

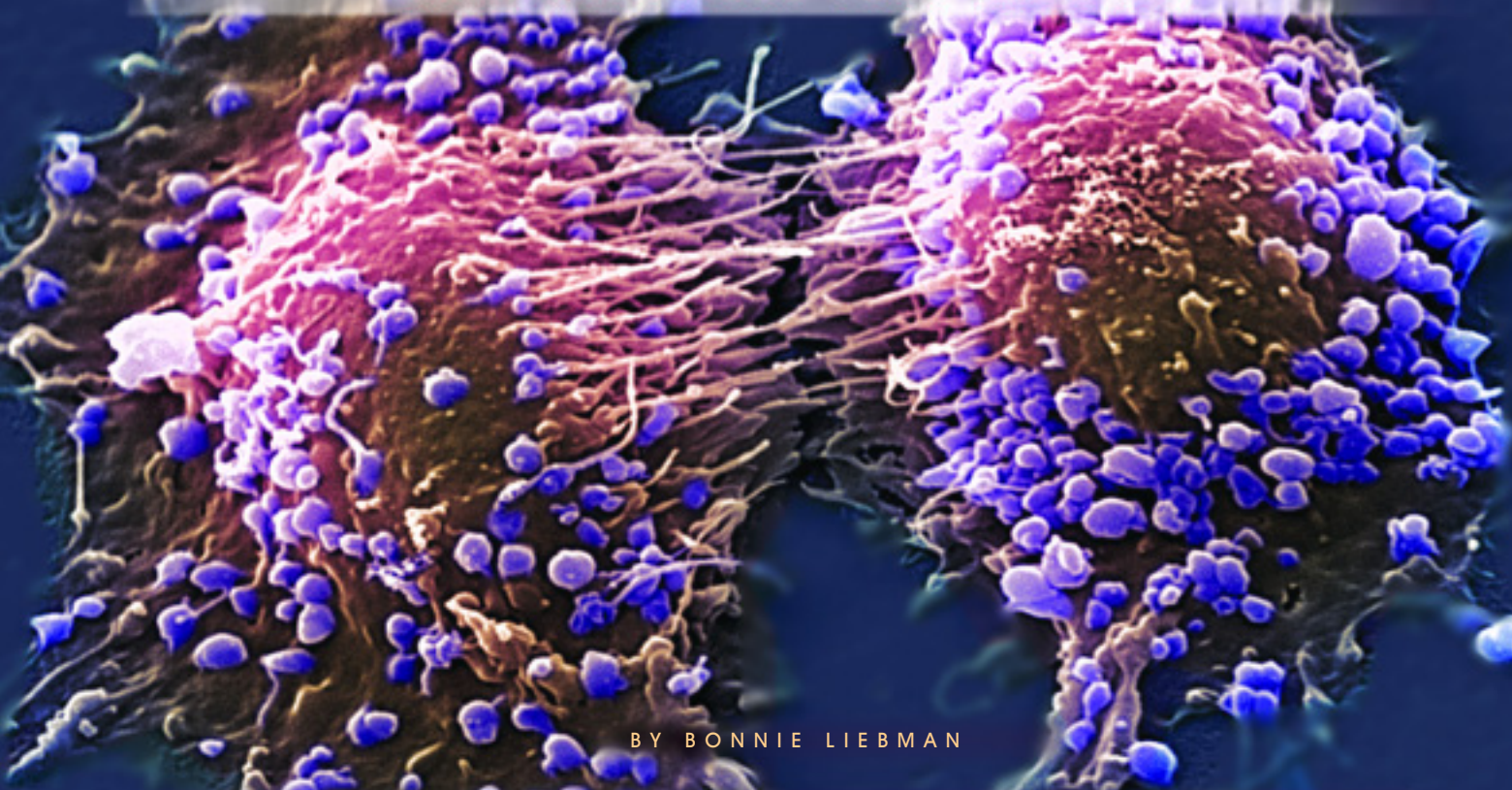


NUTRITION ACTION

HEALTH LETTER™

PROSTATE CANCER

MORE QUESTIONS THAN ANSWERS



BY BONNIE LIEBMAN

HARRY BELAFONTE, Colin Powell, John Kerry, Bob Dole, Arnold Palmer, Norman Schwarzkopf, and Robert Goulet chose surgery. Rudolph Guiliani, Nelson Mandela, Richard Riordan, Charlton Heston, and Rupert Murdoch went with radiation. Gregory Hines, Linus Pauling, Frank Zappa, Telly Savalas, and Timothy Leary died of the disease.

Anyone who's past middle age can add the names of friends, fathers, brothers, and others who have or had prostate cancer. That's what happens when a disease hits one in six men.

Death rates are down 20 percent since the peak in the early 1990s. But prostate cancer is still expected to strike 230,100 men and claim 29,900 lives this year.

Here's the latest on what may—or may not—keep your name off the list.

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Photo: A prostate cancer cell divides.

Photo: VVC/Science Photo Library.

PROSTATE CANCER

More Questions than Answers

It's not the worst cancer you can get. The odds of surviving prostate cancer for five years are 98 percent, up from 67 percent in the mid-1970s. That's a higher survival rate than for any common cancer (except non-melanoma skin). After ten years, 84 percent of patients are still alive.

Nevertheless, prostate cancer is a source of immeasurable suffering and loss. And while researchers have stepped up their efforts to find foods or supplements that might keep tumors from starting or spreading, their findings have yet to yield a slam dunk. Here's an A-to-Z guide to what they've learned so far.

that was a study done in cell lines, not in people or even animals. And they used purified ALA, which is devoid of antioxidants and is kept at high temperatures, not ALA as it is found in the body."

Demark-Wahnefried's studies have found that flaxseed slows the growth of prostate tumors in mice.³ "Those results, plus the slower cancer growth and the drop in PSA we found in men who ate flaxseed during the month before surgery, are compelling," she says. "But I wouldn't stand on a soapbox and tell men to eat flaxseed. We first need well-controlled trials to find out if it can help."

She has now started a clinical trial that will give a low-fat diet supplemented with flaxseed to cancer patients who are scheduled to have their prostate glands removed. (Most men have to wait several weeks before the surgery can be performed.)

"Then when the prostate comes out, we can measure the cell proliferation rate," she says. "That's more reliable than measuring PSA."

Demark-Wahnefried suggests several mechanisms to explain why flaxseed might work. "The lignans could be acting like estrogen," which slows prostate cell growth. "Or they could bind to testosterone in the GI tract, just as the beta-glucan fiber in oat bran binds to cholesterol. That would enhance testosterone excretion."

But until more research results are in, it makes sense to avoid too much ALA, especially from concentrated sources like flaxseed oil supplements.

"We found an increased risk of prostate cancer in men who consumed 1.5 grams of ALA a day compared to those who got 0.7 grams," says Ed Giovannucci of the Harvard School of Public Health. Every 1,000 mg of flaxseed oil in a typical supplement contains roughly 500 mg (0.5 grams) of alpha-linolenic acid.

His advice: "ALA is a tough one because we have good evidence that it's beneficial for heart disease, but men can certainly reduce the ALA they consume by eating less red meat." That might protect the prostate without jeopardizing the heart.

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Until researchers know more, hold off on taking flaxseed oil.



Alpha-Linolenic Acid & Flaxseed

It seems contradictory.

In studies of thousands of men, the risk of prostate cancer is 70 percent higher in those who consume more alpha-linolenic acid, or ALA—an omega-3 fat found in meat, vegetable oils, and other foods.¹ (The body may convert ALA to the longer-chain omega-3s that are found in fish oil.)

"At first we thought that ALA was associated with a higher risk of prostate cancer because men who consumed more ALA also consumed more meat," says Walter Willett, who chairs the nutrition department at the Harvard School of Public Health in Boston. "But now it looks like the ALA in oils like soy and canola are also linked to prostate cancer."

So it seems surprising that flaxseed, one of the richest sources of alpha-linolenic acid, lowered PSA levels (from 8.5 to 5.7, on average) in a pilot study of 15 men who were scheduled to have a repeat biopsy.² (The men added an ounce a day of ground flaxseed to a lower-fat diet for six months.)

"The findings are conflicting, but people don't eat isolated nutrients—they eat foods," says researcher Wendy Demark-Wahnefried of Duke University in Durham, North Carolina. "We tested the whole flaxseed, which has a host of nutrients—not just ALA, but lignans, which are fiber-rich plant estrogens."

A recent study at the University of Michigan found that ALA promoted prostate cell growth, she notes. "But

Calcium

Calcium is everywhere—fruit juices, breakfast cereals, pancake mixes, and dozens of other foods. You'd never guess that too much calcium may raise a man's risk of prostate cancer. Yet that's what several studies show.⁴

"In earlier studies, we saw roughly four times the risk of advanced prostate cancer only in men who consumed at least 2,000 mg of calcium a day, compared with men who consumed less than 500 mg a day," says Giovannucci.

"But now that we have more precise measurements, we see that the risk is roughly double in men who exceed 1,500 mg," he adds, referring to a new, unpublished study. That's more than the 1,200 mg a day that experts recommend for men, but it's not much more.

How could calcium harm the prostate? Some researchers believe that a high calcium intake lowers levels of vitamin D in the blood. (Taking extra vitamin D doesn't help.) Less D may make it easier for cells to lose their normal structure and to proliferate, two hallmarks of cancer cells.

"That's far from proven," says Giovannucci. "But there's no benefit from getting 1,500 mg or more of calcium a day anyway."

And with the food industry fortifying so many foods with calcium, consuming that much isn't hard. "Ten years ago, it wasn't a problem," says Giovannucci, "but now you can get a lot of calcium from different sources without thinking about it."

Fish vs. Red Meat

Go with surf, not turf.

The Health Professionals Follow-up Study has tracked more than 47,000



Eating more fish may protect the prostate.

men since 1986. Those who reported eating fish more than three times a week had a 44 percent lower risk of metastatic prostate cancer over the next 12 years compared with those who reported eating fish less than twice a month.⁵ (Fish oil supplements had no impact on risk.)

It's unclear why fish (a good source of long-chain omega-3 fats) might protect the prostate, while alpha-linolenic acid (a shorter-chain omega-3 fat) might increase the risk.

Fish may appear protective because people who eat more seafood often eat less red meat, which is linked to a higher risk of prostate cancer in some studies.⁶ "It's hard to tease that out," says Giovannucci.

If meat does promote cancer, it's not clear how. "It could be related to meat fat, or the nitrites in processed meats, or cooking meat at high temperatures," he explains. "At this point we can't say for sure."

He's more sure about what men should eat.

"Only a few studies suggest that fish may protect against advanced prostate cancer, but it's still prudent to increase fish and to decrease red meat to reduce the risk of heart disease."

Green Tea

American men are three times more likely than Japanese men—and 18 times more likely than Chinese men—to die of prostate cancer. Why?

One theory is that green tea may protect Asian men. When researchers gave green tea extracts—equal to six cups of tea a day—to mice that spontaneously get metastatic prostate cancer, it stopped the spread of cancer cells.⁷

But mice aren't people.

"We tested green tea on men with advanced prostate cancer because we had data showing that green tea components were effective in killing prostate cancer cells in the laboratory," explains Aminah Jatoi, an oncologist at the Mayo Clinic in Rochester, Minnesota.

Jatoi and other physicians in the North Central Cancer Treatment Group gave six cups of



Green tea slowed the spread of prostate cancer in mice, but not men.

tea a day (each made with one gram of green tea powder) to 42 cancer patients whose PSA levels hadn't dropped despite treatment with hormones.⁸ Their PSAs kept rising.

"It's possible that green tea might work at earlier stages," says Jatoi. "But it wasn't effective in patients with advanced cancer."

Since then, a study found that Chinese men who had prostate cancer were less likely to be tea drinkers than men without cancer.⁹ But researchers need far more evidence to reach any conclusions.

"It would be wonderful if everything that works in cell lines also worked in people," says Jatoi. "We need more clinical trials to find out."

Low-Fat Diet, etc.

"We put men on a vegan diet of fruits, vegetables, whole grains, beans, and soy products instead of dairy," says Dean Ornish, describing a study he conducted with Peter Carroll and their colleagues at the Preventive Medicine Research Institute in Sausalito and the University of California at San Francisco.

"They exercised three hours a week and did an hour of meditation or other stress-management techniques every day. They also took part in a weekly support group."

Ornish studied 90 men who had chosen to "watch and wait" rather than have surgery or other treatment for their early-stage prostate cancer. After one year, the men on the vegan diet (who were getting 10 percent of their calories from fat) had a small but statistically significant drop in PSA levels, while the control group had a rise in PSA, Ornish reported at a recent scientific meeting. But until the study is

published, the results are difficult to evaluate.

"It's encouraging that Ornish saw a drop in PSA," says Mark Moyad, director of complementary and alternative medicine at the University of Michigan Urology Center in Ann Arbor. "But cancer is difficult to fight, especially when it's aggressive."

When it comes to healthy men, similar but less drastic diet changes had no impact on PSA levels.

In a four-year study of 1,350 healthy men, researchers at Sloan-Kettering Memorial Hospital in New York found that those who ate a low-fat diet (20 percent of calories from fat) high in fiber, fruits, and vegetables had no lower PSAs than those who were simply given a brochure on a healthy diet.¹⁰

Still, says Moyad, any diet that protects against heart disease is worth eating.

"The worst-case scenario is that you only reduce the risk of the number-one cause of death. We have plenty of men who have beaten prostate cancer only to die of something else. The goal is to live long—not to beat just one disease."

Selenium

The good news: the National Cancer Institute is testing whether selenium (and vitamin E) can prevent prostate cancer in more than 32,000 men nationwide. The bad news: results are not expected until 2013.

Selenium was thrust into the spotlight in 1996 when researchers looked at its ability to prevent recurring skin cancers in the southeastern U.S., where levels of selenium in the soil—and therefore in locally grown foods—are low.

"In the initial report on the study, they found no difference in skin cancer, but they noticed a decrease in prostate cancer incidence," says W. Robert Lee of the Wake Forest University Baptist Medical Center in Winston-Salem, North Carolina.

Since then, other studies have found a higher risk in men with low selenium levels in their blood or toenails.¹¹

"Selenium holds the most promise for men who are deficient in selenium," says Lee. "In subsequent analyses of the skin-cancer trial, only those men benefited from selenium."¹²

It's too early to know if Lee is right. But the buzz about selenium may be causing other problems.

"We've got a population of men overdosing on the stuff," says Moyad. Too much selenium is toxic, he points out. "We've seen some men showing up with hair loss and dizziness." (To avoid toxicity, don't exceed 200 mcg a day, the dose used in most studies.)

"Men should have a blood test before they start taking a selenium supplement to see if their levels are low," says Moyad. "Taking selenium without a blood test ignores all we know about the mineral and could be dangerous."

Soy

The soy story is still unfolding.

"Prostate cancer rates are low in Asia, though they're increasing dramatically," says Mark Messina, an adjunct professor at Loma Linda University in California who has consulted for the soy industry.

So far, soy hasn't cut PSA levels in healthy men or prostate cancer patients.



"But we have no large studies in the U.S. because Americans don't eat enough soy." A recent Asian study suggests that soy protects the prostate, he adds.¹³

Without large numbers of soy eaters to track, researchers have instead tested soy—or isoflavones extracted from soy—on PSA levels. (In animal studies, the estrogen-like isoflavones curb the growth of prostate tumors.)

Soy failed to lower PSA levels in three studies on men, and slowed the rise in PSA in a fourth.¹⁴⁻¹⁷

"So far, it looks like not a lot happens to PSA when people eat soy," says Wake Forest's Lee. Many doctors don't consider a treatment effective unless it lowers PSA levels by at least 50 percent. Smaller changes are difficult to interpret.

"There's no question that if a prostate cancer patient's PSA goes up quickly—say, if it doubles in three to six months—especially after treatment, they're in trouble," Lee explains.

"But if you slow down the doubling time, say, from three to four years to five to eight years, we don't know what that means. It's too much of a stretch to say that PSA doubling time is a surrogate for time to death."

PSA isn't a perfect measure of a cancer's growth, says Lee. "If you do nothing, PSA can sometimes go up or down. For example, bike riding, a biopsy, prostatitis, catheterization, urinary retention, or trauma can raise PSA."

On the other hand, some researchers think that traditional soy foods are worth the gamble. "Soy is heart-healthy and the number-one cause of death in men is heart disease," says Lee.

But there's a catch. "The problem with soy is that people get fixated on bars and pills," says Moyad. "Some bars have 250 calories and some are high in saturated fat. And they may not have the isoflavones and proteins that are in traditional soy foods."

Tomato Sauce & Lycopene

"A new study says men who eat ten pizzas a week are less likely to develop prostate problems," joked Jay Leno in December 1995. "They're more likely to develop size 54 pants."

It's been nearly a decade since Ed Giovannucci and colleagues at the Harvard School of Public Health discovered that men who eat tomatoes at least twice a week have a lower risk of prostate cancer. Dozens of studies followed.¹⁸

"Researchers recently looked at all the literature and found a 20 percent reduced risk in studies that looked at cooked, not raw, tomatoes," says Giovannucci.

Lycopene may explain why cooked tomatoes seem to be more protective than raw. "One serving of tomato sauce has much more lycopene than a tomato or a glass of tomato juice," says Giovannucci.

Lycopene—the pigment that gives tomatoes, pink grapefruit, watermelon, and guava their red color—is also an antioxidant that's concentrated in the prostate gland. When Giovannucci looked at men who were older than 65



Men who eat tomato sauce at least twice a week have a lower risk of prostate cancer.

and had no family history of prostate cancer, those with higher blood levels of lycopene had roughly half the risk of getting the disease than those with lower blood levels.¹⁹

"In younger men with a family history, the risk might be more related to genetics," he explains. "But those men comprise only about 10 percent of people with prostate cancer, so lycopene may still be protective for the majority."

It's too early to know, though, whether it's the lycopene or something else in tomatoes that matters. When researchers recently gave rats a carcinogen, they found fewer prostate tumors if the animals were fed tomato powder, but not if they were fed lycopene.²⁰

"We always inferred that lycopene explained the link between tomatoes and prostate cancer," says Giovannucci. "Lycopene may be a factor, but it may also be a marker for something else in tomatoes that's beneficial."

Meanwhile, Aminah Jatoi and the North Central Cancer Treatment Group at the Mayo Clinic are testing lycopene in patients with advanced cancer.

"The dose—30 milligrams a day—is comparable to a diet with a lot of spaghetti sauce," she explains. In fact, her patients will take their lycopene in tomato sauce.

She expects results in about two years. In the meantime, says Giovannucci, "we don't have enough evidence to recommend that men take lycopene, but we do have enough to recommend that they eat tomato products twice a week."

Just remember that you don't need cheese-heavy dishes like pizza or lasagna to enjoy tomato sauce.

Vitamin E

Vitamin E, once the darling of antioxidant enthusiasts, has lost its luster when it comes to staving off heart attacks. "It's been a bust in studies on more than 55,000 people and cardiovascular disease," notes the University of Michigan's Mark Moyad.

It's too early to say whether the antioxidant will prevent prostate cancer. Most of the promising evidence comes from research in smokers.

"Smokers are notorious for low levels of vitamin E and other antioxidants," says Moyad. "What do you tell a non-smoking man about vitamin E? No one has any idea what it can do in non-smokers."

In the SELECT trial, healthy men are taking 400 IU of vitamin E (alpha-tocopherol) every day for seven to 12 years. That's considerably higher than the U.S. Recommended Daily Allowance (30 IU), or the 50 IU that seemed to cut the risk of prostate cancer in smokers.

High doses may not be harmless, notes Moyad. "They may increase the risk of bleeding in people who take aspirin or other blood-thinning drugs."

Zinc

"Zinc deficiency results in prostate enlargement...larger supplemental doses, commonly between 50 and 100 mg daily, may help shrink a swollen prostate," says www.doctoryourself.com.

Yet researchers found more than double the risk of advanced prostate cancer in men who got more than 100 mg a day from supplements, compared with those who got less than 25 mg.²¹ Either the zinc takers had prostate problems to begin with or zinc damages the prostate.

"Zinc is concentrated in the prostate, so some people say that it's bad if you're not getting enough," says Giovannucci. "But we found an increased prostate cancer risk at intakes well beyond the U.S. Recommended Daily Allowance," which is only 15 mg.

"Zinc is a disaster," says Moyad. "Large doses increase bad cholesterol, decrease good cholesterol, suppress the immune system, interfere with some bone-building drugs, and potentially raise testosterone levels."

"It's the number-one touted product for the prostate, and there's no good evidence for taking it." ♦

The Bottom Line

- Cut back on red meat and shoot for two or three servings of fish a week.
- Try for at least two servings a week of tomato sauce (preferably on pasta or other dishes that aren't smothered in cheese).
- Take a multivitamin with roughly a day's worth of vitamin E (30 IU) and selenium (55 mcg).
- Don't take more zinc than you'd get in an ordinary multivitamin (15 mg).
- Don't assume that more calcium is better. Don't exceed the recommended calcium intakes (1,200 mg a day for men over 50 and 1,000 mg a day for men 50 and under, from food and supplements combined).
- Until researchers know more about alpha-linolenic acid (ALA), avoid flaxseed oil supplements.

¹ *Journal of Nutrition* 134: 919, 2004.

² *Urology* 63: 900, 2004.

³ *Urology* 60: 919, 2002.

⁴ *Epidemiol. Rev.* 23: 87, 2001.

⁵ *Cancer Epidemiol. Biomarkers Prev.* 12: 64, 2003.

⁶ *Cancer Causes Control* 12: 557, 2001.

⁷ *Proc. Nat. Acad. Sci.* 98: 10350, 2001.

⁸ *Cancer* 97: 1442, 2003.

⁹ *Int. J. Cancer* 108: 130, 2004.

¹⁰ *J. Clin. Oncol.* 20: 3592, 2002.

¹¹ *J. Nat. Cancer Inst.* 96: 696, 2004.

¹² *BJU Int.* 91: 608, 2003.

¹³ *Cancer Epidemiol. Biomarkers Prev.* 12: 665, 2003.

¹⁴ *Cancer Epidemiol. Biomarkers Prev.* 13: 644, 2004.

¹⁵ *Journal of Urology* 169: 507, 2003.

¹⁶ *Prostate* 59: 141, 2004.

¹⁷ *Nutr. Cancer* 47: 111, 2003.

¹⁸ *Cancer Epidemiol. Biomarkers Prev.* 13: 340, 2004.

¹⁹ *Cancer Epidemiol. Biomarkers Prev.* 13: 260, 2004.

²⁰ *J. Nat. Cancer Inst.* 96: 554, 2004.

²¹ *J. Nat. Cancer Inst.* 95: 1004, 2003.