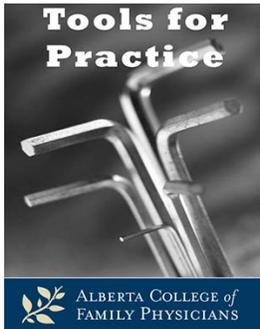


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Evidence Updated: New meta-analysis, moved Context references to Evidence Bottom Line: No change

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Antioxidant Vitamin Cure-Alls: Will Good Theories Ever Die?

Clinical Question: Does daily supplementation of antioxidant vitamins (A, E, and C) decrease mortality in the general population?

Bottom-line: The current evidence does not support the use of antioxidant supplementation, and patients should be dissuaded from using beta-carotene, vitamin E, and perhaps high-dose vitamin A, as they appear to increase mortality by about 1 in every 250 over ~5 years.

Evidence:

- One Cochrane review¹ of 78 Randomized Controlled Trials (RCTs) with 296,707 patients (~75% healthy participants, ~25% pre-existing condition):
 - Focusing on high-quality RCTs:
 - Antioxidants increased mortality with a Relative Risk (RR) of 1.04 (1.01-1.07), Number Needed to Harm (NNH)=238.
 - Specifically:
 - Beta-carotene (pro-vitamin A): RR 1.05 (1.01-1.09).
 - Vitamin E: RR 1.03 (1.00-1.05).
 - No statistically significant difference in mortality for:
 - Vitamin A, all doses: RR 1.07 (0.97-1.18).
 - High-dose vitamin A appears to increase mortality (p=0.002).
 - High-dose not clearly defined, but appears to be ≥ 5000 IU.
 - Vitamin C: RR 1.02 (0.98-1.07).
 - Selenium: RR 0.97 (0.91-1.03).
 - If baseline mortality risk were around 10% over 3.5 years, about one in every 100 to 250 people taking antioxidants would die because of the supplements.
- Other meta-analyses report similar results. Examples:
 - Antioxidant vitamins do not reduce the incidence of cardiovascular disease or cancer when taken for primary prevention.²
 - Beta-carotene: Statistically significant increased mortality (NNH=167-326).²⁻⁴
 - Vitamin E:

- No difference in mortality in 101,343 healthy individuals: RR 1.01 (0.98-1.04).²
- High-dose (≥ 400 IU): Statistically significant increased mortality (NNH=257).^{5,6}

Context:

- While theories and previous observational studies suggested potential benefit with antioxidant vitamins, this has been disproven by higher-level evidence.
 - Theories of disease and treatment/prevention are common in medicine. We must guard against the superficial appeal of these theories and rely on evidence of benefit or harm to guide the care of our patients.

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