In the name of God

Taher Entezari-Maleki

US Preventive Services Task Force | Evidence Report

FREE

June 21, 2022

Vitamin and Mineral Supplements for the Primary Prevention of Cardiovascular Disease and Cancer

Updated Evidence Report and Systematic Review for the US Preventive Services Task Force

Top of Article

Multivitamins

- Evidence suggested a possible small benefit for
- Cancer Any cancer incidence: OR, 0.93 (95% CI,
- 0.87-0.99); but small to no benefit for all-cause
- mortality or CVD

- Harm
- Cataract, small increase of rash and epixtaxis

Beta carotene (Vitamin A)

- Paradoxical
- Small increase of CV mortality : OR, 1.10 (95% CI, 1.02-1.19); 5 RCTs (n = 95 506);

- Harm
- The most substantial serious harms are the paradoxical harms of increased all-cause mortality, CVD mortality, and lung cancer
- Trials generally showed no statistically significant findings for other adverse events other than hypercarotenodermia and GI symptoms

- Two cohort studies in women found an elevated but not statistically significantly increased risk of hip fracture

Vitamin E

- Most evidence indicated that vitamin E had no benefit for mortality, CVD

- Harm
- Hemorrhagic stroke: low for increased risk
- Cataracts, hospitalization from pneumonia, other nonserious: low for no increased risk

Vitamin D (with or without calcium)

- No benefit on CVD
- 32 RCTs (n = 123 140
- observations)
- CVD events: 1.00 (95% CI, 0.95-1.05); 7 RCTs (n = 74 925)

- Harm
- Both trial and cohort evidence suggested an increased risk of kidney stones with 1000 IU/d or more of vitamin D over ≥7 y
- Most evidence supported no increased risk of GI-related symptoms

Calcium

- Most evidence indicated no benefit for mortality, CVD,
- All-cause mortality: 1.05 (95% CI, 0.92-1.21; 6 RCTs [n = 8394])
- CVD events: 1.11 (95% CI, 0.90-1.36; 4 RCTs [n = 4076])

- Harm
- Findings suggested an increased risk of constipation and GI symptoms and possibly kidney stones

Micronutrient Supplementation to Reduce Cardiovascular Risk

Dec 05, 2022

Authors: An P, Wan S, Luo Y, et al.

Citation: Micronutrient Supplementation to Reduce Cardiovascular Risk. *J Am Coll Cardiol* 2022;80:2269-2285.

Summary By: Elizabeth A. Jackson, MD, FACC

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Mar 06, 2023 | **ACC News Story**

RCTs

Antioxidant Micronutrient		Randomized Controlled Trials on CVD Risk Factors		Blood Pressure		Blood Lipid				Blood Glucose		
		Median Dose [Range]	Median Duration [Range], Month	Systolic Blood Pressure	Diastolic Blood Pressure	Total Cholesterol	Low-Density Lipoprotein Cholesterol	High-Density Lipoprotein Cholesterol	Triglyceride	Hemoglobin A1c	Fasting Blood Glucose	Fasting Blood Insulin
Fatty Acid	n-3	2 g/d [0.28-9.50 g/d]	3 [0.69-60]	●	●	●	●	▲	▼	●	●	●
	n-6	4.25 g/d [1-20 g/d]	2.07 [0.69-24]	●	●	▼	▼	▲	●		●	
	n-9		1.38 [0.46-1.84]			●	●	●	▲			
Amino Acid	L-arginine	6 g/d [1.3-30 g/d]	1.50 [0.23-30]	▼	▼	●	●	●	●	●	▼	▼
	L-citrulline	6 g/d [2-6 g/d]	1.15 [0.23-1.84]	▼	▼	●	●	●	●			
Vitamin	Folic Acid	5 mg [0.25-15 mg]	1.84 [0.23-53.85]	▼	▼	▼	▼	●	▼	●	▼	▼
	Vitamin C	500 mg/d [50-3,000 mg/d]	1.84 [0.33-60]	●	●	●	●	▲	●	●	●	●
	Vitamin C + E	1,400 mg/d [300-1,400 mg/d]	3 [1.84-5.52]	●	●	●	●	●	●			
	Vitamin D	3,410 IU/d [40-120,000 IU/d]	3 [1.38-84]	●	●	●	●	●	●	▼	▼	●
	Vitamin E	400 mg/d [3-1,800 mg/d]	2 [0.69-72]	●	●	●	●	●	●	▼	●	●

Direction	Cardiometabolic Health
▼ Decrease	Benefit
▲ Increase	Benefit
▲ Increase	Harm
● Unchanged	Neutral

Evidence Quality
High Quality
Moderate Quality
Low Quality
Very Low Quality

		Randomized Controlled Trials on CVD Risk Factors		Blood Pressure		Blood Lipid				Blood Glucose		
		Median Dose [Range]	Median Duration [Range], Month	Systolic Blood Pressure	Diastolic Blood Pressure	Total Cholesterol	Low-Density Lipoprotein Cholesterol	High-Density Lipoprotein Cholesterol	Triglyceride	Hemoglobin A1c	Fasting Blood Glucose	Fasting Blood Insulin
Mineral	Magnesium	400 mg/d [200-729 mg/d]	2.76 [1-6]	▼	▼	•	•	▲	▼	•	•	•
	Selenium	200 μg/d [100-960 μg/d]	2.76 [1.38-6]	•	•	•	•	•	•	•	•	•
	Zinc	30 mg/d [5-200 mg/d]	2 [0.92-12]	•	•	▼	•	•	▼	▼	▼	▼
Antioxidant Supplement	α-Lipoic Acid	600 mg/d [100-2,400 mg/d]	2.96 [1.84-16.57]	▼	▼	•	•	▲	•	•	•	•
	β-carotene											
	Coenzyme Q10	300 mg/d [60-1,200 mg/d]	2.76 [0.56- 6]	▼	•	•	•	•	▼	▼	•	•
	Lycopene	15 mg/d [5-30 mg/d]	2 [1.38-6]	▼	•	•	•	•	•			
	Melatonin	5 mg/d [1-24 mg/d]	1.84 [0.46-12]	•	•	▼	•	•	•		•	•

		Randomized Controlled Trials on CVD Risk Factors		Blood Pressure		Blood Lipid				Blood Glucose		
		Median Dose [Range]	Median Duration [Range], Month	Systolic Blood Pressure	Diastolic Blood Pressure	Total Cholesterol	Low-Density Lipoprotein Cholesterol	High-Density Lipoprotein Cholesterol	Triglyceride	Hemoglobin A1c	Fasting Blood Glucose	Fasting Blood Insulin
Polyphenol	Anthocyanin	160 mg/d [1.65-1,024 mg/d]	1.84 [0.46-6]	●	●	▼	▼	▲	▼	●	▼	●
	Catechin	456 mg/d [20-1,344 mg/d]	2.76 [0.46-12]	●	●	▼	●	●	●	▼	▼	●
	Curcumin	500 mg/d [80-2,400 mg/d]	2.76 [2.38-5.52]	▼	●	●	●	▲	●	▼	▼	▼
	Flavanol	805 mg/d [6.5-20,000 mg/d]	1.18 [0.46-11.97]	▼	●	●	●	▲	●	●	▼	▼
	Flavonoid		4.14 [0.46-12]	●	▼	●	▼	●	●			
	Genistein	54 mg/d [50-90 mg/d]	6 [2.76-36]	▼	▼	▼	▼	●	●		▼	▼
	Hesperidin	500 mg/d [290-500 mg/d]	2.76 [0.69-3]	●	●	●	●	●	●		●	●
	Isoflavone	66 mg/d [10-165 mg/d]	2.76 [0.46-48]	●	●	●	●	●	●	●	●	●
	Quercetin	150 mg/d [50-1,000 mg/d]	1.38 [0.23-2.76]	▼	●	●	●	●	●		●	▼
	Resveratrol	390 mg/d [75-3,000 mg/d]	2.76 [0.92-6.44]	▼	▼	●	●	●	●	●	●	●

- Evidence-based maps summarizing 256 meta-analyses of 884 randomized controlled trials investigating the interventional effects of 27 antioxidant micronutrients on cardiovascular disease risk factors (top) and cardiovascular disease and type 2 diabetes events (bottom

Micronutrient		Blood Pressure		Blood Lipid				Blood Glucose		
		Systolic Blood Pressure	Diastolic Blood Pressure	Total Cholesterol	Low-Density Lipoprotein Cholesterol	High-Density Lipoprotein Cholesterol	Triglyceride	Hemoglobin A1c	Fasting Blood Glucose	Fasting Blood Insulin
Fatty acid	n-3	●	●	●	●	▲	▼	●	●	●
	n-6	●	●	▼	▼	▲	●		●	
	n-9			●	●	●	▲			
Amino acid	L-arginine	▼	▼	●	●	●	●	●	▼	▼
	L-citrulline	▼	▼	●	●	●	●			
Vitamin	Folic acid	▼	▼	▼	▼	●	▼	●	▼	▼
	Vitamin C	●	●	●	●	▲	●	●	●	●
	Vitamin C+E	●	●	●	●	●	●			
	Vitamin D	●	●	●	●	●	●	▼	▼	●
	Vitamin E	●	●	●	●	●	●	▼	●	●
Mineral	Magnesium	▼	▼	●	●	▲	▼	●	●	●
	Selenium	●	●	●	●	●	●	●	●	●
	Zinc	●	●	▼	●	●	▼	▼	▼	▼
Antioxidant supplement	α-lipoic acid	▼	▼	●	●	▲	●	●	●	●
	Coenzyme Q10	▼	●	●	●	●	▼	▼	●	●
	Lycopene	▼	●	●	●	●	●			
	Melatonin	●	●	▼	●	●	●		●	●
Polyphenol	Anthocyanin	●	●	▼	▼	▲	▼	●	▼	●
	Catechin	●	●	▼	●	●	●	▼	▼	●
	Curcumin	▼	●	●	●	▲	●	▼	▼	▼
	Flavanol	▼	●	●	●	▲	●	●	▼	▼
	Flavonoid	●	▼	●	▼	●	●			
	Genistein	▼	▼	▼	▼	●	●		▼	▼
	Hesperidin	●	●	●	●	●	●		●	●
	Isoflavone	●	●	●	●	●	●	●	●	●
	Quercetin	▼	●	●	●	●	●		●	▼
	Resveratrol	▼	▼	●	●	●	●	●	●	●

Effects of Antioxidant Micronutrient on Cardiovascular Disease and Type 2 Diabetes Events

Micronutrient		All-Cause Mortality	Cardiovascular Disease Mortality	Myocardial Infarction	Stroke	Coronary Heart Disease	Arrhythmia	Type 2 Diabetes
Fatty acid	n-3	●	▼	▼	●	▼	●	●
	n-6							●
Vitamin	Folic acid	●	●	●	▼			
	Vitamin C	●	●	●	●			
	Vitamin D	●	●	●	●	●		
	Vitamin E	●	●	●	●			●
Mineral	Selenium	●	●	●	●	●		
Antioxidant supplement	β-carotene	▲	▲	●	▲			●
	Coenzyme Q10	▼						

Direction	Cardiometabolic Health
▼ Decrease	Benefit
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● Unchanged	Neutral

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Thank you