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.

Evidence
- Meta-analysis\(^1\) of 21 RCTs, with 91,074 patients (54% men) randomized to multivitamins or placebo for 3.5 years.
  - 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 heterogeneity.
- Heavily publicized RCT\(^2,3\) of 14,641 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 RCT\(^4\) 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 people\(^8\) 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 age-related 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