Daily multivitamins to reduce mortality, cardiovascular disease, and cancer

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Clinical question

Does daily multivitamin supplementation reduce mortality, cardiovascular disease (CVD), or cancer?

Bottom line

Current evidence does not support the routine use of multivitamins to reduce mortality, CVD, or cancer for people in developed countries.

- Meta-analysis¹ of 21 RCTs, with 91074 patients (54% men) randomized to multivitamins or placebo for 3.5
 - -No effect on overall mortality, relative risk (RR) = 0.98 (95% CI 0.94 to 1.02); cancer mortality, RR=0.96 (95% CI 0.88 to 1.04); or CVD mortality, RR = 1.01 (95% CI 0.93 to 1.09).
 - -Multiple subgroup testing found no differences.
 - -No evidence of publication bias or meaningful het-
- Heavily publicized RCT^{2,3} of 14641 men (mean age 64.3 years) randomized to multivitamin or placebo, followed for 11.2 years.
 - -No effect on overall mortality, hazard ratio (HR) = 0.94 (95% CI 0.88 to 1.02); cancer mortality, HR=0.88 (95% CI 0.77 to 1.01); CVD mortality, HR=0.95 (95% CI 0.83 to 1.09); or CVD events, HR=1.01 (95% CI 0.91 to 1.10). -Reduced cancer incidence, HR=0.92 (95% CI 0.86 to 0.998).
 - —These HRs were adjusted (for unclear reasons).
 - —Unadjusted HR for cancer incidence was not significant, RR=0.94 (95% CI 0.87 to 1.003).
 - -Issues: lots of exclusion (eg, removing noncompliant patients), adjustments always in favour of multivitamins.

Context

- Vitamin supplementation might help reduce overall mortality in undernourished populations.4 However, in this RCT⁴ of 4 different vitamin interventions, only 1 reduced mortality, RR=0.91 (95% CI 0.84 to 0.99).
- Meta-analyses of vitamin components on mortality: -No effect with B vitamins.5
 - -Increase with antioxidants, RR=1.04 (95% CI 1.01 to 1.07), vitamin E, beta-carotene, and high-dose vitamin A; but no effect with vitamin C and selenium.6
 - -Decrease with vitamin D, RR=0.97 (95% CI 0.94 to 1.00).7 -Increases and decreases are small (numbers needed to harm or treat around 200 over 5 years).

Implementation

Approximately 33% of the population takes daily multivitamins.8 Users are generally healthier people8 who believe multivitamins improve or maintain overall health.9 Multivitamin use is most common in the elderly,8 a population with an increasing polypharmacy burden. One review suggested multivitamins should be among the first medications to discontinue in this population owing to their lack of benefit.¹⁰ The approximate cost for daily vitamin consumption is \$32 to \$62 per year. While patients with intermediate or higher agerelated macular degeneration derive some benefits from ocular vitamins,11 multivitamins are generally not helpful, and Canadians might be spending as much as \$500 million per year on false hopes of improved health with multivitamins.

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References

- 1. Macpherson H, Pipingas A, Pase MP. Multivitamin-multimineral supplementation and mortality: a meta-analysis of randomized controlled trials. Am J Clin Nutr 2013;97(2):437-44.
- 2. Gaziano JM, Sesso HD, Christen WG, Bubes V, Smith JP, MacFadyen J, et al. Multivitamins in the prevention of cancer in men: the Physicians' Health Study II randomized controlled trial. JAMA 2012;308(18):1871-80.
- 3. Sesso HD, Christen WG, Bubes V, Smith JP, MacFadyen J, Schvartz M, et al. Multivitamins in the prevention of cardiovascular disease in men: the Physicians' Health Study II randomized controlled trial. JAMA 2012;308(17):1751-60.
- 4. Blot WJ, Li JY, Taylor PR, Guo W, Dawsey S, Wang GQ, et al. Nutrition intervention trials in Linxian, China: supplementation with specific vitamin/mineral combinations, cancer incidence, and disease-specific mortality in the general population. J Natl Cancer Inst 1993;85(18):1483-92.
- 5. Clarke R, Halsey J, Lewington S, Lonn E, Armitage J, Manson JE, et al. Effects of lowering homocysteine levels with B vitamins on cardiovascular disease, cancer, and cause-specific mortality: meta-analysis of 8 randomized trials involving 37485 individuals. Arch Intern Med 2010;170(18):1622-31
- 6. Bjelakovic G, Nikolova D, Gluud LL, Simonetti RG, Gluud C. Antioxidant supplements for prevention of mortality in healthy participants and patients with various diseases. *Cochrane Database Syst Rev* 2012;(3):CD007176.
- 7. Bjelakovic G, Gluud LL, Nikolova D, Whitfield K, Wetterslev J, Simonetti RG, et al. Vitamin D supplementation for prevention of mortality in adults. Cochrane Database Syst Rev 2011;(7):CD007470.
- 8. Bailey RL, Gahche JJ, Lentino CV, Dwyer JT, Engel JS, Thomas PR, et al. Dietary supplement use in the United States, 2003-2006. *J Nutr* 2011;141(2):261-6.

 9. Bailey RL, Gahche JJ, Miller PE, Thomas PR, Dwyer JT. Why US adults use dietary
- supplements. JAMA Intern Med 2013;173(5):355-61
- 10. Steinman MA, Hanlon JT. Managing medications in clinically complex elders: "there's got to be a happy medium." JAMA 2010;304(14):1592-601.
- 11. Kolber MR, Tennant M, Nickonchuk T. Vitamins for age-related macular degeneration demonstrate minimal differences. Can Fam Physician 2013;59:503.



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