

# **New Evidence on Vitamin E Safety**

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An important review published in the American Journal of Clinical Nutrition in April, 2005 sheds new light on the safety of Vitamin E.

Statistical experts have already largely discredited the extremely poor meta-analysis announced last Fall by the medical journal Annals of Internal Medicine that re-analyzed only 19 studies on Vitamin E. The experts' overwhelmingly negative responses are posted on that journal's web site. Combining studies that did not use consistent forms or doses unfairly added variables while ignoring positive effects of the vitamin. The authors acknowledged that their findings do not apply to healthier populations and are not definitive.

The new review of Vitamin E published in the American Journal of Nutrition on April 1, 2005 states that after adjusting for variables in supplementation, the actual dose of Vitamin E that may have been slightly harmful to these seriously ill patients was statistically significant only at levels where patients took over 2,000 IU per day, well above the 400 IU suggested by the original Annals analysis.

A recent JAMA article on Vitamin E also used very sick patients but subjected positive data on Vitamin E's benefits to different, more stringent statistical methods than the equally skimpy negative data to produce a negative result and thereby tainting the study, which had been already been rejected by the journal Lancet a year earlier.

The national Institute of Medicine's safe upper limit of 1,500 I.U. per day of natural Vitamin E is based on their own expert review of hundreds of well-designed studies.

The National Institutes of Health (NIH) supports the ongoing Selenium and Vitamin E Cancer Prevention Trial (SELECT), a multi-center, long-term, double-blind, randomized trial that includes 35,534 men age 55 and older taking 400 IU of vitamin E daily to verify earlier evidence of it preventing prostate cancer. NIH researchers carefully examined the data from these few negative reports and decided not to change their protocol, still believing that Vitamin E at this dose is unlikely to cause any harm to their patients.

This confirms the new American Journal of Nutrition review stating that there is no good evidence that levels of Vitamin E under 1,600 IU have been shown to increase health risks.

Two large observational studies (the Nurses' Health Study and the Health Professionals Follow-up Study) show that people taking Vitamin E supplements of 400 IU or more for at least two years had between 20-40% reduction in coronary heart disease. In the GISSI Prevention Trial of 11,000 heart attack survivors, Vitamin E reduced the number both of sudden deaths and deaths due to cardiovascular disease.

The scientific method of giving only one isolated nutrient has generated some brutal publicity for individual members of the antioxidant "family" because antioxidants function inter-dependently. For example, Beta-carotene has been cited in one study as putting smokers at greater risk of lung cancer, but a more thorough follow up analysis - looking at their diet plus other dietary supplements taken - revealed that the smokers' actual danger was due to low total antioxidant levels.

One caution is that people should not try to take a high dose of any one supplement without considering that it may increase our need for other nutrients. And elderly, sick people especially need a more holistic approach, rather than using a single nutrient in high doses as if it were a drug. Nutrients just don't work well in isolation from each other. Vitamins are essential to health and life, but the average American gets only 1/3 of the recommended daily intake of Vitamin E, the amount that the Institute of Medicine determined to be needed by the typical adult to prevent serious illnesses. Most people would benefit from taking a multiple vitamin and a Vitamin E supplement, and it would be even safer than just the Vitamin E alone.

There are also differences between natural and synthetic Vitamin E, with most studies using only the synthetic forms, which are composed of different-shaped molecules only half as effective as natural Vitamin E. Natural Vitamin E is called d-alpha tocopherol and synthetic Vitamin E is called dl-alpha tocopherol. It is known that alpha tocopherol can block absorption of gamma tocopherol, an important antioxidant. Vitamin E complexes with several forms of natural tocopherols, along with the related tocotrienols, are far better than just one kind of Vitamin E. The alpha forms have preferential absorption versus the other forms, for both tocopherols & tocotrienols, making it important to have the right balance so all can work together, as they do in healthy foods.

People with serious heart diseases are more likely to take a Vitamin E supplement than the general population, but a single supplement may not work very quickly or effectively on these seriously ill people and should not be blamed for their illnesses without some more convincing science to back it up.

There is no published evidence that the average person taking a mixture of antioxidants is at greater risk of any disease, but plenty of studies show that

people eating a variety of antioxidant nutrients receive some protection from various diseases. In the case of antioxidants, there is safety in numbers.

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#### MAIN REFERENCES:

1. Margaret E. Wright , Susan T. Mayne, Rachael Z. Stolzenberg- Solomon, Zhaohai Li, Pirjo Pietinen, Philip R. Taylor, Jarmo Virtamo and Demetrius Albanes. American Journal of Epidemiology. July 2004. Development of a Comprehensive Dietary Antioxidant Index and Application to Lung Cancer Risk in a Cohort of Male Smokers.  
[http://aje.oupjournals.org/cgi/content/abstract/160/1/68?maxtoshow=&HITS=10&hits=10&RESULTFORMAT=1&andorexacttitle=and&andorexacttitleabs=and&fulltext=beta+carotene&andorexactfulltext=and&searchid=1100534768534\\_1530&stored\\_search=&FIRSTINDEX=0&sortspec=relevance&fdate=7/1/2004&tdate=7/31/2004&journalcode=amjepid](http://aje.oupjournals.org/cgi/content/abstract/160/1/68?maxtoshow=&HITS=10&hits=10&RESULTFORMAT=1&andorexacttitle=and&andorexacttitleabs=and&fulltext=beta+carotene&andorexactfulltext=and&searchid=1100534768534_1530&stored_search=&FIRSTINDEX=0&sortspec=relevance&fdate=7/1/2004&tdate=7/31/2004&journalcode=amjepid)
2. Edgar R. Miller, III, MD, PhD; Roberto Pastor-Barriuso, PhD; Darshan Dalal, MD, MPH; Rudolph A. Riemersma, PhD, FRCPE; Lawrence J. Appel, MD, MPH; and Eliseo Guallar, MD, DrPH. High-dose vitamin E supplementation may increase all-cause mortality, a dose response meta- analysis of randomized trials. Annals of Internal Medicine: Online: Nov. 10, 2004: Print: 4 January 2005 | Volume 142 Issue 1  
<http://www.annals.org/cgi/content/full/0000605-200501040-00110v1>  
<http://www.annals.org/cgi/content/short/142/1/37>  
<http://www.annals.org/cgi/eletters/0000605-200501040-00110v1>
3. Satia-Abouta J, Kristal AR, Patterson RE, Littman AJ, Stratton KL, White E. Dietary supplement use and medical conditions. Am Journal Preventive Medicine 24:43-51, January 2003. <http://www.ajpm-online.net/article/PIIS0749379702005718/fulltext>
4. Huang HY, Appel LJ. Supplementation of diets with alpha-tocopherol reduces serum concentrations of gamma- and delta-tocopherol in humans. J Nutr. 2003 Oct;133(10):3137-40

[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list\\_uids=14519797](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=14519797)

5. The Lewin Group, DaVanzo, J. et al. Improving Public Health, Reducing Health Care Costs: An Evidence-Based Study of Five Dietary Supplements. September 22, 2004.

<http://www.supplementinfo.org/contentman/anmviewer.asp?a=156&z=14>

6. The Lewin Group, Al Dobson, Ph.D., et al. A Study of the Cost Effects of Daily Multivitamins for Older Adults. Prepared for: Wyeth Consumer Healthcare

<http://www.lewin.com/NR/rdonlyres/exul3vts44kvq5kr35iw6vt3sc6nhtmj3hwope245srdtp3iw7bco4dctska6gilvhewvhivcbujnl/StudytheCostEffectsDailyMultivitaminsforOlderAdult.pdf>

7. Richer S, Stiles W, Statkute L et al. Double-masked, placebo- controlled, randomized trial of lutein and antioxidant supplementation in the intervention of atrophic age-related macular degeneration: the Veterans LAST study (Lutein Antioxidant Supplementation Trial). *Optometry*. 2004;75:216-30.

<http://www.nutrition4health.org/NOHAnews/Biographies/April%202004%20Optometry%20LAST%20Study.pdf>

8. John N Hathcock, Angelo Azzi, Jeffrey Blumberg, Tammy Bray, Annette Dickinson, Balz Frei, Ishwarlal Jialal, Carol S Johnston, Frank J Kelly, Klaus Kraemer, Lester Packer, Sampath Parthasarathy, Helmut Sies and Maret G Traber. REVIEW ARTICLE: Vitamins E and C are safe across a broad range of intakes. *American Journal of Clinical Nutrition*, Vol. 81, No. 4, 736-745, April 2005. <http://www.ajcn.org/cgi/content/full/81/4/736>

### **Conflict of Interest:**

Formulator for dietary supplement manufacturer, but this is my own response.