

Epidemiology Shows That Vitamin C Helps Us Live Longer

© Interview With Dr. James E. Enstrom
Interviewed By Richard A. Passwater Ph.D.

In May, very exciting nutrition headlines captured the interest of nearly everyone. [1,2] A long-time colleague and friend of mine, Dr. James E. Enstrom of the UCLA School of Public Health, published his latest research on how men taking vitamin C, about 300 milligrams or more per day, on average live six years longer than those who receive less than 50 milligrams of vitamin C daily. [3] The scientific journal also included an editorial by Dr. Gladys Block that concluded, "The results of Enstrom et al indicate that increased attention should be given not only to dietary sources of these nutrients, but also to the possible benefits of vitamin supplements. [4]

I called Dr. Enstrom to congratulate him, and I thought that you might like to share in that conversation.

James E. Enstrom, Ph.D., M.P.H.

Dr. James E. Enstrom is an Associate Research Professor and Epidemiologist at the University of California School of Public Health in Los Angeles. He received his Ph.D. in Physics from Stanford in 1970 and a M.P.H. in Epidemiology from UCLA in 1976. He has been conducting epidemiologic research at the UCLA School of Public Health and Jonsson Comprehensive Cancer Center since 1974. Also, he has been a consulting epidemiologist for the Linus Pauling Institute of Science and Medicine.

Passwater: Congratulations, Dr. Enstrom, your latest study made national headlines and may have been just the impetus needed to get more researchers excited about studying the role of nutrients and health beyond deficiencies.

The headlines concentrated on the longer lifespans of those taking vitamin C, but I see several other interesting revelations in your article.

I often refer to the fact that 30 million Americans have been taking vitamin C and vitamin E supplements for decades now, and heart disease has decreased in step with this. You also point out, "the last 20 years of large increases in the consumption of supplements containing vitamin C and large declines in age-adjusted death rates (total, cardiovascular disease and stomach cancer) in the general population that are only partially explained by established risk factors." Would you elaborate on this point?

Enstrom: One line of evidence that must be used in assessing epidemiologic associations is temporal changes in etiologic (causative) factors and disease rates, such as, the changes that have occurred in cigarette smoking and lung cancer rates during this century. In this regard, **it's worth noting that there has been about a ten-fold increase in consumption of vitamin supplements, particularly vitamin C, during the past 25 years and the age-adjusted death rates for Americans have declined since 1970 by about 30% for all causes, 45% for all cardiovascular diseases, and 40% for stomach cancer.**

Obviously, time trends themselves do not prove an association. However, **since changes in the established risk factors for cardiovascular diseases (e. g. smoking, serum cholesterol and blood pressure) do not fully explain the changes in cardiovascular disease death rates, it is reasonable to look at other potential risk factors such as vitamin C as a partial explanation.** [5]

Passwater: I have been stressing in this column for years that antioxidant nutrient intake is more important than cholesterol intake for the average healthy person.

You note that "the inverse relation of total mortality to vitamin C intake is stronger and more consistent in this population than the relation of total mortality to serum cholesterol and dietary fat intake, two variables on which strong public health guidelines have been issued over the years." Would you mind telling me more about this point?

Enstrom: Serum cholesterol was measured very carefully in the HANES I Epidemiologic Follow-up Study (NHEFS) cohort (group) and its relationship to mortality is a U-shaped curve, with the total death rate being highest at the highest and lowest serum cholesterol levels. Even though the bulk of epidemiological data indicate no benefits of low serum cholesterol with respect to total mortality in the population as a whole, these data have been largely ignored in the heart disease community, which prefers to focus on the positive relationship between serum cholesterol and coronary heart disease among middle-aged white men.

Two major books in the last four years have been written which point out many weaknesses in the serum cholesterol - heart disease data. [6,7] Even if serum cholesterol has a positive relation to coronary heart disease in some segments of the population, **serum cholesterol does not have a positive relation to total mortality and this lessens its importance to overall health.**

Passwater: Your study actually showed a benefit in taking supplements beyond that of the "adequate" intake from foods. Do you think that this fact will be noticed by others in the nutrition community?

Enstrom: It is hard to know what the nutrition community will do with this study, but I have been surprised with the relative lack of criticism. I hope I have stated my findings in such a qualified way that they will not invite criticism. **The healthiest persons were those who consumed substantial dietary vitamin C and used supplements containing vitamin C on a daily basis.** However, the supplement usage in this study involved more than just vitamin C pills because most supplement users consumed multivitamin pills which contain several basic nutrients. The use of supplements may be a marker for other healthy behavior, but **my results suggest an effect for vitamin C even after controlling for ten potentially confounding variables in addition to age and sex** (smoking, alcohol consumption, recreational exercise, dietary fat, dietary calories, serum cholesterol, dietary vitamin A, disease history, education and race).

Passwater: Your study concentrated on vitamin C -- why did you select vitamin C?

Enstrom: Vitamin C was selected because of theories proposed by Dr. Linus Pauling related to the fact that vitamin C is not naturally produced in the human body and may be beneficial to humans in amounts greater than those needed to prevent a deficiency disease like scurvy. Very little epidemiologic research has been done on vitamin C and total mortality, and this makes it an area worthy of more investigation. **Another reason for investigating vitamin C is the fact that it is relatively easy to change this risk factor if it is shown to have value.**

Passwater: What about the other antioxidant vitamins. Does your data allow a study of vitamins A or E? If so, will we be treated to a companion article on them?

Enstrom: The NHEFS did measure all the foods consumed during a 24 hour period before the initial interview. Calculations were done to convert these food lists into dietary vitamin C and dietary vitamin A intake as part of the original data processing using standard food conversion tables. Similarly, it is possible to calculate intake levels of beta carotene and vitamin E from these same foods. I am in the process of doing this now. **It is my intention to construct an antioxidant index and reanalyze the mortality data with regard to the antioxidant hypothesis.**

Passwater: That will be a major advance! There are so many studies out there that miss the point. They look at the quintiles of one antioxidant without regard for the confounding actions of the other antioxidants.

Thus, they miss the protective effects of the antioxidants not being studied -- which will distort the quintile rankings -- and they will miss their synergistic effects. I hope other investigators will follow your lead and fine-tune their published data with your antioxidant index to extract more information.

Will you also examine the effects pro-oxidants? There is an urgent question now concerning blood ferritin levels and possibly dietary iron intake.

Enstrom: I will examine pro-oxidants like iron to the extent possible with the data collected in the NHEFS. If the recently reported relationships between cardiovascular diseases and vitamin C and iron hold up in subsequent studies, they could represent major new risk factors.

Passwater: You did a study similar to the NHEFS study earlier with Linus Pauling. That study, published in the Proceedings of the National Academy of Sciences (PNAS) used data from my 1974 Prevention study. [8] Yet, when your study was published in 1982, it received very little attention. Do you think the attitudes have changed or do you think it's just the strength of the data?

Enstrom: My 1982 paper in PNAS with Linus Pauling involved a highly selected cohort of 479 elderly California Prevention subscribers who completed a very simple questionnaire. Thus, the data were very limited and inconclusive, and this probably explains the relative lack of attention that this paper received. Also, the scientific community seems more receptive to this area of investigation now.

Passwater: What did the 1982 data show?

Enstrom: The 1982 paper showed that this cohort of 479 elderly (65+ years) Prevention magazine subscribers was substantially healthier than the general population (with a total death rate about two-thirds that of similarly aged Americans). Also, this cohort was healthier than typical nonsmokers, but tended to be similar to the health conscious nonsmokers in some other questionnaire surveys. It was hard to analyze the selection factors for this group because it included persons who were very health conscious currently -- but many of them had poor health in the past. The results were inconclusive with regard to benefits of vitamin E supplements because there were so few (14) non-users of supplements. Also, the total number of deaths (107) was too small to do any detailed analyses.

Passwater: How did your recent study improve upon this?

Enstrom: The NHEFS was a far better study because it involved a nationally representative sample with many more persons (11,348) and many more follow-up deaths (1,809). It collected much more information about the dietary habits and health characteristics of the persons studied. Thus, it was possible to make detailed analyses which showed a significant beneficial effect for vitamin C among men even after controlling for ten potential confounding variables.

Passwater: How well do the two studies correlate?

Enstrom: Precise comparison is difficult because of the much different way the cohorts were assembled. Roughly speaking, the Prevention cohort as a whole is healthier than the elderly NHEFS nonsmokers, but fairly similar to the elderly NHEFS non-smokers who had high vitamin C intake. The females appear to be much healthier than the males in the Prevention cohort compared with sex differences in the NHEFS cohort.

Passwater: I remember sorting through the 17,894 responses by hand in my 1974 study for one variable at a time. Now you use computers and sophisticated analytical programs. Is there a chance that you can go back and use these new tools to extract more information from the old data? Can you follow up any of the respondents from that study?

Enstrom: It would be difficult to follow the nearly 18,000 persons you questioned in 1974 because of the limited identifying information that you collected.

However, I have continued to follow the California portion (those in my 1982 PNAS paper) to a limited extent and the results remain roughly similar. The main problem with analyzing the specific effect of vitamin supplements in this cohort is that there were very few non-users of supplements to serve as a control group.

Passwater: Will there be a follow-up study of the NHANES participants, and, if so, when will you have access to the data to do a follow-up of your present study?

Enstrom: There is ongoing follow-up of the NHEFS cohort, and I am now conducting an analysis of follow-up through 1987 -- along with an analysis of disease incidence in the cohort.

Passwater: In my books, I write about your studies showing the benefits of a moderate lifestyle. You have done several studies -- what are the main points learned from these studies?

Enstrom: My studies on Mormons, Prevention magazine readers, Alameda County residents practicing good health habits, physicians who have stopped smoking, and the NHEFS cohort have all been analyzed with respect to major lifestyle variables with the goal of identifying lifestyles that result in a low overall death rate. [3, 8-11] I think that **they indicate substantial benefits of non-smoking, family structure, health consciousness, good health habits, and vitamin C intake in reducing premature deaths.**

Passwater: Can we assume that you will be continuing to follow these same groups?

Enstrom: Yes, I am continuing to follow these groups. I believe in long-term studies of overall health in well defined populations. More results from these studies will be forthcoming in the next few years.

Passwater: What will you be looking into next?

Enstrom: Recently I have begun a collaboration with the American Cancer Society to conduct a follow-up of their 1959 Cancer Prevention Study through 1991. I will then analyze the Cancer Prevention Study data over a 32 year period (1960-1991) to determine mortality trends in relation to smoking cessation and to identify the most important lifestyle factors associated with reduced mortality over a long period of time.

Passwater: Wow! Are you one busy scientist. Thanks for taking the time to chat about your research.

NOTE !!!

Since Dr. Enstrom's research was published, a Harvard research team has published an abstract that vitamin C reduces the risk for heart disease. [12]

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