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Effect of Supplemental Antioxidants Vitamin C, Vitamin E, and Coenzyme Q10 for the Prevention and Treatment of Cardiovascular Disease

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Preface

The Agency for Healthcare Research and Quality (AHRQ), through its Evidence-Based Practice Centers (EPCs), sponsors the development of evidence reports and technology assessments to assist public- and private-sector organizations in their efforts to improve the quality of health care in the United States. The reports and assessments provide organizations with comprehensive, science-based information on common, costly medical conditions and new health care technologies. The EPCs systematically review the relevant scientific literature on topics assigned to them by AHRQ and conduct additional analyses when appropriate prior to developing their reports and assessments.

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AHRQ expects that the EPC evidence reports and technology assessments will inform individual health plans, providers, and purchasers as well as the health care system as a whole by providing important information to help improve health care quality.

We welcome written comments on this evidence report. They may be sent to: Director, Center for Practice and Technology Assessment, Agency for Healthcare Research and Quality, 540 Gaither Road, Rockville, MD 20850.

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Structured Abstract

Objectives. The purpose of this study was to conduct a systematic review of the scientific literature to identify and assess the evidence for the efficacy of the antioxidant supplements vitamin C, vitamin E, and coenzyme Q10 for the prevention and treatment of cardiovascular disease or modification of known risk factors for cardiovascular disease. It was our intention to perform meta-analyses where possible. The results may be used to develop a research agenda as well as to assist clinicians in advising patients who desire to take antioxidants to modify their risk of cardiovascular disease.

Search Strategy. A comprehensive search was conducted for citations in English and other languages using 15 databases. We used the search terms antioxidant, vitamin E, vitamin C, coenzyme Q10, and all pharmacologic synonyms in combination with the MeSH term cardiovascular disease. We also identified appropriate literature by searching the bibliographies of review articles and asking our experts for articles.

Selection Criteria. The literature search was confined to controlled trials assessing supplements of the three antioxidants—vitamin E, vitamin C, and coenzyme Q10—and cardiovascular disease. Cardiovascular disease included coronary artery disease and its sequelae as well as stroke, heart failure, and peripheral vascular disease. Primary emphasis was given to studies reporting clinical outcomes such as mortality or myocardial infarction. Studies were also included if they affected risk factors for cardiovascular disease such as blood lipids or hypertension. Language of publication was not a barrier to inclusion.

Data Collection and Analysis. Information was collected about trial design and quality, number and characteristics of patients, details on the intervention, and time between intervention and outcome measurement. Two physicians independently reviewed each article, abstracted data, and resolved differences by consensus. Data were synthesized qualitatively or quantitatively as appropriate. For this report, pooled analysis was performed of the effects of vitamin E alone and in combination on death, myocardial infarction, and blood lipid levels.

Main Results. Our literature search process identified 156 articles that represented results from 159 reports on 144 unique trials (i.e., those reporting data not duplicated in another publication). Of the 159 reports, one-third were judged to be of high quality using the Jadad method.

Studies reporting on the outcomes of death, myocardial infarction, and/or blood lipid levels were selected for further analysis. For the interventions of vitamin E alone and in combination with other antioxidants, sufficient numbers of studies existed to perform pooled analysis.

Both the pooled analyses of smaller studies and the results of larger studies did not show, in general, any beneficial effect of vitamin E supplementation on cardiovascular outcomes. Some trials reported beneficial effects on only one outcome or in subgroups, but these results were either not confirmed or were contradicted by other studies.

We did not find evidence in the pooled analysis of smaller trials that vitamin E alone or in combination had a significant effect on levels of TC, LDL, or HDL. For the Heart Prevention Study, a small increase in LDL and HDL was reported.

We identified one meta-analysis of the effect of coenzyme Q10 that reported mostly beneficial effects on measures of cardiac function in patients with heart failure. Five placebo-controlled, randomized studies that measured clinically relevant outcomes, enrolled at least 60 patients, and had at least 6 months duration of treatment were identified and reported mixed results.

Four studies were identified that assessed the effect of vitamin C (mostly in combination with other antioxidants) on clinical outcomes in patients with or at high risk for cardiovascular disease using a placebo-controlled, randomized design, enrolling at least 60 patients, and having at least 6 months duration of treatment. The results were uniformly negative.

Conclusions. For the combinations and conditions studied, the pooled analysis of smaller studies does not show evidence of an effect of vitamin E alone or in combination with other agents on all-cause mortality, cardiovascular mortality, fatal or nonfatal MI, or blood lipid levels. Results from a number of large clinical trials not included in the pooled analysis were substantially in agreement with this conclusion. Large studies of vitamin C in combination with other antioxidants for the prevention of cardiovascular disease reported no favorable outcomes. There is no convincing evidence either supporting or refuting the value of coenzyme Q10 in cardiovascular disease.

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