

Canadian Task Force on Preventive Health Care

RECOMMENDATION STATEMENT: The Role of Vitamin E Supplements in the Prevention of Cardiovascular Disease and Cancer

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RECOMMENDATIONS

The CTFPHC concludes that there is insufficient evidence to recommend for or against the use of routine vitamin E supplementation for the primary prevention of CVD events (**I Recommendation**). There is good evidence to recommend against the use of vitamin E for the secondary prevention of CVD in patients with established CVD or risk factors for CVD (**D Recommendation**). The CTFPHC concludes that there is good evidence to recommend against the use of routine vitamin E supplementation for the prevention of lung cancer (**D Recommendation**). There is insufficient evidence to recommend for or against the use of routine vitamin E supplementation for the prevention of cancers in the general population (**I Recommendation**).

BACKGROUND

Cardiovascular disease (CVD) and cancer are the leading causes of death in Canada, accounting for 37% and 27% of all deaths respectively.¹ Premature death from cardiovascular disease is responsible for an estimated 294,000 years of life lost.² Almost one-third of the cancer deaths in men and almost one-quarter in women are due to lung cancer alone. Cancer was the leading cause of potential years of life lost (PYLL) for men and women: 894,000 potential years were lost due to cancer, representing 29% of the PYLL resulting from all causes of death.³ Simple, accessible and safe preventive therapies that will decrease the incidence and mortality of CAD and cancer are expected to have a great effect on public health.

Epidemiologically, lower rates of heart disease and cancer have been noted among Vitamin E users.⁴⁻⁸ Vitamin E's antioxidant properties are felt to be responsible for this association. Oxidative modification of Low Density Lipoproteins (LDL) is an important step in the development and progression of atherosclerosis.^{9,10} Antioxidants such as vitamin E have been shown to slow atherosclerosis.¹¹

Several in vitro experiments with cells in culture exposed to pro-oxidant carcinogens showed antioxidant vitamins to have a significant protective role against cancer.¹²⁻¹⁴ In experimental animals deficiencies of certain nutrients such as vitamin E may enhance carcinogenesis, while supplementation of these nutrients may inhibit tumor formation.^{15,16} α -tocopherol is the most common naturally occurring compound of vitamin E.¹⁷

Given the high prevalence of both cardiovascular disease and cancer, the potential population at risk is broad. In the last 5 years, multiple randomized trials have been published examining the effect of vitamin E in the primary prevention of cancer and cardiovascular disease as well as the secondary prevention of cardiac events.

MANEUVERS

- Use of vitamin E for the prevention of cardiovascular events and cancer.

POTENTIAL BENEFITS & HARMS

Benefits

- Reduction of total mortality
- Primary prevention of cardiovascular disease
- Secondary prevention of coronary events in patients with established cardiovascular disease
- Primary prevention of lung, stomach, esophageal, colorectal, genitourinary and prostate cancer

Harms

- Increase in mortality from hemorrhagic stroke
- Increase in CVD mortality
- A small but statistically significant increase of total cholesterol levels

EVIDENCE & CLINICAL SUMMARY

- Vitamin E did not have beneficial effects on the primary prevention of CVD events.
- The evidence regarding the effects of vitamin E on the secondary prevention of CVD is conflicting, but mostly does not show benefit.
- In the ATBC trial there was a significant increase in mortality from hemorrhagic stroke in patients taking vitamin E (RR 1.49 (1.03-3.17)).^{18,19} This finding was based on a small number of events and it was not reported in other large vitamin E trials.
- There was a significant increase in CVD mortality (age adjusted) in the ATBC subset trial (RR 1.51 (1.02-2.24)) in the vitamin E group (with B-carotene), which remained but lost its statistical significance in the vitamin E group (alone) (RR 1.33 (0.86-2.05)).²⁰ Additionally, this association was not noted in the original cohort: CVD mortality in the ATBC trial was not affected in the vitamin E (with B-carotene) group (RR 0.98 (0.89-1.08)).¹⁸ This finding was not replicated in other large trials, which evaluated the role of vitamin E in the primary or secondary prevention of CVD.
- In the HPS trial, participants allocated to the vitamin group had a small but statistically significant increase of total cholesterol levels (mean difference 0.15 mmol/L, p=0.024).²¹
- Vitamin E did not affect the incidence or mortality of lung cancer. Half of the participants in the vitamin E group of the ATBC trial received B-carotene which might mask any protective effect of vitamin E against lung cancer. B-carotene was shown to increase the risk of lung cancer in two large RCTs, the ATBC trial and in the CARET trial (RR 1.16 (1.02-1.33) and RR 1.28 P <0.05, respectively).^{18,22}
- There is one fair quality RCT, which showed a marginal benefit of vitamin E (with B-carotene), in the reduction of prostate cancer incidence, but the discernment of this secondary endpoint is not well defined.²³ This finding was not replicated in the large HPS trial (RR 0.9 (0.74 - 1.1)).²¹
- There is conflicting evidence to recommend for or against the use of vitamin E for the prevention of stomach cancer. In one large good quality trial there was a marginal significant reduction of stomach cancer mortality and morbidity in patients taking vitamin E (with B-carotene and

selenium).²⁴ This study was done in Linxian, a rural area in china with a population that has a high rate of gastric cancer and subclinical deficiencies of several micronutrients including vitamin E.^{25,26} In addition, it is not clear if the beneficial effect comes from vitamin E alone or with selenium and B-carotene or with these supplements combined. The findings of this trial were not replicated in the large ATBC and HPS trials.^{18,21}

- There is an insufficient evidence to make a recommendation about the role of vitamin E in the prevention of esophageal, colorectal, urothelial (bladder, renal pelvis, ureter) and renal cell cancer.

RECOMMENDATIONS OF OTHERS

In 2003, the US Preventive Services Task Force concluded that the evidence is insufficient to recommend for or against the use of supplements of vitamins A, C, or E; multivitamins with folic acid; or antioxidant combinations for the prevention of cancer or cardiovascular disease.²⁷

Authorship Contributions:

Abdullah Alkhenizan and Valerie A. Palda co-authored the original systematic evidence review and the current article.

The Canadian Task Force on Preventive Health Care critically reviewed the evidence and developed the recommendations according to its methodology and consensus development process.

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