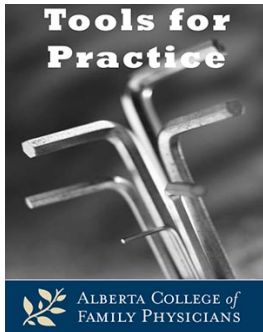


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Reviewed: August 21, 2016

**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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Tools for Practice is a biweekly article summarizing medical evidence with a focus on topical issues and practice modifying information. It is coordinated by G. Michael Allan, MD, CCFP and the content is written by practising family physicians who are joined occasionally by a health professional from another medical specialty or health discipline. Each article is peer-reviewed, ensuring it maintains a high standard of quality, accuracy, and academic integrity. If you are not a member of the ACFP and would like to receive the TFP emails, please sign up for the distribution list at <http://bit.ly/signupfortfp>. Archived articles are available on the ACFP website.

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