

Another Flawed Attack against Antioxidants

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In today's media frenzied world, science is practiced by *ambush*. The very day a medical study is published, it can become the headline news story of the day. This denies an opportunity for those who might disagree with the study's design and methodologies to rebut what might be junk science. In the case of a recent study questioning the value of certain antioxidant nutrients, the flaws are so significant as to cause its findings to have little or no meaning.

Within five days of this blatant attempt to discredit certain **antioxidants**, the **Life Extension Foundation** prepared this rebuttal to expose the flaws of this irrational and highly biased attack that the media used to disparage popular dietary supplements.

Overview

Oxidative stress is a well-recognized factor directly implicated in a number of human diseases¹⁻², and a great deal of scientific information supports and validates the role of antioxidants to decrease oxidative damage.³⁻⁶

The latest attack against antioxidants emblazoned across headlines is from a convoluted statistical review published in the February 28, 2007 edition of *JAMA (Journal of the American Medical Association)*.

This statistical review was developed by the same group of researchers that denounced antioxidants as without significant benefit in an article published in 2004⁷. It takes the bold step of not only discounting all of the well-established scientific support for antioxidants in preventing disease, but brazenly declares that antioxidant vitamins increase all-cause mortality (death from all causes).

Suboptimal dosages, outdated formulations, and inadequate study duration

One of the problems with dietary supplement research is that it frequently evaluates nutrients that were initially popularized in the 1960s and 1970s, but comprise a mere fraction of what health conscious individuals are actually using today based upon current, up-to-date research.

The *JAMA* review that attacked the value of antioxidants included vitamins A, C, E, and selenium and evaluated these very basic nutrients in a very wide & inconsistent dosage range:

Supplement	Dose range
Vitamin A (synthetic)	1,333-200,000*** IU
Alpha Tocopherol (synthetic)	10-5,000 IU
Vitamin C (synthetic)	60 – 2,000 mg
Selenium (natural)	20 – 200 mcg

As an example of the strange decisions made by the *JAMA* authors as to which studies to exclude or include in their analysis, they selected a single dose study*** of patients using 200,000 IU of vitamin A, who were subsequently followed for 3 months.⁸

Several critical nutrients taken by health-conscious individuals were omitted from the *JAMA* analysis, along with optimal forms of these nutrients such as gamma tocopherol & natural alpha tocopherol succinate in the case of vitamin E, and CoQ10. Among the critically important nutrients that were completely or mostly ignored included fish oil, lipoic acid, carnitine, standardized fruit & vegetable extracts, B-vitamins, and minerals such as magnesium, zinc, and calcium.

Life Extension long ago warned members about the potential implications of taking only the alpha tocopherol form of vitamin E. Whether this was a factor in the studies in which vitamin E did not show a positive health benefit is unknown, but the role of gamma tocopherol was not discussed as a possible reason for the synthetic alpha tocopherol failing to work in the minority of hand-selected studies used in this evaluation.

For serious supplement consumers interested in maximum benefit, the nutrients that were evaluated in the negative JAMA study make up a small percentage of the many complimentary nutrients they have been taking for the past 10-20 years or more.

The average duration of the studies selected for the analysis was 3.3 years, and the average age of the study subjects was 62 years. The belief that the administration of these very basic antioxidant supplements, in a wide range of suboptimal doses, could somehow reverse a lifetime of oxidative damage strains scientific credibility.

Exclusion of over 91% of antioxidant studies

Out of a potential total of 815 studies that assessed the effects of antioxidant supplements in the *JAMA* statistical review, only 68 were chosen for inclusion in this statistical review – this means that fully 91% of eligible antioxidant studies were arbitrarily excluded from the *JAMA* statistical analysis. Furthermore, 405 of the excluded studies showed no deaths whatsoever in any of the groups.

Of the studies that were included in this flawed statistical review, several were completely misinterpreted:

- The JAMA statistical review incorrectly included 30 deaths from a study published in 2001, yet actual review of this study shows that there was only one death in the placebo group, one death in the drug plus antioxidant group, and no deaths in the group given only antioxidants;⁹
- The JAMA statistical review failed to account for pre-existing risk factors in 399 of 800 Parkinson's disease patients assigned to 2000 IU of vitamin E per day in the DATATOP trial - in fact, after adjustment for pre-existing risk factors, there was no excess mortality in the group assigned to vitamin E, nor did researchers observe any evidence of increased mortality for each additional year of exposure to high-dose through 13 years of observation.¹⁰

Even more disturbing than the studies that were misinterpreted by the *JAMA* authors is the fact that many large studies of significant trial duration showing benefit with antioxidants were excluded from this flawed & biased statistical review: A few examples of intentionally omitted positive studies were:

- A study involving over 29,092 male smokers aged 50-69 years followed prospectively for 19 years showed that men with the highest serum alpha-tocopherol levels had a 28% lower risk of total and cause-specific mortality than did those with the lowest levels, and a 21%, 29%, and 30% lower risk of deaths due to cancer, cardiovascular disease, and other causes;¹¹
- A study in 3,254 people (1,260 males and 1,994 females) aged from 39 to 85 years followed from 1989 to 1995 showed that higher serum levels of carotenoids with pro-vitamin A activity significantly reduces the risk of mortality from cardiovascular disease and colorectal cancer;¹²
- A study in aging women that showed those with the lowest levels of alpha- and beta-carotene, lutein/zeaxanthin, and total carotenoids were significantly more likely to have increasing IL-6 levels over a period of 2 years, and those aging women with the lowest selenium levels had a significantly higher 54% risk of death over a 5-year period;¹³
- A study in patients with aggressive, small cell lung cancer showed a clinically significant 35% decreased risk of death associated with antioxidant supplement use after adjustment for tumor stage and other risk factors;¹⁴
- A study in 1,168 elderly men and women followed for 10 years showed that plasma carotene concentrations were associated with a 21% lower mortality risk for every 0.39 micromol/L increase in plasma carotene, a 41% lower mortality risk for cancer, and a 17% lower risk of mortality due to cardiovascular disease;¹⁵
- A study that evaluated the effect of Vitamin E, beta carotene, and vitamin C on prostate cancer risk in over 29,000 men during 8 years of follow-up showed that supplemental beta-carotene intake at a dose level of at least 2000 micrograms per day was associated with a highly significant 52% decreased prostate cancer risk in men with low dietary beta-carotene intake as well as a dramatic, 71% decreased risk of advanced prostate cancer with increasing dose and duration of supplemental vitamin E;¹⁶
- A study in 1,214 persons age 75-84 studied for over 4 years showed that those people with the lowest vitamin C plasma levels (< 17 micromol/L) had the highest mortality, whereas those aging people with the highest vitamin C plasma levels (> 66 micromol/L) had a mortality risk nearly 50% less;¹⁷
- A study that examined vitamin E and vitamin C supplement use in relation to mortality risk in 11,178 persons aged 67-105 years (Established Populations for Epidemiologic Studies of the Elderly) in 1984-1993 showed that vitamin E reduced the risk of all-cause mortality by 34%, reduced the risk of coronary disease mortality by 47%, and the simultaneous use of vitamins E and C was associated with a 42% lower risk of total mortality and 53% lower risk of coronary mortality;¹⁸
- A study (Chicago Western Electric Study) that followed over 1,800 middle-aged men over a 30-year period showed that during 46,102 person-years of follow-up the risk of fatal stroke was 29% lower in the group taking the highest amount of vitamin C and beta-carotene;¹⁹
- Two studies with different designs conducted in Linxian, an area of north central China with some of the world's highest rates of esophageal and stomach cancer and a population with a chronically low intake of several nutrients, showed significant reductions in mortality associated with antioxidant intake:

- One study showed that in 3,318 persons with esophageal dysplasia, a precursor to esophageal cancer, significantly lower total and cancer mortality risk was observed in those Chinese receiving beta-carotene, vitamin E, and selenium, and a whopping 55% decrease in mortality due to cerebrovascular disease;²⁰
- A second study in 29,584 adult Chinese followed from March 1986-May 1991 showed a significantly lower total mortality among those receiving supplementation with beta carotene, vitamin E, and selenium, with a significant 23% reduction in stomach cancer in this high-risk population;²¹
- A study in 1,078 pregnant women infected with HIV given daily multivitamin supplements including vitamins A, C, and E showed reductions in risk of death, reduction in risk of HIV progression, and reduction in viral load;²²
- A study involving 15,419 children over one year showed the risk of death in the group supplemented with synthetic vitamin A (8,333 IU daily) was 54% less;²³
- A study with lung cancer patients over age 60 showed that those patients taking supplements including antioxidant vitamins like A, C, and E had a dramatic 68% increase in survival, from only 11 months in non-users to an astounding 41 months for the vitamin users (median survival);²⁴
- A study that showed daily oral administration of high-dose vitamin A (300,000 IU daily) was effective in reducing the number of lung cancers related to tobacco consumption and improved disease-free interval in patients surgically-treated for stage I lung cancer;²⁵
- A study in 595 critically-ill ICU patients showed that supplemental vitamin C and vitamin E reduced the risk of multiple organ system failure by an amazing, statistically significant 57% along with a shorter duration of mechanical ventilation and length of ICU stay.²⁶

Respected scientists agree with *Life Extension's* evaluation of the flawed *JAMA* statistical review

Meir Stampfer, Professor of Nutrition and Epidemiology at the Harvard School of Public Health

- "This study does not advance our understanding, and could easily lead to misinterpretation of the data."²⁷

Balz Frei, Director and Endowed Chair, Linus Pauling Institute, Professor, Department of Biochemistry and Biophysics, Oregon State University

- "This is a flawed analysis...the totality of the evidence indicates that antioxidants from foods or supplements have many health benefits, including reduced risk for cardiovascular disease, some types of cancer, eye disease, and neurodegenerative disease...they are a key to an enhanced immune system and resistance to infection."²⁸

Jeffrey Blumberg, Director of the Antioxidants Research Laboratory at Tufts University in Boston, Massachusetts

- "One of the major premises of doing such a meta-analysis is that the studies should be comparable...here, they looked at primary prevention, treatment, old people, young people, smokers, nonsmokers. Only when they used their own criteria of what was good and what was bad were they able to show an increase in all-cause mortality."²⁹

Life Extension is always vigilant in providing our members with rigorous scientific review of information on health & disease prevention

Statistical analysis is a tool used to interpret and assess information. The quality of the statistical result depends in large part upon the criteria used to evaluate the data. Regrettably, *Life Extension* fears that the greater impact of the *JAMA* analysis will be to tragically cut short the lives of people who may otherwise derive lifesaving benefit from antioxidant supplements, but avoid these dietary ingredients out of fear generated by this deeply-flawed, biased statistical review.

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treatment. You should consult with a healthcare professional before starting any diet, exercise or supplementation program, before taking any medication, or if you have or suspect you might have a health problem. You should not stop taking any medication without first consulting your physician.