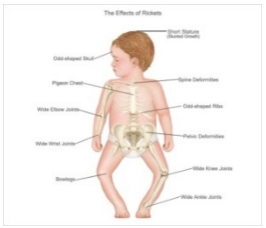



The Netherlands



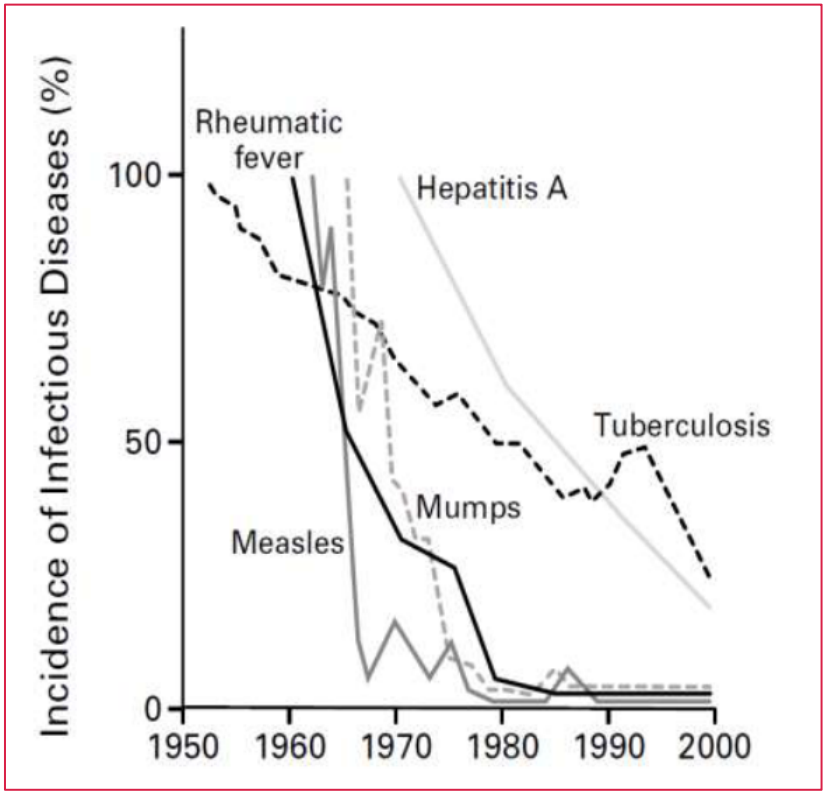

Troesch et al BJN 2012

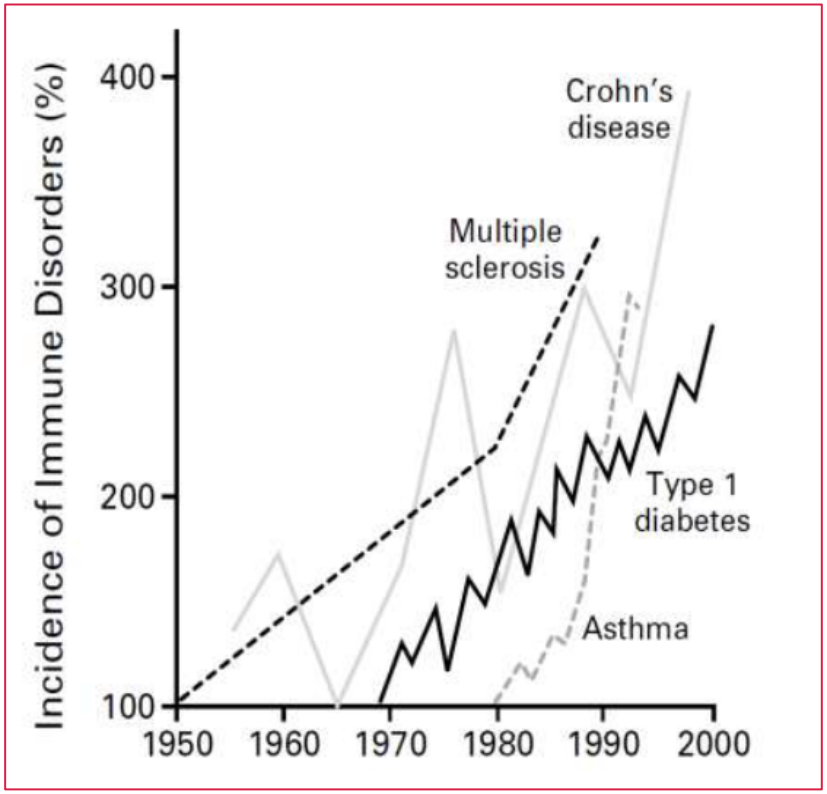
# Inadequate micronutrient intake affects long term health and performance

| Nutrient status | Metabolic response | | | |
|---|---|---|---|---|
| **Desirable** | Long term health, wellness, vitality |  |  |  |
| **Insufficient** | Impaired functions, higher risk for non-communicable diseases |  |  |  |
| **Deficient** | Deficiency disease |  |  |  |

**An adequate intake of all essential nutrients is required for long-term health, healthy aging and risk reduction of NCDs**

# Health and risk for diseases changed in the last century



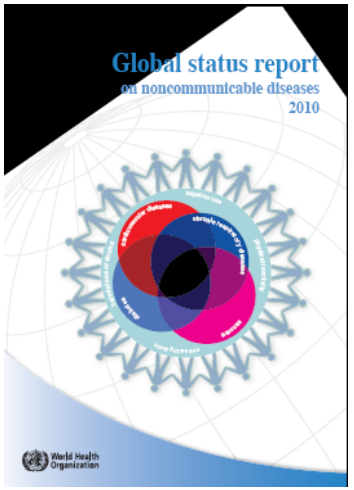

**We achieved a lot of progress in infectious diseases however face an unprecedented rise in non-communicable diseases**

Source: Bach et al, NEJM 2012

**More than 40% of nutrition related diseases take place before the age of 70**

**Approximately one third of cancers can be prevented**

**Up to 80% of heart disease, stroke and diabetes type 2 deaths are preventable.**




*http://www.who.int/gho/ncd/en/index.html*

# Micronutrient challenges and opportunities: where do we stand?

- Inadequate micronutrient intake is a global issue
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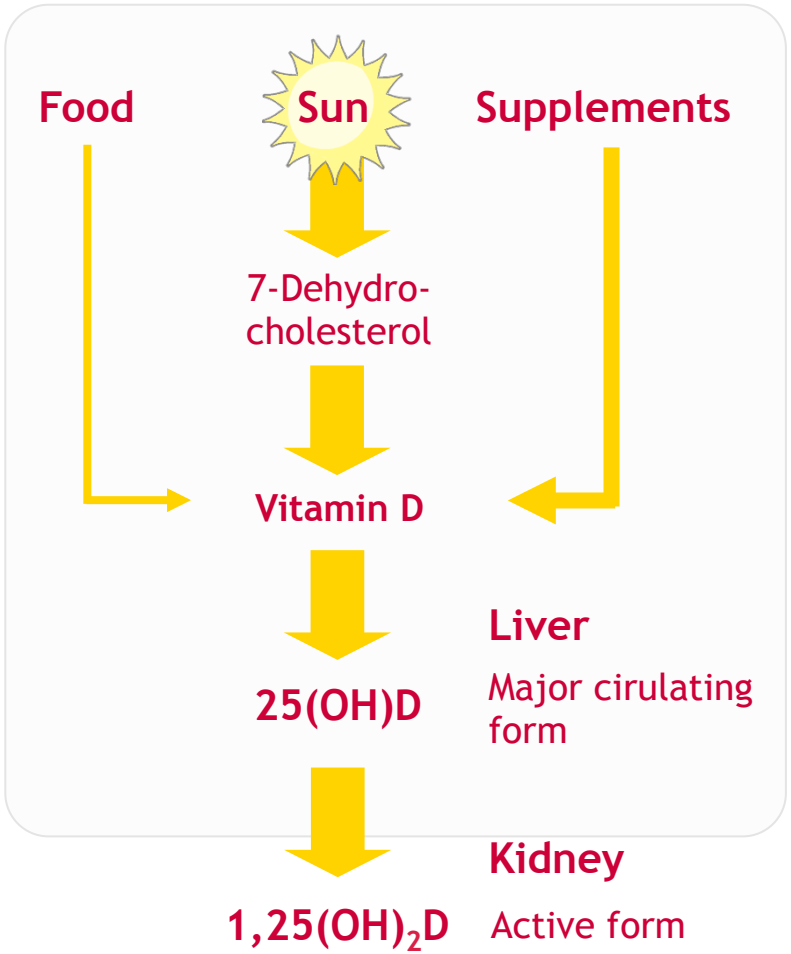
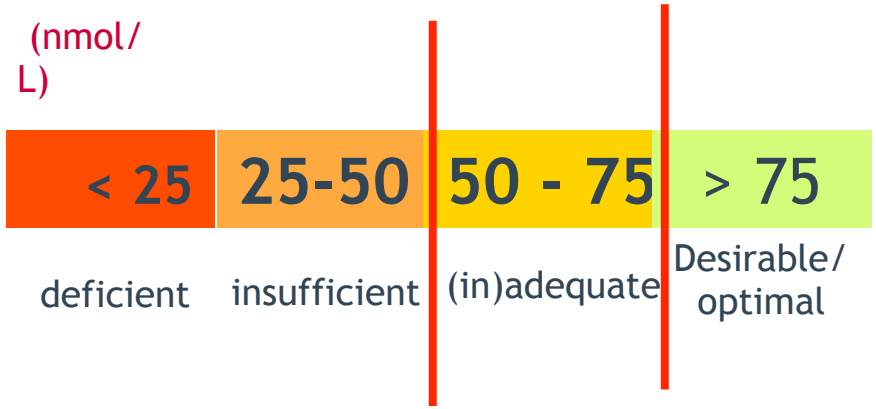
# Vitamin D comes from different sources
# Serum level is an indicator for individual status




**25(OH)D serum level (nmol/L) is a sensitive indicator of Vitamin D status**
(IOM 1997)

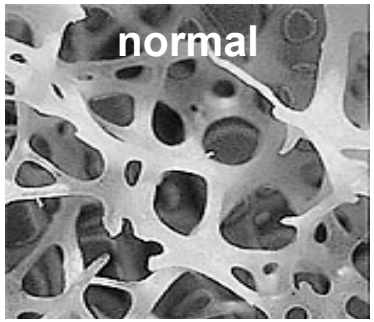
Four ranges are suggested to assess the individual status:



# Vitamin D: the inadequate status impacts a number body functions

## Classical role of vitamin D: bone health

- Improves **bone mineral density** through calcium absorption and deposition
- Necessary to prevent rickets & osteomalacia

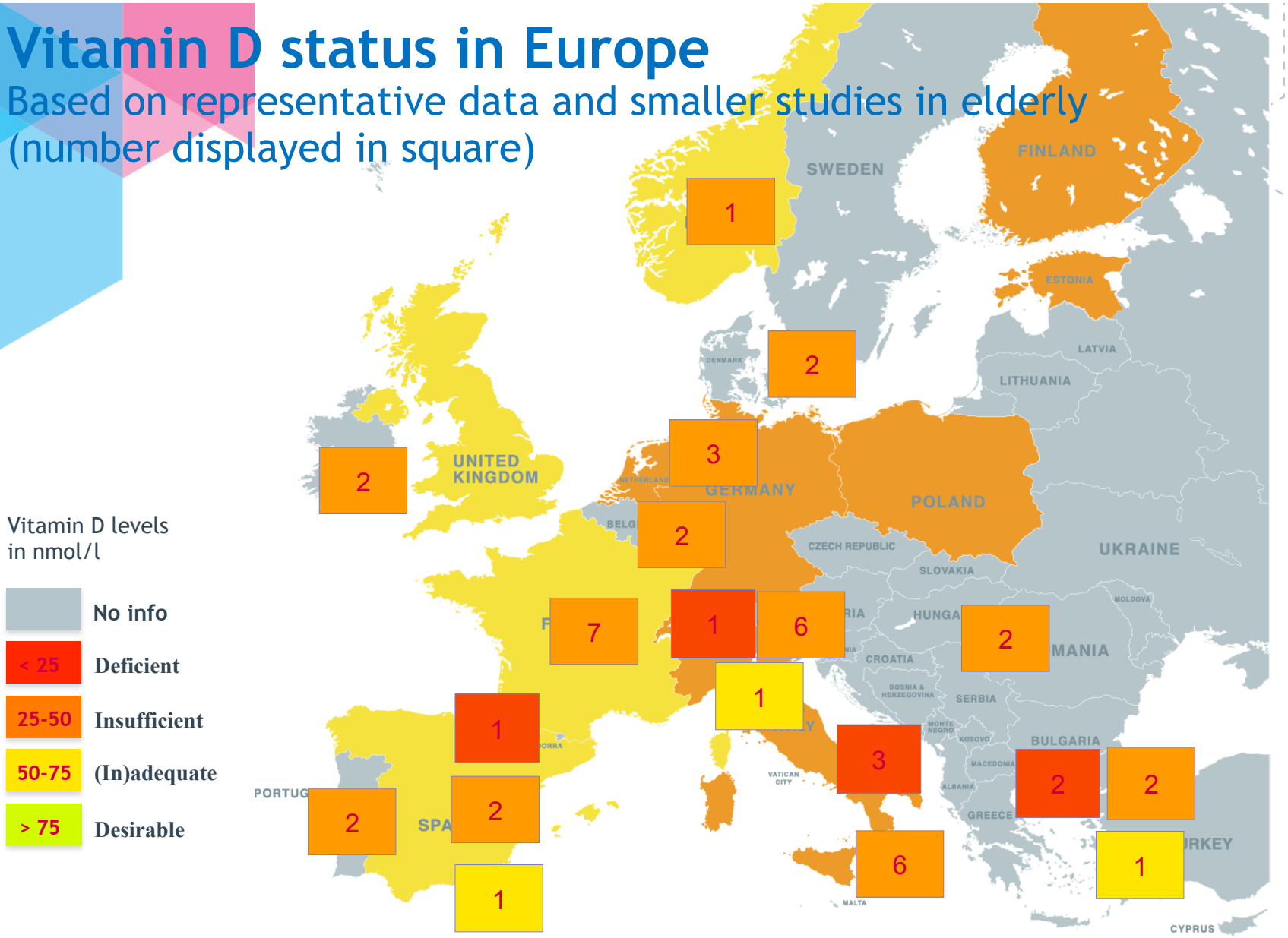



## Emerging health benefits of vitamin D

- Muscle - Reduces risk of falling by improving muscle strength
- Immunity - Strengthens the immune system
  - Reduces risk of multiple sclerosis and diabetes type
- Cardiovascular - Lowers blood pressure
- Cancer - Inhibits cell proliferation

# Vitamin D status in Europe

## Based on representative data and smaller studies in elderly (number displayed in square)

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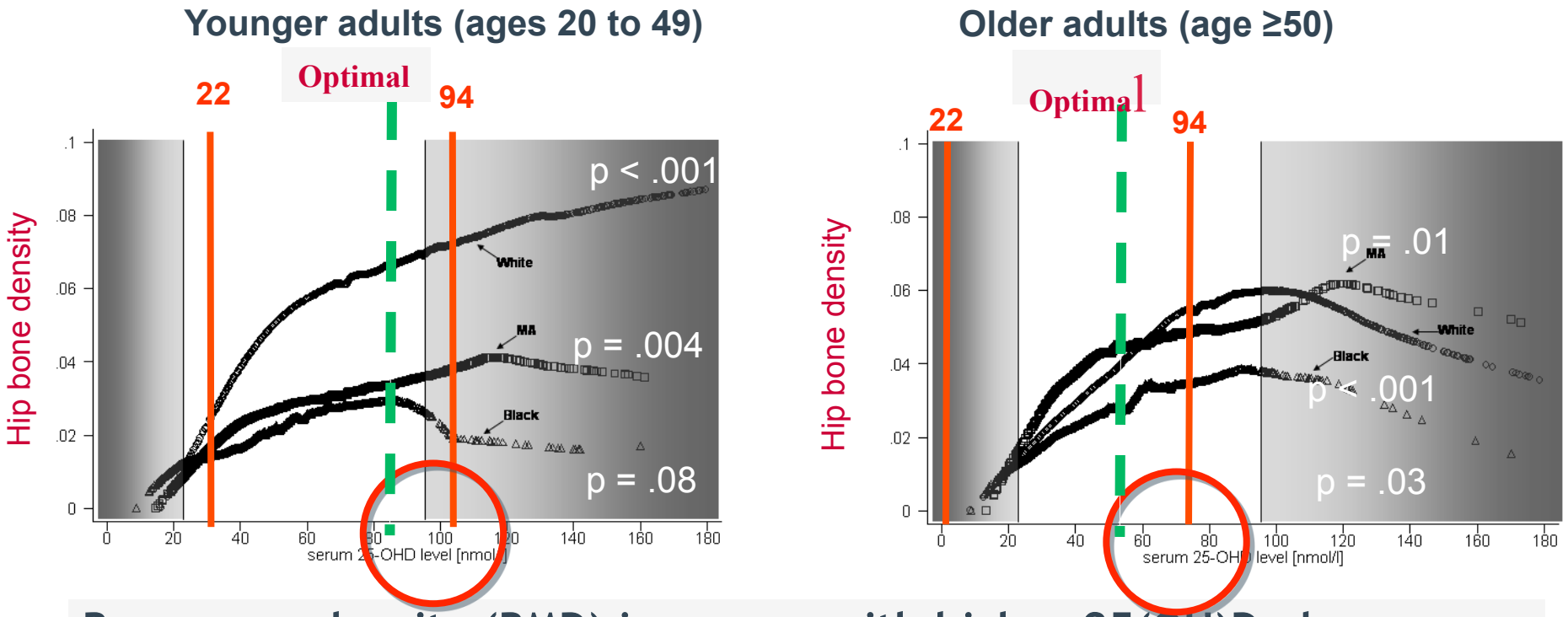
# A higher hip bone density depends on the 25(OH)D plasma levels



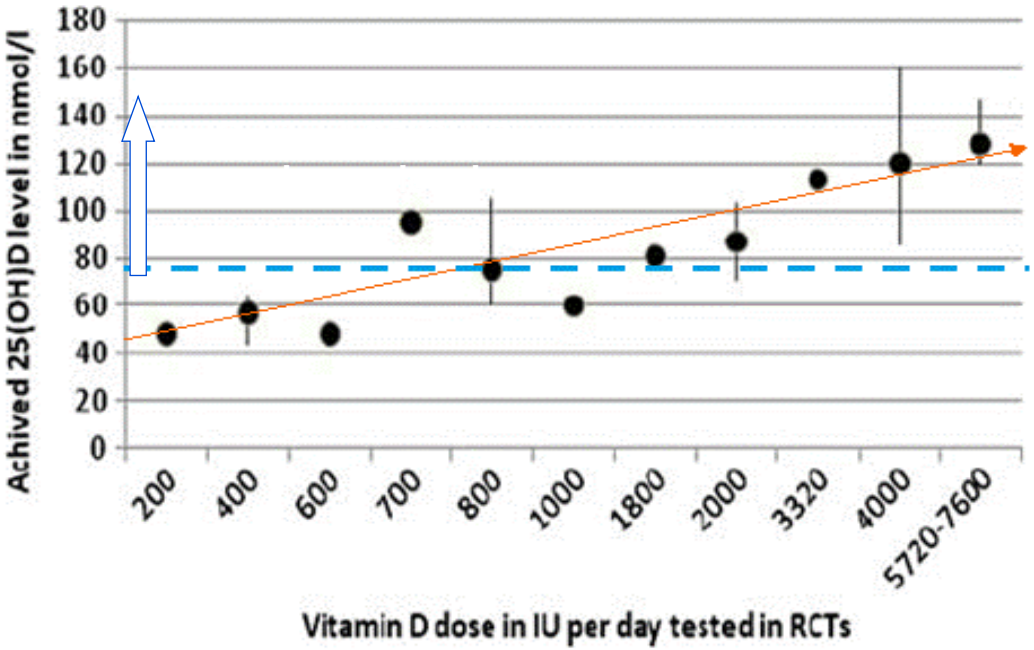

**Bone mass density (BMD) increases with higher 25(OH)D plasma level in younger and in older adults of different ethnicities**

Bischoff-Ferrari HA, Stähelin HB, et al. Am J Med 2004

# Intake of vitamin D and achieved 25(OH)D plasma level, a clear dose-relationship

## RCTs analyzed

RCTs 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 -110 nmol/L
- **These levels can be best obtained with oral doses in the range of 700 IU - 2000 IU**
- Benefit is clearly dose dependent

Bischoff-Ferrari, 2009 Osteoporos Int

# 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)

**Net socio-economic benefit ranges from* :** ⇨ **585 mio €**

Including medical and therapeutic costs for prevention, treatment and supplementation costs vitamin D

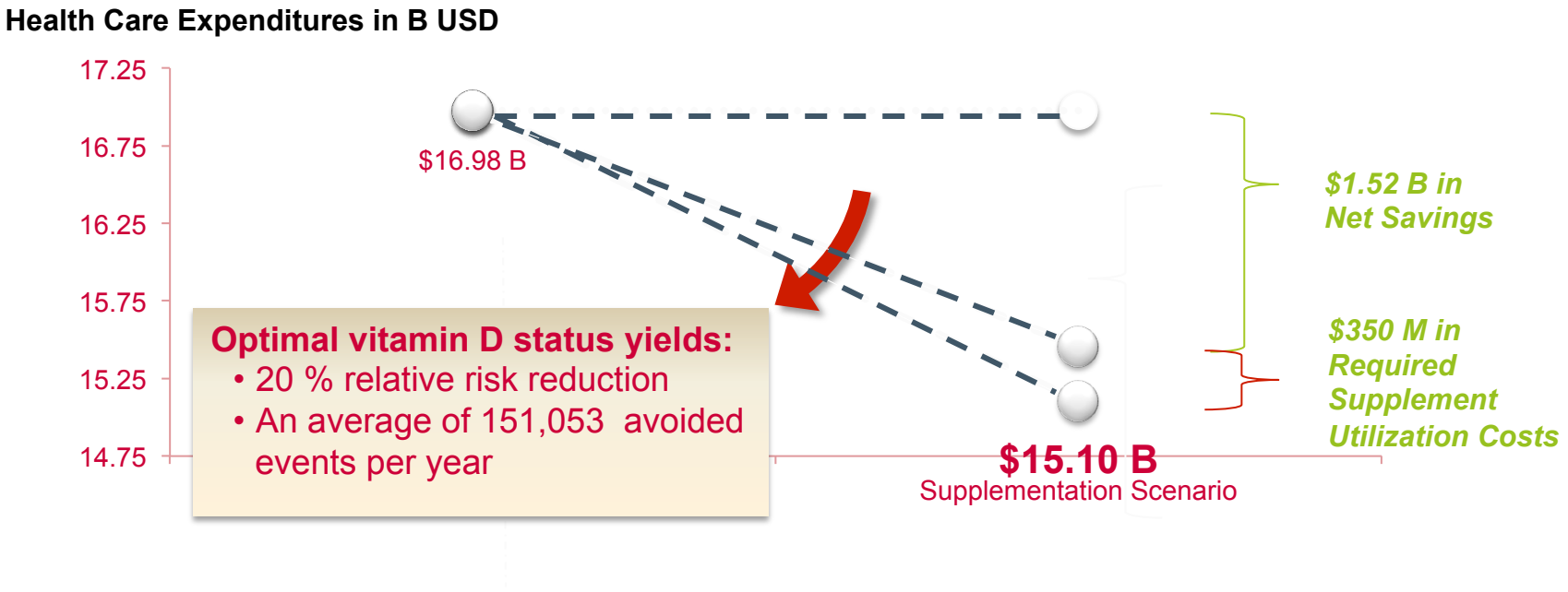
**up to** ⇨ **778 mio €**

Including societal perspective, e.g. family care, reha costs

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.




*Source: Frost & Sullivan analysis.*

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# Vitamin C deficiency is common – also in the Western world

**Table 1.** Prevalence of vitamin C deficiency in larger cross sectional population studies

| Study | Subjects (*n*) | Severe vitamin C deficiency (< 11 μmol/l) | Marginal vitamin C deficiency (11–23 μmol/l) | Suboptimal vitamin C status (23–50 μmol/l) | Comment |
|---|---|---|---|---|---|
| NHANES III[50] | 15 769 | 14 % (M)<br>10 % (F) | 20 % (M)<br>17 % (F) | NR | 31 % (M) and 25 % (F) of the smokers alone were diagnosed with severe vitamin C deficiency |
| NHANES II[51] | 11 592 | 2 % | 8 % | NR | 7 and 20 %, respectively, in smokers alone |
| NHANES II[41] | 8453 | NR | 9 % (NS)<br>30 % (S) | 31 % (NS)*<br>35 % (S) | Subpopulation aged 30 years or older |
| CARDIA[52] | 2637 | NR | 8 % (NS)<br>26 % (S) | 33 % (NS)†<br>40 % (S) | Numbers with marginal vitamin C deficiency include those with severe vitamin C deficiency |
| Third Glasgow MONICA population survey[53] | 1267 | 26 % (M)<br>14 % (F) | 22 % (NSM)<br>16 % (NSF)<br>30 % (SM)<br>30 % (SF) | NR | 36 % (M) and 23 % (F) of the smokers alone were diagnosed with severe vitamin C deficiency |
| French population study[54] | 1039 | 7–12 % (M)<br>3–5 % (F) | 10–46 % (M)‡<br>3–15 % (F) | NR | Values are ranges of various age groups |

NHANES III, Third National Health and Nutrition Examination Survey; M, males; F, females; NR, not reported; NHANES II, Second National Health and Nutrition Examination Survey; NS, non-smokers; S, smokers; CARDIA, Coronary Artery Risk Development in Young Adults Study; MONICA, Monitoring of Trends and Determinants in Cardiovascular Disease; NSM, non-smoking males; NSF, non-smoking females; SM, smoking males; SF, smoking females.

* Range used: 23 to 55 μmol/l.
† Range used: 23 to 45 μmol/l.
‡ Range used: 11 to 19 μmol/l.

**> $10^8$ have chronic Vitamin C deficiency**
**No one knows the consequences…**

Lykkesfeldt og Poulsen, Brit. J. Nutr. (2010)

# Observational studies report positive health effects associated with elevated vitamin C plasma levels

| Ref. | Study population | Mean vitamin C level associated with health effect | Disease outcome | Main results |
|---|---|---|---|---|
| Simon et al., 2001 | 8,453 adults | 45.4 μmol/L (normal) and 79.5 μmol/L | CVD, all-cause mortality | Subjects with normal or saturating serum ascorbic acid levels (45.4 μmol/L and 79.5 μmol/L, respectively) had a "marginally" signi… 21–25% decreased risk of fatal CVD and a significant 25… decreased risk of all-cause mortality compared to… serum ascorbic acid levels (23.0 μmol/L). |
| Boekholdt et al., 2006 | 979 cases and 1794 controls | 77.1 μmol/L | CHD | Subjects with the highest vitamin C pla… 77.1 μmol/L) had a 33% lower… bottom quartile (mean… |
| Khaw et al., 2001 | 19,496 men and women | 72.6 μmol/L in men and 85.1 μmol/L in women | CVD, cancer, all-cause mortality | Subjects in the top… and 85.1 μ… and … |
| Simon et al., 1998 | 6,624 adults | 85.2 μmol/L | | …ch. A 20 …with about a …min C (saturation, 85.2 …ke and 27% reduction in CHD …ast category (low to marginal, 17.0 |
| Nyyssonen et al., 1997 | 1,605 men | Observational st… | | …plasma or serum levels of vitamin C … had a 4-fold higher risk of myocardial infarction compared to …jects with the highest levels (> 64.8 μmol/L), after adjustment for age, season, and year of examination. |
| Langlois et al., 2001 | 85 patie… | | …se | Serum ascorbic acid concentrations were low among PAD patients (median, 27.8 μmol/L) despite comparable smoking status and dietary intake with the other groups (median, 51.7 μmol/L in healthy subjects and 49.6 μmol/L in hypertensive patients without PAD). |
| Gale et al. | | | Stroke | Subjects with the highest vitamin C plasma levels (> 27.8 μmol/L) had a 30% lower risk of death from stroke compared to subjects with lower vitamin C levels. |
| | | …/L | Stroke | Subjects in the top quartile of baseline plasma vitamin C (78.1 μmol/L) had a 42% lower risk of stroke than those in the bottom quartile (28.2 μmol/L), independent of age, sex, BMI, systolic blood pressure, smoking, alcohol consumption, cholesterol, social class, physical activity, diabetes, myocardial infarction, or supplement use. |
| | …women | 64.0 μmol/L | Stroke | Subjects with the highest vitamin C serum levels (≥ 64 μmol/L, top quartile) had a 41% lower risk of all stroke than those with the lowest levels (≤ 40 μmol/L, bottom quartile). The corresponding risk reductions for cerebral infarction and hemorrhagic stroke were 49% and 55%, respectively. |

**Cohorts with elevated vitamin C levels have lower CHD risk by 20 - 42 %**

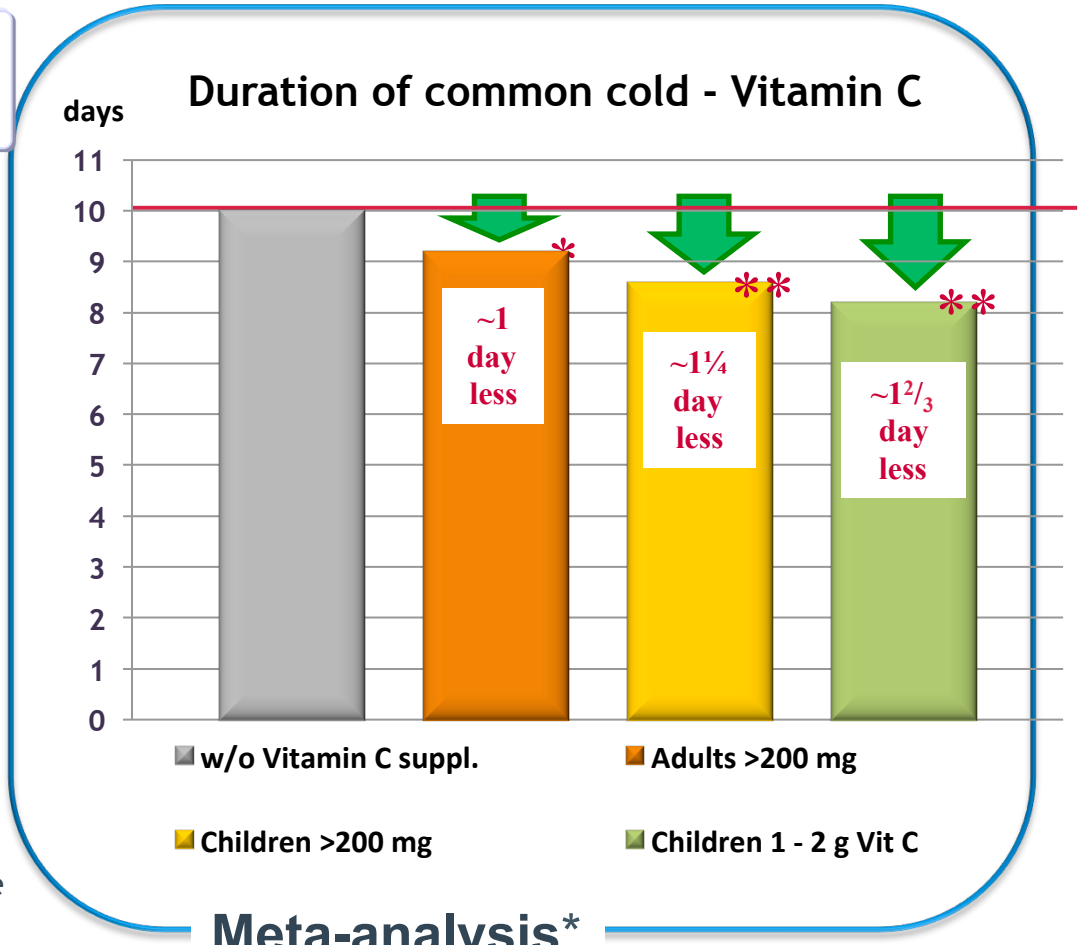
Source: B. Frei et al.

# Vitamin C – reduces *duration* of colds

**Taking regularly**
**≥ 200 mg/d Vitamin C**

Regular supplementation with Vitamin C reduces the duration of colds in adults* and in children**
*(17 trials, 8%; p=0.0002)
**(14 trials, 14% / 18%; p<0.0001)

No drug has a similiar benefit like vitamin C
➡ communicate!




**Meta-analysis***

*Hemilä H., Chalker E.: Cochrane Database Syst Rev. 2013

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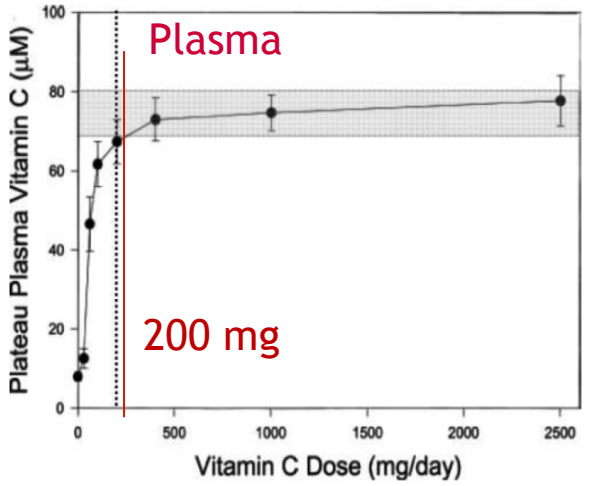
# Vitamin C - optimal intake is 200mg per day

Based on the evidence from human metabolic, pharmaco-kinetic, and observational studies and RCTs, we conclude:

**200 mg per day is the optimum dietary intake of vitamin C**

to maximize the potential health benefits with the least risk of inadequacy or adverse health effects.




Near-saturation plateau plasma vitamin C, 200 mg

**Figure 1** Two hundred milligrams of vitamin C (vertical dotted line) as optimum daily intake based on a) near-saturating plateau plasma vitamin C concentration of ≥ 70 $\mu$M (shaded area) and b) first dose beyond the steep, linear increase in plasma concentration at vitamin C intakes of 30–100 mg/day. (Adapted from (Levine et al., 2001; 1996))

Frei B. et al. 2012

Source: http://www.cdc.gov/nutritionreport/pdf/Nutrition_Book_complete508_final.pdf

# Omega-3 Fatty Acids and Heart Health

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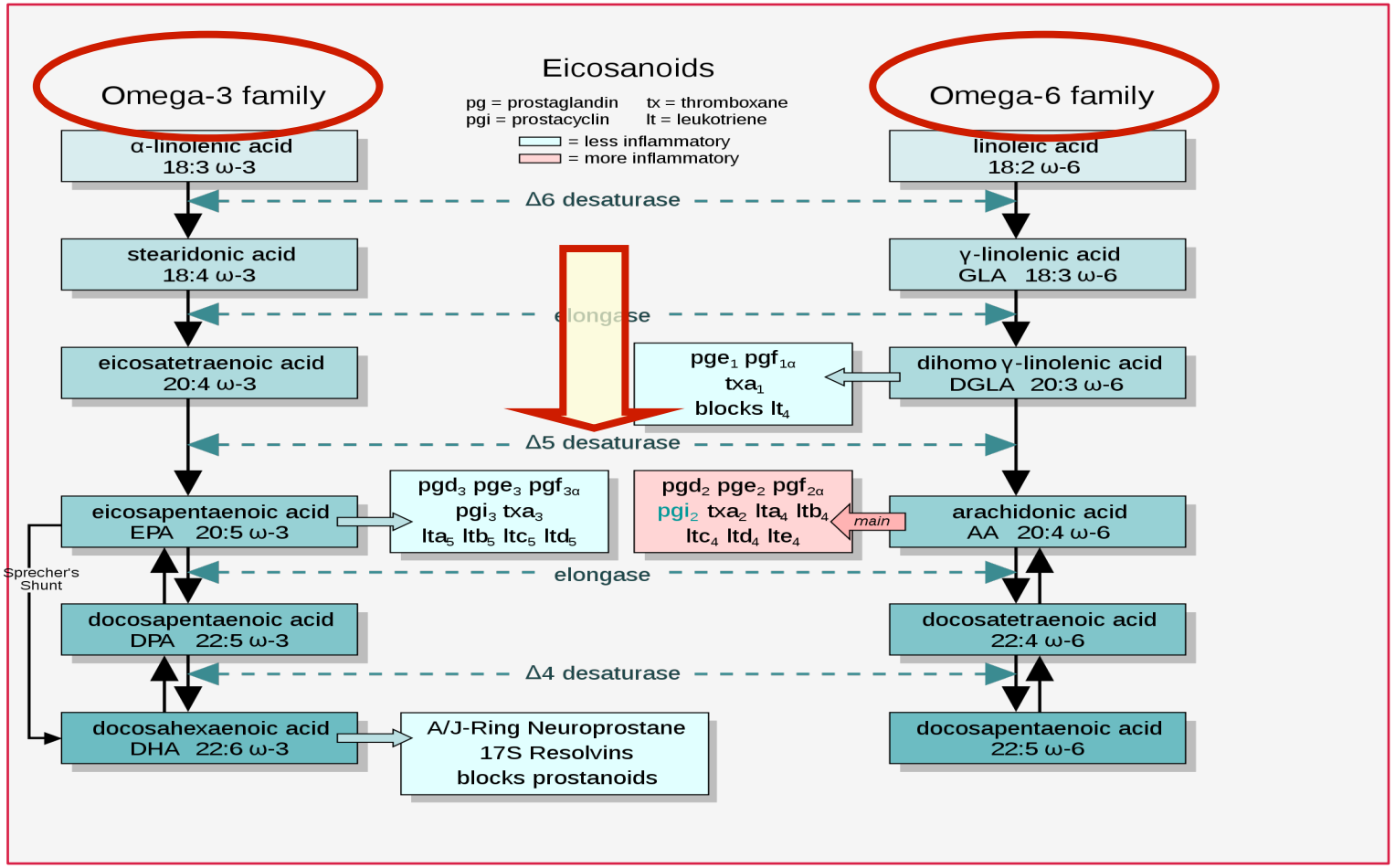


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# Omega-3s Affect Several Functions/ Structures

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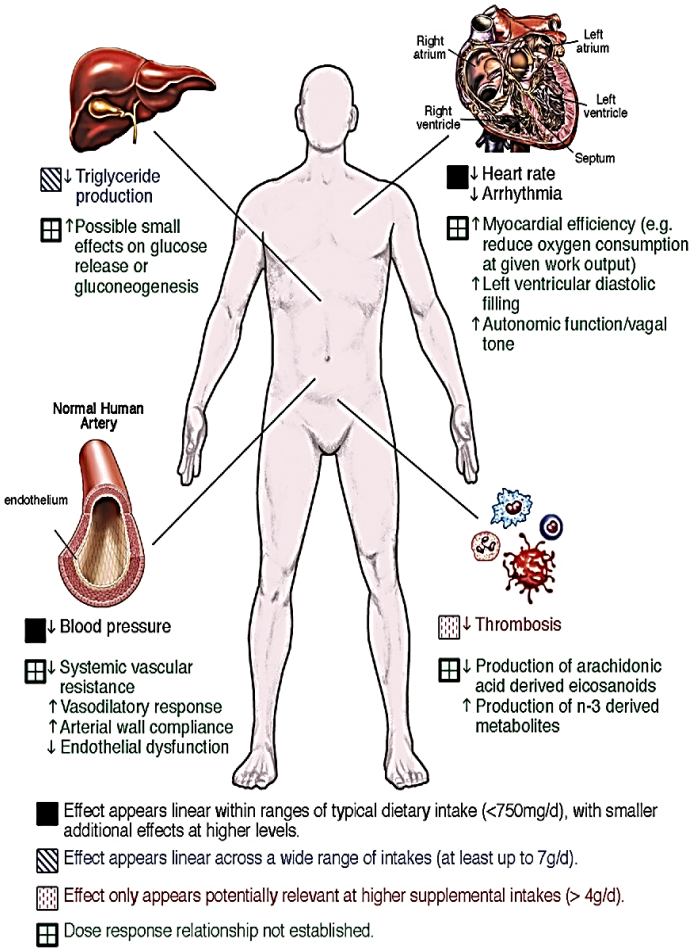


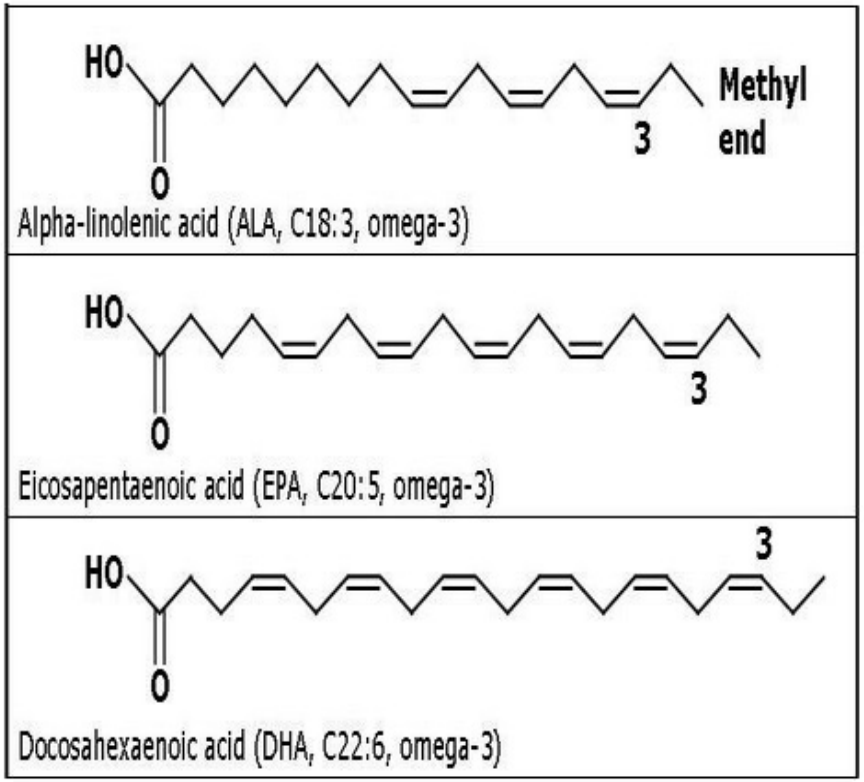


Taken from Mozaffarian et al. 2011 J Am Coll Cardiol 58:2047

# Omega-3 Intake and Risk of Sudden Death
# Physicians' Health Study

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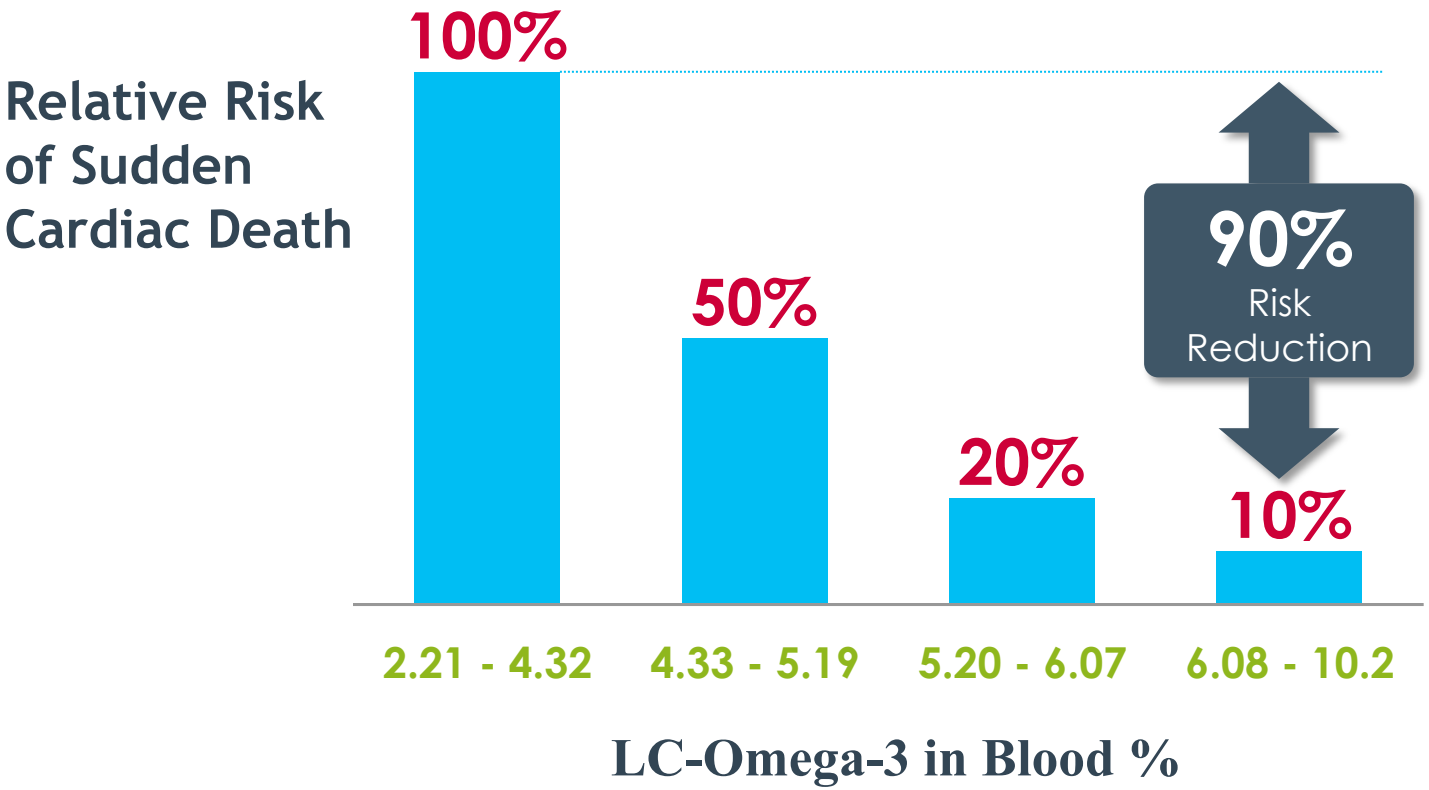


Source: 2002 NEJM 346:1113-1118

# Fish Oil Supplements Reduce Mortality
# GISSI-Prevenzione RCT

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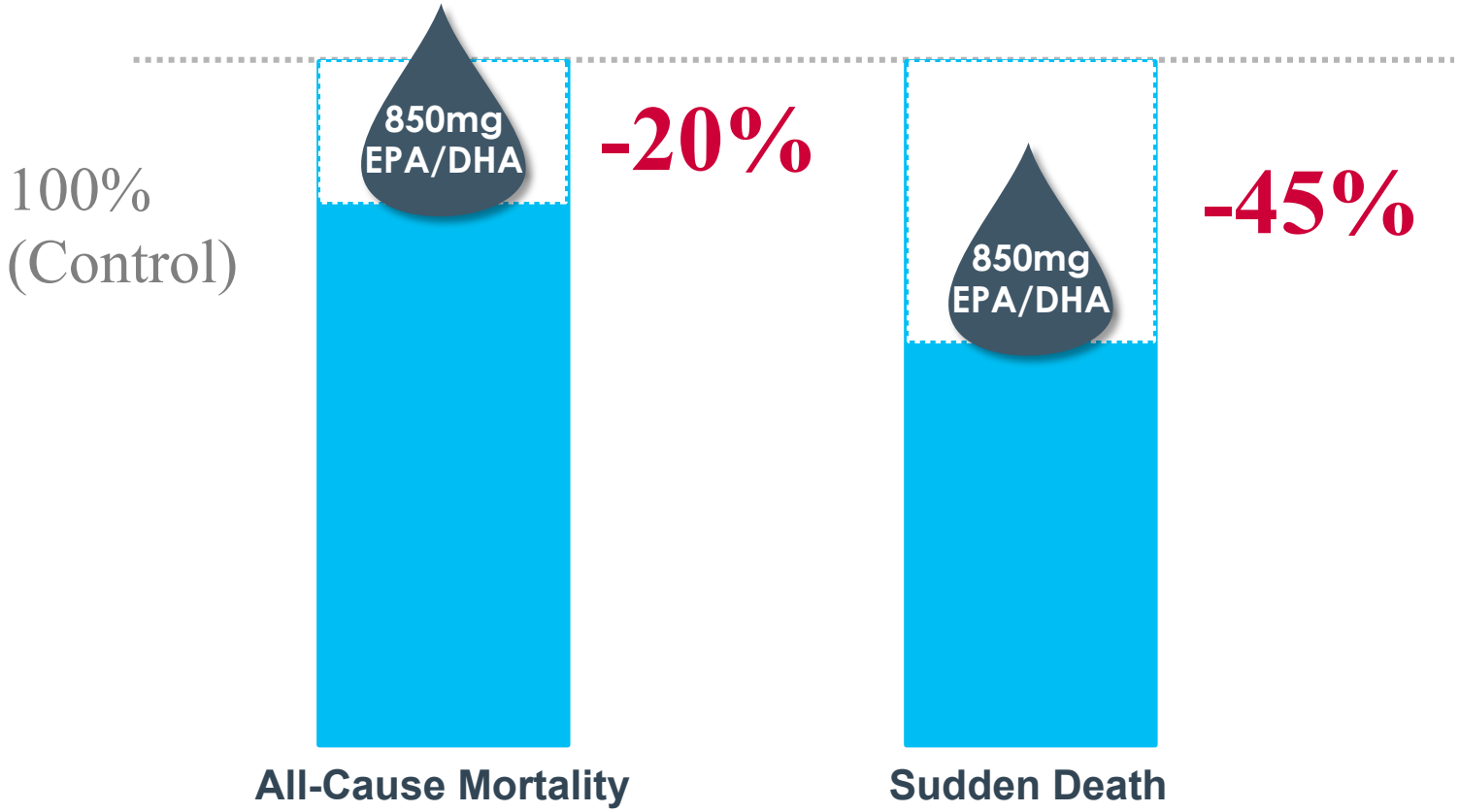


*Source: Lancet 1999; 354:447-455*

# EPA and Major Coronary Events
# Japan EPA Lipid Intervention Study (JELIS)

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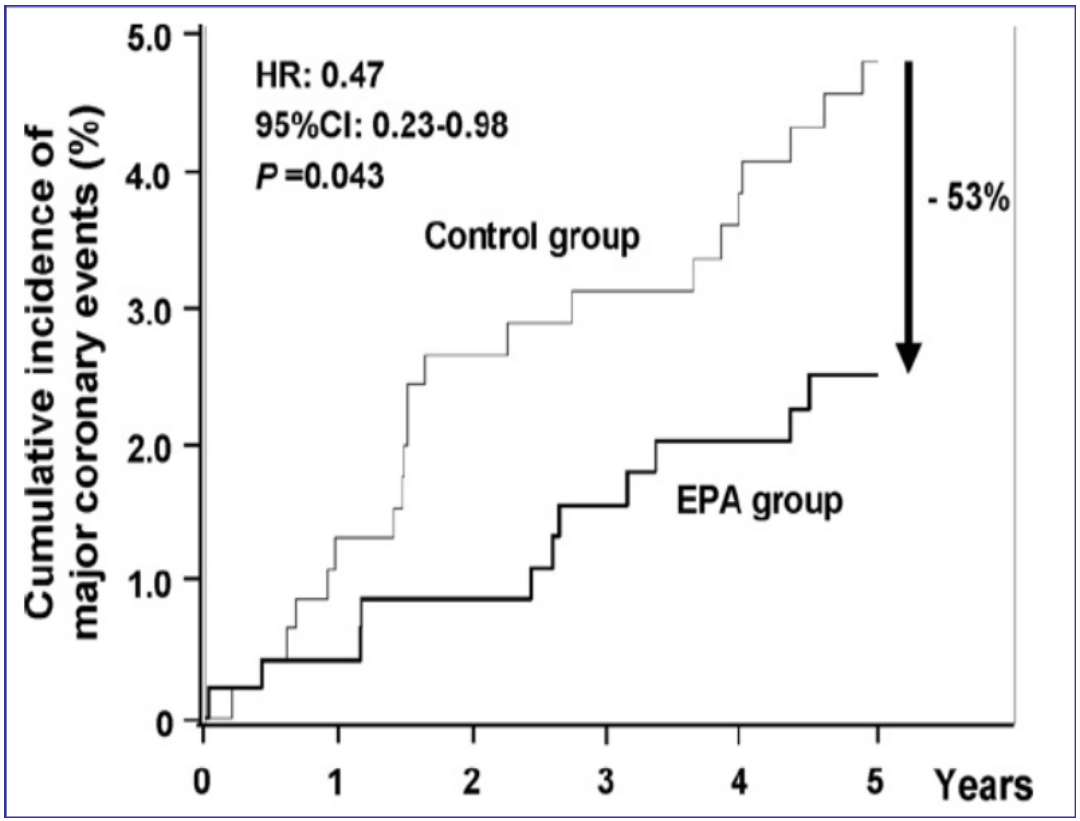


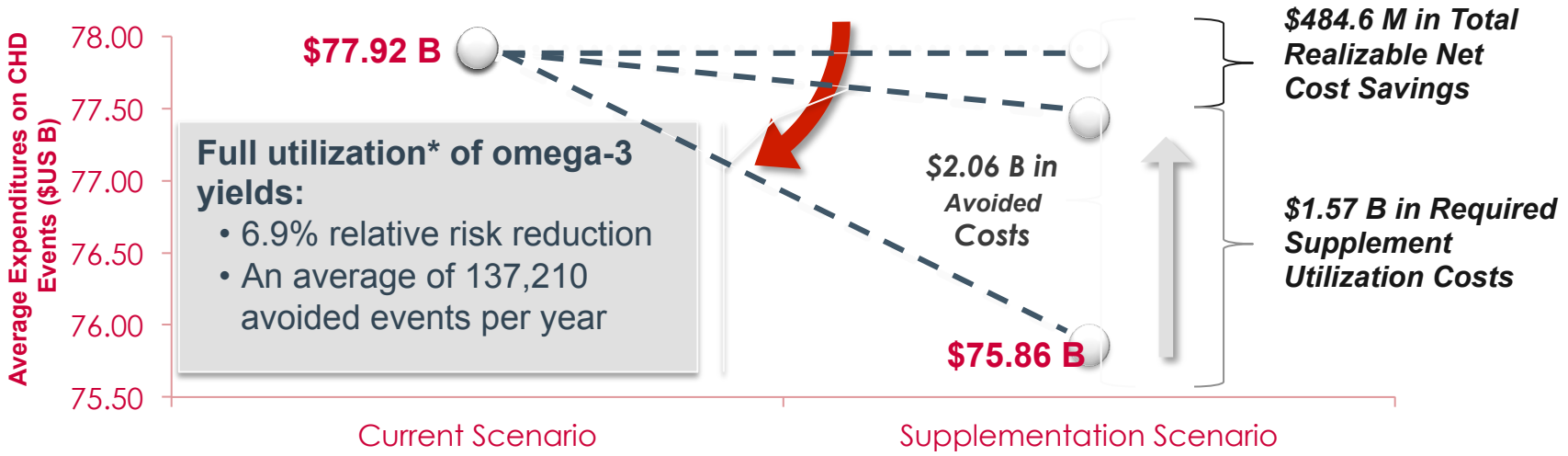

- Hypercholesterolemic patients
- High omega-3 intakes in Japan
- Benefits seen even with statin use

Source: Saito et al. 2008 Atheroscler 200:135

# Benefits of Omega-3—Potential CHD Cost Savings

**The potential net savings in avoided CHD events derived from the use of omega-3 supplements would be an annual average of $484.6 M per year**

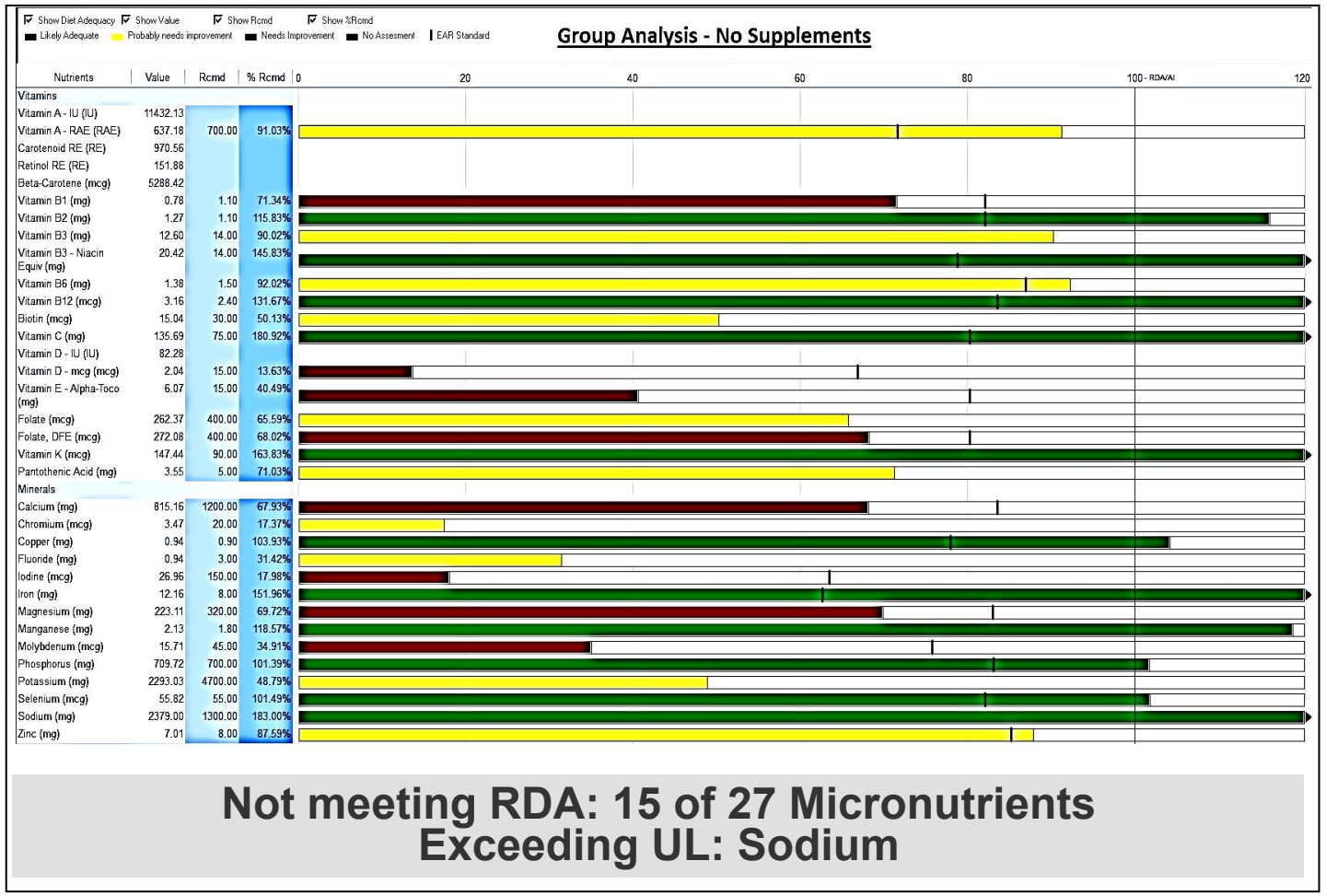
**Net Annual Average Cost Savings due to Avoided Health Care Expenditures through Omega-3 Intervention, 2013–2020**




Source: Frost & Sullivan analysis. Note: * Among all adults over the age of 55 with CHD

# How to close micronutrient gaps?

3-day food diaries; “Food Processor” (USDA National Nutrient Database)

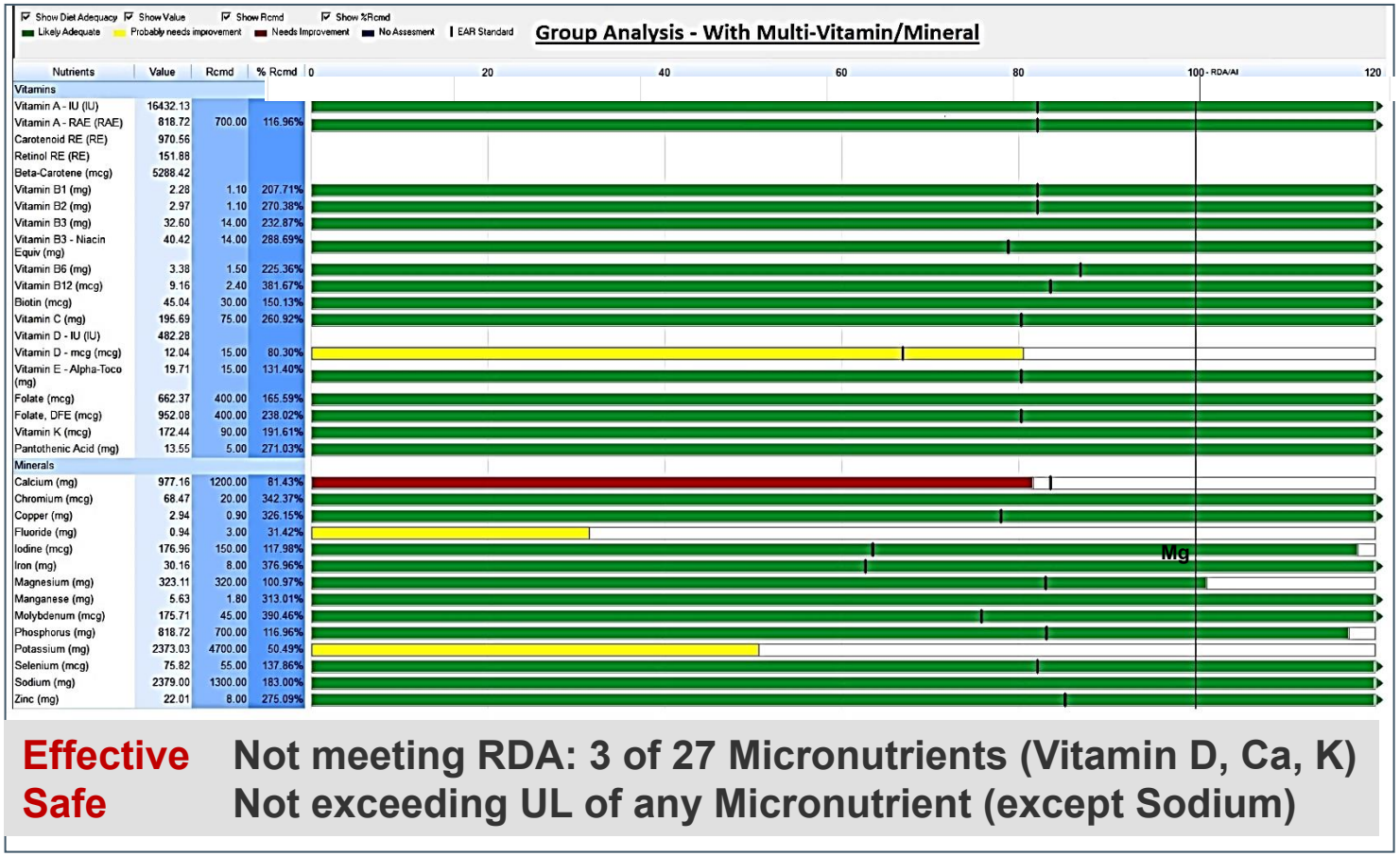



| Nutrients | Value | Rcmd | % Rcmd |
|---|---|---|---|
| Vitamins | | | |
| Vitamin A - IU (IU) | 11432.13 | | |
| Vitamin A - RAE (RAE) | 637.18 | 700.00 | 91.03% |
| Carotenoid RE (RE) | 970.56 | | |
| Retinol RE (RE) | 151.88 | | |
| Beta-Carotene (mcg) | 5288.42 | | |
| Vitamin B1 (mg) | 0.78 | 1.10 | 71.34% |
| Vitamin B2 (mg) | 1.27 | 1.10 | 115.83% |
| Vitamin B3 (mg) | 12.60 | 14.00 | 90.02% |
| Vitamin B3 - Niacin Equiv (mg) | 20.42 | 14.00 | 145.83% |
| Vitamin B6 (mg) | 1.38 | 1.50 | 92.02% |
| Vitamin B12 (mcg) | 3.16 | 2.40 | 131.67% |
| Biotin (mcg) | 15.04 | 30.00 | 50.13% |
| Vitamin C (mg) | 135.69 | 75.00 | 180.92% |
| Vitamin D - IU (IU) | 82.28 | | |
| Vitamin D - mcg (mcg) | 2.04 | 15.00 | 13.63% |
| Vitamin E - Alpha-Toco (mg) | 6.07 | 15.00 | 40.49% |
| Folate (mcg) | 262.37 | 400.00 | 65.59% |
| Folate, DFE (mcg) | 272.08 | 400.00 | 68.02% |
| Vitamin K (mcg) | 147.44 | 90.00 | 163.83% |
| Pantothenic Acid (mg) | 3.55 | 5.00 | 71.03% |
| Minerals | | | |
| Calcium (mg) | 815.16 | 1200.00 | 67.93% |
| Chromium (mcg) | 3.47 | 20.00 | 17.37% |
| Copper (mg) | 0.94 | 0.90 | 103.93% |
| Fluoride (mg) | 0.94 | 3.00 | 31.42% |
| Iodine (mcg) | 26.96 | 150.00 | 17.98% |
| Iron (mg) | 12.16 | 8.00 | 151.96% |
| Magnesium (mg) | 223.11 | 320.00 | 69.72% |
| Manganese (mg) | 2.13 | 1.80 | 118.57% |
| Molybdenum (mcg) | 15.71 | 45.00 | 34.91% |
| Phosphorus (mg) | 709.72 | 700.00 | 101.39% |
| Potassium (mg) | 2293.03 | 4700.00 | 48.79% |
| Selenium (mcg) | 55.82 | 55.00 | 101.49% |
| Sodium (mg) | 2379.00 | 1300.00 | 183.00% |
| Zinc (mg) | 7.01 | 8.00 | 87.59% |

**Not meeting RDA: 15 of 27 Micronutrients**
**Exceeding UL: Sodium**

# Supplements close most dietary micronutrient gaps

3-day food diaries; “Food Processor” (USDA National Nutrient Database)




| Nutrients | Value | Rcmd | % Rcmd |
|---|---|---|---|
| **Vitamins** | | | |
| Vitamin A - IU (IU) | 16432.13 | | |
| Vitamin A - RAE (RAE) | 818.72 | 700.00 | 116.96% |
| Carotenoid RE (RE) | 970.56 | | |
| Retinol RE (RE) | 151.88 | | |
| Beta-Carotene (mcg) | 5288.42 | | |
| Vitamin B1 (mg) | 2.28 | 1.10 | 207.71% |
| Vitamin B2 (mg) | 2.97 | 1.10 | 270.38% |
| Vitamin B3 (mg) | 32.60 | 14.00 | 232.87% |
| Vitamin B3 - Niacin Equiv (mg) | 40.42 | 14.00 | 288.69% |
| Vitamin B6 (mg) | 3.38 | 1.50 | 225.36% |
| Vitamin B12 (mcg) | 9.16 | 2.40 | 381.67% |
| Biotin (mcg) | 45.04 | 30.00 | 150.13% |
| Vitamin C (mg) | 195.69 | 75.00 | 260.92% |
| Vitamin D - IU (IU) | 482.28 | | |
| Vitamin D - mcg (mcg) | 12.04 | 15.00 | 80.30% |
| Vitamin E - Alpha-Toco (mg) | 19.71 | 15.00 | 131.40% |
| Folate (mcg) | 662.37 | 400.00 | 165.59% |
| Folate, DFE (mcg) | 952.08 | 400.00 | 238.02% |
| Vitamin K (mcg) | 172.44 | 90.00 | 191.61% |
| Pantothenic Acid (mg) | 13.55 | 5.00 | 271.03% |
| **Minerals** | | | |
| Calcium (mg) | 977.16 | 1200.00 | 81.43% |
| Chromium (mcg) | 68.47 | 20.00 | 342.37% |
| Copper (mg) | 2.94 | 0.90 | 326.15% |
| Fluoride (mg) | 0.94 | 3.00 | 31.42% |
| Iodine (mcg) | 176.96 | 150.00 | 117.98% |
| Iron (mg) | 30.16 | 8.00 | 376.96% |
| Magnesium (mg) | 323.11 | 320.00 | 100.97% |
| Manganese (mg) | 5.63 | 1.80 | 313.01% |
| Molybdenum (mcg) | 175.71 | 45.00 | 390.46% |
| Phosphorus (mg) | 818.72 | 700.00 | 116.96% |
| Potassium (mg) | 2373.03 | 4700.00 | 50.49% |
| Selenium (mcg) | 75.82 | 55.00 | 137.86% |
| Sodium (mg) | 2379.00 | 1300.00 | 183.00% |
| Zinc (mg) | 22.01 | 8.00 | 275.09% |

**Effective** Not meeting RDA: 3 of 27 Micronutrients (Vitamin D, Ca, K)

**Safe** Not exceeding UL of any Micronutrient (except Sodium)

# Micronutrient challenges and opportunities: Where do we stand?

- Inadequate micronutrient intake is a global issue
- Opportunities: Case studies
  - Vitamin D
  - Vitamin C
  - Omega-3
- Challenges in micronutrients
- Summary and outlook

# Challenges in micronutrients

- Media reports are often negative and challenging concerning the role of vitamins for health and well-being
- We need updated recommendations for nutrients (WHO, CODEX,…)
- We lack European harmonization
- We need more funding for nutrition science and the role of micronutrients
- Dietary risk are the key factor for mortality; we miss data

# Media reports are often negative and challenging

EDITORIAL | Annals of Internal Medicine

## Enough Is Enough: Stop Wasting Money on Vitamin and Mineral Supplements

Three articles in this issue address the role of vitamin and mineral supplements for preventing the occurrence or progression of chronic diseases. First, Fortmann and colleagues (1) systematically reviewed trial evidence to update the U.S. Preventive Services Task Force recommendation on the efficacy of vitamin supplements for primary prevention in community-dwelling adults with no nutritional deficiencies. After reviewing 3 trials of multivitamin supplements and 24 trials of single or paired vitamins that randomly assigned more than 400 000 participants, the authors concluded that there w
beneficial effect of supplements o
diovascular disease, or cancer.

Second, Grodstein and cow
efficacy of a daily multivitamin to
among 5947 men aged 65 yea
in the Physicians' Health Study I
up, there were no differences b
and placebo groups in overall
verbal memory. Adherence to th
and the large sample size resu
showing that use of a multivitan
nourished elderly population did
cline. Grodstein and coworkers'
with a recent review (3) of 12 f
that evaluated dietary supplem
mins, B vitamins, vitamins E a
acids, in persons with mild cogn
to moderate dementia. None of t
cognitive function.

Third, Lamas and associates
benefits of a high-dose, 28-comp
plement in 1708 men and wom

U.S. adults from 30% between 1988 to 1994 to 39% between 2003 to 2006, while overall use of dietary supplements increased from 42% to 53% (9). Longitudinal and secular trends show a steady increase in multivitamin supplement use and a decline in use of some individual supplements, such as β-carotene and vitamin E. The decline in use of β-carotene and vitamin E supplements followed reports of adverse outcomes in lung cancer and all-cause mortality, respectively. In contrast, sales of multivitamins and other supplements have not been affected by major

BIOMEDICAL RESEARCH

## Antioxidants Could Spur Tumors by Acting on Cancer Gene

Many people take vitamins such as A, E, and C thinking that their antioxidant properties will ward off cancer. But some clinical trials have suggested that such antioxidants, which sop up DNA-damaging molecules called free radicals, have the opposite effect and raise cancer risk in certain people. Now, in a provocative study that raises unsettling questions about the widespread use of vitamin supplements, Swedish researchers have showed that moderate doses of two widely used antioxidants spur the growth of early lung tumors in mice.

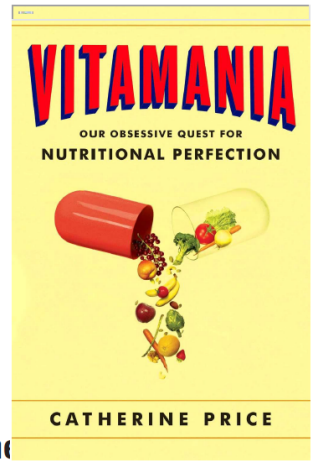
Some cancer specialists caution against basing public health advice on the study, published online this week in *Science Translational Medicine*. "You can't extrapolate from this study to make

drug used to thin mucus in people with lung disease, and fat-soluble vitamin E. They gave mice genetically engineered to develop lung tumors a dose of NAC comparable to what a patient would receive or chow containing about 10 times more vitamin E than is in ordinary mouse food. "A lot of vitamin pills contain a lot more than that. It's a conservative dose," Bergö says.

Compared with mice on a normal diet, the mice consuming the antioxidants developed more lung tumors, their tumors were more aggressive, and they lived only half as long. Follow-up studies suggested that by reducing reactive oxidative species and DNA damage in the cell, the antioxidants turn down a gene, *p53*, that is key to keeping cell growth in check and is often inactivated in cancer.

Laboratory in New York. "Perhaps we should look more carefully at what's available over the counter." But he would like to see a more detailed explanation of how the cell's sensing of reactive species controls *p53* activity. Lung disease researcher Shyam Biswal of Johns Hopkins University in Baltimore, Maryland, wonders if the results would be the same in mice with cancer sparked by a carcinogen, rather than an existing mutation. "The model is great, but it's a very aggressive model," Biswal says.

Another huge caveat, Kramer adds, is that in the earlier lung cancer prevention trials, only


# We need a share of science-based voice in the ongoing debate on the role of nutrients for health

**FROM SCIENCE TO ECONOMICS**

THE POTENTIAL VALUE OF SUPPLEMENTATION

IADSA

International Alliance of Dietary/
Food Supplement Associations

# We need updated recommendations for nutrients

**Micronutrient recommendations during pregnancy**

Currently, the WHO recommends pregnant women to take Iron and Folic Acid supplements only!

*However, many micronutrients, including iron and folic acid are essential during pregnancy……*

| DRI | Females | Pregnancy | Change during Pregnancy |
|---|---|---|---|
| Vitamin A (µg RE) | 700 | 770 | Declines in malnourished pop. |
| Vitamin D (IU) | 600 | 600 | Increases in late gestation |
| Vitamin E (mg) | 15 | 15 | Increases |
| Vitamin K (µg) | 90 | 90 | Little data |
| Folate (µg DFE) | 400 | 600 | Declines due to hemodilution |
| Thiamine (mg) | 1.1 | 1.4 | No change |
| Riboflavin (mg) | 1.1 | 1.4 | No change |
| Niacin (mg) | 14 | 18 | No change |
| Vitamin B-12 (µg) | 2.4 | 2.6 | Declines due to hemodilution |
| Vitamin B-6 (mg) | 1.3 | 1.9 | Declines due to hemodilution & hormonal factors |
| Vitamin C (mg) | 75 | 85 | Declines due to hemodilution |
| Iodine (µg) | 150 | 220 | UI decreases |
| Iron (mg) | 18 | 27 | Declines due to hemodilution and deficiency |
| Zinc (mg) | 8 | 11 | Declines due to hemodilution and deficiency |
| Calcium | 1000 | 1000 | Declines until 34 week |

**The benefit of multi-micronutrient complex is demonstrated**

# We miss aligned recommendations in Europe (Example vitamin E)

**Table 2** Comparison of recommended daily intakes (RDAs/PRIs) of vitamins and minerals for adults derived from different countries and organisations

| Vitamins | $B_1$ Thiamine (mg) | $B_2$ Riboflavin (mg) | Niacin (mg) | $B_6$ (mg) | Folates (µg) | $B_{12}$ (µg) | C (mg) | A (µg RE#) | D (µg) | E (mg) | K (µg) | Pantothenic acid (mg) | Biotin (µg) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| European Union (including Greece), 1992[4] | 1.1/0.9 | 1.6/1.3 | 18/14 | 1.5/1.1 | 200 | 1.4 | 45 | 700/600 | 0-10 | 0.4*/ >4->3 | - | 3-12 | 15-100 |
| Belgium, 2000[9] | 1.1/0.9 | 1.6/1.3 | 18/14 | 1.7/1.2 | 200 | 1.4 | 70 | 700/600 | 2.5-10 | 10 | - | 3-12 | 15-100 |
| France, 2001[10] | 1.3/1.1 | 1.6/1.5 | 14/11 | 1.8/1.5 | 330/300 | 2.4 | 110 | 800/600 | 5 | 12 | 45 | 5 | 50 |
| Germany, Austria, Switzerland, 2000[11] | 1.2/1.0 | 1.4/1.2 | 16/13 | 1.5/1.2 | 400 | 3.0 | 100 | 1000/800 | 5 | 15/12 | 70/60 | 6 | 30-60 |
| Ireland, 1999[12] | 1.1/0.9 | 1.6/1.3 | 18/14 | 1.5/1.1 | 300 | 1.4 | 60 | 700/600 | 0-10 | - | - | - | - |
| Italy, 1996[13] | 1.2/0.9 | 1.6/1.3 | 18/14 | 1.5/1.1 | 200 | 2 | 60 | 700/600 | 0-10 | >8 | - | - | - |
| Netherlands, 1989, 2000, 2003[14,15,16] | 1.1 | 1.5/1.1 | 17/13 | 1.5 | 300 | 2.8 | 70 | 1000/800 | 2.5-5 | 11.8/ 9.3 | - | 5 | - |
| Nordic countries, 1996[17] | 1.4/1.1 | 1.8/1.3 | 19/15 | 1.5/1.2 | 300 | 2.0 | 60 | 900/800 | 5 | 10/8 | - | - | - |
| Portugal, 1982[18] | 1.5/1.2 | 1.6/1.4 | 18/14 | 2.2 | 400 | 3.0 | 75 | 1000 | - | - | - | - | - |
| Spain, 1994-1998[19] | 1.2/0.9 | 1.8/1.4 | 20/15 | 1.8/1.6 | 200 | 2.0 | 60 | 750 | 2.5 | 12 | - | - | - |
| United Kingdom, 1991[20] | 1.0/0.8 | 1.3/1.1 | 17/13 | 1.4/1.2 | 200 | 1.5 | 40 | 700/600 | - | >4/>3 | 74/60 | 3-7 | 10-200 |
| United States, 1997, 1998, 2000, 2001[22,23,24,25] | 1.2/1.1 | 1.3/1.1 | 16/14 | 1.3 | 400 | 2.4 | 90/75 | 900/700 | 5 | 15 | 120/ 90 | 5 | 30 |
| FAO/WHO, 2002[26] | 1.2/1.1 | 1.3/1.1 | 16/14 | 1.3 | 400 | 2.4 | 45 | 600/500 | 5 | 10/7.5 | 65/55 | 5 | 30 |
| **Reference Labelling Value (RLV)** | **1.1** | **1.4** | **16** | **1.4** | **400** | **2.5** | **80** | **800** | **5** | **12** | **75** | **6** | **50** |

When there are 2 values, the left-hand side value represents the contribution advised for men, that of right-hand side for women. When a range of values is proposed, it is indicated by sign "-".

# Retinol equivalents. * mg/g PUFA.

# We need more funding for nutrition science and the role of micronutrients

Nutrition and its role for prevention has a low priority on the agenda of funding bodies (EU, national level)

Very few universities engage in micronutrient research

However, there is a renaissance in micronutrients ….

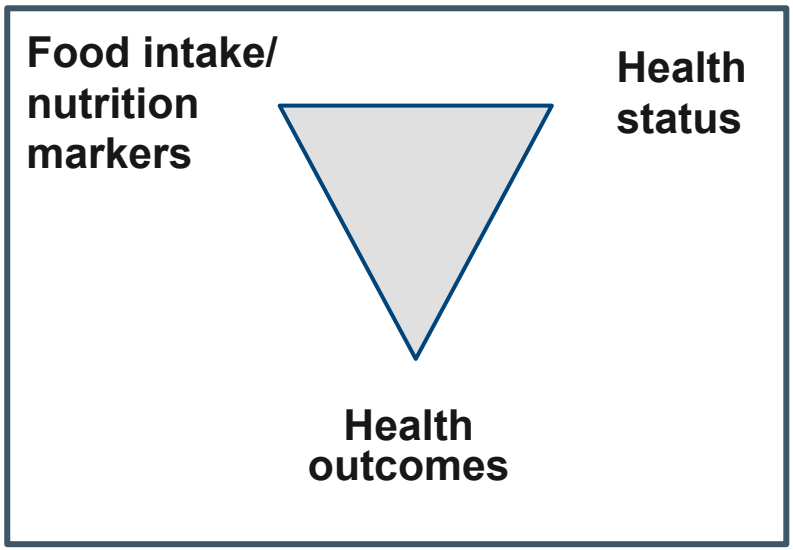
- Understanding nutrient-gene interactions
- Progress in analytics
- Personalized nutrition

## A demand for new scientifc approaches

# Dietary risks are the key factor for mortality

**.. a need for generating data on vitamin status and health outcomes to understand underlying cause and action**


Cohort with >160000 people
- Grandparents
- Parents
- Children




Assessment of vitamin status in low versus high socio-economic groups of the North-Netherlands LifeLines population and explore the phenotype of marginal/subclinical micro-nutrient deficiency

# Micronutrient challenges and opportunities: Where do we stand?

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- Opportunities: Case studies
  - Vitamin D
  - Vitamin C
  - Omega-3
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# Summary

- Inadequate intake and status of essential nutrients is common in many countries, also in the Western world
- Adequate status is a relevant factor to improve public health
- Supplements are an effective and safe way to close the nutrient gap
- A continuous effort is required to manage challenges and generate awareness from the regulatory, media and the scientific environment.

# Thank you!

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# Support for 200 mg Vitamin C intake

Per 2012 CDC 2nd Nutrition Report, 200 mg C daily intake for the majority of the adult population is needed to maximize the vitamin's potential health benefits with the least risk of inadequacy or adverse health effects.

Source: http://www.cdc.gov/nutritionreport/pdf/Nutrition_Book_complete508_final.pdf

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## Authors' Perspective: What is the Optimum Intake of Vitamin C in Humans?

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*The recommended dietary allowance (RDA) of vitamin C has traditionally been based on the prevention of the vitamin C deficiency disease, scurvy. While higher intakes of vitamin C may exert additional health benefits, the limited Phase III randomized placebo-controlled trials (RCTs) of vitamin C supplementation have not found consistent benefit with respect to chronic disease prevention. To date, this has precluded upward adjustments of the current RDA. Here we argue that Phase III RCTs—designed principally to test the safety and efficacy of pharmaceutical drugs—are ill suited to assess the health benefits of essential nutrients; and the currently available scientific evidence is sufficient to determine the optimum intake of vitamin C in humans. This evidence establishes biological plausibility and mechanisms of action for vitamin C in the primary prevention of coronary heart disease, stroke, and cancer; and is buttressed by consistent data from prospective cohort studies based on blood analysis or dietary intake and well-designed Phase II RCTs. These RCTs show that vitamin C supplementation lowers hypertension, endothelial dysfunction, chronic inflammation, and Helicobacter pylori infection, which are independent risk factors of cardiovascular diseases and certain cancers. Furthermore, vitamin C acts as a biological antioxidant that can lower elevated levels of oxidative stress, which also may contribute to chronic disease prevention. Based on the combined evidence from human metabolic, pharmacokinetic, and observational studies and Phase II RCTs, we conclude that 200 mg per day is the optimum dietary intake of vitamin C for the majority of the adult population to maximize the vitamin's potential health benefits with the least risk of inadequacy or adverse health effects.*

# Omega-3 and Heart Health Summary

- **Structure-function relationship established**
  - Omega-3 fatty acids required for cell membranes and signaling molecules
  - Desaturation and elongation of ALA to EPA and DHA is limited
  - Increased omega-3 fatty acid status helps maintain health
- **Claims sanctioned in many countries**