Antioxidants and Vitamin Supplements

Edgar R. Miller III, M.D., Ph.D.
Professor of Medicine and Epidemiology
Johns Hopkins Medical University

Disclosures: none
Medical Management - A routine clinical visit

- 64 years old woman
- overweight
- Hypertension
- High cholesterol
- Medication
  - Altace 10 mg/d
  - Lipitor 20 mg/d
  - ASA 81 mg/d

- **Findings**
  - BP 122 / 82
  - LDL 92 mg/dl
  - Glucose 82 mg/dl
  - PE - unremarkable
Doc, should I continue to take these to lower my risk of heart attack?

- “Definitely help – continue”
- “Probably helpful - ok to continue”
- “Ok to continue - but at a lower dose”
- “Probably won’t hurt”
- “I’d recommend stopping them”
What is a Vitamin?

• A vitamin is a vital nutrient that the body requires in limited amounts
• Thirteen are recognized (A, B, C, D, E, K)
• Classified by biological and chemical activity
  – Antioxidant (vitamin E, vitamin C and Beta Carotene)
  – Co-factors in metabolic enzymes (B vitamins including folic acid)
  – Hormone-like functions (vitamin D)
Vitamin Deficiencies

• Vitamin A – night blindness
• Vitamin B – Anemia, birth defects
• Vitamin C – scurvy
• Vitamin D – rickets and osteoporosis
• Vitamin E – very rare (sterility)
• Vitamin K - increased risk of bleeding
Figure 1. Percent of US population using dietary supplements
Data derived from Radimer et al., 2004 and NHANES 1999 – 2000.
Learning Objectives

• Enhance understanding of:
  – What is the evidence from clinical trials that vitamin supplements are effective at preventing or treating chronic disease in humans

• What questions should you ask in making individual informed decisions on supplements
Are Vitamins relevant to Cardiovascular Disease Risk?

Coronary arteries

Percent subjects with lesions

- any lesion type (I to VI)
- only minimal lesions (I or II)
- preatheroma (III) or advanced (IV to VI) lesions

Age groups (years)  
<1+  2-3  4-7  8-11  12-15  16-19  20-23  24-27  28-31  32-35  36-39

Number of subjects per age group (total n = 691)

45  19  28  26  39  99  141  118  75  53  48
Relationship between serum cholesterol levels and death due to coronary heart disease (CHD) in 361,662 men screened for the Multiple Risk Factor Intervention Trial.
Fig. 1. Association of serum total cholesterol (TC) levels and coronary heart disease (CHD) mortality rates over 25 years of follow-up in the Seven Countries Study. From Verschuren et al. [2].
Antioxidants
Vitamin E
Beta carotene
Vitamin C

Free Radical Activity
Or “Oxidative stress”

LDL-Cholesterol

oxidized LDL

Atherosclerosis

Heart Attack and Stroke
**Fig. 1. Oxidation of plasma components** (left axis; scale, 0–
Consuming antioxidant vitamins lowers oxidative stress.

**FIGURE 1.** Mean changes (and 95% CIs) in urinary 8-iso-prostaglandin F$_{2\alpha}$ (PGF$_{2\alpha}$): 9.0 (−125.1, 143.1) in the placebo group, −150.0 (−275.4, −24.6) in the vitamin C group, −141.3 (−230.5, −52.1) in the vitamin E group, and −112.5 (−234.8, 9.8) in the vitamins C + E group. There was no synergistic interactive effect of vitamins C and E ($P = 0.12$).
Biological Evidence

• Vitamins are necessary for life

• Oxidized molecules are associated with chronic diseases
  – DNA – cancer
  – Cholesterol - heart disease

• Antioxidant vitamins prevent oxidation

• Does supplementation with antioxidants lower your risk of heart disease?
# Nurses Health Study

**Design:** Prospective Cohort Study  
**Participants:** 121,700 female nurses free of diagnosed cardiovascular disease  
**Exposure Assessment:** Dietary questionnaire at baseline  
**Follow-up:** 8 years  
**End Points:** 1) Major Coronary Disease  
2) Non-fatal MI  
3) Deaths Due to Coronary Disease  

### Evidence for Benefit: Nurses' Health Study: 8 year risk of heart disease by use supplements

<table>
<thead>
<tr>
<th>Vitamin Use</th>
<th>Risk Reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multivitamin only</td>
<td>15%</td>
</tr>
<tr>
<td>Vitamin E alone</td>
<td>60%</td>
</tr>
<tr>
<td>Vitamin E + multivitamin</td>
<td>50%</td>
</tr>
</tbody>
</table>

Do Vitamin supplements reduce risk?

- Observational studies have problems—vitamin E takers exercise more, weigh less, eat healthier, and smoke less often that non-vitamin users.

- Benefits can only be assessed in randomized controlled clinical trials.
Can pills, tablets, or capsules of B-vitamins or vitamins C, D, or E reduce the risk of heart disease?

American family diet. The Revis family of Raleigh, North Carolina, USA, in their kitchen with a week's worth of food. The family spend US $341.98 a week in groceries. Time Magazine 2011
β-carotene Supplement trials
ATBC Study

- Design: Randomized, double-blind, placebo-controlled primary prevention trial
- Participants: 29,133 male Finnish smokers, age 50-69
- Intervention:
  1) Vitamin E 50 IU/day
  2) B-carotene 20 mg/day
  3) Combination
  4) Placebo
- Follow-up: 5-8 years
- End Points: Incident lung cancer & deaths

ATBC, 1993 NEJM
Figure 3: **Kaplan-Meier estimates of mortality**
ATBC Trial Results

- Beta-carotene group (20 mg/day)
  - increase in total mortality (9%)
  - increased incidence of angina (13%)*
  - increased CVD mortality (11%)*
  - increased incidence of lung cancer (18%)*
CARET Study

- **Design:** Randomized, double blind, placebo-controlled primary prevention trial

- **Participants:** 18,314 smokers, former smokers, and workers exposed to asbestos

- **Intervention:** 1) B-carotene (30 mg/day) and vitamin A (25,000 IU/day) 
  2) Placebo

- **Follow-up:** 4 years

- **End Points:** Incident lung cancer or Cardiovascular Disease
CARET Study Results

- Beta-carotene (30mg + 25,000 IU retinol/day)
  - higher total mortality (17%)
  - higher total CVD mortality (26%)
  - higher incidence of lung cancer (28%)*

Omenn, 1996 NEJM
# Effects of Beta-carotene on Myocardial Infarction, Stroke, or Death

<table>
<thead>
<tr>
<th>Study</th>
<th>Dose</th>
<th>Time</th>
<th>N</th>
<th>Relative risk (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PHS</td>
<td>50*</td>
<td>12.0</td>
<td>22,000</td>
<td>1.00 (0.91 - 1.09)</td>
</tr>
<tr>
<td>ATBC</td>
<td>20**</td>
<td>5.3</td>
<td>29,000</td>
<td>1.19 (0.97 - 1.45)</td>
</tr>
<tr>
<td>CARET</td>
<td>30***</td>
<td>4.0</td>
<td>18,000</td>
<td>1.26 (0.99 - 1.61)</td>
</tr>
</tbody>
</table>

* every other day dosing - dose equivalent of 2 carrots per day
**dose equivalent of three carrots per day
*** (also took 25,000 IU of retinol per day - dose equivalent of 4 carrots per day)
Reason for a lack of effect of Beta-carotene

• Toxic levels of beta-carotene accumulate?
  – ATBC 4x, PHS 9x CARET 12x increase in serum levels

• Too short a duration of supplements to see a protective effect

• Beta-carotene absorbed by plaque makes it unstable
Vitamin C Supplementation

Effects on: Oxidative stress markers
Blood pressure
Long-term Clinical events
A Randomized Factorial Trial of Vitamins C and E and Beta Carotene in the Secondary Prevention of Cardiovascular Events in Women

Results From the Women’s Antioxidant Cardiovascular Study

Nancy R. Cook, ScD; Christine M. Albert, MD; J. Michael Gaziano, MD; Elaine Zaharris, BA; Jean MacFadyen, BA; Eleanor Danielson, MIA; Julie E. Buring, ScD; JoAnn E. Manson, MD, DrPH

- 8171 women, health professionals
- ≥ 3 CVD risk factors
- Vitamin C 500 mg/day
- Outcome:
  - CVD events, stroke, CVD mortality

Arch Intern Med. 2007;167(15):1610-1618
From: Vitamins E and C in the Prevention of Cardiovascular Disease in Men: The Physicians' Health Study II Randomized Controlled Trial


14,641 US male physicians, 400 IU vitamin E/day, 500 mg vitamin C /day , 8 years, CVD composite end point
Meta-analysis of vitamin C and mortality

- 29 trials
- 3637 dead/36,659 (9.9%) in vitamin C arm
- 2717 dead/29,283 (9.3%) in placebo arms;
- RR 1.02, 95% CI 0.98 to 1.07)

Vitamin D Supplementation in the age of lost innocence (fractured evidence)

Elmer McCollum PhD Johns Hopkins
First described health benefits of Vitamin D

WHAT SHALL WE HAVE FOR DINNER?

It is only within the last four or five years that anyone could say what constitutes a satisfactory diet but we now know definitely that the regular diet of a large portion of the people of the United States is

The diet of rat No. 1 consisted from weaning time of unhulled wheat flour 20, degenerated cornmeal 10, cooked and dried potato 39, peas 10, Navy beans 10, beets 5, turnips 5, and cooked and dried beets. 10 per cent.

When photographed it was 300 days old. The life of the domestic rat is about 2 years, and this animal corresponded approximately in age to a man of 28 or 30 years. Note the small size, thin hair, and general old and miserable appearance. This diet afforded wide variety, has an appropriate chemical composition insofar as analysis could show, was palatable, and included only natural food products of recognized wholesomeness, and from both animal and vegetable

• At Johns Hopkins University, Nina Simmonds, J. E. Becker and Elmer V. McCollum studied vitamin E, whose effect on sterility Drs. Herbert M. Evans and K. S. Bishop of the University of California discovered little more than a year ago (TIME, Feb. 15, 1926). The presence of vitamin E in the body permits fecundity; its absence causes sterility. It occurs in lettuce, wheat germs, alfalfa, egg yolks, liver.
Supplements: “Good for your chest, too”.

Green M BMJ 2011;343:bmj.d7505
Figure 3. Age-, sex-, season- and race/ethnicity-adjusted mortality rates per 1,000 person-years by 25(OH)D groups among adults without eGFR <60 ml/min/1.73 m2.

http://www.plosone.org/article/info:doi/10.1371/journal.pone.0047458
**Figure 1** Dose–response analysis of serum 25-hydroxyvitamin D levels after vitamin D3 supplementation


Vitamin D supplementation of CVD endpoints – is there benefit or harm?

Calcium/Vitamin D Supplementation and Cardiovascular Events
Judith Hsia, Gerardo Heiss, Hong Ren, Matthew Allison, Nancy C. Dolan, Philip Greenland, Susan R. Heckbert, Karen C. Johnson, JoAnn E. Manson, Stephen Sidney and Maurizio Trevisan

Circulation. 2007;115:846-854
Woman's Health Initiative

- Objective: test the effects of Calcium/Vitamin D supplementation on CVD risk
- Design: randomized controlled trial
- Dose: calcium 1 gram/d + vitamin D 400IU/d or placebo
- Participants: 36,282 postmenopausal women
- Duration: 7 years
- Outcome: CVD including MI, Stroke and total mortality
Medscape

**Myocardial infarction**

Hazard ratio 1.31 (95% CI 1.02 to 1.67), \( P = 0.035 \)

Cumulative incidence (%)

- **Calcium**
  - No at risk: 4097, 3870, 3539, 2670, 1294, 373
- **Placebo**
  - No at risk: 4054, 3865, 3588, 2728, 1320, 388

**Stroke**

Hazard ratio 1.20 (95% CI 0.96 to 1.50), \( P = 0.11 \)

Cumulative incidence (%)

- **Calcium**
  - No at risk: 4097, 3865, 3541, 2659, 1294, 373
- **Placebo**
  - No at risk: 4054, 3859, 3589, 2730, 1312, 386

**Composite of myocardial infarction, stroke, or sudden death**

Hazard ratio 1.18 (95% CI 1.00 to 1.39), \( P = 0.057 \)

Cumulative incidence (%)

- **Calcium**
  - No at risk: 4097, 3848, 3517, 2635, 1271, 360
- **Placebo**
  - No at risk: 4054, 3875, 3566, 2692, 1292, 376

**Death**

Hazard ratio 1.09 (95% CI 0.96 to 1.23), \( P = 0.18 \)

Cumulative incidence (%)

- **Calcium**
  - No at risk: 4097, 3889, 3580, 2699, 1322, 389
- **Placebo**
  - No at risk: 4054, 3875, 3618, 2767, 1340, 399

Source: BMJ © 2010 BMJ Publishing Group Ltd
Interaction between baseline use of calcium supplementation and risk of CVD with CaD supplementation?

<table>
<thead>
<tr>
<th>Cardiovascular end point</th>
<th>No personal use of calcium</th>
<th>Any personal use of calcium</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CaD (n=8429)</td>
<td>Placebo (n=8289)</td>
</tr>
<tr>
<td></td>
<td>Hazard ratio (95% CI)</td>
<td>P value</td>
</tr>
<tr>
<td>Clinical MI</td>
<td>1.22 (1.00 to 1.50)</td>
<td>0.05</td>
</tr>
<tr>
<td>Total MI†</td>
<td>1.20 (0.99 to 1.47)</td>
<td>0.07</td>
</tr>
<tr>
<td>Revascularisation</td>
<td>1.15 (0.98 to 1.34)</td>
<td>0.09</td>
</tr>
<tr>
<td>Stroke</td>
<td>1.17 (0.95 to 1.44)</td>
<td>0.1</td>
</tr>
<tr>
<td>Total MI or CHD death</td>
<td>1.15 (0.97 to 1.38)</td>
<td>0.1</td>
</tr>
<tr>
<td>Clinical MI or revascularisation</td>
<td>1.16 (1.01 to 1.34)</td>
<td>0.04</td>
</tr>
<tr>
<td>Clinical MI or stroke</td>
<td>1.16 (1.00 to 1.35)</td>
<td>0.05</td>
</tr>
<tr>
<td>Total MI, CHD death, or revascularisation</td>
<td>1.13 (0.99 to 1.29)</td>
<td>0.07</td>
</tr>
<tr>
<td>Death from all causes</td>
<td>0.99 (0.86 to 1.14)</td>
<td>0.9</td>
</tr>
</tbody>
</table>

CaD=allocation to calcium and vitamin D supplement. MI=myocardial infarction. CHD=coronary heart disease.
*Interaction between CaD allocation and use or non-use of personal calcium supplements for each end point, testing the difference between subgroups.
†includes clinically silent myocardial infarction diagnosed from changes in routine serial electrocardiograms.

Conclusions

• Elmer McCollum
  
  – “eat what you need, then eat what you want”
  
  – “In his later years, McCollum regarded drugstore vitamin pills and supplements as “snake-oil quackery”
Bone mass

With treatment, you can maintain bone mass.

Without treatment, more bone can be lost.

Age

5 10 15 20 25 30 35 40 45 50 55 60 65 70 75 80 85 90

Peak bone mass

Menopause

Normal bone matrix

Osteoporosis
Potential Indicators of Adverse Outcomes Associated With Excess Intake of Calcium and Vitamin D

Calcium
- Hypercalcemia
- Hypercalciuria
- Vascular and soft-tissue calcification
- Nephrolithiasis (kidney stones)
- Prostate cancer
- Interactions with iron and zinc
- Constipation

Vitamin D
- Intoxication and related hypercalcemia and hypercalciuria
- Serum calcium
- Measures in infants: retarded growth, hypercalcemia
- Emerging evidence for all-cause mortality, cancer, cardiovascular risk, falls, and fractures

Photo credit: Qizhi He/James Martin/iStockphoto.com
Vitamin E supplementation: what’s the harm in that?

Edgar R Miller III\(^{a,b,c,d}\) and Eliseo Guallar\(^{a,b,c,e}\)

Clinical Trials 2009; 6: 47–49
Vitamin E

\[
\text{α-Tocopherol 2-Dimensional Representation}
\]
HOPE Trial

• Design: Randomized, double blind, placebo-controlled primary prevention trial
• Participants: 9,541 men and women at high risk for cardiovascular disease
• Intervention: 1) Vitamin E (400 IU / day)  
   2) Placebo
• Follow-up: 4.5 years
• End Points: MI, stroke and death from CVD

HOPE, NEJM 2000 & 2006
Figure 1. Kaplan–Meier Estimates of the Effect of Vitamin E on the Composite Outcome of Nonfatal Myocardial Infarction, Stroke, or Death from Cardiovascular Causes.

The relative risk of the composite outcome in the vitamin E group as compared with the placebo group was 1.05 (95 percent confidence interval, 0.95 to 1.16; P=0.33).
Vitamin E
placebo

HOPE-TOO trial, JAMA 2005
The Selenium and Vitamin E Cancer Prevention Trial (SELECT)

- 35,533 men
- Follow-Up 6 years
- Randomized:
  - Vitamin E : 400 IU/day
  - Selenium
  - Placebo
  - Both

Select trial 2013 JAMA
Probability of developing Prostate Cancer
Meta-Analysis: High-Dosage Vitamin E Supplementation May Increase All-Cause Mortality

Edgar R. Miller III, MD, PhD; Roberto Pastor-Barriuso, PhD; Darshan Dalal, MD, MPH; Rudolph A. Riemersma, PhD, FRCPE; Lawrence J. Appel, MD, MPH; and Eliseo Guallar, MD, DrPH

Background: Experimental models and observational studies suggest that vitamin E supplementation may prevent cardiovascular disease and cancer. However, several trials of high-dosage vitamin E supplementation showed non-statistically significant increases in total mortality.

Purpose: To perform a meta-analysis of the dose–response relationship between vitamin E supplementation and total mortality by using data from randomized, controlled trials.

Patients: 135,967 participants in 19 clinical trials. Of these trials, 9 tested vitamin E alone and 10 tested vitamin E combined with other vitamins or minerals. The dosages of vitamin E ranged from 16.5 to 2000 IU/d (median, 400 IU/d).

Data Sources: PubMed search from 1966 through August 2004, complemented by a search of the Cochrane Clinical Trials Database and review of citations of published reviews and meta-analyses. No language restrictions were applied.

Data Extraction: 3 investigators independently abstracted study reports. The investigators of the original publications were contacted if required information was not available.

Data Synthesis: 9 of 11 trials testing high-dosage vitamin E (≥400 IU/d) showed increased risk (risk difference > 0) for all-cause mortality in comparisons of vitamin E versus control. The pooled all-cause mortality risk difference in high-dosage vitamin E trials was 39 per 10,000 persons (95% CI, 3 to 74 per 10,000 persons; P = 0.035). For low-dosage vitamin E trials, the risk difference was −16 per 10,000 persons (CI, −41 to 10 per 10,000 persons; P > 0.2). A dose–response analysis showed a statistically significant relationship between vitamin E dosage and all-cause mortality, with increased risk of dosages greater than 150 IU/d.

Limitations: High-dosage (≥400 IU/d) trials were often small and were performed in patients with chronic diseases. The generalizability of the findings to healthy adults is uncertain. Precise estimation of the threshold at which risk increases is difficult.

Conclusion: High-dosage (≥400 IU/d) vitamin E supplements may increase all-cause mortality and should be avoided.

Results - Trial Characteristics

• 135,967 men and women

• 12,500 deaths

• Doses: 17 to 2000 IU/day
  – Median dose 400 IU/d

• Vitamin E alone: 9 of 19 trials
  – 10 of 19 multivitamin trials

• Mean age range 47 to 84 years
  – Most participants at high risk for CVD

• Average follow-up: 1.4 to 8.2 years
Vitamin E supplementation and all-cause mortality – Summary

• A significant relationship between vitamin E dose and mortality

• In high dose trials (>400 IU/day), there was a 6% increased risk of death in those assigned to vitamin E compared to those assigned to placebo

• There was evidence of possible benefit in the low-dose trial (special populations)
Arafat dies, leaves void

Bush calls death 'significant moment in Palestinian history'

Sorrow and hope embraced

study: High dose of vitamin E may increase death risk

Bush chooses counsel for attorney general
CRN Questions Conclusions Reached by Researchers in Recent Vitamin E Meta-Analysis

John N. Hathcock, Ph.D., vice president, scientific and international affairs, for the Council for Responsible Nutrition (CRN)

"This is an unfortunate misdirection of science in an attempt to make something out of nothing for the sake of headlines," comments John Hathcock, Ph.D., vice president, scientific and international affairs, CRN.
“I think that study is flawed,” charges Donald Berry, chairman of the Department of Biostatistics and Applied Mathematics at the University of Texas MD Anderson Cancer Center in Houston. “It is based on a most inappropriate model and is an inappropriate and rather naive analysis. Any reasonable model comes to a different conclusion.”
• **Vitamin E in Wonderland**

“You might suspect the fix is in when the first person quoted by the WSJ is cardiologist Edgar R. Miller, author of one of the most criticized and denounced studies ever done on vitamin E. Eminent vitamin E researchers called his analysis, claiming common doses of vitamin E boosted death rates 4% to 6%, a case study in the misuse of statistics with laughable conclusions”.
Further Evidence from Trials of Vitamin E supplementation
New Vitamin E trials

- Head and Neck trial
- ASAP
- WHS
- WACS
- IARC
- ALS trial

All-Cause Mortality Risk Difference vs. Vitamin E Dosage (IU/d)
From: Multivitamins in the Prevention of Cardiovascular Disease in Men: The Physicians' Health Study II Randomized Controlled Trial


14,641 male physicians, mean age 64.3 years, MVI, outcome composite CVD events, 11 yrs, 75 mg Vitamin C/day

Y-axis range shown in blue indicates cumulative incidence from 0 to 0.06. The reduction in the numbers at risk from 10 to 12 years reflects the 2 phases of Physicians' Health Study II recruitment; men in the Physicians' Health Study I initially enrolled in phase 1 starting in 1997 were followed up longer on average (mean, 13 years) than the men recruited in phase 2 starting in 1999 (mean, 10 years).
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 nutrit-

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

Eltheo Guallar, MD, DrPH
Johns Hopkins Bloomberg School of Public Health
Baltimore, Maryland

Saverio Stranges, MD, PhD
Warwick Medical School, University of Warwick
Coventry, United Kingdom

Cynthia Mulrow, MD, MSc
Annals of Internal Medicine, American College of Physicians
Philadelphia, Pennsylvania

Lawrence J. Appel, MD, MPH
Edgar R. Miller III, MD, PhD
Johns Hopkins School of Medicine
Baltimore, Maryland

“…we believe that the case is closed— supplementing the diet of well-nourished adults with (most) mineral or vitamin supplements has no clear benefit and might even be harmful. These vitamins should not be used for chronic disease prevention. Enough is enough.”
Annals of Internal Medicine

Original Research

Oral High-Dose Multivitamins and Minerals After Myocardial Infarction
A Randomized Trial
Gervasio A. Lamas, MD; Robin Bolmeau, MD, MA; Christine Goertz, DC, PhD; Daniel B. Mark, MD, MPH; Yves Rosenberg, MD; Mario Stylianou, PhD; Theodore Rozema, MD; Richard L. Nahin, PhD, MPH; Lauren Lindblad, MS; Eldrin F. Lewis, MD; Jeannie Drisko, MD; and Kerry L. Lee, PhD, for the TACT (Trial to Assess Chelation Therapy) Investigators

Original Research

Long-Term Multivitamin Supplementation and Cognitive Function in Men
A Randomized Trial
Francine Grodstein, ScD*; Jacqueline O’Brien, ScD*; Jae Hee Kang, ScD; Rimma Dushkes, PhD; Nancy R. Cook, ScD; Olivia Okereke, MD; JoAnn E. Manson, MD, DrPH; Robert J. Glynn, PhD; Julie E. Buring, ScD; J. Michael Gaziano, MD, MPH; and Howard D. Sesso, ScD, MPH

Review

Vitamin and Mineral Supplements in the Primary Prevention of Cardiovascular Disease and Cancer: An Updated Systematic Evidence Review for the U.S. Preventive Services Task Force
Stephen P. Fortmann, MD; Brittany U. Burda, MPH; Caitlyn A. Senger, MPH; Jennifer S. Lin, MD, MCR; and Evelyn P. Whitlock, MD, MPH
Multivitamin researchers say "case is closed" after studies find no health benefits

Experts: Don't Waste Your Money on Multivitamins

Are multivitamins a waste of money?
Editorial in medical journal says yes

3 Reasons Multivitamins Are For N.J. Suckers
• When they get paid to publish an article, what do you expect?

Oh please. Try reading the stats. Pharmaceutical companies have KNOWINGLY suppressed results from drugs in order to rake in the big bucks. …..These are the same bozos that have tried saying that Vitamin E is dangerous.

Most people don't think that vitamins prevent heart attacks. This whole article constructs a fake argument so that it can then be debunked to make the authors appear intelligent. Maybe they should do follow-up research proving how vitamins can't make you fly.
Conclusions

• Vitamin C, D, E, Folate supplementation highly tested in setting of RCT’s

• Evidence to support recommendations for widespread use for high-dose supplements in the general population remains insufficient

• “Trial data available to date are unable to demonstrate a significant reduction in mortality or cardiovascular disease risk associated with vitamin C, D, E, Folate supplementation – watch for the harm”.
Reasons for a lack of Benefit of Vitamin Supplements

- Reducing free radicals may interfere with essential defense mechanisms linked to apoptosis, phagocytosis, detoxification.

- Pro-oxidant effects at high doses (in vitro evidence)

- Displaces other antioxidants (changes balance) or suppress endogenous antioxidant mechanisms
Recommendations for Antioxidant supplement intake

- High dose vitamin supplements should be discouraged until there is evidence of efficacy from randomized controlled trial
- Take proven medications to treat underlying diseases (e.g. hypertension, cholesterol, etc)
- Adopt a healthy diet, lose weight if overweight, stop smoking, and exercise
Recommended! The DASH Diet

• Emphasizes:
  – Fruits, Vegetables, Low-fat Dairy Products

• Includes:
  – Whole Grains, Nuts, Poultry, Fish

• Reduced in:
The DASH diet
Conlin et al., Am J Hypertens, 2002

Change in Systolic Blood Pressure (mmHg)

- Control Diet
- Fruits-and-vegetables Diet
- DASH

Intervention Week

Baseline 1 2 3 4 5 6 7 and 8

* **
Summary

• Eat fruits and vegetables

• High dose antioxidant supplements do not help and may lead to harm

• Do not take antioxidant supplements during cancer treatment unless MD directed
### What is recommended?

<table>
<thead>
<tr>
<th>VITAMIN</th>
<th>Prior Guidelines</th>
<th>NEW Recommendations</th>
<th>Upper Limit of Intake</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin A (beta-carotene)</td>
<td>5000 IU</td>
<td>3000 IU</td>
<td>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</td>
<td>600 IU</td>
<td>2000 IU</td>
</tr>
<tr>
<td>Vitamin E</td>
<td>20 mg</td>
<td>15 mg</td>
<td>1000 mg</td>
</tr>
<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</td>
<td>400 mcg (food)</td>
<td>1000 mcg</td>
</tr>
<tr>
<td>Vitamin B-12</td>
<td>6 mcg</td>
<td>2.4 mcg</td>
<td>ND</td>
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Institute of Medicine report 2007
Summary

• Apply critical thinking to when considering using dietary supplements

• Question the source of information and whether studies support the recommendations

• General Suggestion: do not take supplements that provide levels that are greater that twice the level that can be achieved with a healthy diet
  – i.e. low dose antioxidant vitamin probably ok