



Complete Summary

GUIDELINE TITLE

The role of vitamin E supplements in the prevention of cardiovascular disease and cancer.

BIBLIOGRAPHIC SOURCE(S)

Alkhenizan A, Palda VA. The role of vitamin E supplements in the prevention of cardiovascular disease and cancer. London (ON): Canadian Task Force on Preventive Health Care (CTFPHC); 2003 May. 6 p. [27 references]

GUIDELINE STATUS

This is the current release of the guideline.

A complete list of planned reviews, updates, and revisions is available under the What's New section at the [Canadian Task Force on Preventive Health Care \(CTFPHC\) Web site](#).

COMPLETE SUMMARY CONTENT

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IDENTIFYING INFORMATION AND AVAILABILITY
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SCOPE

DISEASE/CONDITION(S)

Cardiovascular disease and cancer (including lung, esophageal, stomach, colorectal, urological, and prostate cancer)

GUIDELINE CATEGORY

Assessment of Therapeutic Effectiveness
Prevention

CLINICAL SPECIALTY

Cardiology
Family Practice
Gastroenterology
Internal Medicine
Nutrition
Oncology
Preventive Medicine
Pulmonary Medicine
Urology

INTENDED USERS

Advanced Practice Nurses
Physicians

GUIDELINE OBJECTIVE(S)

To establish evidence-based guidelines for the use of vitamin E in the prevention of cardiovascular disease (CVD) and cancer

Specifically the guidelines sought to answer the following questions:

- What is the direct evidence that vitamin E reduces adverse clinical outcomes in the general population?
 - What is the direct evidence that vitamin E reduces total mortality?
 - What is the direct evidence that vitamin E reduces cardiovascular outcomes?
 - What is the direct evidence that vitamin E reduces cancer outcomes?
- What is the optimal dose of vitamin E in the prevention of CVD and cancer?
- What are the short-term and long-term side effects and toxicity of vitamin E?

TARGET POPULATION

Adults (>18 years of age, males and nonpregnant females) including those at risk of cardiovascular disease and cancer, and those with preexisting cardiovascular disease

INTERVENTIONS AND PRACTICES CONSIDERED

Vitamin E supplementation of diet

MAJOR OUTCOMES CONSIDERED

- Overall mortality
- Cardiac mortality
- Cancer mortality
- Incidence of nonfatal myocardial infarction
- Incidence of lung cancer and other cancers (prostate, urological, esophageal, stomach, colorectal).

- Side effects and toxicity of vitamin E supplements

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

A computerized search of Ovid MEDLINE, PREMEDLINE, the Cochrane database, and EMBASE for English language articles published between January 1966 and December 2000 was conducted using the Medical Subject Heading (MeSH) terms "coronary disease", "vitamin E", "alpha-tocopherol", "vitamins", "myocardial ischemia", "neoplasms", "colonic polyps", "polyps", "prevention", "primary prevention", "side effects", "toxicities", and "secondary prevention". These terms were used in various combinations. Relevant articles were also retrieved through a manual review of references. The search was updated for key new evidence in March 2003. Trials were included if they were randomized controlled trial (RCT) design, looked at clinical (not surrogate) outcomes of cardiovascular disease (CVD) or cancer as a primary or a secondary end point, and included only adults (age >18 years). Exclusion criteria were studies with sample size <100, non-English language publications, and studies with more than 5 different supplements in the vitamin E arm.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of Evidence

Research Design Rating

I: Evidence from at least one randomized controlled trial (RCT)

II-1: Evidence from controlled trial(s) without randomization

II-2: Evidence from cohort or case-control analytic studies, preferably from more than one centre or research group

II-3: Evidence from comparisons between times or places with or without the intervention; dramatic results in uncontrolled experiments could also be included here

III: Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees

Quality (Internal Validity) Rating

Good: A study that meets all design-specific criteria* well.

Fair: A study that does not meet (or it is not clear that it meets) at least one design-specific criterion* but has no known "fatal flaw."

Poor: A study that has at least one design-specific* "fatal flaw," or an accumulation of lesser flaws to the extent that the results of the study are not deemed able to inform recommendations.

*General design-specific criteria are outlined in Harris RP, Helfand M, Woolf SH, Lohr KN, Mulrow CD, Teutsch SM, Atkins D. Current Methods of the U.S. Preventive Services Task Force: A Review of the Process. Am J Prev Med 2001;20(suppl 3):21-35.

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The evidence was systematically reviewed using the methodology of the Canadian Task Force on Preventive Health Care. Recommendations were based on studies included in the evidentiary tables.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Recommendations Grades for Specific Clinical Preventive Actions

A: The Canadian Task Force (CTF) concludes that there is **good** evidence to recommend the clinical preventive action.

B: The CTF concludes that there is **fair** evidence to recommend the clinical preventive action.

C: The CTF concludes that the existing evidence is **conflicting** and does not allow making a recommendation for or against use of the clinical preventive action; however, other factors may influence decision-making.

D: The CTF concludes that there is **fair** evidence to recommend against the clinical preventive action.

E: The CTF concludes that there is **good** evidence to recommend against the clinical preventive action.

I: The CTF concludes that there is **insufficient** evidence (in quantity and/or quality) to make a recommendation; however, other factors may influence decision-making.

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Comparison with Guidelines from Other Groups
External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

External Peer Review

The Canadian Task Force on Preventive Health Care sent the final review and recommendations to selected external expert reviewers and their feedback was incorporated.

Comparison with Guidelines from Other Groups

The 2003 recommendations of the US Preventive Services Task Force on 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 were also reviewed.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Recommendation grade [**A, B, C, D, E**] and level of evidence [**I, II-1, II-2, II-3, III, good, fair, poor**] are indicated after each recommendation. Definitions for these grades and levels are repeated following the recommendations.

The Canadian Task Force on Preventive Health Care (CTFPHC) concludes that there is insufficient evidence to recommend for or against the use of routine

vitamin E supplementation for the primary prevention of cardiovascular disease (CVD) events in the general population and in male smokers (**Grade I recommendation**) ("MRC/BHF Heart Protection Study," 2002 [**I, good**]; de Gaetano, 2001 [**I, fair**]; Virtamo et al., 1998 [**I, fair**]).

The CTFPHC concludes that 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 (**Grade D recommendation**) ("MRC/BHF Heart Protection Study," 2002 [**I, good**]; Yusuf et al., 2000 [**I, good**]; Virtamo et al., 1998 [**I, fair**]; Rapola et al., 1997 [**I, fair**]; "Dietary supplementation," 1999 [**I, fair**]; Stephens, et al. 1996 [**I, fair**]).

The CTFPHC concludes that there is good evidence to recommend against the use of routine vitamin E supplementation for the prevention of lung cancer (**Grade D recommendation**), ("The effect of vitamin E," 1994 [**I, good**]; "MRC/BHF Heart Protection Study," 2002 [**I, good**]).

The CTFPHC concludes that 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 (**Grade I recommendation**), ("MRC/BHF Heart Protection Study," 2002 [**I, good**]; "The effect of vitamin E," 1994 [**I, fair**]; Blot et al. 1993 [**I, fair**]; Albanes et al., 2000 [**I, fair**]; Virtamo et al., 2000 [**I, fair**]; Heinonen et al., 1998 [**I, fair**]).

Definitions:

Levels of Evidence - Research Design Rating

Research Design Rating

I: Evidence from at least one randomized controlled trial (RCT)

II-1: Evidence from controlled trial(s) without randomization

II-2: Evidence from cohort or case-control analytic studies, preferably from more than one centre or research group

II-3: Evidence from comparisons between times or places with or without the intervention; dramatic results in uncontrolled experiments could also be included here

III: Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees

Quality (Internal Validity) Rating

Good: A study that meets all design-specific criteria* well.

Fair: A study that does not meet (or it is not clear that it meets) at least one design-specific criterion* but has no known "fatal flaw."

Poor: A study that has at least one design-specific* "fatal flaw," or an accumulation of lesser flaws to the extent that the results of the study are not deemed able to inform recommendations.

*General design-specific criteria are outlined in Harris RP, Helfand M, Woolf SH, Lohr KN, Mulrow CD, Teutsch SM, Atkins D. Current Methods of the U.S. Preventive Services Task Force: A Review of the Process. Am J Prev Med 2001;20(suppl 3):21-35.

Recommendations Grades for Specific Clinical Preventive Actions

A: The Canadian Task Force (CTF) concludes that there is **good** evidence to recommend the clinical preventive action.

B: The CTF concludes that there is **fair** evidence to recommend the clinical preventive action.

C: The CTF concludes that the existing evidence is **conflicting** and does not allow making a recommendation for or against use of the clinical preventive action; however, other factors may influence decision-making.

D: The CTF concludes that there is **fair** evidence to recommend against the clinical preventive action.

E: The CTF concludes that there is **good** evidence to recommend against the clinical preventive action.

I: The CTF concludes that there is **insufficient** evidence (in quantity and/or quality) to make a recommendation; however, other factors may influence decision-making.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

REFERENCES SUPPORTING THE RECOMMENDATIONS

[References open in a new window](#)

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

Maneuver: Vitamin E for the primary prevention of cardiovascular disease (CVD)

Level of Evidence:

I, good (one study); I, fair (two studies)

Maneuver: Vitamin E for the secondary prevention of CVD in patients with established CVD or risk factors for CVD

Level of Evidence:
I, good (two studies); I, fair (four studies)

Maneuver: Vitamin E for the prevention of lung cancer

Level of Evidence:
I, good (two studies)

Maneuver: Vitamin E for the prevention of other cancers (esophageal, stomach, colorectal, urological, and prostate)

Level of Evidence:
I, good (one study); I, fair (five studies)

Refer to the "Major Recommendations" field.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

The guideline recommendations may provide guidance to health care providers on the use of Vitamin E for prevention of cardiovascular events and cancer.

POTENTIAL HARMS

Not stated

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

The Canadian Task Force on Preventive Health Care (CTFPHC) recognizes that in many cases, patient-specific factors need to be considered and discussed, such as the value the patient places on the clinical preventive action; its possible positive and negative outcomes; and the context and/or personal circumstances of the patient (medical and other). In certain circumstances where the evidence is complex, conflicting, or insufficient, a more detailed discussion may be required.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Staying Healthy

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Alkhenizan A, Palda VA. The role of vitamin E supplements in the prevention of cardiovascular disease and cancer. London (ON): Canadian Task Force on Preventive Health Care (CTFPHC); 2003 May. 6 p. [27 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2003 May

GUIDELINE DEVELOPER(S)

Canadian Task Force on Preventive Health Care - National Government Agency [Non-U.S.]

SOURCE(S) OF FUNDING

The Canadian Task Force on Preventive Health Care (CTFPHC) is funded through a partnership between the Provincial and Territorial Ministries of Health and Health Canada.

GUIDELINE COMMITTEE

Canadian Task Force on Preventive Health Care (CTFPHC)

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

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GUIDELINE AVAILABILITY

Electronic copies: Available from the [Canadian Task Force on Preventive Health Care \(CTFPHC\) Web site](#).

Print copies: Available from Canadian Task Force on Preventive Health Care, Clinical Skills Building, 2nd Floor, Department of Family Medicine, University of Western Ontario, London, Ontario N6A 5C1, Canada.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Stachenko S. Preventive guidelines: their role in clinical prevention and health promotion. Ottawa: Health Canada, 1994. Available from the [Canadian Task Force on Preventive Health Care \(CTFPHC\) Web site](#).
- CTFPHC history/methodology. Ottawa: Health Canada, 1997. Available from the [CTFPHC Web site](#).
- Quick tables of current recommendations. Ottawa: Health Canada, 2003. Available from the [CTFPHC Web site](#).
- Alkhenizan, A., Palda, V.A., and the Canadian Task Force on Preventive Health Care. The role of vitamin E supplements in the prevention of cardiovascular

disease and cancer: systematic review and recommendations. CTFPHC Technical Report 03-6. May 2003. London, ON: Canadian Task Force. Available from the [CTFPHC Web site](#).

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on October 18, 2004. The information was verified by the guideline developer on November 2, 2004.

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