The good news: if you’re diagnosed with prostate cancer, your odds of surviving 10 years are roughly 93 percent. And death rates have dropped since 1990. The bad news: researchers haven’t figured out how to prevent prostate cancer. That could be because they’re looking at two different versions of the disease.

“With PSA screening, you find a lot of slow-growing, indolent tumors that would never bother people at all,” says Walter Willett of the Harvard School of Public Health in Boston. “They’ll die at 90 of a heart attack or something else.”

And that may lead to contradictory results. “The risk factors for these indolent cancers seem to be different than the risk factors for aggressive cancers,” says Willett. “But many studies haven’t sorted them out or don’t have enough of the aggressive, potentially fatal tumors.”

Here’s what might protect or harm the prostate. The evidence comes from studies that look at healthy men as well as studies of men who already have cancer.

**WHAT MIGHT HARM**

**SELENIUM**

“Did you know that there are more new cases of prostate cancer each year than any other cancer?” asked the radio ad. “Now there is something that you can do.”

What you can do, implied the ad, is switch to Bayer One A Day Men's Formula, a “complete multivitamin plus selenium, which emerging research suggests may reduce the risk of prostate cancer.” (Bayer pulled the ads in June, after the Center for Science in the Public Interest, Nutrition Action’s publisher, threatened to sue over the false claim.)

Maybe that’s what emerging research suggested 10 years ago. In 1996, researchers reported a surprise. The Nutritional Prevention of Cancer trial had given men and women in the southeastern United States who had skin cancer either selenium or a placebo to see if selenium would lower their risk of a recurrence. (It didn’t.) But the selenium-taking men had a lower risk of prostate cancer.

By 2001, the National Cancer Institute had launched a $118 million study called SELECT (Selenium and Vitamin E Cancer Prevention Trial), which tested selenium and vitamin E on 35,000 healthy U.S. and Canadian men. In October 2008, researchers halted the trial when they found that those taking selenium (200 mcg a day), vitamin E (400 IU a day), or both had no lower risk of prostate cancer than those who took a placebo.

“Physicians should not recommend selenium or vitamin E or any other antioxidant supplements to their patients for preventing prostate cancer,” wrote Peter Gann of the University of Illinois at Chicago in an editorial that was published with the SELECT results.

What’s more, the risk of diabetes was slightly—though not significantly—higher in the men who took selenium.

“SELECT dashed hopes that selenium somehow would be useful for the average man,” says Gann. Selenium might still matter to people with certain genes, he adds, but that’s not a simple story.

For example, a recent study of men who had been diagnosed with prostate cancer looked at two variants of a gene that regulates manganese superoxide dismutase, an enzyme that cells use to detoxify harmful oxygen radicals.

“If you just look at men with the AA genotype, it seemed to be beneficial to have higher levels of selenium,” says lead

---

Nutrition Action Healthletter • September 2009
investigator June Chan of the University of California, San Francisco. In those men, high levels of selenium in the blood were linked to a lower risk of aggressive cancer.8

“But the flip side was true for the V carriers,” adds Chan. In those men, high blood selenium levels were linked to a higher risk of aggressive cancer. And 75 percent of men are V carriers.

Should men with prostate cancer get their genotypes tested? “Not now,” says Chan. “It’s just one study, and we want to follow the men to see how selenium is associated with the risk of metastasis or recurrence.”

In the meantime, the SELECT results are somewhat reassuring. “There wasn’t an elevated risk of prostate cancer for taking selenium in that large trial,” says Chan. But, she adds, the SELECT results mean that “you can’t make a good argument for taking selenium or vitamin E to prevent prostate cancer.”

VITAMIN E

Until recently, vitamin E was a potential friend to the prostate. Now it’s a possible foe.

The SELECT trial gave men a high dose of the vitamin (400 IU a day) because in the 1990s the ATBC (Alpha-Tocopherol, Beta-Carotene) trial found a 34 percent lower risk of prostate cancer in Finnish smokers who were given a lower dose of vitamin E (50 IU a day) in an attempt to lower their risk of lung cancer.7 (It didn’t work.)

But in the SELECT trial, vitamin E takers had a 13 percent higher risk of prostate cancer. While the increased risk wasn’t statistically significant, it was close.

Why would two trials yield almost opposite results?

“A few things were different,” says Demetrius Albanes, a SELECT co-author and senior investigator at the National Cancer Institute. First, “the ATBC included only smokers.” Less than 10 percent of the men in SELECT were smokers.

Second, the dose in SELECT was eight times higher than in ATBC. “We may have gone beyond the physiological levels that are beneficial,” says Albanes, “and jumped to a much higher, pharmacological level that disturbed the body’s routine maintenance mechanisms.”

For example, some studies suggest that the gamma-tocopherol form of vitamin E protects the prostate. (Most vitamin E supplements contain the alpha-tocopherol form.) “The high doses of alpha-tocopherol in SELECT may have displaced the gamma-tocopherol,” says Albanes. “The alpha-tocopherol group in SELECT had a pretty substantial decline in gamma-tocopherol levels.”

Another possibility: SELECT screened out men who were found to have prostate cancer before they entered the study. “By screening, we may have taken out early, small tumors that vitamin E would have blocked from growing,” Albanes suggests. “But that’s just conjecture.”

One comfort: the risk of prostate cancer was no higher in other trials that gave men high doses of vitamin E (400 IU or 600 IU a day) to see if it could prevent heart disease.8,9 (It didn’t.)

The bottom line: Despite ads that still tout vitamin E as a potent antioxidant, don’t expect it to protect your prostate.

CALCIUM & DAIRY

What can men do to lower their risk of prostate cancer? “Avoid high milk intake,” says Harvard’s Walter Willett.

But the evidence is confusing. For example, in the NIH-AARP study, which tracked nearly 300,000 men for six years, those who reported drinking at least two glasses of skim milk a day had a 23 percent higher risk of advanced prostate cancer than those who drank no skim milk.10 Yet the study found no link with low-fat

Prostate Cancer Death Rates Vary

Death rates for prostate cancer vary dramatically worldwide, as shown by this sampling of countries. Overall, rates are higher in developed countries. However, there are exceptions. For example, Japan has low rates, while many African countries have high rates.

milk—which is virtually identical to skim milk—or with whole milk, yogurt, or cheese.

Other studies have seen a link with dairy protein or dairy foods, while still others find no link at all.11,12

How might milk promote prostate tumors?

“Milk increases levels of insulin-like growth factor-1,” says Willett. “And we have evidence that higher levels of IGF-1 are related to aggressive prostate cancer.”

In a meta-analysis of 12 studies on a total of 9,000 men, those with the highest IGF-1 levels had a 38 percent higher risk of prostate cancer than those with the lowest levels.13

Cheese and yogurt may not raise IGF-1, notes Willett, because “the IGF-1 may be denatured by the fermentation process.”

Another possibility: Excess calcium may account for the higher prostate cancer risk.

In the Health Professionals Follow-up Study, which tracked 47,000 men for 16 years, those who consumed 1,500 to 1,999 milligrams of calcium a day from food and supplements combined had an 87 percent higher risk of fatal prostate cancer, compared to those who got less than 750 mg a day.14 And the risk was 2½ times higher in those who consumed at least 2,000 mg a day.

“In most studies, calcium and dairy intake are so highly correlated that it’s hard to pull them apart,” says Willett. Like the dairy evidence, the calcium findings aren’t uniform. But three of the best four studies found a higher prostate cancer risk in men with calcium intakes over 1,500 mg or 2,000 mg a day, according to a new review by the government’s Agency for Healthcare Research and Quality (AHRQ).15

A clearer picture may be coming.

“We’re looking at the impact of milk, calcium, and other foods on aggressive prostate cancer by pooling the original data from a number of studies,” says Willett. “But it will be a couple of years before it’s published.”

Until scientists know more, it’s probably best to avoid excess.

“The highest prostate cancer risk was seen in people who were most likely taking a calcium supplement,” says the University of California’s June Chan.

It’s not just supplements. Calcium is now added to some brands of orange juice, breakfast cereals, energy and granola bars, and other foods. “And some people may be taking a lot of calcium in antacids like Tums and not realize it,” adds Chan.

**VITAMIN D**

“Of all the things made just for men, maybe this is one of the most important,” says the recent TV ad. “New Centrum Silver Ultra Men’s—a complete multivitamin for men over 50. It has antioxidants and vitamin D to support your prostate and colon.”

Vitamin D supports the prostate? Not exactly.

Most studies find no link between levels of vitamin D in the blood and the risk of prostate (or colon) cancer, according to the government’s AHRQ review.16 (One study even found a higher risk of aggressive prostate cancer in men with all but the lowest vitamin D blood levels, but it was unusual.17)

“The data for vitamin D are complicated,” says Willett. “It’s tangled up in this issue of types of prostate cancer, and we don’t have enough large studies with blood levels to look at.”

Does that sound like vitamin D supports the prostate?

**OBESITY**

In the Cancer Prevention Study II, which tracked 70,000 men for roughly 10 years, the risk of fatal or metastatic prostate cancer was 54 percent higher in those who were obese, compared to those who were normal weight.17

“Obesity raises the risk of dying of prostate cancer.”

In other studies, men who were overweight or obese had no higher risk of being diagnosed with prostate cancer, but once diagnosed, they were more likely to die of the disease.18

“Obesity or overweight is related to aggressive, but not to indolent, prostate cancer,” says Willett. “So avoiding aggressive prostate cancer may be the 102nd reason to stay lean and active.”

**MEAT**

Recent studies have seen a stronger possible link with well-done meat than with other red meat. For instance, in a study of 29,000 men, those who averaged at least 2½ ounces of very-well-done meat a week had a 40 percent higher risk of prostate cancer than those who ate no very-well-done meat.19

“The results on red meat aren’t clear,” says Willett. “We hope to sort it out when we pool data on aggressive cancers.”

**ZINC**

“Zinc was thought to be beneficial, but studies have not consistently borne that out,” says the National Cancer Institute’s Demetrius Albanes. That’s for sure. In one study, men who got more than 100 milligrams a day of zinc from supplements had double the risk of advanced prostate cancer, compared with men who didn’t take zinc supplements, though the number of men was small.20

And in a trial that gave men 80 mg a day of zinc to see if it could reduce their risk of eye disease, the zinc takers were more likely to be hospitalized for genitourinary complications (benign enlarged prostate, urinary tract infections, kidney stones, or kidney failure) than those who took no zinc.21

Oops.
WHAT MIGHT HELP

TOMATOES & LYCOPENE

You can find lycopene in watermelon, carrots, and papayas, but we get most of the bright red carotenoid from tomato sauce.

Lycopene gained fame in the mid-1990s, when Harvard researchers reported that men who ate more than 10 servings a week of foods (like pizza) that are made with tomato sauce had a 35 percent lower risk of prostate cancer than men who ate less than 1½ servings a week. But since then, the evidence has been mixed.

For example, in a study that tracked 137,000 men in eight European countries for six years, those who had the highest levels of lycopene in their blood were 60 percent less likely to be diagnosed with advanced prostate cancer than those who had the lowest levels. But other studies found no link with lycopene.

FLAXSEED

Flaxseed isn’t exactly a household staple, but researchers suspect that its estrogen-like compounds might protect the prostate.

“We’ve been focusing on two lignans, enterodiol and enterolactone,” says Wendy Demark-Wahnefried of the MD Anderson Cancer Center in Houston.

Her research team randomly assigned 161 men who were scheduled for prostate cancer surgery to eat three tablespoons of flaxseed a day or to continue with their usual diets. After three weeks, the scientists found that cells were dividing more slowly in the prostate glands of the men who had eaten flaxseed. That could mean that their tumors were growing more slowly.

“We’re not ready to stand on a soapbox and say you have to have flaxseed, because we need to do further studies,” says Demark-Wahnefried. “But the findings are compelling.”

One disappointment: earlier studies had suggested that flaxseed would curb PSA levels, but in Demark-Wahnefried’s study, PSA scores dropped whether the men ate flaxseed or not. Stress might explain why.

“There’s a whole literature to suggest that when men are under stress their testosterone levels drop, and therefore it may be fairly common for men’s testosterone levels to plummet as they approach surgery,” she explains. “And testosterone drives the PSA.”

Her results underscore why studies testing any treatment for prostate cancer need a control group.

“Prior to this study, we were singing praises about flaxseed lowering PSAs,” says Demark-Wahnefried. “We didn’t realize that our control group’s PSAs would drop just as much. Unless you have that control, you lose all your ability to compare.”

Ironically, alpha-linolenic acid (ALA), an omega-3 fat found in flaxseed (and many other foods), has raised red flags. Some (but not all) studies find a higher risk of prostate cancer in men who consume more ALA, though usually not from flaxseed.

“Americans get ALA primarily from salad dressing, meat, and dairy products,” says Demark-Wahnefried. “Flaxseed has been virtually extinct from the American diet for over a century.”

Also reassuring: In Demark-Wahnefried’s study, men who ate flaxseed showed no increases in ALA in either their red blood cells or prostates.

However, the flaxseed eaters did have higher levels of EPA, one of the two main omega-3 fats in fish oil.

GREEN TEA

In a study of 50,000 Japanese men, the risk of advanced prostate cancer was 50 percent lower in those who drank at least five cups of green tea a day than in those who drank less than one cup a day. But another, smaller Japanese study found no link.

Few populations drink enough green tea to detect a link if there were one. So researchers in Italy gave a daily green tea extract (600 milligrams of catechins) or a placebo to 60 men with high-grade PIN, or prostate intraepithelial neoplasia. (An estimated 30 percent of men with high-grade PIN are diagnosed with prostate cancer within a year.)

After one year, biopsies revealed prostate cancer in just one of the men who took the tea extract but in nine of those who got a placebo.

“There are critics of the study, but the basics seem okay,” says University of Illinois researcher Peter Gann.
The problem is that it's tough for researchers to get a green tea extract that's well-defined enough for the National Cancer Institute (NCI). "When NCI got interested in green tea, it bought a large amount of an extract called polyphenon E from a company in Japan," says Gann. But now there's none left for researchers to use. "NCI's stock is committed and the company isn't making any more available because it's trying to get the Food and Drug Administration to approve polyphenon E as a prescription drug," he adds. "As soon as an extract looks good, access gets restricted."

**DIET, EXERCISE, ETC.**

The 93 men had decided to treat their early-stage prostate cancer with "watchful waiting." Dean Ornish, a clinical professor of medicine at the University of California, San Francisco, and colleagues randomly assigned them to get "usual care" from their doctors or to take part in "intensive lifestyle changes."

The lifestyle group ate mostly fruits, vegetables, whole grains, beans, and soy (but no eggs, dairy, meat, poultry, or fish) with little or no fats or oils (except fish oil supplements). They walked for 30 minutes six times a week, did stress management (like stretching, breathing, and meditation) for an hour a day, and met for a one-hour support group each week.

After two years, 13 men in the usual-care group, but only two in the lifestyle group, had undergone conventional treatment for prostate cancer (surgery, radiation, etc.).

Good news? Maybe. "The decision to undergo conventional treatment is not always a question of whether the disease is progressing or not," notes Ornish. Men often opt for surgery because of fear. "Well-meaning family or friends often say, 'Don't you think you should have this treatment?' Or the patient's wife will say, 'I don't want to lose you.' And every six months, he goes to the urologist, who says, 'You need to get this taken out before it spreads.' And the patient says, 'Okay, take it out,' not because he got worse but because he got scared."

The study also looked at PSA levels, which dropped 4 percent (from 6.23 to 5.98) after one year in the lifestyle group and rose 6 percent (from 6.36 to 7.64) in the usual-care group. "Those aren't huge amounts," says Ornish. But PSA isn't a good marker for whether the disease is progressing, he adds. "There really aren't good markers. It's frustrating."

What if Ornish's program only changed the men's attitudes toward treatment? Even if that didn't save lives, it could save much misery (and money). "Unless you have a very aggressive form of prostate cancer or are younger, most treatments don't do much and they often leave men incontinent or impotent or both," says Ornish.

"So if you're more likely to die with prostate cancer than from it, I think we need to be cautious about doing these interventions. To me the first rule in medicine is: First, do no harm."

**OTHER FOODS**

**Pomegranate.** In a study of 46 men who had rising PSA levels after surgery or radiation, the increase slowed after they started drinking a cup of pomegranate juice every day. (Instead of doubling every 15 months, their PSAs took an average of 54 months to double.) However, there was no control group, so it's hard to know if pomegranate made a difference.

**Vegetables.** Men who ate more vegetables had a lower risk of aggressive prostate cancer in a study that tracked 29,000 men for four years. But in a four-year trial of 1,200 men, PSA levels—and the risk of prostate cancer—were no different in those who were randomly assigned to eat a lower-fat diet rich in fruits and vegetables (6½ instead of 4 servings a day).

**Soy.** In the Multi-Ethnic Cohort Study, which tracked 82,000 men in Hawaii and Los Angeles, those who ate more soy foods or isoflavones to treat prostate cancer didn't have less cancer. Clinical studies that gave men soy foods or isoflavones to treat prostate cancer haven't had great success, but more are under way.

---

5 JAMA 301:102, 2009.
8 JAMA 293:1338, 2005.
15 Agency for Healthcare Research and Quality (AHRQ) report: Relationships of Vitamin D and Calcium Intakes to Nutrient Status Indicators and Health Outcomes (www.ahrq.gov/clinic/tp/vitadcaltp.htm).
19 Cancer Res. 65:11779, 2005.