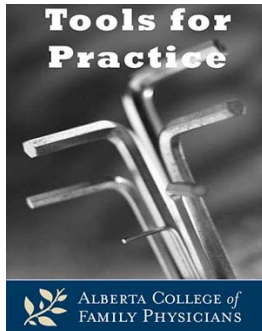


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Antioxidant vitamin cure-alls: Will good theories ever die?

Clinical Question:

Does daily supplementation of anti-oxidant vitamins (A, E and C) in general population decrease mortality?

Evidence

- Two virtually identical systematic reviews were published by the same authors in JAMA¹ and Cochrane².
 - Systematic review and meta-analysis of 68 randomized controlled trials (RCT) with 232,606 patients (70% healthy participants, 30% pre-existing condition).¹
 - Focusing on high-quality RCTs:
 - Antioxidants increased mortality with a relative risk (RR) of 1.05 (1.02-1.08)¹ for number needed to harm (NNH) of 180.³
 - Specifically:
 - Beta-Carotene (Provitamin A): RR 1.07 (1.02 - 1.11)
 - Vitamin A: RR 1.16 (1.10 - 1.24)
 - Vitamin E: RR 1.04 (1.01 - 1.07)
 - There was no statistical difference in mortality for vitamin C RR 1.06 (0.94-1.20) or selenium 0.90 (0.80-1.01).²
 - Selenium is the only one trending towards improved outcomes (but still not statistically significant).

Context

- While theories and previous observational studies suggested potential benefit with anti-oxidant vitamins, this is disputed by higher level evidence.
- Previous meta-analyses report similar results to the meta-analysis^{1,2} above. Examples:
 - Beta-Carotene⁴: Statistically significant increase mortality NNH=326
 - High dose vitamin E ($\geq 400\text{IU}$)⁵: Statistically significant increase mortality NNH=257
- RCTs published since continue to support the findings that anti-oxidants are not beneficial⁶ or increase mortality⁷.

- 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.

Bottom-line: The current evidence does not support the use of anti-oxidant supplementation, and patients should be dissuaded from using beta-carotene and vitamins A & E as they appear to increase mortality.

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1. [JAMA. 2007;297:842-57](#)
2. [Cochrane Database Syst Rev. 2008;\(2\):CD007176](#)
3. [ACP Journal Club 2007; 147\(1\): 4](#)
4. [Lancet. 2003;361:2017-23](#)
[ACP Journal Club 2004; 140\(2\); 45](#)
5. [Ann Intern Med. 2005;142:37-46](#)
[ACP Journal Club 2005; 143\(1\): 1](#)
6. [JAMA. 2008;300:2123-33](#)
7. [BMJ 2008;337:a1840](#)

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. Archived articles are available on the Towards Optimized Practice website and the ACFP website.

This communication reflects the opinion of the author and does not necessarily mirror the perspective and policy of the Alberta College of Family Physicians.