

Preliminary Rebuttal to Recent Attacks Against Dietary Supplements

By William Faloon

The media recently ran headline news stories claiming that vitamins C, D and E do not prevent heart attack, stroke or breast cancer. This report represents *Life Extension's* preliminary response to these media attacks that are based on egregiously flawed studies. We will submit this report for formal peer review and referencing and expect to post our official report within a few weeks.

Needless to say, when these biased attacks are launched, we are not given prior notice so that our side of the story makes it into the mass media.

In the early **1990s**, several large population studies showed significant reductions in cardiovascular disease in those who consumed **vitamin C** or **vitamin E**.

The most widely reported study emanated from UCLA, where it was announced that men who took **800 mg** a day of **vitamin C** lived **six years longer** than those who consumed the recommended daily allowance of **60 mg** a day. The study, which evaluated 11,348 participants over a 10-year period of time, showed that higher vitamin C intake reduced cardiovascular disease mortality by **42%**.

These kinds of findings did not go unnoticed by the federal government, who subsequently invested hundreds of millions of dollars in an attempt to ascertain if relatively *modest* vitamin doses could prevent common age-related diseases.

In a study that received extensive media coverage, four groups of male doctors were given various combinations of vitamin C and/or vitamin E or placebo. After eight years, there was no reported difference in heart attack or stroke incidence among the groups. This led the media to state that consumers should not buy these supplements.

As you will read, there were so many egregious flaws in this study that the findings are rendered meaningless. Regrettably, consumers who trust their lives to the mainstream media may fall victim to this latest charade to discredit validated methods to reduce cardiovascular disease risk.

DO YOU TAKE YOUR VITAMINS EVERY OTHER DAY?

The study subjects in the **vitamin E** groups were told to take one **400 IU** capsule of synthetic *alpha* tocopherol every other day. This design flaw raises several issues that are rather obvious to *serious* supplement takers.

First of all, we don't take our vitamins every other day. Free radicals are constantly being generated in our bodies, and supplement users today seek to take their *antioxidants* with most meals, as oxidative damage is generally the greatest after eating.

It is rather ludicrous to think that these study subjects would reduce their vascular disease risk by taking modest dose, every other day, of a form of vitamin E with inferior anti-oxidant capacity.

If one were to rely only on synthetic *alpha* tocopherol, the minimum daily dose needed has been shown to exceed **800 IU**, far greater than the **400 IU** ingested every other day by the subjects in this poorly designed study.

Serious supplement users normally take 400 IU every day of natural vitamin E along with a plethora of complimentary nutrients. We would not expect 400 IU of synthetic vitamin E taken every other day to produce much of an effect. Yet that is the dose given to these study subjects with the expectation that this would show a reduction in cardiovascular disease. This is by no means the only flaw of this study.

NATURAL VERSUS SYNTHETIC VITAMIN E

There was a long standing debate as to whether natural or synthetic vitamin E is better. For most vitamins, there is no difference between natural and synthetic. In fact, for most vitamins, the only forms available are synthetic. With vitamin E, however, the natural form has proven far superior.

Natural vitamin E is distributed throughout the body much better than the synthetic form. The reason is that specific *carrier proteins* in the liver selectively bind to natural vitamin E and transport it through the blood to cells throughout the body. These *carrier proteins* only recognize a portion of synthetic vitamin E and ignore the remainder.

Japanese researchers gave *natural* or *synthetic* vitamin E to young women to measure how much vitamin E actually made it into their blood. It took only **100 mg** (149 IU) of natural vitamin E to produce blood levels that required **300 mg** (448 IU) of synthetic vitamin E.

Most studies show that synthetic vitamin E is only **half** as active in the body as the natural form. As it relates to the flawed study claiming that vitamin E does not prevent heart attack, the **400 IU** of synthetic *alpha* tocopherol given every other day equates to only **100 IU** a day of the natural form.

We would not expect **100 IU** of natural vitamin E a day *by itself* to necessarily reduce vascular disease risk. As you continue to read, however, there are many *other* flaws in this study that render its conclusions useless.

Note: When checking vitamin labels, natural vitamin E is usually stated as the “*d*” form (for example *d-alpha tocopheryl acetate*, *d-alpha tocopherol*, and *d-alpha tocopheryl succinate*). Synthetic vitamin E will have a “*l*” after the “*d*” (for example, *dl-alpha tocopheryl acetate*, *dl-alpha tocopheryl succinate*, *dl-alpha tocopherol*). Remember – “*dl*” signifies synthetic vitamin E, whereas “*d*” signifies natural vitamin E. Remember that if you are getting 400 IU of natural *d-alpha tocopherol* (*d-alpha tocopheryl succinate* or *acetate*) it is equal to about 800 IU of synthetic *dl-tocopherol* (*dl-alpha tocopheryl acetate* or *succinate*).

VITAMIN C POTENCIES TOO LOW

If all you are going to take to protect against *free radical* damage is **vitamin E** and/or **vitamin C**, then you will need far greater potencies than were given to the study subjects in this flawed study.

Published studies that document vascular benefits in response to vitamin C typically use doses of **1,000-6,000 mg** each day. The authors of the flawed study alluded to this when they stated:

“In a pooled analysis of 9 cohorts, vitamin C supplement use exceeding 700 mg/day was significantly associated with a 25% reduction in coronary heart disease risk.”

Since the doctors who designed the flawed study knew that vitamin C intakes exceeding 700 mg a day significantly reduce heart attack rates, we can not figure out why they limited their subject’s daily dose to only 500 mg.

Two-time Nobel Prize laureate **Linus Pauling** and his associates advocated daily doses of vitamin C ranging from **10,000 to 20,000 mg** to protect against heart attack. Linus Pauling’s theory was that atherosclerosis is primarily caused by insufficient vitamin C intake. Dr. Pauling compared the high amount of vitamin C *naturally* synthesized in the bodies of animals that don’t typically die of heart attacks. A 150 pound goat, for example will maintain an ascorbate blood concentration equivalent to ingesting **13,000 mg** of vitamin C.

Unlike most animals, humans lack an internal *enzyme* needed to manufacture vitamin C in their body. If humans don’t obtain enough vitamin C from external sources, they die acutely from *scurvy*, or according to Linus Pauling...slowly suffer *atherosclerotic occlusion*. Dr. Pauling crusaded to educate humans about the need to take mega-doses of **vitamin C**.

Dr. Pauling and his associates published papers stating that when *vitamin C* levels are insufficient, the body uses *cholesterol* to repair the inner lining of arteries. Dr. Pauling believed that cholesterol’s involvement in atherosclerosis was a direct result of insufficient vitamin C.

Life Extension has long recommended that its members take at least **2,000 mg** a day of vitamin C, along with potent plant extracts to enhance the biological benefits of ascorbate inside the body. The **500 mg** daily dose of vitamin C given to the subjects of this flawed study was clearly inadequate. This did not stop the headline-hungry media and many conventional doctors from recommending that aging humans avoid these supplements altogether.

As we noted already, the dose of **vitamin E** used in this study was also too low to expect a reduction in vascular disease events. While *alpha tocopherol* **vitamin E** is a classic *antioxidant*, its free radical quenching efficacy pales in comparison to *polyphenol* extracts from **green tea**, **pomegranate**, **grape-seed** and **blueberry**.

Based on the superior *antioxidant* properties of plant extracts such as **pomegranate**, health conscious people today are able to obtain *greater* protection against free radicals and enhance the efficacy of the vitamin C without necessarily having to take the mega-doses recommended by Linus Pauling. On the flip-side, to attack the value of vitamin C based on a group of doctors who took

only 500 mg a day does not correspond to the doses scientific studies show are needed to prevent heart attack.

ALPHA TOCOPHEROL DISPLACES GAMMA TOCOPHEROL

An increasing number of scientists are questioning the wisdom of administering *alpha* tocopherol vitamin E *by itself*. The reason is that *alpha* tocopherol displaces critically important *gamma* tocopherol in the body. The authors of the flawed study admitted that the failure to include *gamma tocopherol* may have been a reason that no effect was seen in the *alpha tocopherol* groups. Here is a quote directly from the flawed study:

"Moreover, PHS II and other prevention trials have used alpha-tocopherol, whereas the gamma-tocopherol isomer also may have a role in cardiovascular disease prevention because it has greater efficacy than alpha-tocopherol to inhibit lipid peroxidation and it may be suppressed in the presence of alpha-tocopherol."

The above admission understates the critical importance that *gamma* tocopherol plays in maintaining arterial health. While *alpha* tocopherol helps protect against lipid peroxidation, *gamma* tocopherol is required to neutralize the dangerous *peroxynitrite* free radical. *Peroxnitrite* damages arteries because:

1. *Peroxnitrite* promotes the oxidation of *alpha* tocopherol, thereby depleting the body of the **vitamin E** needed to protect against oxidation of the lipid moiety (part) of **LDL**. LDL is composed of both lipid and protein parts (moieties), and oxidation associated with both moieties has been implicated in atherosclerosis. In a fascinating paradox, when *alpha* tocopherol is given without *gamma* tocopherol, the result is that *alpha* tocopherol itself can be neutralized in the body by the *peroxynitrite* free radical. This in turn promotes oxidation of the lipid moiety of LDL, a major step on the path towards atherosclerosis.
2. *Peroxnitrite* promotes LDL *protein oxidation*. While *alpha* tocopherol inhibits LDL *lipid* peroxidation, *gamma* tocopherol is needed to protect against oxidation of the *protein* moiety (part) of LDL.

In the absence of *gamma* tocopherol, which can occur when *alpha* tocopherol is given without *gamma* tocopherol, both LDL *lipid* and *protein* oxidation is increased, which reveals the egregious mistake of trying to prevent vascular disease by administering only *alpha* tocopherol. Health conscious individuals should be assured that other nutrients such a *lipoic acid* and *polyphenol* plant extracts also block *protein* and *lipid* LDL oxidation.

Some studies suggest that only *gamma* tocopherol prevents heart attacks. As it relates to atherosclerosis, *gamma* tocopherol blood concentrations have been reported to be significantly lower in coronary heart disease patients than in healthy control subjects. While *alpha* and *gamma* tocopherols each perform life-sustaining functions, only *gamma* tocopherol increases endothelial *nitric oxide* protein expression. As I will describe next, a deficit of *nitric oxide* in the endothelium is a primary cause of arterial disease.

PRIMER ON ALPHA AND GAMMA TOCOPHEROL

Alpha tocopherol and *gamma* tocopherol are the two major forms of **vitamin E** in human plasma. The dietary intake of *gamma* tocopherol is generally two- to four-fold higher than that of *alpha* tocopherol. *Alpha* tocopherol plasma levels, however, are about four-fold higher than those of *gamma* tocopherol. One reason is that there is a preferential cellular uptake of *gamma* tocopherol over *alpha* tocopherol.

Scientific studies consistently show that *gamma* tocopherol plays a significant role in modulating intracellular antioxidant defense mechanisms. Interestingly, the presence of *gamma* tocopherol dramatically increases the cellular accumulation of *alpha* tocopherol.

A HIDDEN CAUSE OF HEART ATTACK AND STROKE

Even when all conventional risk factors are controlled for, the progressive decline of *nitric oxide* involving the arterial wall (the endothelium) too often leads to coronary heart attack and stroke.

Seven years ago, *Life Extension* researchers identified a critical compound (tetrahydrobiopterin) that is essential for the synthesis of *nitric oxide* in the endothelium. We spent several hundred thousand dollars trying to develop an affordable way to manufacture this compound as it offered tremendous promise for eradicating atherosclerosis.

We failed to find an affordable way to make *tetrahydrobiopterin*. The good news is that nutrients that suppress *peroxynitrite* (like *gamma tocopherol* and *pomegranate*) increase endothelial *nitric oxide* by blocking the oxidation of *tetrahydrobiopterin*.

Indeed, clinical studies show that supplemental *gamma* tocopherol enhances platelet endothelial *nitric oxide synthase* activity. Furthermore, a diet high in *gamma* tocopherol rich walnuts improved endothelium-dependent vasodilation in those with high cholesterol.

By administering only *alpha* tocopherol as was done in the flawed study, one would expect *gamma* tocopherol to be suppressed, *peroxynitrite* levels to increase, and precious *tetrahydrobiopterin* to be oxidized, thus depriving the endothelium of the *nitric oxide* it needs to protect against heart attack and stroke. Is it any wonder that this study failed to show vascular disease reduction in those given only *alpha* (but not *gamma*) tocopherol?

FAILING TO ACCOUNT FOR ALL VASCULAR RISK FACTORS

Numerous independent risk factors are associated with the development of *atherosclerosis* and subsequent heart attack and stroke risk. A major flaw in this study was expecting low-dose vitamin C and/or E to somehow overcome all of these underlying causes of artery disease.

We know it is impossible for vitamins C and E to overcome these many risk factors, but this did not stop the media from recommending that Americans discard their supplements.

The following represents a succinct list of documented vascular disease risk factors:

1. Low testosterone (in men)
2. Excess fibrinogen
3. Low HDL
4. Excess LDL and total cholesterol
5. Excess glucose
6. Excess C-reactive protein
7. Excess homocysteine
8. Hypertension
9. Low EPA/DHA
10. Low vitamin D
11. Excess insulin
12. Excess estrogen (in men)
13. Oxidized LDL
14. Excess platelet activity
15. Nitric oxide deficit (endothelial dysfunction)

The basis for doing this study, as outlined by the study's authors, was to use vitamins C and/or E to:

1. Trap organic free radicals
2. Deactivate excited oxygen molecules
3. Prevent tissue damage
4. Inhibit LDL oxidation
5. Modify platelet activity
6. Reduce thrombotic potential
7. Modify vascular reactivity

As one can clearly see, there are **15** documented cardiovascular risk factors. Yet only **3** of these risk factors are what formed the basis for conducting this clinical trial using low-dose vitamin C and/or E. The **3** known risk factors the authors of the flawed study expected to favorably influence with vitamins C and E were:

1. LDL oxidation
2. Platelet activity and thrombotic potential
3. Vascular reactivity (another term for endothelial dysfunction)

For every one mechanism the study's authors proposed might enable low-dose vitamin C and/or E to work, there were five additional risk factors that would not be corrected. For instance, vitamins C and E in these low doses are not going to reduce C-reactive protein, homocysteine, fibrinogen, or glucose. Vitamins C and E in any dose are not going to increase testosterone, decrease estrogen, or provide cardio-protective EPA/DHA and vitamin D.

On the contrary, as we have already shown, by giving only *alpha* but not *gamma* tocopherol, one might expect increased LDL oxidation and impaired endothelial function. That's because *alpha* tocopherol displaces *gamma* tocopherol in the body. *Gamma*-tocopherol suppresses the *peroxynitrite* radical that oxidizes both LDL *protein* and the *tetrahydrobiopterin* that is needed to produce endothelial *nitric oxide*.

As far as platelet activity and thrombotic potential (abnormal clotting inside a blood vessel) are concerned, gamma tocopherol is

significantly more potent than alpha tocopherol in inhibiting platelet aggregation that can lead to a heart attack or stroke. By displacing gamma tocopherol, the alpha tocopherol used alone in this study may have increased abnormal platelet aggregation risk.

From everything we know today, this study was *designed* to fail. Not only did it not correct for the major causes of vascular disease, but it may have *exacerbated* some of the more dangerous ones.

NONE OF WHAT I WROTE SO FAR MAY REALLY MATTER

You have just learned why low-dose vitamin C and/or E supplementation would not be expected to reduce heart attack and stroke risk.

I have saved the biggest shocker for last. It turns out that a significant number of the study subjects (who were all medical doctors) who were supposed to take the vitamin C and/or E supplements did not take their pills. Yet when the calculations for heart attack or stroke incidence were made, those who took as little as **66%** of their low-dose vitamin C and/or E supplements were counted as having taken the entire dose.

At the end of the study, **28%** of the study subjects admitted they had not even taken **66%** of their low-dose vitamin C and/or E supplements.

Even more troubling is the method used to track who was really taking their supplements. Participants were asked to remember and track supplement usage for over 8 years' time without any verification of actual pill counts, compliance by plasma antioxidant analysis, or *in vivo* surrogate markers of oxidant stress. Relying upon participants' memory & recollection over a lengthy time period of many years is a rather pathetic way of ensuring adherence, and renders the author's so called "sensitivity analysis" meaningless.

The lack of adherence, i.e. the fact that a significant percentage of the study participants were not even taking their vitamins may be the most significant flaw to this study. No one in the mainstream media bothered to report this, or any of the other flaws that jumped out at us.

Instead, the media's message was don't waste your money on vitamin C or E pills. Many supplement users who are taking the right form and dose of their vitamin C and E nutrients may believe the media's biased reporting. Even those who take low-dose vitamin supplements may discontinue, which as you will read next is regrettable from a public health standpoint (but great news for the pharmaceutical companies).

SHOCKING DEFICIENCIES OF VITAMIN E

The media used this horrifically flawed study as a basis to steer Americans away from vitamin C and E supplements. It's as if all of the previous positive published studies disappeared overnight.

What was omitted is the fact that **93%** of American men and **96%** of American women do not consume the recommended dietary allowance of vitamin E in their diet. The federal government says Americans need only **15** milligrams a day of vitamin E, yet even this minute amount is not found in the diets of the vast majority of people.

This means that most Americans require a vitamin E supplement to avoid a chronic deficiency, but this important fact was conveniently left out of the news stories.

Conventional medicine says that severe vitamin E deficiency results mainly in neurological symptoms such as impaired balance and coordination and muscle weakness. These neurological symptoms do not develop for 10-20 years; as it takes time for free radicals to inflict nerve damage in the absence of sufficient vitamin E. The reality is that chronic vitamin E deficiency adversely impacts virtually every cell of the body.

A MEDIA COUP FOR PHARMACEUTICAL COMPANIES

The optimal moment of the year to get your message to the masses is the second week of November. This is a time in between holidays, when winter is setting in, and few people are on vacation. The television networks consider this their most important "sweeps week" as it provides the most accurate measurement of their ratings.

The timing of the release of this horrendously flawed vitamin C and E study could not have been more perfect for pharmaceutical interests. It came out less than one week after the November election when the media was primed to sensationalize any story that would attract viewers for their all important "sweeps week".

On the very same day the media launched its attack on vitamins C and E, the same news sources reported that the statin drug

Crestor® reduced heart attack rates by 44% in healthy people who had high C-reactive protein levels. Just think, as an uneducated consumer, you read on the same day that vitamins C and E are worthless and an expensive statin drug works miracles.

Financial analysts predict a windfall for the makers of Crestor® based on this widely distributed report. In retrospect, conducting this study only on people with high C-reactive protein (but not particularly high LDL) was a brilliant marketing strategy. It had a high probability of a successful outcome, and if the study failed, Crestor® was never approved to lower C-reactive protein or be used in this population group anyway, so the pharmaceutical company had nothing to lose.

We at *Life Extension* have long warned about the vascular dangers of elevated *C-reactive protein* and even recommended statin drugs if natural approaches fail to reduce C-reactive protein. We don't believe most people have to purchase expensive brand name drugs like Crestor®, as generic *simvastatin* (name brand Zocor®) or *pravastatin* (name brand Pravachol®) can provide similar benefit at a fraction of the price.

MEDIA ALSO ATTACKS VITAMIN D

Not content to bash only vitamins C and E, the media the very next day in November ran a headline story stating that "*Supplements don't reduce breast cancer risk*". This story was based on a study of women who received only 400 IU a day of supplemental vitamin D.

As has been reported for years in this and other health publications, 400 IU a day of vitamin D is clearly inadequate. To reduce breast cancer risk by around 50%, a daily dose of 1000 IU and higher is required. The major flaw in this study is that participants in the active and placebo group were allowed to take vitamin D outside the study, which rendered the findings meaningless even if the proper dose has been given.

The fact that the media made this study headline news is regrettable because only about 20% of the study population achieved a 25-hydroxy vitamin D at the minimum dose required to prevent breast cancer (greater than 30 ng/mL). In other words, most participants in the active or placebo group failed to achieve even the minimal blood concentrations of vitamin D that other studies document are needed to protect against breast cancer. So all this study did was help confirm what vitamin D experts have been saying for over five years now, i.e. a minimum of **800 IU to 1000 IU** of vitamin D a day is required.

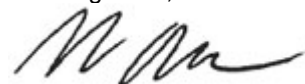
DON'T BE A VICTIM OF THIS FLAWED PROPAGANDA

It is in the economic interests of drug companies to steer Americans away from healthier lifestyles and dietary supplements. As more Americans fall ill to degenerative disease, drug company profits increase exponentially.

Enormous amounts of pharmaceutical dollars are spent influencing Congress, the FDA, and other federal agencies. The result is the promulgation of policies that cause Americans to be deprived of effective, low-cost means of protecting themselves against age-related disease.

As a member of the *Life Extension Foundation*, you gain access to scientific information that is interpreted in the context of what health conscious people are really doing to protect themselves against common diseases. This information is too often distorted by the government, drug companies and the media.

For longer life,



William Faloon

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