

Multivitamin use among middle-aged, older men results in modest reduction in cancer

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In a randomized trial that included nearly 15,000 male physicians, long-term daily multivitamin use resulted in a modest but statistically significant reduction in cancer after more than a decade of treatment and follow-up, according to a study appearing in *JAMA*. The study is being published early online to coincide with its presentation at the Annual American Association for Cancer Research Frontiers in Cancer Prevention Research meeting.

"Multivitamins are the most common dietary supplement, regularly taken by at least one-third of U.S. adults. The traditional role of a daily multivitamin is to prevent nutritional deficiency. The combination of essential vitamins and minerals contained in multivitamins may mirror healthier dietary patterns such as fruit and vegetable intake, which have been modestly and inversely associated with cancer risk in some, but not all, epidemiologic studies. Observational studies of long-term multivitamin use and cancer end points have been inconsistent. To date, large-scale randomized trials testing single or small numbers of higher-dose individual vitamins and minerals for cancer have generally found a lack of effect," according to background information in the article.

"Despite the lack of definitive trial data regarding the benefits of multivitamins in the prevention of chronic disease, including cancer, many men and women take them for precisely this reason."

J. Michael Gaziano, M.D., M.P.H., of Brigham and Women's Hospital and Harvard Medical School, Boston, (and also Contributing Editor, *JAMA*), and colleagues analyzed data from the Physicians' Health Study

(PHS) II, the only large-scale, randomized, double-blind, placebo-controlled trial testing the long-term effects of a common multivitamin in the prevention of chronic disease. The trial includes 14,641 male U.S. physicians, initially age 50 years or older, including 1,312 men with a history of cancer at randomization, who were enrolled in a multivitamin study that began in 1997 with treatment and follow-up through June 1, 2011. Participants received a daily multivitamin or equivalent placebo. The primary measured outcome for the study was total cancer (excluding nonmelanoma skin cancer), with prostate, colorectal, and other site-specific cancers among the secondary end points.

PHS II participants were followed for an average of 11.2 years. During multivitamin treatment, there were 2,669 confirmed cases of cancer, including 1,373 cases of prostate cancer and 210 cases of colorectal cancer, with some men experiencing multiple events. A total of 2,757 (18.8 percent) men died during follow-up, including 859 (5.9 percent) due to cancer. Analysis of the data indicated that men taking a multivitamin had a modest 8 percent reduction in total cancer incidence. Men taking a multivitamin had a similar reduction in total epithelial cell cancer. Approximately half of all incident cancers were prostate cancer, many of which were early stage. The researchers found no effect of a multivitamin on prostate cancer, whereas a multivitamin significantly reduced the risk of total cancer excluding prostate cancer. There were no statistically significant reductions in individual site-specific cancers, including colorectal, lung, and bladder cancer, or in cancer mortality.

Daily multivitamin use was also associated with was a reduction in total cancer among the 1,312 men with a baseline history of cancer, but this result did not significantly differ from that observed among 13,329 men initially without cancer.

The researchers note that total cancer rates in their trial were likely influenced by the increased surveillance for prostate-specific antigen

(PSA) and subsequent diagnoses of prostate cancer during PHS II follow-up starting in the late 1990s. "Approximately half of all confirmed cancers in PHS II were prostate cancer, of which the vast majority were earlier stage, lower grade prostate cancer with high survival rates. The significant reduction in total cancer minus prostate cancer suggests that daily multivitamin use may have a greater benefit on more clinically relevant cancer diagnoses."

The authors add that although numerous individual vitamins and minerals contained in the PHS II multivitamin study have postulated chemopreventive roles, it is difficult to definitively identify any single mechanism of effect through which individual or multiple components of their tested multivitamin may have reduced cancer risk. "The reduction in total cancer risk in PHS II argues that the broader combination of low-dose vitamins and minerals contained in the PHS II multivitamin, rather than an emphasis on previously tested high-dose vitamins and mineral trials, may be paramount for cancer prevention. ... The role of a food-focused cancer prevention strategy such as targeted fruit and vegetable intake remains promising but unproven given the inconsistent epidemiologic evidence and lack of definitive trial data."

"Although the main reason to take multivitamins is to prevent nutritional deficiency, these data provide support for the potential use of multivitamin supplements in the prevention of cancer in middle-aged and older men," the researchers conclude.

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