Nutritional Supplements
Exploring Evidence-Based Use in Cancer Prevention and Cardiovascular Health

Presented by:
Karen Collins, MS, RDN, CDN, FAND

1-Credit Continuing Education Webinar
Disclosures

Karen Collins
MS, RDN, CDN, FAND

Karen is Nutrition Advisor to the American Institute for Cancer Research (AICR) and serves as consultant to the National Processed Raspberry Council
Learning Objectives

Suggested CDR Learning Codes:  2000, 4000, 4040, 5150, 5160, 9020 ; Level 2

1. Describe current overall research conclusions regarding adult use of supplements, including antioxidants, vitamin D, omega-3 fatty acids and multivitamins, to reduce risk of cardiovascular disease and cancer.

2. Explain factors to consider in evaluating contradictory findings among studies addressing supplements’ potential role in cardiovascular health and cancer prevention.

3. Identify sources of reliable information on nutritional supplements for professional reference and patient information.
Our Target for Today

- Adults
- Cardiovascular Health
- Reducing Cancer Risk
Who’s Using Supplements?

• Americans spent > $36 billion in 2014\(^1\)
• NHANES 2007-2010: \(^2\)
  48.8% of adults: 43.1% of men, 54.4% of women
  Variation by age: 67.4% over age 60
• Survey for Council for Responsible Nutrition: \(^3\)
  Any use 2007 to 2011: 64% - 69%
  Regular use: 48% - 53%
How Common is Intake Below Average Requirements?

Percent of U.S. Population with Average Intake Below EAR

Vitamin D > Vitamin E > Magnesium > Calcium > Vitamin A > Vitamin C > Zinc > Vitamin B6 > Folate > Iron > Thiamin > Copper > Phosphorus > Selenium > Vitamin B12 > Niacin > Riboflavin

Scientific Report of the 2015 Dietary Guidelines Advisory Committee, Fig. D1.1

From: What We Eat in America, NHANES 2007-2010
Questions to Consider

• Evidence of Benefit
• Patient’s Perspective
• Evidence of Risk
• Degree of Burden
Individualized Perspective

• Current intake: naturally-occurring, fortified foods, supplements
• Estimated needs
• Baseline health risks
• Individual values, beliefs, barriers
Antioxidant Supplements
Oxidative Stress and Disease

External Exposures
- Pollution
- Tobacco smoke
- Radiation

Internal Exposures
- Aerobic metabolism
- Immune
- Enzymatic reaction

Free Radicals (& other ROS, RNS)*

Direct Cell Damage
- Proteins
- Lipoproteins
- Cell membranes

Inflammation

Chronic Disease
- Cancer
- CVD
- T2 Diabetes
- Dementia

*ROS= Reactive Oxygen Species  RNS= Reactive Nitrogen Species
## Our Antioxidant Defense System

### Endogenous Antioxidants

<table>
<thead>
<tr>
<th>Enzymatic</th>
<th>Non-enzymatic</th>
<th>Metal-binding Proteins</th>
</tr>
</thead>
<tbody>
<tr>
<td>Superoxide dismutase (SOD)</td>
<td>Glutathione (GSH)</td>
<td>Ferritin</td>
</tr>
<tr>
<td>Glutathione peroxidase (GPx)</td>
<td>Lipoic acid</td>
<td>Lactoferrin</td>
</tr>
<tr>
<td>Glutathione reductase</td>
<td>Melatonin</td>
<td>Transferrin</td>
</tr>
<tr>
<td>Thioreducan reductase</td>
<td>Uric acid</td>
<td>Ceruloplasmin</td>
</tr>
<tr>
<td>Catalase (CAT)</td>
<td>NADPH</td>
<td></td>
</tr>
<tr>
<td>Glucose-6-phosphate dehydrogenase</td>
<td>Bilirubin</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ubiquinol (formed from CoQ10)</td>
<td></td>
</tr>
</tbody>
</table>
Our Antioxidant Defense System

Exogenous Antioxidants

- Vitamin C
- Vitamin E (tocopherols & tocotrienols)
- Selenium
- Carotenoids (α-carotene, β-carotene, lycopene, lutein, zeaxanthin, β-cryptoxanthin)
Evolving Understanding: Health-Supporting Balance

Low level ROS:
- Cell signaling to modulate cell proliferation & apoptosis
- Immune response regulation
- Vascular activation of eNOS
- Gene expression
- Triggers body’s endogenous antioxidant defense system

High level ROS:
- Toxic to lipids & proteins

Physiologic level:
- Antioxidant
- Anti-inflammatory

Supraphysiologic level:
- Pro-oxidant
- Pro-inflammatory

ROS Exposure
- External
- + Internal

Antioxidant Defense
- Endogenous
- + Exogenous

Individual Variation

Genetic Microbiota
Antioxidant Levels & Mortality
Potential Models

Higher Risk

Lower Risk

Increasing Serum Antioxidant Level →

Prevent Deficiency

More is Better

Optimum Target (U-shaped curve)

Examples:
Rayman, Lancet 2012, 379:1256;
Goyal, Cancer Epid Bio Prev 2013, 22:2202
Antioxidants & CVD Risk
Observational Data from Prospective Cohorts

• Decreased serum or dietary levels link to increased CVD risk in some – but not all – studies for β-carotene, vit C, vit E

• Dose-response meta-analysis – CHD risk

  Vit C: q 30 mg/day ◊ RR 1.01 (0.99-1.02)
  Vit E: q 30 IU/day ◊ RR 0.96 (0.94-0.99)
  β-carotene: q 1 mg/day ◊ RR 1.00 (0.88-1.14)

• Q1 to Q2 or Q3 often biggest drop in risk

• Confounders – dietary & lifestyle -- significant

2 Goyal, Cancer Epid Bio Prev 2013, 22:2202
Antioxidants & Risk of Myocardial Infarction: RCTs

<table>
<thead>
<tr>
<th>Study</th>
<th>Followup</th>
<th>Comparison</th>
<th>Mantel-Haenszel RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beta-carotene</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WHS</td>
<td>4.1</td>
<td>Beta-carotene vs. no beta-carotene</td>
<td>0.84 (0.56, 1.27)</td>
</tr>
<tr>
<td>PHS-I</td>
<td>12</td>
<td>Beta-carotene vs. no beta-carotene</td>
<td>0.96 (0.85, 1.08)</td>
</tr>
<tr>
<td>Subtotal (I-squared = 0.0%, p = 0.551)</td>
<td></td>
<td></td>
<td>0.95 (0.84, 1.07)</td>
</tr>
<tr>
<td>Vitamin E</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PHS-II</td>
<td>8</td>
<td>Vitamin E vs. no vitamin E</td>
<td>0.89 (0.75, 1.05)</td>
</tr>
<tr>
<td>WHS</td>
<td>10.1</td>
<td>Vitamin E vs. no vitamin E</td>
<td>1.01 (0.83, 1.22)</td>
</tr>
<tr>
<td>Subtotal (I-squared = 0.0%, p = 0.347)</td>
<td></td>
<td></td>
<td>0.94 (0.82, 1.07)</td>
</tr>
<tr>
<td>Selenium</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NPC</td>
<td>7.6</td>
<td>Selenium vs. placebo</td>
<td>0.95 (0.63, 1.42)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Subtotal (I-squared = .%, p = .)</td>
<td>0.95 (0.63, 1.42)</td>
</tr>
<tr>
<td>Vitamin C</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PHS-I</td>
<td>8</td>
<td>Vitamin C vs. no vitamin C</td>
<td>1.03 (0.87, 1.23)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Subtotal (I-squared = .%, p = .)</td>
<td>1.03 (0.87, 1.23)</td>
</tr>
</tbody>
</table>

Fortmann, 2013
AHRQ Publication No. 14-05199-EF-1
SELECT: Selenium, Vit E & Prostate Cancer Risk

Cumulative Incidence of Prostate Cancer: Vitamin E vs Placebo

National Cancer Institute, 2015
Selenium, Vit E & Prostate Cancer Risk

SELECT – RCT of Se (200 mcg) ± Vit. E (400 IU)

2008 (5.5 years):
• Study stopped – no effect on prostate cancer risk
• Non-significant increase in DM with Se alone

2011:
Vitamin E alone – 17% incr prostate cancer

2014:
• High baseline Se
  – Se supplement: 91% increased risk high-grade prostate ca
• Low baseline Se
  – Vit E supplement: >2x risk high-grade prostate ca
• High baseline Vit E
  – Se supplement with or without E: 2x risk prostate ca

Antioxidants & Cancer Risk: Observational Studies

Vitamin E

• Iowa Women’s Health Study\(^1\)
  Vit E from food + supplements & colon cancer
  High (>35.7 IU/d) vs Low (<5.7 IU/d) RR=0.32

• Nurses’ Health Study & Health Prof. Follow-up Study\(^2\)
  Vit E from supplements:
  No sig link to colon cancer risk

Carotenoids

• Nurses’ Health Study\(^3\)
  Plasma carotenoids High vs Low: breast cancer RR 0.77 (.63-.94)

• Meta-analysis\(^4\)
  Blood carotenoids High vs Low: breast cancer RR 0.74 (.57-.96)
  Beta-carotene supplement intake: no link to breast cancer

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## Antioxidant Supplements & Risk of Any Cancer Incidence
### Meta-Analysis of RCTs

<table>
<thead>
<tr>
<th>Study</th>
<th>Years of Followup</th>
<th>comparison</th>
<th>Random Effects RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>WHS</td>
<td>4.1</td>
<td>Beta-carotene vs. no beta-carotene</td>
<td>1.02 (0.89, 1.18)</td>
</tr>
<tr>
<td>PHS-I</td>
<td>12.9</td>
<td>Beta-carotene vs. no beta-carotene</td>
<td>0.97 (0.90, 1.04)</td>
</tr>
<tr>
<td>Subtotal</td>
<td>(I-squared = 0.0%, p = 0.509)</td>
<td>Inestimable predictive distribution with &lt;3 studies</td>
<td>0.98 (0.92, 1.05)</td>
</tr>
<tr>
<td>Vitamin E</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PHS-II</td>
<td>8</td>
<td>Vitamin E vs. no vitamin E</td>
<td>1.03 (0.95, 1.12)</td>
</tr>
<tr>
<td>WHS</td>
<td>10.1</td>
<td>Vitamin E vs. no vitamin E</td>
<td>1.01 (0.94, 1.08)</td>
</tr>
<tr>
<td>SELECT</td>
<td>12</td>
<td>Vitamin E vs. placebo</td>
<td>1.07 (0.99, 1.15)</td>
</tr>
<tr>
<td>Subtotal</td>
<td>(I-squared = 0.0%, p = 0.518)</td>
<td>with estimated predictive interval</td>
<td>1.03 (0.99, 1.08)</td>
</tr>
<tr>
<td>Selenium</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NPC</td>
<td>7.4</td>
<td>Selenium vs. placebo</td>
<td>0.78 (0.62, 0.98)</td>
</tr>
<tr>
<td>SELECT</td>
<td>12</td>
<td>Selenium vs. placebo</td>
<td>1.02 (0.94, 1.10)</td>
</tr>
<tr>
<td>Subtotal</td>
<td>(I-squared = 78.9%, p = 0.029)</td>
<td>Inestimable predictive distribution with &lt;3 studies</td>
<td>0.91 (0.70, 1.16)</td>
</tr>
<tr>
<td>Vitamin C</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PHS-II</td>
<td>8</td>
<td>Vitamin C vs. no vitamin C</td>
<td>1.00 (0.92, 1.09)</td>
</tr>
</tbody>
</table>

Fortmann, 2013; AHRQ Publication No. 14-05199-EF-1
Antioxidants: Lots of Questions

• Potential benefit of higher amounts?
  - Vitamin C or Vitamin E for endothelial function?
  - For higher-risk groups?
  - If started at younger age, continued longer?
  - If different forms?

• Potential risk of higher amounts?
  - Could β-carotene or Vitamin E in doses > RDA pose risk even if < UL?

Ashor, Br J Nutr 2015; 113(8):1182-94
Bjelakovic, PlosOne 2013; 8(9):e74558
Shaping our Messages: Shifting the Talk about Antioxidants

• “In vitro” does not equal “in your body”

• Health-promoting balance (homeostasis) is the goal

• Supporting antioxidant defenses is one part of a strategy based on multiple effects of nutrients and natural compounds in food...working together with healthy body composition, activity and lifestyle

• A healthy eating pattern supports a wide range of systems in our body
Resources

Antioxidant-Related Summaries

• National Center for Complementary & Integrative Health (NCCIH)
  Antioxidants and Health
  https://nccih.nih.gov/health/antioxidants/introduction.htm

• National Cancer Institute (NCI)
  Antioxidants and Cancer Prevention
Multivitamin and Multivitamin-Mineral Supplements
Multivitamins: Watching the Research

What counts?

• Most common definition in studies: 3 or more vitamins, with or without minerals

• Some federal use (CDC, NHANES): 3 or more vitamins and minerals

• More common understanding: At least 10-15 vitamins and minerals

• Variables:
  – With botanicals, amino acids, omega-3’s, carotenoids?
  – Dosed at or near 100% DV? Or high-dose also?
Multivitamins & Health
Observational Studies

• Several prospective cohort studies: \(^1\)
  No effect on CVD risk, cancer risk or mortality
  - Relatively healthy middle age & older adults
  - Follow-up 5.5 to 11 years

• A prospective cohort linking to mixed benefit: \(^2\)
  NHS: Use for ≥15 yrs → 75% lower colorectal cancer
  - No effect breast cancer
  - Use for ≥10 yrs → nearly 2x greater N-H Lymphoma

MultiVits & CVD or Cancer Risk Meta-Analysis of RCTs

<table>
<thead>
<tr>
<th>Health Outcome</th>
<th>Relative Risk</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any CVD event</td>
<td>1.02</td>
<td>0.94-1.10</td>
</tr>
<tr>
<td>CVD mortality</td>
<td>0.97</td>
<td>0.85-1.11</td>
</tr>
<tr>
<td>Any Cancer incidence</td>
<td>0.94</td>
<td>0.89-1.00</td>
</tr>
<tr>
<td>• Breast cancer</td>
<td>0.94</td>
<td>0.71-1.24</td>
</tr>
<tr>
<td>• Prostate cancer</td>
<td>0.99</td>
<td>0.89-1.06</td>
</tr>
<tr>
<td>• Colorectal cancer</td>
<td>0.89</td>
<td>0.68-1.17</td>
</tr>
<tr>
<td>• Lung cancer</td>
<td>0.84</td>
<td>0.62-1.15</td>
</tr>
<tr>
<td>Any Cancer mortality</td>
<td>0.88</td>
<td>0.78-1.01</td>
</tr>
</tbody>
</table>

Fortmann, 2013; AHRQ Publication No. 14-05199-EF-1
Total Folate Intake & Breast Cancer Incidence

Effect Varies with Level of Intake
Top vs Bottom Quintile

Malmo Diet & Cancer
456 ug vs 160 ug
HR 0.56 (p=.006)

PLCO Cancer Screening
>853 ug vs ≤336 ug
HR 1.27 (p=.05)

Folic Acid Issues

Folic Acid & Fortification
Absorption 2 times greater than dietary folate
NHANES 2011-2012: Adult supplement users avg. 652 mcg/d
UL 1000 mcg: applies to supplemental + fortification folic acid only
- People over 50: 5% exceed
- People over 50 with supplement >400 mcg: 50% exceed

Potential Double-Edged Sword in Colon & Breast Cancer?
Colorectal Cancer Risk:
- NIH-AARP Study \(^2\): \(\geq 400\) mcg DRI: 20-25% lower CRC vs <200 mcg
  \(\diamond \) No significant benefit beyond 400 mcg
- Meta-analysis \(^3\): No significant link to blood folate or total intake
- Effects on risk could vary with age & timing?
Risk reduction related to alcohol consumption

\(^1\) Yang, Amer J Clin Nutr 2010, 91:64; \(^2\) Gibson, Amer J Clin Nutr 2011
\(^3\) WCRF/AICR Continuous Update Project Report, Colorectal Cancer 2011
Multivitamins: Other Nutrients of Interest

• Vitamin B-12
  - 10-30% of people >50 years at risk: IOM advises getting RDA of 2.4 mcg in supplement or fortified food
  - 40% of Daily Value meets RDA (DV = 6 mcg)

• Vitamin A (retinol)
  - Too much of a good thing: liver abnormalities, birth defects, potential bone fracture risk if excessive
  - Caution for smokers and ex-smokers
  - 46-60% of Daily Value meets RDA (DV=5000 IU)

• Iron
  - Nutrient of concern for pre-menopausal women
  - Men & post-mp women look for “senior” or no-iron
Multivitamins & Fortified Foods

Is there the equivalent of an MVM in someone’s fortified foods?

– Breakfast cereal (note portion, use for snacks)
– Juice and blended juice drinks, smoothies
– Bars
– Fortified grains

Generally not excessive intake, but is MVM supplement duplication?
Resources

Multivitamin/Mineral Supplements Reviews & Summaries

• National Center for Complementary & Integrative Health (NCCIH): https://nccih.nih.gov/health/vitamins

• Nutrition Action by Center for Science in the Public Interest (CSPI): “Should I Take a Multivitamin?” http://bit.ly/1SWlIz8

• “Addressing nutritional gaps with multivitamin and mineral supplements” (Nutrition Jrnal 2014, 13:72; by Elizabeth Ward, MS, RD; *honorarium by Pfizer) http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4109789/
Vitamin D Supplements
**Vitamin D – Basic Science Matters**

- **Sun-UVB** → **Skin**
- **Intestine** → **Diet**
- **Liver**
- **25(OH)D**
  - **Kidney**
  - **Target Tissues**
    - **1α,25(OH)₂D**
    - **1α,25(OH)₂D**

**Plasma levels:** biomarker of Vit D status

**Active form of Vit D**

**Endocrine Function** (Intestine, Bone, Kidney)

**Produced & Acting Locally** (Endothelium, Colon, Breast, Endometrium, Pancreas, Adipose, Immune, others)

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Vitamin D and CVD Risk

Potential CVD Protection
• Inhibit vascular smooth muscle cell proliferation?
• Anti-inflammatory?
• Promote blood pressure control via renin-angiotensin-aldosterone system?

Intervention Trials:
No significant effect of Vit D supplements (alone or with calcium) on any CVD incidence
• Doses too low? How low at baseline?

Schnatz, Clin Chem 2014; 60(4):600-609
Fortmann, 2013; AHRQ Publication No. 14-05199-EF-1
Caution: Beware of Headlines on Vitamin D & Cancer

“Recent Study Confirms Relationship between Vitamin D and Breast Cancer”
Vitamin D & Cancer Risk
Laboratory evidence

- Promotes cell differentiation
- Reduces inflammatory cytokines
- Inhibits proliferation
- Induces apoptosis

Toner, JADA 2010, 110(10):1492
Vitamin D & Cancer Risk
Population studies

Each 10 ng/ml increase in 25(OH)D \(^1\) [25 nmol/L]

- Colorectal cancer meta-analysis: 15% decreased risk
- Breast cancer meta-analysis: 11% decreased risk
  
  **Much less consistent; often obesity/waist confounding**
- Benefits not seen in all studies

**High vs low comparisons:**

- Meta-analysis 25(OH)D weak link to breast cancer risk, but \(~\)40% lower all-cause and breast cancer mortality in breast cancer \(^2\)
- 14% lower cancer mortality for high vs low 25(OH)D \(^3\)
- U-shaped curve for prostate cancer? \(^4\)

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\(^1\) Gandini, Int J Cancer 2011
\(^2\) Kim, Br J Cancer 2014; 110(11):2772
\(^3\) Chowdhury, BMJ 2014
\(^4\) Kristal, Cancer Epid Biom Prev 2014
Vitamin D & Cancer Risk
Controlled Intervention Trials

- Meta-analysis shows little if any effect on cancer incidence
- Combined all doses and all types of cancer
- No difference total vitamin D supplements or vitamin D₃
- No difference when participants had vitamin D baseline levels < 20 ng/mL versus when baseline ≥ 20 ng/mL
- No difference with or without concomitant calcium

Vitamin D Questions

What is optimal blood level?
- IOM\(^1\): ≥ 20 ng/ml (50 nmol/L) for bones
- Endocrine Society\(^2\): ≥ 30 ng/ml (75 nmol/L) for bones/falls
- VITAL trial in progress: target 30-36 ng/ml (75-90 nmol/L)
- U-shaped curve: risk > 45, 150 ng/ml ??

Confounders: Age, BMI, time outside = activity?

Is testing everyone the answer?
- Problems with consistent lab assays
- Problems with interpreting normal values
USPSTF: insufficient evidence to assess benefits versus harms of screening asymptomatic individuals.
Endocrine Society: recommends screening only people at risk

\(^1\)IOM (Institute of Medicine) 2011 Dietary reference intakes for calcium and vitamin D.
\(^2\)Clinical Practice Guidelines: Holick, J Clin Endocrinol Metab. 2011; 96(7):1911-30
Vitamin D: How Much is Enough?

*Based on skeletal benefits only*

**Institute of Medicine**
- RDA 600 IU (800 IU if >70 yrs)
- UL 4000 IU (age ≥ 9 years)

**Endocrine Society**
- Adults 19-70 – at least 600 IU
- Adults 70+ years – at least 800 IU
- For 25(OH)D >30 ng/ml: may need ≥ 1500–2000 IU/day
- For people with obesity, malabsorption syndromes, or medications affecting vitamin D metabolism – suggest 2-3 times higher dose

**Individual differences:** genetics, skin, clothing, pollution

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1 IOM (Institute of Medicine) 2011 Dietary reference intakes for calcium and vitamin D.
2 Clinical Practice Guidelines: Holick, J Clin Endocrinol Metab. 2011; 96(7):1911-30
Can We Reach Healthful Amounts of Vitamin D without Supplements?

- USDA Dietary Pattern 2015
  - 1600 kcals = 266 IU Vitamin D
  - 2000 kcals = 274 IU
  - 2400 kcals = 294 IU

- Adjusted 2000 kcal pattern reaches 400 IU EAR

- Note: EAR & RDA assume minimal sun

Scientific Report of the 2015 Dietary Guidelines Advisory Committee, Appendix E-3.3: Meeting Vitamin D Recommended Intakes in USDA Food Patterns
## What Does It Take to Reach Vitamin D EAR or RDA without a Supplement?

<table>
<thead>
<tr>
<th>Food Group</th>
<th>Vit D Content</th>
<th>Dietary Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fortified Milk or Yogurt</td>
<td>115 IU / cup</td>
<td>Limit cheese to ≤ 1/4 of dairy (std pattern based on ~1/2 dairy as cheese)</td>
</tr>
<tr>
<td>Fortified Juice</td>
<td>100 IU/8 oz cup</td>
<td>Replace unfortified juice</td>
</tr>
<tr>
<td>Fortified Grains</td>
<td>Wh grains 21 IU/oz equiv, Fort’d cereals/bars 38-100 IU/eqv</td>
<td>Choose fortified grains when possible (versus 6 IU/oz wh grns, 1 IU/oz ref grns)</td>
</tr>
<tr>
<td>Seafood: High n-3 types</td>
<td>99 IU/ounce on average; some 150-250 IU/oz</td>
<td>Choose high n-3 fish for all 8 oz/ week of fish in pattern</td>
</tr>
<tr>
<td>Seafood: Low n-3 types</td>
<td>20 IU/ounce average</td>
<td>Choose seafood more often (versus poultry 1 IU/oz avg, meat 4 IU/oz avg)</td>
</tr>
<tr>
<td>Eggs</td>
<td>44 IU each (yolk only)</td>
<td>Choose eggs as appropriate; consider eggs from enriched feeding (120 IU)</td>
</tr>
<tr>
<td>Mushrooms</td>
<td>UV: 700-1000 IU/cup (3 oz) raw</td>
<td>Choose UV-exposed or maitake</td>
</tr>
</tbody>
</table>

Adapted from Scientific Report of the 2015 Dietary Guidelines Advisory Committee, Appendix E-3.3: Meeting Vitamin D Recommended Intakes in USDA Food Patterns

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Resources
Vitamin D Supplements
Reviews & Summaries

• NIH Office of Dietary Supplements Vitamin D Fact Sheets
  For Health Professionals:
  For Consumers:
  https://ods.od.nih.gov/factsheets/VitaminD-Consumer/

• NIH Office of Dietary Supplements Summary & Videos of Conference (2014):
  “Vitamin D: Moving Toward Evidence-Based Decision Making in Primary Care,”
  http://1.usa.gov/1R3LGTd

• National Cancer Institute: Vitamin D and Cancer Prevention
Omega-3 Fatty Acids
and
Fish Oil Supplements
Omega-3 Fatty Acids: Protective ♥ Potential

Valid Hypothetical Mechanisms $^{1,3}$
Anti-inflammatory potential through prostaglandins
Decreased susceptibility to arrhythmia
Decreased platelet activation
Reduced triglycerides
  *mainly if TG $\geq 500$ mg/dl with doses of 2-4 g/day supervised

Observational cohort studies
Support link to fish consumption and lower CVD
  Fish 1 svg/wk or 2-4 svg/wk: 16-21% lower CHD mortality $^2$
  250 mg EPA+DHA/day: 36% lower CHD mortality $^3$

$^1$ Jacobson, National Lipid Assoc Recommendations Pt 2, J Clin Lipid 2015
Long-Chain Omega-3 Fatty Acid Supplements & CVD Controlled Trials

Positive Studies
• DART
• GISSI-Prevenzione
• GISSI Heart Failure
• JELIS

Neutral Studies
• Alpha-Omega
• DART-2
• OMEGA
• Su.Fol.Om3
• ORIGIN

What’s Different?
• Background medication
• Omega-3 intake
• Who’s in the study
• Outcome
Non-Significant Trend Only – 12% lower risk per 100 gm Fish Consumption
Omega-3 Fatty Acids Without Supplements?

Fish

- High n-3 average 451 mg EPA+DHA per ounce
- Low n-3 average 102 mg EPA+DHA per ounce
- CVD Prevention: 8 oz. fish/week, prefer high n-3*
- 250 mg EPA+DHA/day:
  - 4 oz/week all high n-3
  - or 8 oz/week typical U.S.
  - or 12 oz/week all low n-3
- 500 mg EPA+DHA/day:
  - 8 oz/week all high n-3
  - or 12 oz/week if half high n-3

*Recommended by American Heart Association & Dietary Guidelines for Americans 2010
Omega-3 Fatty Acids
Without Supplements OR Fish?

Alpha-Linolenic Acid (ALA) – Natural Plant sources
• Walnuts, Flaxseeds (ground) or oil, Chia seeds, Hemp seeds, Avocado, Dark leafy greens, Seaweed, Soynuts,
• Canola & Soybean oil

Omega-3 Fortified Foods
• Total n-3 ≈ 115 mg per large egg
• EPA+ DHA ≈ 30-50 mg/svg
  Cheese, Milk, Peanut Butter, Orange Juice, Bread, Spreads(?)
• ALA ≈ 180-500 mg /svg (sometimes 1000 mg)
  Pasta, RTE Cereal, Oatmeal, Frozen Waffles, Spreads
Omega-3 Fatty Acid Supplement Considerations

• Grams of Fish Oil ≠ Grams EPA+ DHA
  - 1 g fish oil may contain 80 – 800 mg EPA+DHA

• Fish liver oils: contain vitamins A & D in very high amounts (potential for excess)

• Calamari oil: good source of DHA especially

• Algal oil: vegetarian, source of DHA especially
Resources
Omega-3 Fatty Acids & Seafood Options

Seafood for Omega-3’s

• *Seafood: Food Pattern Modeling Analysis* for 2010 Dietary Guidelines Advisory Committee Report, Appendix E-3.10
  http://www.cnpp.usda.gov/sites/default/files/dietary_guidelines_for_americans_AppendixE-3-10-Seafood.pdf

• *Seafood Health Facts: Making Smart Choices* - joint project of several universities with information on seafood choices, including EPA+DHA content and recommended amounts for demographic groups. Free downloadable consumer handout.
  http://seafoodhealthfacts.org/

Omega-3 Supplements

• *Omega-3 Supplements: An Introduction for Consumers* - National Center for Complementary & Integrative Health (NCCIH):
The Search for Reliable Information

Dealing with Contradictory Findings
Putting Together Pieces of Evidence

Laboratory Cell and Animal Studies
Long-Term Observational Cohort Studies
Human Clinical Trials
Individual Factors – Medical dx & pharma, Eating choices & barriers
Looking Beyond Supplement Headlines: Some Good Questions

• Study of humans, animals or cells?
• In humans, is group representative of person of interest?
• Compared to what other treatment or condition?
• What was the dose?
• Controlled for other influences (confounders)?
• How long an intervention and follow-up?
• Results: biomarkers, risk factors, or clinical outcomes?
• How closely did participants comply?
• Especially for review or meta-analysis, what is publication date?
American Heart Association

• Eat a healthy diet.
• Patients with heart disease should consume about 1 gram of EPA + DHA, ideally from fish. This can be hard to get by diet alone, so a supplement could be needed. As always, consult with a physician first.
• If you have elevated triglycerides, try to get 2-4 g/day EPA+DHA.
• Don’t take antioxidant vitamin supplements such as A, C and E.
• Do not rely only on supplements. There isn’t sufficient data to suggest that healthy people benefit by taking certain vitamin or mineral supplements in excess of the daily recommended allowance. Some observational studies have suggested that using these can lower rates of cardiovascular disease and/or lower risk factor levels. However, it’s unclear in these studies whether supplements caused these improvements.

American Institute for Cancer Research (AICR)

• Don't use supplements to protect against cancer.

• To reduce your risk of cancer, choose a balanced diet with a variety of foods rather than taking supplements.

• In some dietary or health circumstances, supplements may be valuable.
A diet rich in vegetables, fruits, and other plant-based foods may reduce the risk of cancer, but there is little proof that dietary supplements can reduce cancer risk.

- One exception may be calcium supplements, which may reduce the risk of colorectal cancer.
- Some high-dose supplements may actually increase cancer risk.
- Some dietary supplements may be beneficial for other reasons for some people, such as pregnant women, women of childbearing age, and people with restricted dietary intakes.
Based on a current review of the literature, specific dietary supplements are not recommended for cancer prevention.

[Recommendation 16; Grade 1A = Strong recommendation, high-quality evidence]
## U.S. Preventive Services Task Force 2014 Recommendations

<table>
<thead>
<tr>
<th>Population</th>
<th>Recommendation</th>
<th>Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>Use of Multivitamins to Prevent Cardiovascular Disease or Cancer</td>
<td>The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of the use of multivitamins for the prevention of cardiovascular disease or cancer.</td>
<td>I</td>
</tr>
<tr>
<td>Single- or Paired-Nutrient Supplements for Prevention of Cardiovascular Disease or Cancer</td>
<td>The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of the use of single- or paired-nutrient supplements (except β-carotene and vitamin E) for the prevention of cardiovascular disease or cancer.</td>
<td>I</td>
</tr>
<tr>
<td>Use of β-carotene or Vitamin E for Prevention of Cardiovascular Disease or Cancer</td>
<td>The USPSTF recommends against the use of β-carotene or vitamin E supplements for the prevention of cardiovascular disease or cancer.</td>
<td>D</td>
</tr>
</tbody>
</table>

Professional Resources: Published Statements

American Heart Association
   Science Advisory on Antioxidant Vitamin Supplements & CVD
   http://circ.ahajournals.org/content/110/5/637.full
American Institute for Cancer Research (AICR)
   Recommendations for Cancer Prevention (see #8 on Supplements)
   http://www.aicr.org/reduce-your-cancer-risk/recommendations-for-cancer-prevention/
American Cancer Society
   Guidelines on Nutrition and Physical Activity for Cancer Prevention (see “Common Questions”)
Society for Integrative Oncology – Clinical Practice Guidelines
United States Preventive Health Services Task Force
   Vitamin Supplementation to Prevent Cancer and CVD (2014)
   USPSTF Statement for Patients:
# Supplement Labels

![Image of a supplement label showing nutritional facts and certifications marks (USP, NSF, ConsumerLab.com)]
### Do Labels Mean What You Think?

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>DV</th>
<th>EAR</th>
<th>RDA (or AI)</th>
<th>UL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin A</td>
<td>5000 IU</td>
<td>500-625 mcg</td>
<td>700-900 mcg</td>
<td>3000 mcg</td>
</tr>
<tr>
<td></td>
<td></td>
<td>= 1665-2081 IU</td>
<td>=2330-3000 IU</td>
<td><em>retinol</em></td>
</tr>
<tr>
<td>Vitamin C</td>
<td>60 mg</td>
<td>60-75 mg</td>
<td>75-90 mg</td>
<td>2000 mg</td>
</tr>
<tr>
<td>Vitamin D</td>
<td>400 IU</td>
<td>400 IU</td>
<td>600-800 IU</td>
<td>4000 IU</td>
</tr>
<tr>
<td>Vitamin E</td>
<td>30 IU</td>
<td>12 mg α-tocoph</td>
<td>15 mg α-tocoph</td>
<td>1000 mg α-tocoph</td>
</tr>
<tr>
<td></td>
<td></td>
<td>= 18-27 IU</td>
<td>=22-33 IU</td>
<td></td>
</tr>
<tr>
<td>Folate</td>
<td>400 mcg</td>
<td>320 mcg</td>
<td>400 mcg</td>
<td>1000 mcg</td>
</tr>
<tr>
<td>Calcium</td>
<td>1000 mg</td>
<td>800-1000 mg</td>
<td>1000-1200 mg</td>
<td>2000-2500 mg</td>
</tr>
<tr>
<td>Iron</td>
<td>18 mg</td>
<td>5.6 mg / 8.1 mg</td>
<td>8 mg / 18 mg</td>
<td>45 mg</td>
</tr>
<tr>
<td>Magnesium</td>
<td>400 mg</td>
<td>255-350 mg</td>
<td>320-420 mg</td>
<td>350 mg <em>supp only</em></td>
</tr>
<tr>
<td>Selenium</td>
<td>70 mcg</td>
<td>45 mcg</td>
<td>55 mcg</td>
<td>400 mcg</td>
</tr>
<tr>
<td>Potassium</td>
<td>3500 mg</td>
<td>--</td>
<td>( 4700 mg )</td>
<td>--</td>
</tr>
</tbody>
</table>

DV= Daily Value; EAR = Est’d Avg Requirement; RDA = Rec’d Dietary Allowance; AI = Adequate Intake; UL = Tolerable Upper Intake Level
What Do We Say?

• Supplements can play an important role – as “Supplements”
• Intake < RDA level does not mean “deficient”
• More is not necessarily better
• Food & supplements are not the same
• Base choices on expert recommendations & reports, not single studies and hearsay
• Supplement decisions are individual – assess needs & baseline
Professional Resources

• NIH Office of Dietary Supplements Dietary Supplement Label Database
  http://dsld.nlm.nih.gov/dsld/

• NIH Office of Dietary Supplements Fact Sheets for Professionals
  http://ods.od.nih.gov/factsheets/list-all/

• National Center for Complementary & Integrative Health (NIH)
  https://nccih.nih.gov/

• Integrative Medicine Center, Memorial Sloan Kettering Cancer Center -- “About Herbs, Botanicals & Other Products” (online info & app)  http://bit.ly/1HRqvAF

• Natural Standard Database through personal or institutional subscription or as part of some dpg memberships

• Consumer Lab.com available through subscription
Resources for the Public

• U.S. Preventive Services Task Force: Vitamin, Mineral, and Multivitamin Supplements to Prevent Cardiovascular Disease and Cancer: Consumer Guide
  Annals of Internal Medicine Patient Summary of USPSTF Report (1 page pdf)
  http://annals.org/article.aspx?articleid=1832965

• NIH Office of Dietary Supplements
  Fact Sheets in English & Spanish - http://ods.od.nih.gov/factsheets/list-all/
  FAQ -- http://1.usa.gov/1HRmPPi

• American Institute for Cancer Research (AICR)
More Resources for the Public

- U.S. Food & Drug Administration (FDA)
  Tips for Supplement Users - [http://1.usa.gov/1umyeN0](http://1.usa.gov/1umyeN0)

- National Center for Complementary & Integrative Health (NIH)
  [https://nccih.nih.gov/](https://nccih.nih.gov/)

- Integrative Medicine Center, Memorial Sloan Kettering Cancer Center
  About Herbs, Botanicals & Other Products – online info & app with details on vitamins, botanicals, etc.
Let’s Keep the Conversation Going!

For More on
Healthful Eating Research & How-to’s

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Credit Claiming

You must complete a brief evaluation of the program in order to download your certificate. The evaluation survey will be available on www.CE.TodaysDietitian.com for 1 year following the live presentation.

RDs should list CPE activity type 175 in their professional development portfolio.