Vitamins aren't a cure-all

In fact, taking them does nothing to fight cancer, studies find.

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They were some of the most promising medicines of the 1990s -- wonder pills that appeared to fight cancer, heart disease, stroke and other ailments.

Laboratory tests and initial studies in people suggested that lowly vitamins could play a crucial role in preventing some of the most intractable illnesses, especially in an aging population. The National Institutes of Health gave them the same treatment as top-notch pharmaceutical drugs, investing hundreds of millions of dollars in elaborate clinical trials designed to quantify their disease-fighting abilities.

Now the results from those trials are rolling in, and nearly all of them fail to show any benefit from taking vitamin and mineral supplements.

This month, two long-term trials with more than 50,000 participants offered fresh evidence that vitamin C, vitamin E and selenium supplements don't reduce the risk of prostate, colorectal, lung, bladder or pancreatic cancer. Other recent studies have found that over-the-counter vitamins and minerals offer no help in fighting other cancers, stroke or cardiovascular disease.

Research has even suggested that in some circumstances, the supplements can be unsafe.

Some physicians now advise their patients not to bother with the pills, and to rely instead on a healthy diet to provide needed vitamins and minerals.

"These things are ineffective, and in high doses they can cause harm," said Dr. Edgar R. Miller, a professor of medicine and epidemiology at Johns Hopkins University School of Medicine in Baltimore. "People are unhappy with their diets, they're stressed out, and they think it will help. It's just wishful thinking."

Yet faith in vitamins runs deep. The Council for Responsible Nutrition, a trade group in Washington, estimates that 64% of American adults take vitamin and mineral supplements.

Despite the steady drumbeat of reports questioning their efficacy, sales have risen
steadily, from $5 billion in 1995 to $10 billion this year, according to the Nutrition Business Journal.

Scientists remain convinced that vitamins are essential to health. But they have puzzled over how their obvious benefits could be so elusive in randomized controlled trials, the gold standard of medical research.

"You really do need vitamin E. You really do need vitamin C. You really do need selenium," said Jeffrey Blumberg, director of the U.S. Department of Agriculture's Antioxidants Research Laboratory at Tufts University in Boston. "Without them, you die."

Blumberg and others now believe that a combination of factors -- including the versions of vitamins that were tested and the populations they were tested in -- probably doomed the studies from the start.

"In retrospect, maybe the expectations were a little bit unrealistic," said Blumberg, whose research has been funded in part by supplement makers.

Unlike observational studies, which look backward at groups of people to identify factors that are associated with a particular disease, a forward-looking randomized controlled trial has the power to show whether a particular factor can prevent the disease.

The studies rely on thousands of participants who are randomly assigned to receive a medicine or a placebo. Researchers carefully track the participants so they can account for other factors that might affect health outcomes, such as age, diet and amount of physical activity. After several years, the researchers compare the number of people in each group who developed a particular disease and use statistical tools to see whether the medicine made a difference.

Vitamin A and beta carotene were the first supplements to be tested that way. In observational studies from the 1980s, researchers noticed that people who ate lots of vegetables rich in beta carotene, a form of vitamin A, were less likely to be diagnosed with lung cancer and other cancers compared with people who didn't. Thus, they reasoned, the vitamin supplements probably reduced the risk of lung cancer.

The thinking was, "Let's get a bunch of people who smoked for 30 years and see if it's going to be a magic bullet for them," said nutritionist Andrew Shao, a vice president for scientific and regulatory affairs for the Council for Responsible Nutrition, a trade association for the supplement industry. "We were all guilty of wanting to go for that home-run-style randomized trial that would validate everything once and for all."

It didn't.

One trial that followed 29,000 male smokers in Finland for an average of six years found that men who took beta carotene were 18% more likely to be diagnosed with lung cancer
and 8% more likely to die during the study than men who didn't.

A second trial involved 18,000 American men and women who were smokers or former smokers or who were exposed to asbestos at work. That study found that after an average of four years, lung cancer rates were 28% higher among those who took beta carotene and vitamin A, and their overall risk of death during the trial jumped by 17%.

Further research revealed that beta carotene curbs the body's ability to metabolize vitamin A, which is needed to keep cancer cells in check, Shao said.

Researchers tried again and again with other combinations of vitamins and minerals. Among the multimillion-dollar studies sponsored by the National Institutes of Health:

* The Women's Health Study followed 39,876 women for an average of 10 years. Those who took vitamin E were just as likely to develop heart disease, stroke and a variety of cancers as the women who took a placebo, according to results published in 2005 in the Journal of the American Medical Assn.

* The Women's Antioxidant Cardiovascular Study tested the effects of vitamins C and E and beta carotene in 8,171 women with signs of heart disease for an average of 9.4 years. None of the supplements had any effect, according to results published in 2007 in the Archives of Internal Medicine.

* The Physicians' Health Study tested vitamins C and E in 14,641 male doctors for an average of eight years and found the supplements didn't make their hearts healthier. The results were published last month in the Journal of the American Medical Assn.

* The Women's Health Initiative tracked 36,282 women for an average of seven years and found that vitamin D plus calcium didn't protect against invasive breast cancer, according to results published last month in the Journal of the National Cancer Institute. Previous studies of these women found that the supplements offered modest protection against hip fractures but didn't prevent other bone fractures or colorectal cancer.

* The Selenium and Vitamin E Cancer Prevention Trial tested those supplements in 35,533 men for more than five years and found that they didn't reduce the risk of prostate cancer, according to results released this month in the Journal of the American Medical Assn. The trial was halted early, in part because the supplements were associated with a slight increase in the risk of prostate cancer and diabetes.

For several reasons, researchers say, vitamins don't lend themselves to randomized controlled trials. Chief among them is that there is no true placebo group when it comes to vitamins and minerals, because everyone gets some in their diet.

"For drugs, someone either has [the anti-impotence drug] Cialis in their system or he doesn't have Cialis," said Paul Coates, director of the NIH Office of Dietary Supplements in Bethesda, Md. But with vitamins, "there's a baseline exposure that needs to be taken
into account. It makes the challenge of seeing an improvement more difficult."

A vitamin's benefit may become apparent only if people aren't getting enough of it. That could explain why vitamin D has been linked to reduced rates of heart disease, cancer and diabetes.

"Most people are vitamin-D-deficient, and that's not true for vitamin E," Blumberg said.

Randomized clinical trials are designed to test one factor at a time, but vitamins and minerals consumed as part of a healthy diet work in concert with each other.

"You don't eat a food that just has beta carotene in it," said Dr. Mary L. Hardy, medical director of the Simms/Mann UCLA Center for Integrative Oncology, who focuses on the importance of diet and supplements for cancer patients.

What's more, she said, vitamins manufactured into pills are not identical to vitamins that occur naturally in foods, so the clinical trials don't test the exact compounds that may have been key in earlier studies.

"Is this apples and apples, or is this apples and crab apples, or is this apples and peaches?" said Hardy, who sits on the scientific advisory board of the company that sells Nature Made and other brands of vitamins. "It's hard to know what to say."

The observational studies that originally linked vitamins to better health may have been biased because people who take supplements are often healthier overall than people who don't.

"They tend to be more physically active, better educated, eat better diets, and tend not to be smokers," Coates said. "So you can't say for certain it's your item of interest that causes" the health benefit.

The data collected by these big studies aren't useless. Researchers said they could spend years slicing and dicing the data to see if they can tease out a positive effect in a subgroup, such as black men over 65 or women with a family history of osteoporosis.

But no one expects the NIH -- or anyone else -- to launch studies on vitamins until more is understood about how to measure their effects in the body.

"We clearly don't have much enthusiasm for investing huge amounts of money in clinical trials that aren't going to work," Coates said.

Instead, some researchers have turned their attention to biomarkers that provide reliable indicators of disease risks, such as the prostate-specific antigen protein that is used to screen for prostate cancer.

Advances in personalized medicine may also allow doctors to identify people with
genetic mutations that make them more likely to benefit from specific vitamins and minerals, experts said.

In the meantime, researchers will return to traditional observational studies to learn more about the role of nutrition in fighting disease.

"I'm really comfortable telling you to eat whole grains and fruits and vegetables and cut back on saturated fats," Blumberg said, "even though we don't have clinical trials showing that."

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