Demystifying Vitamins and Supplements

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UCLA Health
Who is taking Vitamins and Supplements?
Who is taking supplements?

- More physically active
- Lower BMI
- Less likely to smoke
- More educated, health conscious
- Older, >65yo
Who is taking Vitamins and Supplements?

The "Life...supplemented" Healthcare Professionals Impact Study (HCP Impact Study) found

• 72% of physicians
• 89% of nurses

Used dietary supplements regularly, occasionally, or seasonally.

Regular use of dietary supplements was reported by 51% of physicians and 59% of nurses.
An Evidence Based Approach

Observational Studies
- Correlation does not imply causation
- Confounding biases

Randomized Clinical Trials

Systematic Reviews and Meta analysis

By Jacknunn - Own work, CC BY-SA 4.0,
https://commons.wikimedia.org/w/index.php?curid=49168037
Supplement Types

1. **Vitamins**
   - ✓ Vitamin A
   - ✓ Vitamin E
   - ✓ Vitamin C
   - ✓ Vitamin D
   - ✓ Vitamin B12

2. **Multivitamins**

3. **Minerals**
   - ✓ Calcium

4. **Fatty acids**
   - ✓ Fish Oil
Vitamins

- Fat-soluble or water-soluble
- Organic compounds essential for normal biochemical and physiological functions.
- Vitamins are multi-functional:
  - serve as structural components in the body,
  - act as co-enzymes in multiple metabolic pathways,
  - and/or act as antioxidants
Minerals

- Minerals are inorganic elements
- Essential to body functions - maintenance of acid-base balance, normal hemoglobin levels and osmotic pressure.
- Components of vitamins, hormones, enzymes in bone and tissues.
- Calcium
Omega-3 fatty acids

- **Lipids**
  - TG ↓
  - RLP ↓

- **Vessels**
  - Inflammation ↓
  - Endothelial function ↑
  - Vasodilation ↑

- **Platelets**
  - Platelet aggregation ↓
  - Blood rheology ↑

- **Plaque stabilization**
  - Arrhythmias ↓
  - Mitochondrial function ↑

- **Cardiovascular protection**

*Image Credit: google.com*
Antioxidants

- Beta carotene/Vitamin A
- Vitamin E
- Vitamin C
Beta carotene/Vitamin A

Red, yellow, orange fruits and vegetables
  Carrots
  Tomatoes
  Sweet potatoes
  Spinach
Helps with vision, immune function, antioxidant
Toxicity: skin yellowing
Observational Data

- Individuals with higher Beta Carotene in blood, got lower rates of cancer.
- Particularly lower incidence of lung cancer
CARET
Beta carotene and Retinol Efficacy Trial

RCT
18,000 smokers, former smokers, ages 45-74, Enrolled in 1985, with 4 year follow up.

Beta carotene 30mg and Vitamin A 25,000IU

Primary end points: lung cancer, death, Cardiovascular health.

Beta carotene- More lung cancer, more death from all causes.
What’s the Bottom line?

Dietary reference intakes (DRIs) represent four concepts:
- Recommended Dietary Allowance (RDA);
- Adequate Intake (AI);
- Estimated Average Requirement (EAR); and
- Tolerable Upper Intake Level (UL).

DRIs are established in the United States by the National Academy of Sciences, National Research Council, and the Institute of Medicine (IOM).
<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Vitamin A (mcg RAE)</td>
<td>RDA</td>
<td>300</td>
<td>400</td>
<td>400</td>
<td>600</td>
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<td>RDA</td>
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<td>7</td>
<td>7</td>
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<td>11</td>
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<td>Thiamin (mg)</td>
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<td>0.6</td>
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<td>1.2</td>
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<td>Riboflavin (mg)</td>
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<td>Niacin (mg)</td>
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<td>8</td>
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<td>14</td>
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<td>Folate (mcg)</td>
<td>RDA</td>
<td>150</td>
<td>200</td>
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<tr>
<td>Vitamin B₆ (mg)</td>
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<td>0.6</td>
<td>0.6</td>
<td>1.0</td>
<td>1.0</td>
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<td>Choline (mg)</td>
<td>AI</td>
<td>200</td>
<td>250</td>
<td>250</td>
<td>375</td>
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<td>Vitamin K (mcg)</td>
<td>AI</td>
<td>30</td>
<td>55</td>
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<td>60</td>
<td>60</td>
<td>75</td>
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<td>90</td>
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<td>120</td>
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## Vitamin A

### Recommended Dietary Allowances (RDAs) for Vitamin A

<table>
<thead>
<tr>
<th>Age</th>
<th>Male</th>
<th>Female</th>
<th>Pregnancy</th>
<th>Lactation</th>
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<tbody>
<tr>
<td>0–6 months*</td>
<td>400 mcg RAE</td>
<td>400 mcg RAE</td>
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<tr>
<td>7–12 months*</td>
<td>500 mcg RAE</td>
<td>500 mcg RAE</td>
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</tr>
<tr>
<td>1–3 years</td>
<td>300 mcg RAE</td>
<td>300 mcg RAE</td>
<td></td>
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</tr>
<tr>
<td>4–8 years</td>
<td>400 mcg RAE</td>
<td>400 mcg RAE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9–13 years</td>
<td>600 mcg RAE</td>
<td>600 mcg RAE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>14–18 years</td>
<td>900 mcg RAE</td>
<td>700 mcg RAE</td>
<td>750 mcg RAE</td>
<td>1,200 mcg RAE</td>
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<tr>
<td>19–50 years</td>
<td>900 mcg RAE</td>
<td>700 mcg RAE</td>
<td>770 mcg RAE</td>
<td>1,300 mcg RAE</td>
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<tr>
<td>51+ years</td>
<td>900 mcg RAE</td>
<td>700 mcg RAE</td>
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<td></td>
</tr>
</tbody>
</table>

### Beta-Carotene

- Antioxidant & converted to vitamin A.

- 1 cup raw carrots: 10,605 mcg
- 1 cup raw kale: 6,182 mcg
- 1 cup raw spinach: 1,688 mcg

### Nonfermentable fiber

- Easy on your stomach and does not cause gas.
- [Low FODMAP](https://www.ibs-uk.org/lifestyle/fodmap-diet/)
- [AIP-FRIENDLY](https://www.ibs-uk.org/anti-inflammatory-diet/)
- [MEDIUM-CARB](https://www.ibs-uk.org/carbohydrates/)

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[Image of carrots with text: The greens are edible too, along with information about fiber.]
# Upper Tolerable Limits

<table>
<thead>
<tr>
<th>VITAMIN</th>
<th>CURRENT RDI*</th>
<th>NEW DRI**</th>
<th>UL***</th>
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</thead>
<tbody>
<tr>
<td>Vitamin A</td>
<td>5000 IU</td>
<td>900 mcg (3000 IU)</td>
<td>3000 mcg (10,000 IU)</td>
</tr>
<tr>
<td>Vitamin C</td>
<td>60 mg</td>
<td>90 mg</td>
<td>2000 mg</td>
</tr>
<tr>
<td>Vitamin D</td>
<td>400 IU (10 mcg)</td>
<td>15 mcg (600 IU)</td>
<td>50 mcg (2000 IU)</td>
</tr>
<tr>
<td>Vitamin E</td>
<td>30 IU (20 mg)</td>
<td>15 mg #</td>
<td>1000 mg</td>
</tr>
<tr>
<td>Vitamin K</td>
<td>80 mcg</td>
<td>120 mcg</td>
<td>ND</td>
</tr>
<tr>
<td>Thiamin</td>
<td>1.5 mg</td>
<td>1.2 mg</td>
<td>ND</td>
</tr>
<tr>
<td>Riboflavin</td>
<td>1.7 mg</td>
<td>1.3 mg</td>
<td>ND</td>
</tr>
<tr>
<td>Niacin</td>
<td>20 mg</td>
<td>16 mg</td>
<td>35 mg</td>
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<tr>
<td>Vitamin B-6</td>
<td>2 mg</td>
<td>1.7 mg</td>
<td>100 mg</td>
</tr>
<tr>
<td>Folate</td>
<td>400 mcg (0.4 mg)</td>
<td>400 mcg from food, 200 mcg synthetic ##</td>
<td>1000 mcg synthetic</td>
</tr>
<tr>
<td>Vitamin B-12</td>
<td>6 mcg</td>
<td>2.4 mcg ##</td>
<td>ND</td>
</tr>
<tr>
<td>Biotin</td>
<td>300 mcg</td>
<td>30 mcg</td>
<td>ND</td>
</tr>
<tr>
<td>Pantothenic acid</td>
<td>10 mg</td>
<td>5 mcg</td>
<td>ND</td>
</tr>
<tr>
<td>Choline</td>
<td>Not established</td>
<td>550 mg</td>
<td>3500 mg</td>
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</tbody>
</table>
Vitamin E

- Fat soluble antioxidant
- **US RDA 15IU in men and women**
- Deficiency is rare
- **Supplements: 200-400IU**
- Food sources: wheat germ, egg yolk, vegetable oil, nuts, green vegetables
- Observational Study: Nurses Health Study:
  - 87,000 female nurses, no cancer, stroke, heart disease, followed 8 years.
  - 34% reduction in heart disease those taking >200IU daily.
Women’s Health Study
Lee JAMA 2005

• 40,000 healthy women >45yo
• RCT, 10 year follow up
• Vitamin E 600IU every other day versus control
• NO BENEFIT
Vitamin C

• Supplementation can lead to 50% reduction in colds
• BUT in marathon runners, soldiers
• 10% reduction in duration for general public
• Women’s Antioxidant Cardiovascular study and Physicians Health Study II
• Tested 500mg/day, mean follow up of 8-9 years
• No overall association with CVD and cancer
Antioxidant Meta analysis

- 47 Randomized control trials
- Vitamin A 16% increase in all cause mortality
- Beta carotene 7% increase
- Vitamin E 4% increase
- Vitamin C 6% increase (not statistically significant)

Mortality in Randomized Trials of Antioxidant Supplements for Primary and Secondary Prevention Systematic Review and Meta-analysis

Goran Bjelakovic, et

doi:10.1001/jama.297.8.842
Vitamin B 12

- Vitamin B12 deficiency is estimated to affect 10%-15% of people over the age of 60,
- Absorption affected in atrophic gastritis
- Metformin and B12
- Recommended daily allowance for vitamin B12 is **2.4 micrograms**,  
- Should try to obtain vitamin B12 from either supplements or fortified foods to ensure adequate absorption from the gastrointestinal tract.
Absorption of B12

1. Vitamin B_12 in food is bound to protein.
2. In the stomach, acid and pepsin help release vitamin B_12 from food proteins.
3. Cells in the stomach lining release intrinsic factor (IF).
4. In the upper portion of the small intestine (duodenum), intrinsic factor binds to vitamin B_12.
5. In the lower part of the small intestine (ileum), the vitamin B_12-intrinsic factor complex binds to receptors on cells, allowing absorption. A small amount of B_12 not bound to intrinsic factor can be absorbed through passive diffusion.
6. In the colon, vitamin B_12 is synthesized by microorganisms but cannot be absorbed.
Vitamin B12 and Cognition

(A)

<table>
<thead>
<tr>
<th>Study name 1st author (year)</th>
<th>Difference in means</th>
<th>Lower limit</th>
<th>Upper limit</th>
<th>Z-value</th>
<th>p-value</th>
<th>Difference in means (95%CI.)</th>
<th>Relative weight</th>
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<tbody>
<tr>
<td>Aisen (2008)</td>
<td>-1.900</td>
<td>-2.981</td>
<td>-0.819</td>
<td>-3.444</td>
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<td>Connelly (2008)</td>
<td>-4.040</td>
<td>-7.239</td>
<td>-0.841</td>
<td>-2.475</td>
<td>0.013</td>
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<td>5.05</td>
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<tr>
<td>Sun (2007)</td>
<td>-2.600</td>
<td>-3.610</td>
<td>-1.590</td>
<td>-5.048</td>
<td>0.000</td>
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<td>50.73</td>
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<tr>
<td>Combined effect</td>
<td>-2.363</td>
<td>-3.082</td>
<td>-1.644</td>
<td>-6.442</td>
<td>0.000</td>
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</table>

Heterogeneity test: Q-value=1.971, df=2, I-squared=0%, p-value=0.373.

(B)

<table>
<thead>
<tr>
<th>Study name 1st author (year)</th>
<th>Difference in means</th>
<th>Lower limit</th>
<th>Upper limit</th>
<th>Z-value</th>
<th>p-value</th>
<th>Difference in means (95%CI.)</th>
<th>Relative weight</th>
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</thead>
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<tr>
<td>Aisen (2008)</td>
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<td>-0.503</td>
<td>1.363</td>
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<td>Sun (2007)</td>
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<td>Combined effect</td>
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<td>0.627</td>
<td>0.108</td>
<td>0.914</td>
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Heterogeneity test: Q-value=0.967, df=2, I-squared=0%, p-value=0.617.
Vitamin D

Shown benefit: Bone health, fracture risk, fall prevention

Conflicting Data (Not supported by evidence):
Autoimmune disease, cancer, cardiovascular disease, depression, dementia, infectious diseases.
Vitamin D and Calcium
Institute of Medicine Report looked at 1000 studies

Bottom line:
- Vitamin D deficient <12
- Insufficient 12-20
- Sufficient >20
- Potentially harmful >50 (150 toxic)
## Vitamin D Supplement

Vitamin D3 (Cholecalciferol) vs. Vitamin D2 (Ergocalciferol)

<table>
<thead>
<tr>
<th>Vitamin D3 (Cholecalciferol)</th>
<th>Vitamin D2 (Ergocalciferol)</th>
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<tbody>
<tr>
<td>Form synthesized in the body</td>
<td>Form found in plant life</td>
</tr>
<tr>
<td>Naturally derived supplement</td>
<td>Synthetically derived supplement</td>
</tr>
<tr>
<td>Significantly increases vitamin D levels in the body*</td>
<td>Moderately increases vitamin D levels in the body*</td>
</tr>
<tr>
<td>Recommended by experts for optimal bone and immune support*</td>
<td>Alternative form appropriate for vegetarians</td>
</tr>
</tbody>
</table>
Calcium

- Bone Structure
- Muscle Contraction
- Cellular Metabolism
- Wound Healing
- Nerve Impulse Transmission
Calcium

Relative Risk (95% CI)
comparing the highest vs. the lowest
category of dietary calcium intake

<table>
<thead>
<tr>
<th>Author (year), Study</th>
<th>Coronary Heart Disease</th>
<th>RR (95% CI)</th>
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<tbody>
<tr>
<td>Vlijver (1992), Dutch Study (men)</td>
<td>1.11 (0.68-1.81)</td>
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<tr>
<td>Vlijver (1992), Dutch Study (women)</td>
<td>0.91 (0.41-2.03)</td>
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<tr>
<td>Bostick (1999), IWHS</td>
<td>0.63 (0.40-0.98)</td>
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<tr>
<td>Al-Delaimy (2003), HPFS</td>
<td>0.93 (0.77-1.14)</td>
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<tr>
<td>Marniemi (2005), Finnish Study</td>
<td>1.14 (0.70-1.84)</td>
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<tr>
<td>Umesawa (2006), JACC (men)</td>
<td>0.92 (0.37-2.29)</td>
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<tr>
<td>Umesawa (2006), JACC (women)</td>
<td>0.87 (0.31-2.45)</td>
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<tr>
<td>Umesawa (2008), JPHC</td>
<td>0.93 (0.58-1.50)</td>
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</table>

Pooled | 0.92 (0.80-1.07) |

Relative Risk (95% CI)
comparing the highest vs. the lowest category of calcium supplement use

<table>
<thead>
<tr>
<th>Author (year), Study</th>
<th>Coronary Heart Disease</th>
<th>RR (95% CI)</th>
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<td>Bostick (1999), IWHS</td>
<td>0.88 (0.64-1.23)</td>
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<tr>
<td>Al-Delaimy (2003), HPFS</td>
<td>0.87 (0.64-1.19)</td>
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<tr>
<td>Pentti (2009), KORFPS</td>
<td>1.24 (1.02-1.52)</td>
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Pooled | 1.01 (0.78-1.30) |

<table>
<thead>
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<th>Author (year), Study</th>
<th>Stroke</th>
<th>RR (95% CI)</th>
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<td>Ascherio (1998), HPFS</td>
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<td>Iso (1999), NHS</td>
<td>0.73 (0.53-1.01)</td>
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<td>Marniemi (2005), Finnish Study</td>
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<tr>
<td>Umesawa (2006), JACC (men)</td>
<td>0.68 (0.37-1.26)</td>
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<tr>
<td>Umesawa (2006), JACC (women)</td>
<td>0.94 (0.51-1.72)</td>
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<tr>
<td>Umesawa (2008), JPHC</td>
<td>0.71 (0.56-0.89)</td>
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<td>Larsson (2008), ATBC</td>
<td>1.10 (0.98-1.26)</td>
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</tbody>
</table>

Pooled | 0.86 (0.69-1.06) |

<table>
<thead>
<tr>
<th>Author (year), Study</th>
<th>Stroke</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ascherio (1998), HPFS</td>
<td>0.88 (0.60-1.27)</td>
<td></td>
</tr>
<tr>
<td>Iso (1999), NHS</td>
<td>0.75 (0.56-1.01)</td>
<td></td>
</tr>
</tbody>
</table>

Pooled | 0.80 (0.63-1.01) |
Calcium

1000mg- 1200mg daily intake (DIET)
If supplementing, <500mg

- Citrate
  - Does not depend on acid for absorption

- Calcium carbonate
  - Oscal
  - TUMS
  - Depends on acid in stomach to be absorbed. If taking Proton pump inhibitor (Protonix, Nexium), may want to avoid
Omega 3 Fatty Acids

Modern diets have an increased ratio of omega-6/omega 3 fatty acids

Sources of omega 3: fish and nuts
Sources of omega 6: corn oil, soybean, sunflower oil.

Omega 3 fatty acids may have cardioprotective effects.
Does Supplementation with Omega-3 PUFAs Add to the Prevention of Cardiovascular Disease?

Twenty-one randomized controlled trials assessed omega-3 supplementation on mortality and cardiovascular-related outcomes. From these studies, as well as from the relevant meta-analyses, we found that omega-3 supplements do not exert a consistent benefit for cardiovascular protection.

Summary
There is uncertainty of a clear profit from omega-3 supplementation in cardiovascular disease.
Multi Vitamins

- Do NOT represent mega dosing as seen for most individual supplements
- Primary goal is to prevent vitamin and mineral deficiency
- Observational studies: inconsistent, some suggest benefits, others have no effect, some risks
Physicians Health Study II

Centrum Silver
RCT, Multivitamin vs placebo
> 50 years of age Males
~14,000 US male physicians,
mean follow up of 11 years.
67% compliance rate
Cancer

Men with no baseline history of cancer
(n = 13,329)

Men with baseline history of cancer
(n = 1312)

Cumulative Incidence of Total Cancer

Crude log-rank $P = .19$

Crude log-rank $P = .02$

No. at risk
Placebo 6946 6772 6554 6304 6033 5738 2682
Multivitamin 6941 6775 6562 6325 6055 5793 2689

Placebo
Multivitamin
Cataracts
Hippocrates Tenet #1

Let food be thy medicine

and medicine be thy food.

— Hippocrates

thisthatnhealth.wordpress.com
"Everything in excess is opposed to nature."
-
Hippocrates

quotographed.com
Hippocrates Tenet #3

FIRST DO NO HARM
Hippocrates (460 - 370 BC)
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