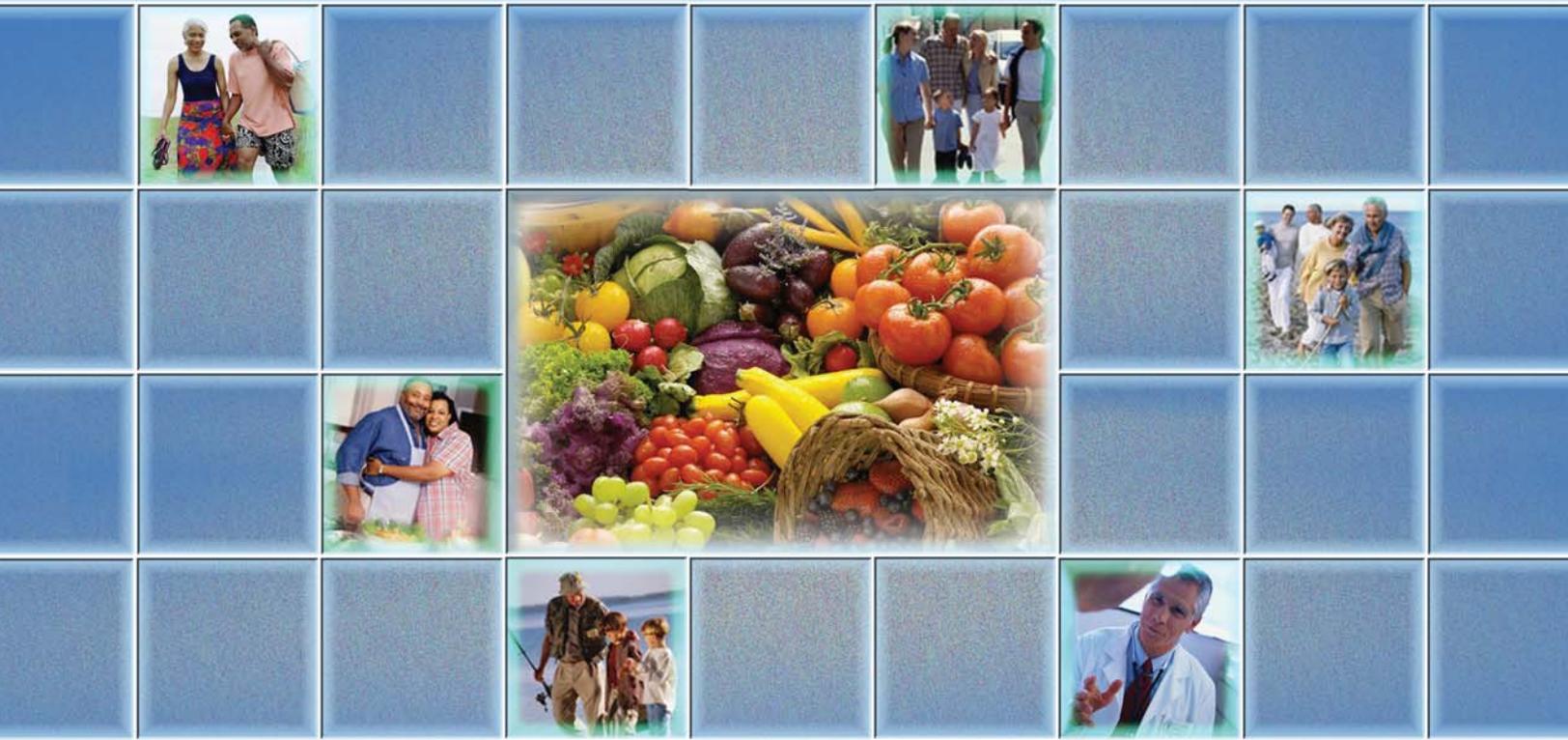




Nutrition and Prostate Cancer



A U T H O R S

Peter H. Gann, MD, ScD
Professor of Preventive Medicine
Feinberg School of Medicine at
Northwestern University
Chicago, Illinois

Edward L. Giovannucci, MD, ScD
Professor of Nutrition and
Epidemiology
Harvard School of Public Health
Boston, Massachusetts



The Prostate Cancer Foundation (PCF) is the world's largest philanthropic source of support for prostate cancer research. Founded in 1993, the PCF has raised more than \$230 million and provided funding for prostate cancer research to more than 1200 researchers at 100 institutions worldwide.

The PCF has a simple yet urgent goal: to find better treatments and a cure for recurrent prostate cancer. The PCF pursues its mission by reaching out to individuals, corporations, and others to marshal support for prostate cancer research. The PCF then provides funding for cutting-edge prostate cancer research and works with research scientists, physicians, government officials, biopharmaceutical industry executives, and others to remove barriers that impede progress toward a cure. The PCF also advocates for greater awareness of prostate cancer and more governmental resources for fighting the disease. For more information, visit <http://www.prostatecancerfoundation.org>.

Contact PCF:

Prostate Cancer Foundation
1250 Fourth Street
Santa Monica, CA 90401

Tel: 800-757-CURE or 310-570-4700

Fax: 310-570-4701

Email: info@prostatecancerfoundation.org

Web: <http://www.prostatecancerfoundation.org>

Managing Editor: Shira Berman

Copyeditor: Sarah Strocchia

Design/Art Direction: Michael Peterson

Copyright © 2005 Prostate Cancer Foundation

Foreword

Each year, dozens of reports are released touting the benefits of a particular diet or lifestyle intervention in the prevention or management of disease, while others question its utility. Some seem to rely on true scientific data, while others seem to hype old, unproven myths and urban legends. What are we to believe? Which diet and lifestyle changes can actually influence the development or progression of disease?

In the fight against prostate cancer, the stakes are at their highest. Far too many men each year are diagnosed with the disease, and far too many men each year die from the disease. When compared with the progress made in other major cancer types, the therapeutic landscape in prostate cancer is relatively young, leaving many men susceptible to the devastating effects that the disease can cause.

Fortunately, more and more researchers are focusing their efforts on identifying dietary and lifestyle changes that can work in tandem with pharmacologic, surgical, and radiotherapeutic approaches and help delay the development and progression of prostate cancer. The *Nutrition and Prostate Cancer* guide summarizes the “best of the best” data and information available in the research arena today, and is designed to help everyone affected by or at risk for prostate cancer understand how key nutritional strategies can be incorporated into everyday life. Culling the data from the published literature, Dr. Peter Gann of Northwestern University and Dr. Edward Giovannucci of the Harvard School of Public Health offer a comprehensive, yet concise overview of where we are today in the search for nutritional approaches to prostate cancer — and remind us how much more we have yet to learn.

The Prostate Cancer Foundation is proud to be part of this effort, first by providing millions of dollars of grants to support the work of nutrition and epidemiology researchers around the world over the past 12 years, and now, by bringing to you this *Guide* to share with your family and discuss with your doctor or qualified nutritional consultant.

Remember: A diagnosis of prostate cancer is just the beginning of your journey, not the end. Adopting some of the key dietary changes discussed in this *Guide* and incorporating them into your everyday life are two important steps on the road to helping your body fight this disease.



Leslie D. Michelson
Vice Chairman and Chief Executive Officer
Prostate Cancer Foundation



Stuart Holden, MD
Medical Director
Prostate Cancer Foundation

Table of Contents

4 Introduction

6 Why Does Nutrition Matter?

7 *When Too Much Good Food Is Bad For You*

8 *How Do We Know What We Know? Where Do The Data Come From?*

11 Nature's Bounty: Fruits And Vegetables

12 *The Whole Might Be Greater Than The Sum Of Its Parts*

12 *Tomatoes And Lycopene: The Evidence Continues To Grow*

14 *Can Tomato-Based Halt Development Of Prostate Cancer?*

16 *Not All Vegetables Are Created Equal*

16 *Focus On Cruciferous Vegetables*

18 *Exploring The Roles Of Polyphenols And Isoflavones*

18 *The Benefits Of Green Tea — And Red Wine?*

19 *What About Soy?*

21 The Building Blocks: Vitamins And Minerals

21 *Beta-Carotene, Vitamin E, And Selenium: The Debate Continues*

24 *The Ups And Downs Of Zinc, Calcium, And Vitamin D*

28 Dietary Fats And Red Meat: Rethinking The American Way

29 *The Skinny On Fat*

31 *The Drawbacks Of Grilling Meat*

33 Charting A Course For The Road Ahead

34 *Changing Your Dietary Habits One Tomato At A Time*

34 *Planning Ahead*

35 *Nutritional Approaches And Therapeutic Strategies Going Hand In Hand*

Introduction

Prostate cancer is the most common non-skin cancer in the United States and is second only to lung cancer as the primary cause of cancer death in men. In 2005, the American Cancer Society estimates that 232,000 men will be diagnosed with prostate cancer, and just over 30,000 will die of the disease.

What does that mean to you and me? One of every six men will develop prostate cancer in his lifetime — making men 33% more likely to be diagnosed with prostate cancer than women are to be diagnosed with breast cancer, and 200% more likely to be diagnosed with prostate cancer than with colorectal cancer. Put another way, a nonsmoking man is more

likely to be diagnosed with prostate cancer than with lung, bronchus, colon, rectal, bladder, lymphoma, melanoma, oral, and kidney cancers *combined*.

The good news is that over 90% of prostate cancers are now diagnosed in the earliest stages, when the long-term survival rate approaches 100%, compared with

barely 70% in the 1970s. In addition, the mortality rate from prostate cancer has slowly but steadily declined since its peak in 1993. Clearly, better detection, better monitoring, and better treatments over the past decades have finally begun to make a difference in the lives of thousands of men.

Yet the toll that prostate cancer exacts is still too high, and the development process for new and better treatments is still too long. In addition, in our zeal to detect cancers at the earliest and most treatable stages, we sometimes find tumors that are so small, the question of whether it is prudent to begin treatment remains unanswered. Prevention strategies have therefore moved to the forefront of many researchers' minds — both primary prevention strategies aimed at halting development of the disease and secondary prevention strategies aimed at identifying more cost-effective screening programs to find and treat early cancers that would otherwise have become life-threatening.

Pharmacologic approaches to primary prevention may still be in their infancy, but the knowledge base on the benefits of nutritional approaches is rapidly expanding. Day after day, the effects of dietary and lifestyle changes on the development and progression of prostate cancer are being discussed and explored by leading researchers in the field, and nutritional strategies for improving outcomes in prostate cancer patient are taking ever more prominent places in treatment protocols.

Which foods and nutrients have been shown to be beneficial for patients with prostate

A nonsmoking man is more likely to be diagnosed with prostate cancer than with lung, bronchus, colon, rectal, bladder, lymphoma, melanoma, oral, and kidney cancers combined.

cancer? How reliable are the data for nutritional strategies in prostate cancer? Are there foods or nutrients that might prevent prostate cancer — or even prevent or delay a recurrence of the disease? How do you get the most benefit from each vitamin and mineral? What should you do now? The *Nutrition and Prostate Cancer* guide will summarize the latest information and help you navigate through the information available about various nutritional approaches so that you can create a strategy that's right for you.

Remember: if the cancer is detected at the earliest stages, over half of men diagnosed will live for more than 15 years.

In other words, your diagnosis of prostate cancer is just the beginning of your journey, not the end. And there might be some relatively simple things that you can do to maximize your body's ability to fight this disease.

A diagnosis of prostate cancer is the beginning of your journey, not the end.

Why Does Nutrition Matter?

When looking at why some people develop cancer and others don't, there are three factors that play a meaningful role and that are unchangeable: age, family history, and race. Depending on the type of cancer, one or more of these can play a pivotal role in increasing or decreasing your risk of developing the disease.

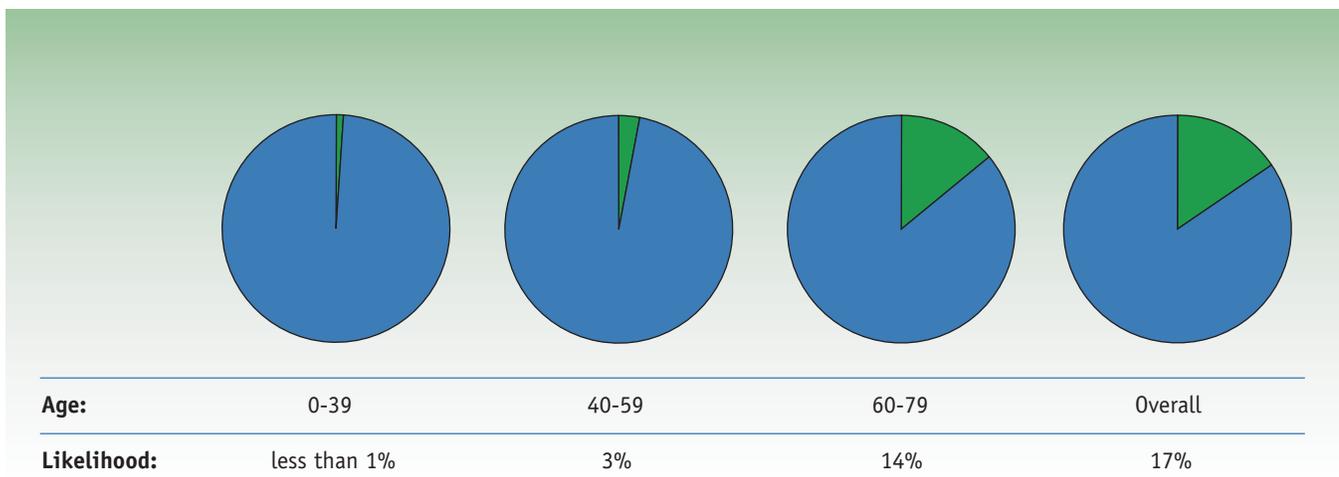
The older you are, the more likely you are to be diagnosed with prostate cancer. Although only 1 in 10,000 under age 40 will be diagnosed, the rate shoots up to 1 in 39 for ages 40 to 59, and 1 in 7 for ages 60 to 79. If you're African-American, you're about 1.5 times as likely as Caucasian patients to be diagnosed, and if you have at least one first-degree relative with prostate cancer — a brother, a father, or even a son — you're more than twice as likely as the average man to be diagnosed.

But these statistics tell only part of the story. There are countless other factors that can influence your risk — factors over which we *do* have control; namely, diet and lifestyle.

The old adage of “you are what you eat” might not be completely true, but there is no question that our environment — and particularly our diet — influences the way our body functions. Think about how you felt the last time you ate that third burrito. How long did it take you to get over it? A few hours? A few days? Now think about all of the foods that you've eaten over the past years. How have our bodies managed to survive it all? Because for every extra bite of something not so smart, we also take in a host of nutrients that help our bodies continue running smoothly, and, in the short term, the effects are not usually noticeably harmful.

It's not much different when it comes to cancer: the body has natural defenses against

The likelihood of developing prostate cancer increases dramatically with age



Source: American Cancer Society. Jemal A, et al. Cancer statistics, 2004. *CA Cancer J Clin.* 2005;55:10-30.

allowing normal cells to become cancerous and allowing cancer cells to grow. But it is a very delicate balance, and it is easily upset by changes in our diet and our environment. For some cancers, the balance is easy to see. Nearly 90% of people in the United States who develop lung cancer are smokers. The longer you smoke, the more damage you cause to your lungs, and the greater your likelihood of developing lung cancer. Take away the cigarettes, and the risk starts to inch its way down.

With prostate cancer, there is not yet evidence of a single causative factor that is likely to dramatically alter your risk. However, research has been showing in the past few years that ingesting certain nutrients might decrease your chances of developing prostate cancer, reduce the likelihood of having a prostate cancer recurrence, or help slow down progression of the disease. Although it will likely take some time before results of these studies

There is no question that our environment — and particularly our diet — influences the way our body functions.

conclusively demonstrate the benefits of nutrition in prostate cancer, there is already good evidence that some of these dietary changes are beneficial in other chronic diseases, particularly heart disease. Adoption of these dietary changes can therefore be seen as an important step in a path toward a more healthy lifestyle overall.

When Too Much Good Food Is Bad For You

In the coming pages, we'll look at the different food types and discuss which nutrients are most likely to be "prostate-cancer protective." But before we do, we need to address the most crucial dietary problem of all — the fattening of America.

Over the past 40 years, the rate of obesity has been steadily climbing. In 2002, the last year for which the data are available, a whopping 65% of adults in the United States were classified as overweight or obese, with a body mass index (BMI) over the accepted normal of 25. Even more disturbing is that 31% of children were classified as overweight or obese, placing them well above the 95th percentile for normal growth for their age.^[1]

Unfortunately, this increase in weight seems unlikely to be offset by an increase in physical activity, as approximately 40% of adults and teenagers do not exercise regularly.^[1] The combination of increased food intake and decreased physical activity has taken its toll on Americans and has resulted in increased rates of a variety of diseases, particularly diabetes.

Although the link between obesity and the risk of developing prostate cancer remains unclear, there is no question that obesity can have a negative effect on disease outcomes. Research has shown that prostate-specific antigen (PSA) test results in obese men can be lower despite the presence of disease, potentially leading to a delay in diagnosis and treatment; recovery from surgery tends to be longer and more difficult; and the risk of dying from prostate cancer can be higher.^[2]

Regardless of the nutritional approach that you ultimately choose, weight management must be an essential component of your overall strategy. Increasing your intake of vegetables can be beneficial — but not if they're swimming in high-fat dressings or sauces. Similarly, nuts can be a great source of some key nutrients but can also be very high in fat and calories.

In addition, it is most important that you be sure to exercise regularly, at least 30 minutes a day at least 3 days each week. Not only will it help to burn off extra calories, but regular stretching exercises will help keep you limber and flexible, while resistance exercises and weight training will help maintain muscle strength and endurance. Walking, jogging, playing tennis or golf, and even gardening can be effective forms of exercise — the key is to stay on the go and stay off the couch.

As you sift through the data in these pages and begin to consider what's right for you, don't forget to talk with your doctor or qualified nutritional consultant about how best to incorporate weight management and exercise strategies into your daily routine.

POINTS TO REMEMBER

1. When it comes to the risk of developing prostate cancer, there are three factors that are unchangeable: age, family history, and race. But there is also no question that our environment — and particularly our diet — influences the way our body functions.
2. Eating certain foods and nutrients might decrease your chances of developing prostate cancer, reduce the likelihood of having a prostate cancer recurrence, or help slow down progression of the disease.
3. Regardless of the nutritional approach you ultimately choose, weight management and exercise should be a core part of your overall strategy.

How Do We Know What We Know? Where Do The Data Come From?

One of the greatest difficulties in medicine today is being able to discern fact from fiction. In addition to the rigorous science being conducted at laboratories and cancer centers across the United States and around the world, far too many people purporting to have all of the answers are publishing their own opinions, making it nearly impossible to find the truth in the noise. Unfortunately, because it's such a common disease, this seems to be particularly true of prostate cancer.

Throughout these pages, we'll be discussing what's currently known about the role of nutrition in prostate cancer development and progression. But we won't present our opinion, and we won't jump to conclusions that can't be supported by the data. Your approach to prostate can-

cer information-gathering should be the same as ours: think and read critically, evaluate the source of the data, compare it with what you already know, and be wary of the extremes.

So where do the “good” data come from?

Suppose we want to test whether a new drug is better than an existing one in delaying progression of prostate cancer. Ideally, we would conduct what is known as a randomized controlled trial. In our study, men with prostate cancer would be randomly assigned to one of two groups, or trial arms: those in one arm would be given standard treatment, while those in the second arm would be given the experimental treatment or the standard treatment plus the experimental treatment. The researchers would assess the patients over time and compare the number of patients in each arm whose disease progresses.

Randomization is an important and powerful tool because it keeps a balance between groups on factors other than the treatment that might explain a difference in disease rates, such as age and family his-

tory. And to ensure that there’s no bias toward one treatment over another, the trial would be “blinded,” so that the researchers and patients won’t know which treatment is which.

But what if we wanted to test the effects of particular eating habits on the progression of prostate cancer? And what if we wanted to see whether dietary changes that we make early in our lives can have long-lasting effects? It would be awfully hard to find a large group of men who would be willing to follow a predetermined diet and lifestyle regimen for decades and decades.

Epidemiologic studies, which track patterns of behavior over many years, are crucial in this area. Like in randomized controlled trials, the researchers in these studies begin with a hypothesis, collect the data, and analyze whether their hypothesis was proven true or false. It is important to note, however, that the ultimate goal of these studies is to use the data to identify and examine factors that can affect the development and/or progression of disease over longer periods of time.

One of the longest running and best known epidemiologic studies is the Framingham Heart Study. In 1948, over 5000 men and women from the town of Framingham, Massachusetts, were recruited to participate in a study designed to identify the common factors or characteristics that contribute to cardiovascular disease; in 1971, an additional study was begun with their children and their spouses. The data culled from the physical examinations and questionnaires completed by the participants have helped to identify what we now know are the classic cardiovascular risk factors: high blood pressure, high blood cholesterol, smoking, obesity, diabetes, and physical inactivity.

In the prostate cancer arena, two epidemiologic studies stand out: the Health Profession-

Your approach to prostate cancer information-gathering should be the same as ours: think and read critically, evaluate the source of the data, compare it with what you already know, and be wary of the extremes.

als Follow-Up Study and the Physicians' Health Study. Neither was designed to specifically look at the effects of diet on prostate cancer, but because they both enrolled only men, it was inevitable that prostate cancer would become a major focus of the studies' results.

The Health Professionals Follow-Up Study, begun in 1986, was designed to look at the effects of various nutritional and lifestyle factors on the development of cancer, cardiovascular diseases, and other serious illnesses affecting men. Every two to four years, over 50,000 men enrolled in this ongoing study complete questionnaires about their health, their smoking status, their level of physical activity, and their diet and nutritional status.

The Physicians' Health Study was a randomized controlled trial begun in 1982 to evaluate the effects of aspirin and beta-carotene on the prevention of cardiovascular disease and cancer. Although that trial technically ended in 1995, a large percentage of the 22,000 male physicians who took part in it continue to complete questionnaires about their health, effectively turning the trial into a long-term epidemiologic study. However, unlike the Health Professionals Follow-Up Study, the Physicians' Health Study focuses more on biomarkers for disease, exploring the link between specific compounds found in the bloodstream and the risk of developing disease.

More than 7000 of the participants in the original Physicians' Health Study plus an additional 7000 men were enrolled in a second trial begun in 1997, examining the effects of vitamin C, vitamin E, beta-carotene, and a multivitamin on the prevention of cardiovascular disease, cancer, age-related eye disease, and early cognitive decline. This trial will run through 2007 but, as with the first trial, will no doubt continue to provide a wealth of information for many years to come.

Because both of these trials have collected huge quantities of data over the years, researchers have been able to mine the data for information on how diet and lifestyle interventions can affect development and progression of different diseases over time. In fact, as we'll see later on, much of what we know today about the benefits of lycopene, beta-carotene, and selenium has stemmed from data collected in these two studies.

POINTS TO REMEMBER

1. Your approach to prostate cancer information-gathering should be the same as ours: think and read critically, evaluate the source of the data, compare it with what you already know, and be wary of extreme statements or "hype" that are not supported by studies published in respected scientific publications.
2. Some very large and respected studies have shown how diet and lifestyle can affect development and progression of different diseases — including prostate cancer — over time.

Nature's Bounty: Fruits And Vegetables

It is unquestionably true that fruits and vegetables are an incredibly rich source of vitamins, minerals, and other naturally occurring chemicals, many of which have strong cancer-fighting properties. However, determining how to maximize the benefits from these nutrient-rich sources has proven quite challenging.

Rather than trying to determine the total number of servings of fruits and vegetables needed to stem the growth of cancer, a strategy that hasn't yet proven very successful, researchers have been looking at certain nutrients in specific types of fruits and vegetables that might have a marked effect on cancer development and progression.

For example, although increased consumption of fruits and vegetables overall seems to have no effect on the risk of developing prostate cancer,^[3] increased consumption of cruciferous vegetables can provide some benefit,^[4] and consumption of specific foods, particularly those derived from tomatoes, has been shown to have a significant effect on the development and progression of prostate cancer.^[5,6]

In this section, we will look at those fruits and vegetables that have generated the greatest excitement in the eyes of prostate cancer researchers and, most importantly, discuss how you can maximize your benefit from their cancer-fighting nutrients.

It is important to remember, however, that regardless of whether studies have shown a benefit of particular types of fruits and vegetables in preventing the development or progression of prostate cancer, every person — male, female, young, and old — should follow the recommendations of the *Dietary Guidelines for America* published jointly by the US Department of Health and Human Services and the US Department of Agriculture and eat 5 to 9 servings a day of fruits and vegetables. In addition to the benefits that they might bring in fighting other types of cancers, there is strong evidence that increased consumption of fruits and vegetables can decrease your risk of heart disease, and evidence is mounting on a variety of other diseases and disorders. Although many questions remain about the specific health benefits of particular types or quantities of foods, there is no question that incorporating a wide variety of fruits and vegetables into your diet will go a long way toward helping you achieve a healthier lifestyle.

Incorporating a wide variety of fruits and vegetables into your diet will go a long way toward helping you achieve a healthier lifestyle.

The Whole Might Be Greater Than The Sum Of Its Parts

Suppose you took a fruit, such a tomato, and broke it down chemically. You would find hundreds of thousands of different compounds, each of which has its own unique properties and mechanisms for interacting with your body's cells. And suppose you were somehow able to isolate a compound that could halt the growth of prostate cancer cells. Which would you think would be a more potent cancer-fighting tool: a supplement containing only that one chemical, or the whole tomato itself?

In fact, many of the benefits that we obtain from whole fruits and vegetables, or even from processed fruits and vegetables, are superior to the benefits seen with supplementation. Why? Simply put, a tomato is not just a collection of individual chemical compounds. The interaction among the compounds within the tomato, with the environment in which the tomato is processed, and with the other foods that are eaten make each of the compounds potentially more effective than they are individually, enabling the body to better utilize them in the fight against prostate cancer.

In this section, as we evaluate the available data on the benefits of various fruits and vegetables, we'll identify the compounds that are most beneficial — and learn why eating the foods might be the preferred route of ingestion over supplementation with the isolated compound alone.

POINTS TO REMEMBER

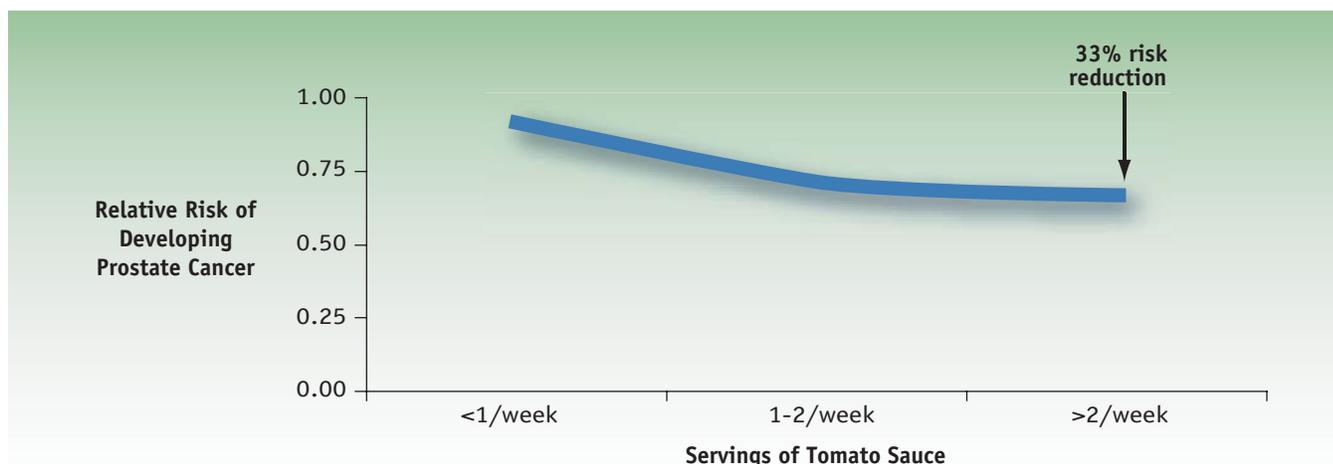
1. Many fruits and vegetables are rich in cancer-fighting nutrients, but determining how to maximize their benefits has proven challenging.
2. Regardless of whether studies have shown a benefit of particular types of fruits and vegetables in preventing the development or progression of prostate cancer, every person — male, female, young, and old — should eat 5 to 9 servings a day of fruits and vegetables in accordance with the USDA's *Dietary Guidelines for America*.

Tomatoes and Lycopene: The Evidence Continues To Grow

Lycopene, a naturally occurring chemical found mostly in tomatoes, but also in watermelons, pink grapefruits, guava, and papaya, has long been touted as one of the most “prostate healthy” compounds available. Why?

Among other things, lycopene acts as a powerful antioxidant and helps protect the body against cancer. During normal cellular processes, extra oxygen atoms, or free radicals, are often produced and are used by the body to destroy foreign invaders like bacteria. However,

Eating at least two servings a week of tomato sauce can significantly decrease the risk of developing prostate cancer



Source: Giovannucci E, et al. *J Natl Cancer Inst.* 2002;94:391-398.

if these free radicals are allowed to roam unchecked, they can cause cellular DNA to break down, mutating the cells and transforming normal cells into cancerous cells. Antioxidants such as lycopene mop up free radicals and thereby might contribute to the protection against cancer.

Although the properties of lycopene have been known for a while, researchers have begun to focus more on understanding what can make lycopene more bioavailable, or more readily accessible and available to the body's tissues.

Often, an important early step in trying to better understand how different compounds react to and interact with human cancer tissues is to test them in animals that have been engineered or otherwise treated to develop human-like cancers. In these animals, the cancers grow very rapidly, so the results of the research initiatives can be realized quickly. For example, in one prostate cancer animal model, hormone-dependent prostate cancer-like tumors develop in 75% of the animals after just one year.

Over the course of 73 weeks, a group of these animals were fed either whole tomato powder or lycopene supplements. Even though the amount of lycopene in the supplements was more than 10 times that found in the tomato powder and the amount of lycopene detected in the bloodstream was more than 30% higher with the supplements, those fed the tomato powder rather than the lycopene lived nearly 20% longer before dying of prostate cancer.^[7]

Why wouldn't the higher levels of lycopene translate into an increased benefit? The researchers theorized that there may well be an upper limit as to how much benefit can be obtained from these nutrients. Something similar was noted in the Physicians' Health Study, where men who had high levels of lycopene in their bloodstreams had a lower risk of prostate cancer — but those who took supplements of beta-carotene, a nutrient with prop-

erties that are similar to lycopene (and discussed in the next section), received the same benefits even when their lycopene levels were lower.^[8] Likewise, in these animals, the amount of lycopene found in the supplements might have been too high for the body to process and therefore had no incremental effect over the tomato powder.

But then why would those fed the tomato powder show a greater benefit? If the researchers' theory is true, and there's an upper limit to the amount of lycopene that the body can absorb, shouldn't the two groups of animals fare the same regardless of how they ingested the compound?

As we noted above, it's possible that the benefits offered by lycopene are best realized when derived from tomato-based sources, both because of the way it interacts with other nutrients in the fruit, and because of the way it is absorbed by the body when ingested from food-based sources. The combination of these factors might therefore make tomato-based foods more potent than lycopene supplementation in the fight against prostate cancer cell growth.

Following along this same theme, other studies have shown that not only are tomatoes better than lycopene alone, but that processed and cooked tomatoes are even better. After studying the dietary habits of the men enrolled in the Health Professionals Follow-Up Study, researchers found that those who consumed at least two servings of tomato sauce a week over the course of the 12-year study demonstrated a 28% lower risk of developing organ-confined prostate cancer, a 35% lower risk of developing locally advanced disease, and a 36% lower risk of developing metastatic disease. At the same time, however, there was no association between prostate cancer risk and the amount of fruits and vegetables overall — including tomatoes — that the study participants consumed.^[5]

Why would tomato sauce be better than tomatoes? It's unclear exactly why, but it seems that processing and cooking a tomato releases compounds such as lycopene from their storage sites within the fruit, changing the way that these nutrients are absorbed and used in the body, and therefore changing the way the lycopene affects the growth of prostate cancer cells.

In an interesting follow-up to this study, the same group of researchers tracked tomato sauce consumption in men from the original study who developed prostate cancer to see if it had a continuing effect on their health. In these men, consuming an extra two servings per week of tomato sauce after diagnosis reduced their risk of disease progression by nearly 20%, demonstrating that the ability of antioxidants to slow cancer cell growth doesn't end even if the tumors are clinically detectable.^[6]

Can Tomato-Based Products Halt The Development Of Prostate Cancer?

That's the question now under investigation in a study being conducted at Northwestern University in Chicago. High-grade prostatic intraepithelial neoplasia, or HGPIN, has long been seen as a precursor to prostate cancer. Because prostate cancer typically grows slowly,

it can be decades before men with HGPIN develop clinical signs of prostate cancer, so the benefits of using standard prostate cancer treatments in these men are unclear. At the same time, however, this is an ideal group of men in which to study preventive agents because these men are far more likely to develop prostate cancer without intervention.

Building on data from studies demonstrating the benefits of lycopene-rich tomato-based foods in delaying disease onset and progression, the researchers at Northwestern University will be administering to men with HGPIN tomato oil extracted from tomatoes specially grown to be high in lycopene. The goal is to see if the tomato oil can prevent the progression from HGPIN to clinically detectable prostate cancer.

So What Does This All Mean?

The benefits of lycopene in delaying prostate cancer growth are likely best obtained through tomato-based products rather than supplementation, and cooked or processed tomatoes seem to be an even better source of the nutrient. A minimum of 2 servings per week of tomato sauce, roughly a half cup per serving, can reduce the risk of developing prostate cancer and of prostate cancer progression, but how much is needed to maximize the benefits, and whether tomato-based foods can prevent the development of prostate cancer in men with HGPIN, remains unknown.

POINTS TO REMEMBER

1. Lycopene, a naturally occurring chemical found mostly in tomatoes, and to a lesser degree in watermelons, pink grapefruits, papaya, and guava, acts as a powerful antioxidant, and helps protect the body against cancer.
2. Because processing and cooking foods change the way that lycopene is absorbed and used in the body, lycopene supplements may not provide the same benefits as cooked tomato products. If possible, you should get your lycopene from regular consumption of cooked tomatoes or tomato products.
3. A very large and long-term study has shown that consuming at least two servings of tomato sauce per week confers a significantly lower risk of developing organ-confined prostate cancer, locally advanced disease, and metastatic disease.

Not All Vegetables Are Created Equal

As we noted above, results from studies evaluating the benefits of fruits and vegetables in protecting against prostate cancer development have been mixed — some showed significant decreases in the risk of developing disease, some showed only modest decreases, and others showed no effect at all. In fact, until a few years ago, the only consistent conclusion was that the true effects of fruits and vegetables were unknown.

The largest study to date on the overall role of fruits and vegetables in prostate cancer was conducted in the 1990s as part of the European Prospective Investigation into Cancer and Nutrition (EPIC).^[3] Using detailed questionnaires, the researchers collected diet and lifestyle information on over 13,000 men in 7 different countries and found no association between fruit and vegetable intake and the risk of developing prostate cancer.

Does that mean that there's no benefit at all to consuming fruits and vegetables? Not necessarily. The study's greatest strength is also its greatest weakness — it measured a vast number of people over a long period of time, which, by definition, included men at all stages of disease. What if some of the cancer-fighting compounds and chemicals found in certain fruits and vegetables are most effective in the earliest stages of disease, or even before the cancer can be detected?

Focus On Cruciferous Vegetables

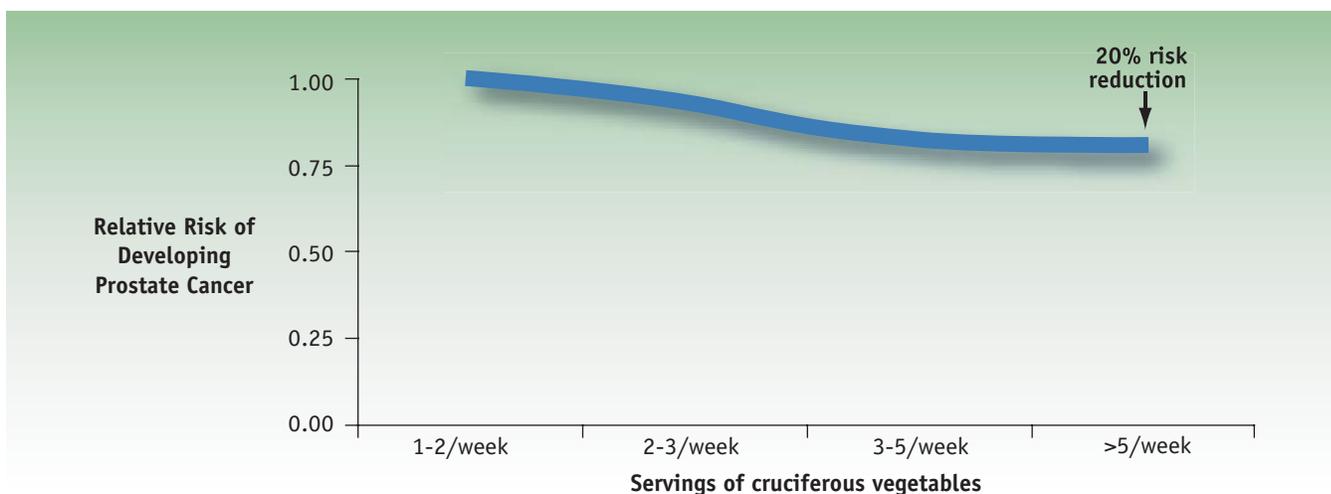
This is precisely the question that was asked of the cruciferous vegetables, such as broccoli, cauliflower, cabbage, Brussels sprouts, bok choy, and kale.

Carcinogens, or substances that are known to cause cancer, are ingested and incorporated into the body on a regular basis. Fortunately, the body's defense system includes specialized proteins that help to clear out the different carcinogens before they wreak havoc. Early in the development of prostate cancer, a group of these protective proteins is knocked out, allowing the damage caused by the carcinogens to spread. Sulforaphane, a compound found in cruciferous vegetables, increases activity of proteins that enable the body to clean up the damage caused by these carcinogens, thereby helping to slow down the cancer growth process.

In both the EPIC trial and the Health Professionals Follow-Up Study, no association was found between cruciferous vegetable intake overall and the risk of prostate cancer development. However, something intriguing was noted in the Health Professionals Follow-Up Study: men who consumed 5 or more servings of cruciferous vegetables per week up to 8 years earlier showed a 10% to 20% lower risk of developing prostate cancer.^[4] Biologically speaking, this makes sense. Because sulforaphane enables the body's protective proteins to do a better job at clearing out carcinogens, it would clearly be most effective during those periods that carcinogens are most active — when the tumor cells are first starting to grow, well before the disease is clinically detectable.

As an interesting side note to this, a recent study performed on animals with human-like

Eating at least five servings a week of cruciferous vegetables can significantly decrease the risk of developing prostate cancer.



Source: Giovannucci E, et al. *Cancer Epidemiol Biomarkers Prev.* 2003;12:1403-1409.

prostate cancers showed a significantly slower rate of tumor growth in those animals fed a combination of broccoli and tomato powder compared with those fed broccoli powder only or tomato powder only.^[9] These data suggest that the benefits of lycopene and sulforaphane might be cumulative — and that each additional cancer-fighting food can further decrease your risk of developing prostate cancer.

So What Does This All Mean?

Eating at least 5 servings each week of cruciferous vegetables, particularly broccoli, might help you decrease your risk of developing prostate cancer. Size-wise, this translates into about a half cup of cooked vegetables per serving. For those who already have detectable prostate cancer, although an increase in cruciferous vegetables might not affect your risk of progressive disease, it will likely help to reduce your risk of cardiovascular disease, and can certainly contribute to the overall health benefits conferred by fruits and vegetables.

POINTS TO REMEMBER

1. Sulforaphane, a compound found in cruciferous vegetables such as broccoli and cauliflower, helps the body to repair the damage caused by cancer-causing substances, thereby helping to slow down the cancer growth process.
2. In a large, long-term study, men who consumed five or more servings of cruciferous vegetables each week showed a lower risk of developing prostate cancer.

Exploring the Roles of Polyphenols and Isoflavones

Unlike the research conducted with many laboratory-engineered pharmacologic agents, research conducted with food-based nutrients often runs backward: an effect is noted in people, and the investigators try to figure out which nutrient might be responsible.

This approach is best seen in the study of Asian men and prostate cancer. Although the rate of prostate cancer development in Asian-born men is considerably lower than that seen in American-born men, the rates tend to equalize after Asian men live in the United States for a number of years.^[10] One of the prevailing theories for this shift is the influence of diet — as men begin to consume a “Western-style” diet that is higher in fat and carbohydrates, their risk of prostate cancer begins to rise. (The association between dietary fat and prostate cancer is discussed in the next section.)

But researchers also offered another possible explanation for this shift. What if the Western-style diet lacks a nutrient that was present in the original diet that offered some protection against prostate cancer development?

The primary candidates in this theory are the isoflavones found in soy and the polyphenols found in green tea, two foods that are abundant in Asian-style diets but that play a far less prominent role in Western-style diets.

Polyphenols, an abundant source of antioxidants, are found to varying degrees in most fruits and vegetables. Their subcomponents, including flavonoids and flavones, have been studied in both prostate cancer cells in the lab and in animals, and have consistently been shown to slow development of disease. The major components of soy, specifically isoflavones or genistein, have also been shown to slow prostate cancer development in the lab.

However, when moving these nutrients to the clinic, researchers were faced with a number of problems. Because the polyphenols and isoflavones seem to exert their effect on prostate cancer through a variety of different mechanisms, the ideal patient population for their benefits remains unknown, and the precise amounts needed to demonstrate the benefits are unclear. Nevertheless, research in this area continues to expand, with the hope of identifying another set of food-based compounds that can be easily incorporated into the diet and that can have a measurable effect on the risk of developing prostate cancer.

The Benefits Of Green Tea — And Red Wine?

Polyphenols have been shown to interrupt the growth pathways of cancer cells, preventing normal cells from transforming into cancerous ones, and promoting death in cancer cells.^[11] This finding would imply that their benefits might best be seen in men with earlier stages of disease, when the cancer cells are first growing, and when disease growth can be halted or prevented.

But other studies have shown that polyphenols inhibit angiogenesis, the process by which tumor cells form new blood vessels to accelerate their own growth.^[12] This and related processes are typically seen when the tumor is spreading to distant sites, implying

that polyphenols would be most helpful in men with metastatic disease.

If polyphenol foods can be helpful in both settings, why aren't we drinking more polyphenol-rich green tea? Unfortunately, the quantities used to induce a positive response in the lab can often exceed normal consumption amounts. For example, in one study of 62 men with high-grade intraprostatic neoplasia, a precursor to prostate cancer, researchers found a significant decrease in the number of men who developed prostate cancer after ingesting polyphenol-rich green tea extracts — but the amount given was the equivalent of drinking over 10 cups of tea per day.^[13] Although that might be par for the course in Asian diets, it's likely far above what the average Westerner will consume regularly.

But other studies have shown that there might be easier ways to increase your intake of polyphenol-rich foods. Because red wine is also rich in polyphenols, a number of researchers have explored whether increasing red wine consumption can alter the risk of developing prostate cancer. Results to date have been mixed. Data from the Health Professionals Follow-Up Study showed only a weak association between overall alcohol intake and prostate cancer risk, and no association at all between red wine intake and prostate cancer risk.^[14] However, a smaller study of men in the Seattle area showed a strong association between red wine intake and prostate cancer risk, with each additional glass per week reducing the risk of developing prostate cancer by nearly 6%.^[15] Pomegranate juice, also rich in polyphenols, has also shown some promise. Confirming data seen in the lab, results from a small study of 48 men with a rising PSA after surgery or radiation therapy demonstrated that drinking 8 oz of pomegranate juice daily can slow the rate at which the disease progresses.^[16] Whether red wine, pomegranate juice, or other polyphenol-rich foods will ultimately prove beneficial in this area remains unknown, but the implication that only small changes in diet can affect prostate cancer development and progression is certainly encouraging.

What About Soy?

As with the polyphenols, studies have shown that isoflavones from soy, specifically genistein, daidzein, and equol (which is formed by bacteria in the gastrointestinal tract by some people), interrupt cell growth pathways and angiogenesis, and therefore might slow both the development and progression of cancer cells. In addition, isoflavones have been shown to influence the production, metabolism, and excretion of testosterone and estrogens, hormones that can play important roles in the development and spread of prostate cancer.^[17]

Unfortunately, assessing the potential effects of soy-based foods on prostate cancer growth has proven challenging. While decreased prostate cancer growth was associated with daidzein, but not genistein, in one study,^[18] the association was found to be true for all isoflavones in a second study.^[19] Why the difference? The first study was conducted in Caucasian men, in whom the average daily intake was extremely low, less than 3 mg. But the second study was conducted in Chinese men, whose average daily intake was over 70 mg — far higher than that seen in Western cultures.

So is the answer simply a question of increasing the amount of soy consumed? Not necessarily. Increased amounts can certainly provide benefit to some men, but identifying the ideal group still remains a challenge. One study evaluating the benefits of 100 mg of soy isoflavone daily in men with a rising PSA did not show a significant enough decrease in PSA levels to indicate that the tumors had shrunk. However, the increased soy did show stabilized PSA levels in most men who had undergone surgery or radiotherapy, and showed a slowing in the rate at which the PSA rises in nearly all men enrolled.^[20] By contrast, a study evaluating the benefits of 83 mg of soy showed no difference in either PSA levels or in the rate at which PSA rises.^[21]

New research is exploring whether the benefits of isoflavones relate more to the processing of the nutrient in the body rather than to the quantity consumed, or whether their hormone-dependent actions and their ability to affect circulating testosterone are the more important factors. A better understanding of these mechanisms will help researchers identify those more likely to benefit from soy-based foods, and will allow them to better evaluate the effects of isoflavones on prostate cancer growth and development.

So What Does This All Mean?

The effects of polyphenols on the development and progression of prostate cancer remain unclear, and whether the addition of polyphenols to the diet by drinking green tea and/or red wine might prove beneficial remains unknown. In the meantime, replacing a cup or two of other less-healthy drinks with green tea is a simple way of adding polyphenols to your diet, but for obvious reasons, too much red wine should most certainly be avoided.

When it comes to isoflavones, the jury is still out on how and why they work, but increased consumption of soy-based foods would seem to be beneficial in slowing the disease process. However, because not all soy-based foods are high in isoflavones and some preparations can be high in fat and low in nutritious value, be sure to discuss the value of adding different types of soy-based foods into your diet with your doctor and/or qualified nutritional consultant.

POINTS TO REMEMBER

1. Polyphenols found in green tea and red wine as well as isoflavones found in soy-based foods have both shown anti-cancer effects in laboratory studies, but it has been difficult to confirm these effects in human clinical studies.
2. Any anti-cancer effects of green tea requires drinking six or more cups per day, and whether there is an anti-cancer benefit to red wine consumption is unclear.
3. Increased consumption of soy products has shown some effect on slowing the rate of PSA rise in several studies, but not all patients responded in the same manner and the results have been inconclusive.
4. Until the effects of these food-based compounds become clearer, it is difficult to recommend their use for preventing and/or slowing the development and progression of prostate cancer.

The Building Blocks: Vitamins and Minerals

The vitamins and minerals found in all foods play an important role in helping to regulate the body’s many processes and functions. As we will discuss in more detail in this section, some of these vitamins and minerals help monitor the balance between cell growth and cell death, and particularly between cancer cell growth and cancer cell death. When this balance is upset, cancer cells can multiply and spread.

Because there are many overlapping layers of control regulating the uncontrolled growth of cancer cells, it’s impossible to point to any specific misstep that can be targeted and corrected through nutritional approaches. Nevertheless, continuing research over the years has shown that the loss of a number of vitamins and minerals can contribute to uncontrolled cancer cell growth — and that, conversely, increased ingestion through foods or supplementation can slow the development and/or progression of the disease.

The challenge, of course, is to figure out how to maximize the benefits from each vitamin or mineral, and to identify the patient population that will benefit most. And, as with all nutritional approaches, it is this area that has proven most difficult.

The best way to increase vitamin and mineral intake is by eating a wide variety of healthy foods

<i>Vitamins and Minerals</i>	<i>Foods</i>
Vitamin A	Apricots, lettuce, spinach, chicken livers
Vitamin B6	Fortified cereals, chickpeas, nuts
Vitamin C	Citrus fruits and juices, red peppers, grape juice
Vitamin D	Sunlight, fortified milk
Vitamin E	Fortified cereals, tomato-based products, nuts, spinach
Beta-carotene	Carrots, pumpkin, sweet potatoes, spinach
Calcium	Dairy products, collard greens, sardines with bones
Lycopene	Tomato-based products, watermelon, pink grapefruits, guava, papaya
Selenium	Nuts, fish, whole-grain wheat flour, garlic
Zinc	Raw or cooked oysters, beef, crab

Source: U.S. Department of Agriculture, Agricultural Research Service. 2004. USDA Nutrient Database for Standard Reference, Release 17. Available at http://www.nal.usda.gov/fnic/foodcomp/Data/SR17/wtrank/wt_rank.html.

Beta-Carotene, Vitamin E, and Selenium: The Debate Continues

As we noted earlier, the greatest amount of research in the quest to find nutritional interventions for prostate cancer has focused on identifying the specific compounds and chemicals that are most likely to offer some benefit.

Early studies had shown that vitamin E, selenium, and beta-carotene, which is converted into vitamin A in the intestines, all seem like good candidates in preventing the growth of cancers in general.

The Alpha-Tocopherol and Beta-Carotene trial was primarily designed to assess the effect of both beta-carotene and a form of vitamin E known as alpha tocopherol on the risk of lung cancer in male smokers in Finland.^[22] Neither supplement had a significant effect on lung cancer; in fact, lung cancer was seen more frequently in the beta-carotene group. However, the effects of vitamin E on prostate cancer were quite striking: supplementation decreased the risk of developing prostate cancer by 32% and decreased the risk of dying from prostate cancer by 41%.

Unlike with vitamin E, this study did not establish a clear link between beta-carotene and prostate cancer. Nevertheless, data from the Physicians' Health Study showed that beta-carotene supplementation can be beneficial. In those who started out with very low levels of beta-carotene and lycopene in their bloodstreams, the vitamin decreased the risk of developing prostate cancer — but it *increased* the risk by about the same rate in those who started with high levels of beta-carotene in their bloodstreams.^[8,23]

Because the Alpha Tocopherol and Beta-Carotene trial was conducted in smokers, some have wondered whether the benefits of vitamin E might be limited to this smaller segment of the population. In 1992, the American Cancer Society mailed questionnaires to over 70,000 men aged 50-74 to obtain diet and lifestyle information. In this group, the use of vitamin E showed no decrease in prostate cancer risk, even in those who reported taking supplements at least 4 times a week.^[24] As with the Alpha-Tocopherol and Beta-Carotene trial, some benefit was seen in smokers, possibly suggesting that, when it comes to prostate cancer, vitamin E might best be suited to men who are already subjected to substances known to cause damage to the body's cells, such as smoking.

This question of a benefit being limited to only specific groups of men might also be true of selenium, a mineral that is found in plant foods, meats, and seafood. The first indication that selenium might play a role in reducing the risk of prostate cancer was seen in the mid 1990s as an incidental finding in a clinical trial examining the effects of selenium on reducing the risk of nonmelanoma skin cancer in high-risk individuals.^[25] After about seven years of follow-up, the researchers' hypothesis was proved wrong, as results showed that selenium supplementation had no significant effect on the incidence of skin cancer. However, the risks of developing other cancers were markedly reduced — including a 50% reduction in the risk of developing prostate cancer.^[26]

Following on these results, investigation into the benefits of selenium supplementation and a reduction in prostate cancer risk continued. In men enrolled in the Health Professionals Follow-Up Study, researchers found that increasingly longer-term consumption of selenium was associated with a lower risk of developing prostate cancer.^[27] Here, too, identifying those men who can benefit most remains unclear. In the Physicians' Health

Study, the association was strongest in men who had a PSA over 10 ng/mL at initial diagnosis, but in the original skin cancer study, the strongest association was seen in men with PSA levels between 4 ng/mL and 10 ng/mL.^[25,28]

To help answer some of the outstanding questions related to these vitamins and minerals, and to better identify the specific groups that might benefit most from both vitamin E and selenium supplementation, the National Institutes of Health has launched the Selenium and Vitamin E Chemoprevention Trial (SELECT), the largest cancer prevention trial evaluating nutrition supplementation ever attempted. Over 30,000 healthy men have been randomized to selenium alone, alpha-tocopherol alone, or the combination for a minimum of 7 years and a maximum of 12 years. Enrollment in this trial began in 2001 and was completed in 2004; the first set of results is anticipated in 2006.

So What Does This All Mean?

Supplementation with additional beta-carotene can be helpful in men who have very low levels of the vitamin, but cannot be recommended at this time because of the potential for an increased risk of lung cancer. The data on selenium and vitamin E are less clear, and many of the true benefits of these elements will likely remain unknown until the results from SELECT are available. For now, the best advice is to carefully monitor your intake of vitamin and mineral supplements to ensure that you're staying within the recommended guidelines, paying particular attention to the amount of vitamins and minerals you're already consuming in your daily multivitamin.

Remember that much of the benefit seen with beta-carotene, vitamin E, and selenium can also be obtained by eating foods that are high in all of these nutrients, specifically fruits and vegetables that are yellow, red, or deep green in color. Although the dietary form of vitamin E is slightly different than that used in most supplements, researchers have shown that the alpha form in supplements and the gamma form in food are both beneficial when it comes to fighting prostate cancer.^[29]

POINTS TO REMEMBER

1. Data from a large, long-term study showed that beta-carotene supplementation in men with low levels of the vitamin in their bloodstreams can decrease the risk of developing prostate cancer, but another long-term study showed that it can increase the risk of lung cancer.
2. Vitamin E supplementation can decrease the risk of developing and dying of prostate cancer, but seems to be most effective in men who are smokers.
3. In one large, long-term study, consumption of selenium was associated with a lower risk of developing prostate cancer, but the benefits might differ depending on each person's PSA levels.

The Ups and Downs of Zinc, Calcium, and Vitamin D

Although high levels of certain vitamins and minerals can negatively affect the development of prostate cancer, as we'll see below, they can also be beneficial in preventing or delaying development of other diseases or disorders. Knowing your personal risk factors for developing prostate cancer and other diseases will help inform your decisions about the benefits of supplementation.

Zinc is a mineral that is found in almost every cell and is essential to many cellular processes. Among other functions, it has been shown to play a role in maintaining a

healthy immune system and in facilitating wound healing. Zinc is abundant in many food sources, including red meat and poultry, beans, nuts, seafood, and whole grains, and can also be found in fortified breakfast cereals.

Because only small amounts of zinc are needed by the body, the average person can usually obtain sufficient amounts through a

well-balanced diet. Nevertheless, zinc has become a standard component in nearly all multi-vitamins and is often taken in doses up to 10 times the recommended amounts.

For unknown reasons, zinc tends to accumulate more in the prostate than in any other location in the body, and early studies in the laboratory suggested that this may offer some protection against prostate cancer cell growth.^[30] However, as data from the Health Professionals Follow-Up Study demonstrate, too much zinc can cause this potentially protective system to backfire.

Analyzing questionnaires completed by the study participants, the researchers found that the average intake was 143 mg per day — or 13 times the recommended daily dose. At these extraordinarily high levels, the protective effects of zinc were overshadowed by its toxic effects. Those who took supplements of over 100 mg per day and those who took supplements for at least 10 years were more than twice as likely to develop advanced prostate cancer compared with those who didn't take supplements at all.^[31]

Although these data imply that avoiding zinc supplementation would seem to be a good idea, 80 mg of zinc per day — nearly 8 times the recommended level — was shown to significantly decrease the risk of disease progression in patients with advancing age-related macular degeneration, the leading cause of legal blindness in people over age 65.^[32] Unfortunately, this is precisely the same age group that is so greatly affected by prostate cancer, and striking a balance between the two can be challenging.^[33]

The same problem is seen with calcium — oversupplementation can lead to an increased risk of developing advanced prostate cancer, but somewhat lower levels of supplementation

Knowing your personal risk factors for developing prostate cancer and other diseases will help inform your decisions about the benefits of supplementation.

can play an important role in protecting against osteoporosis caused by hormone therapy.

Studies have shown that a particularly active form of vitamin D known as 1,25(OH)₂D₃ can protect against growth of prostate cancer cells. In fact, recent data from the Physicians' Health Study indicate that those with high levels of vitamin D in their bloodstreams have as much as a 45% reduction in the risk of developing aggressive prostate cancer.^[34] However, increased intake of calcium lowers the vitamin D levels in the body, and therefore minimizes its protective effects.

Men enrolled in the Health Professionals Follow-Up Study who consumed over 2000 mg of calcium each day had a nearly 5-fold increased risk of developing metastatic prostate cancer compared with those consuming less than 500 mg each day.^[35] Similarly, data from a Swedish study indicate that men who consumed more than 1183 mg of calcium each day had a higher risk of developing prostate cancer compared with those consuming less than 825 mg each day.^[36]

So how much is too much? Data from the Physicians' Health Study showed that each additional increase of 500 mg calcium per day conferred a 16% increase in prostate cancer risk, and that each additional increase of 300 mg of calcium each day significantly lowered levels of 1,25(OH)₂D₃.^[37]

However, keeping calcium intake low is not necessarily a smart move. Both calcium and vitamin D can play important roles in staving off osteoporosis, a disorder that is typically associated with older, postmenopausal women, but that is increasingly being seen in men with prostate cancer undergoing hormone therapy. Researchers have estimated that between 10% and 40% of men with advanced prostate cancer have osteoporotic fractures depending upon the duration of hormone therapy — over and above the 25% of men in the general population whose fractures are caused by the naturally weakened bones of older age.^[38]

Studies have not been conducted on the use of vitamin D and calcium in men at risk for osteoporosis due to hormone therapy, but data seen with postmenopausal women would indicate that 1000-1500 mg of calcium and 400-800 IU of vitamin D each day can help to keep bones strong as part of a preventive regimen for osteoporosis and fracture.^[39] Unfortunately, low levels of vitamin D have been noted in up to 40% of men with prostate cancer, so ensuring that adequate levels of this vitamin are maintained is particularly important.^[39]

So What Does This All Mean?

Building an effective preventive strategy oftentimes means weighing the risks of one disease against another, and trying to find the middle ground between the two. Discussion with your doctor or qualified nutrition consultant about your particular risk factors for one disease or disorder over another will likely help you find that middle ground, and will therefore help you find the nutritional approach that's right for you.

POINTS TO REMEMBER

1. Although high levels of certain vitamins and minerals can increase the risk of developing prostate cancer, they can also be beneficial in preventing or delaying development of other diseases or disorders.
2. One long-term study showed that high doses zinc increases the risk of developing prostate cancer, but a second large study showed that it can improve outcomes in men with age-related macular degeneration.
3. Data from a large, long-term study showed that too much calcium can increase prostate cancer risk and reduce the levels of prostate-cancer-protective vitamin D, but both calcium and vitamin D can play important roles in delaying osteoporosis, a disorder that is increasingly being seen in men with prostate cancer undergoing hormone therapy.
4. Discussion with your doctor or qualified nutrition consultant about your particular risk factors for one disease or disorder over another will help you find the nutritional approach that's right for you.

The Benefits and Drawbacks of Supplementation

It is a common American misconception that if something is good, more of it must be better, and that if something comes in the form of a pill, it's even better. Unfortunately, neither assumption is always true, and the megadoses in some supplement preparations can be harmful.

Because we tend to eat a wide variety of foods and much of our packaged foods — from cereals to orange juice — is fortified with additional vitamins and minerals, true vitamin and mineral deficiency tends to be uncommon in the United States. Therefore, some of the available preparations constitute less a *supplement* and more an *oversupplement*. Why is this a problem? Certain vitamins, such as vitamins A, D, E, and K, are not easily excreted by the body. If taken in extremely high doses, they can build up over time and cause damage to the body's systems.

As you explore the possibility of adding vitamin-rich foods and/or supplements to your diet to help delay prostate cancer development or progression, talk with your doctor or qualified nutrition counselor about establishing a safe balance between healthful vitamin intake and oversupplementation. Remember, vitamin and mineral supplements are meant to be just that, supplements. They should not be used lieu of smart food choices but should be used judiciously in the appropriate setting.

Staying within the recommended ranges for vitamin and mineral intake is a smart choice

	Recommended Intake*	Upper Intake Level†
Vitamin A	3,000 IU/day	10,000 IU/day
Vitamin B6	1.7 mg/day	100 mg/day
Vitamin C	90 mg/day	1,800 mg/day
Vitamin D	400 IU/day	2,000 IU/day
Vitamin E	22.5 IU/day	1,500 IU/day
Calcium	1,200 mg/day	2,500 mg/day
Selenium	55 µg/day	400 µg/day
Zinc	11 mg/day	40 mg/day

Values are for healthy males aged 19-70.

*Recommended dietary allowances or adequate intakes to be used as goals for individual intake.

†The maximum level of daily nutrient intake that is likely to pose no risk of adverse effects; represents total intake from food, water, and supplements.

Source: Institute of Medicine of the National Academies. Dietary reference intakes. Available at <http://www.iom.edu/Object.File/Master/21/372/0.pdf>.

Dietary Fats and Red Meat: Rethinking the American Way

Red meat is an excellent source of protein, iron, zinc, vitamin B6, and vitamin B12, yet the so-called “Western-style diet” that is high in red meat and animal fats and low in fiber, fruits, and vegetables has long been associated with increased risk of obesity, heart disease, and certain cancers.

Unfortunately, this lesson has been hard learned by some immigrant groups. Results from a number of studies suggest that the “Western-style” diet may contribute to the higher rates of prostate cancer seen in Japanese men in the United States compared with those still living in Japan, and may also contribute to their increased risk of dying from prostate cancer.^[10,40] Of note, since the

For every extra bite of meat that's eaten, there's a bite of vegetable that's going uneaten.

1950s, Japan has experienced large increases in the incidence and mortality from prostate, breast and colon cancer, coincidental with the growth of Western influences on lifestyle; China is also beginning to show such trends as it follows this path.

Most people set an upper limit on the quantity of food that they consume on an average day. This means that for every extra bite of meat that's eaten, there's a bite of vegetable that's going uneaten. One contributing factor to the link between the Western diet and cancer might therefore simply be the lack of a positive effect of fruits and vegetables.

But is there something more than just the lack of a protective effect of the “good” foods? Is there something in red meat and other sources of dietary fat that can actually *increase* the risk of developing cancer?

In studying the effects of dietary fat and red meat on prostate cancer, two possible mechanisms have been offered: one focusing on the type of fat and the other focusing on the cooking method. Although the data are still preliminary in both of these areas, results to date suggest that dietary fats and red meat can negatively influence the growth of prostate cancer cells and therefore deserve attention.

First, what is the contribution of fats in general to health and well-being? Much has been made in the past decade of the increasing rates of obesity and of obesity-related disorders such as diabetes and cardiovascular disease. Nevertheless, dietary fat intake is by no means the only factor at play with regard to the increasing rates of obesity in the United States. Simply cutting back on fat has little impact on weight if your diet remains high in calories. And, of course, cutting out fat altogether should never be attempted, as the body utilizes different types of fat in a number of its regular processes, including building cell membranes and transporting certain vitamins and nutrients.

A truly healthful, nutritionally balanced diet should consist of moderate amounts of all different types of food, in combination with a regular exercise program.

The Skinny On Fat

Before we start to look at how different types of fat might affect prostate cancer risk, let's review what fat is, where it comes from, and what it does.

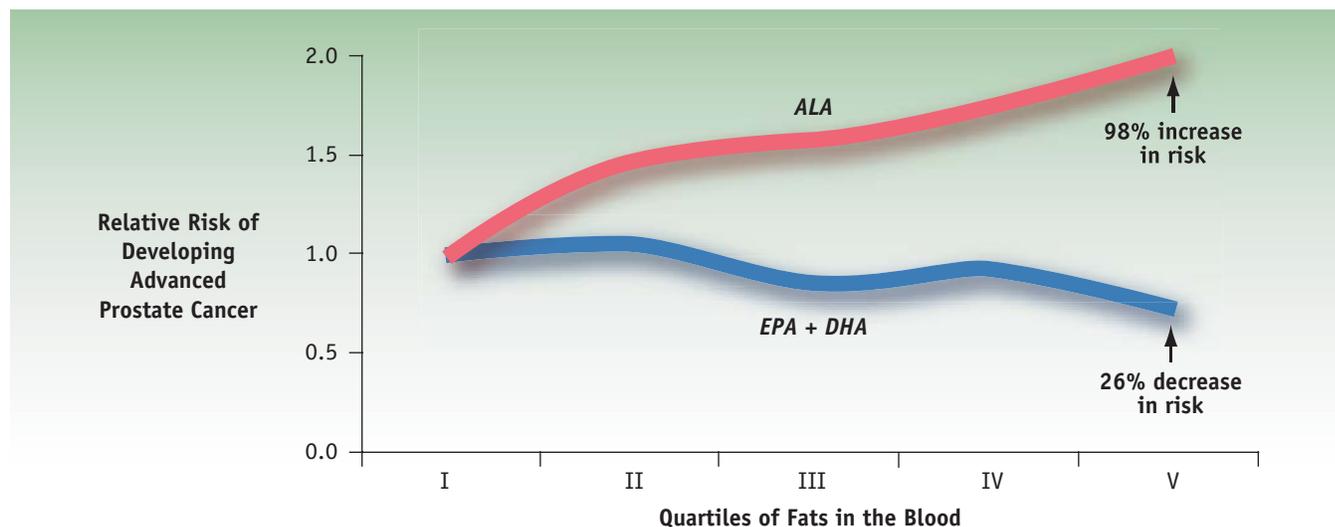
Fat is one of three main types of nutrient molecules used by the body in its everyday processes. (The other two are carbohydrates and proteins.) After fat is ingested, the body breaks it down into smaller components, uses what it needs, and stores the rest for future use.

Although saturated and *trans* fats have been targeted in the fight against cardiovascular disease, more studies in prostate cancer have zeroed in on omega-3 fatty acids, found primarily in fatty fish, fish oils, and certain vegetable oils, including walnut and canola oils.

A number of years ago, the omega-3 fatty acids were studied for their beneficial effects on memory and depression, and particularly on the risk of cardiovascular disease. While the effects on memory and depression are questionable, the benefits of the omega-3 fatty acids in minimizing heart disease seem to have held true, and the American Heart Association continues to promote omega-3 fatty acids as "heart healthy."

In studies of prostate cancer, however, the equation is not so simple.

Eating red meat high in ALA can increase the risk of developing advanced prostate cancer, but eating fish high in EPA and DHA can decrease the risk



Source: Leitzmann F, et al. *Am J Clin Nutr.* 2004;80:204-216.

Using blood samples collected during the Physicians' Health Study, researchers found that men with the highest levels of the omega-3 fatty acid ALA (*alpha-linolenic acid*) in their bloodstreams were three times as likely to develop prostate cancer compared with those in whom the fatty acid could not be detected.^[41] Similarly, data from the Health Professionals Follow-Up Study showed that men who consumed the highest amounts of ALA were approximately twice as likely to develop advanced prostate cancer.^[42] In both of these studies, as in the typical American diet, the primary source of ALA was animal and dairy products, particularly red meat.

At the same time, however, the Health Professionals Follow-Up Study found that consumption of DHA (*docosahexaenoic acid*) and EPA (*eicosapentaenoic acid*), two omega-3 fatty acids found mostly in fatty fish, was associated with a *lower* risk of developing advanced prostate cancer. In fact, eating the equivalent of 3 servings of fish per week cut the risk of developing advanced prostate cancer in half.

Similar findings were seen in a study of over 6,000 Swedish men who were tracked for nearly 30 years. Those who ate fatty fish, such as salmon, sardines, and herring, reduced their risk of developing prostate cancer by 30%, while those who ate no fish had a nearly 3-fold higher risk of developing prostate cancer.^[43]

ALA is an essential fatty acid, meaning it cannot be synthesized by the body, that is used as the building block for certain cellular processes. Therefore, eliminating it from the diet cannot be recommended. Nevertheless, replacing red meat with fatty fish one or two times a week would seem to be a good way to swap out some of the "bad" fat and replace it with some of the "good" fat. And before going off to the health food store to increase your intake of DHA and EPA, keep in mind that the benefits did not extend to those men who were taking fish oil supplements.

POINTS TO REMEMBER

1. The so-called "Western-style diet" that is high in red meat and animal fats and low in fiber, fruits, and vegetables has long been associated with increased risk of obesity, heart disease, and certain cancers.
2. Although the role of saturated fats in prostate cancer remains unknown, a number of studies have shown that different types of omega-3 fatty acids can affect the risk of developing prostate cancer: ALA (*alpha-linolenic acid*), an omega-3 fatty acid found in dairy products and red meat, increases the risk of developing advanced prostate cancer, while DHA (*docosahexaenoic acid*) and EPA (*eicosapentaenoic acid*), two omega-3 fatty acids found mostly in fatty fish, lowers the risk of developing prostate cancer.

The Drawbacks Of Grilling Meat

For the average American, it's nearly impossible to think about red meat without picturing a barbecue grill. Unfortunately, the charring caused by this quintessential American pastime has been linked to a host of cancer-causing substances, or carcinogens.

HAs (*heterocyclic amines*), a group of carcinogens identified first in the 1970s, were added this year by the Department of Health and Human Services to the list of substances "reasonably anticipated to be human carcinogens."^[44] The HA known as *PhIP* is found in grilled beef, pork, chicken, lamb, and fish, and was estimated to comprise about two thirds of the daily HA intake in a study of over 25,000 people conducted by the US Department of Agriculture.^[45]

Studies in animals have shown that PhIP exposure can lead to the development of prostate cancer, but the quantities used in the animals were nearly 1000 times higher than the average daily intake in humans,^[46] raising the question of whether the average man would see a change in risk from his typical diet.

A review of self-reported dietary habits of over 300 men with prostate cancer in New Zealand showed little association between the risk of developing prostate cancer and meat-cooking practices or estimated HA intake.^[47] However, other researchers have shown that self-reported "done-ness" of meat might not be a good indicator of the actual concentration of PhIP in grilled meat, so the question of whether PhIP can directly cause human prostate cancer remains open.^[48]

In the meantime, researchers have been looking at strategies to reduce the amount of PhIP in the diet. Because carcinogens are formed through direct contact with an open flame, one group of researchers examined whether reducing the amount of charring can reduce the amount of PhIP.^[49] Although the amount of PhIP in the meat patty increased as the grill temperature increased, significant reductions in PhIP were noted when the patty was flipped multiple times, presumably because the patty was less charred.

A second group of researchers explored the possibility of reducing the effects of PhIP in the body by increasing the intake of cruciferous vegetables, which, as we saw earlier, have been shown to help clear out carcinogens from the body before they can wreak havoc. At the end of each of the three 12-day phases of the study, the enrolled men ate a well-done steak, but during second phase, they also ate 500 g of Brussels sprouts and broccoli. Examination of the urine at the end of the second phase showed an increase in the amount of PhIP excreted, indicating that the cruciferous vegetables helped to clear the carcinogen from the body before causing long-term harm. Unfortunately, the benefit was limited, and the amount of PhIP excreted rose again during the third phase when the vegetables were absent.^[50]

So What Does This All Mean?

Although the role of dietary fat and red meat in the fight against prostate cancer remains somewhat unclear, findings to date seem to indicate that limiting the intake of red meat might decrease the risk of developing prostate cancer. Start experimenting with new methods for cooking lean red meat — stewing, roasting, or even broiling — and begin to incorporate more fish into your diet. Keep in mind, however, that fish at the top of the food chain, such as king mackerel, tilefish, shark, and swordfish, have high levels of mercury and should therefore be eaten in moderation.

The backyard barbecue will always be a staple in the United States, so dietary changes that try to eliminate charred and grilled meat completely are unlikely to prove realistic in the long-run. Therefore, when you barbecue, be careful to minimize charring of the meat by flipping the meat multiple times, or by scraping off the charred portion before eating. Lower the flame and grill at a lower temperature, but don't undercook the meat in your zeal to reduce carcinogens caused by the heat.

Keep in mind that the goal, as with all dietary and nutritional approaches, is not to impose harsh restrictions on your daily life. Radical dietary changes tend to be difficult to sustain over long periods of time, so their potential benefits are often not realized. Rather, you should work with your doctor or qualified nutritional counselor to formulate a plan that incorporates a wide variety of different types of healthful foods and that attempts to eliminate, as much as possible, those foods that might adversely affect your risk of developing prostate cancer.

POINTS TO REMEMBER

1. Exposure to high levels of a cancer-causing substance known as PhIP, which is found in grilled meats, has been associated with the development of prostate cancer in laboratory animals.
2. In humans, lowering the grill temperature and minimizing char on the meat resulted in lower absorption of PhIP, as did an increase in cruciferous vegetable intake.
3. Although further research in this area is needed to help define the optimal strategy for reducing exposure to cancer-causing substances, flipping the meat more frequently while grilling to avoid char can help play a role in minimizing their effect on cancer risk.

Charting a Course for the Road Ahead

There's no question that the dietary and lifestyle habits of Americans have changed significantly over the past few decades, and, for the most part, it hasn't been for the better. On the whole, we're fatter, we exercise less, and we're developing heart disease, diabetes, and cancer at rates our grandfathers never could have imagined.

To combat this trend, many people go to extremes. Cut out the carbs, and focus on the proteins, or cut out the proteins and focus on the carbs. Only fruits in the morning and vegetables in the afternoons, or fruits and vegetables all day long as long as they're not eaten together. Although some of these diets might help some people lose

weight initially, none of them teach people how to make smart choices over the long term. So when they find themselves stuck in an airport for four hours with nothing but old wilted salad and cranberry juice cocktail as the healthy options, they end up standing in line with everyone else ordering the extra large soft drink and two donuts to go.

Nutritional strategies in the management of prostate cancer are no different. If you renounce all animal products, you will, by definition, maximize your intake of nutrient-rich fruits and vegetables. But what happens when the choices are limited? Do you know how to make smart choices with what you have in front of you? Or can you only stick to your diet if you're within 100 yards of a health-food store?

A recent study evaluating four popular weight-loss plans showed that the majority of the dieters dropped out within just a few months. But those who were enrolled in programs that could be more easily adaptable to the ups and downs of everyday life stuck to their diets for a longer time. The lesson here is clear: integrate smarter choices gradually, making simple, small changes to your existing diet on a regular basis. After just a few short months, you'll be set on a road toward a healthier lifestyle.

Dietary and lifestyle habits of Americans have changed significantly over the past few decades: we're fatter, we exercise less, and we're developing heart disease, diabetes, and cancer at rates our grandfathers never could have imagined.

POINTS TO REMEMBER

1. Any attempt to combat the trend of the increase in obesity in the United States is important, but extreme or fad diets don't teach people how to make smart choices over the long term.
2. A recent study evaluating four popular weight-loss plans showed that those who were enrolled in programs that could be more easily adaptable to everyday life stuck to their diets for a longer time.

Changing Your Dietary Habits One Tomato at a Time

Although cutting back on food intake and managing portion size are important for weight management strategies, remember that when it comes to prostate cancer, the *quality* of the food is often more important than the *quantity*.

Suppose instead of pouring an Alfredo sauce on your bowl of fettuccini, you use a tomato-based sauce with fresh tomatoes, broccoli florets, and small chunks of grilled tuna? You've just added lycopene, sulforaphane, and omega-3 fatty acids. Morning coffee? Skip the skim and add in some soy milk that's chock full of isoflavones. The boys coming over to watch the game? Assuming crudités and tofu dip aren't an option, try replacing the chips and dip with baked, fat-free chips and lycopene-rich salsa.

Because none of these changes require you to completely overhaul your existing diet, they can more easily become integrated into your normal routine. However, they will all require you to pay attention to what you eat, to alter your food shopping habits, and to think creatively when you go out to eat.

Planning Ahead

Before you go food shopping, sit down for a few minutes and think about what you eat on an average day. If you know you like to snack in the later afternoons, add vegetable chips to your list. If you usually drink orange juice at lunch, throw a container or two of tomato juice into your cart. If you relax with a cup of herbal tea after dinner, try replacing it with green tea. The more options you have on hand, the easier it'll be to make smarter choices, and the easier it'll be to incorporate your choices into your everyday routine.

Of course, it's far easier to make those smart choices when you're in your own "safe"

environment and when you have free access to healthful foods. How do we make smart choices when we're out in the real world?

Although it might not be apparent from the menu, nowadays, almost every restaurant, fast food joint, and even small sandwich shop has healthy food. The key is to

think before you order and to consider whether there are better options to be had before you get ready to order the usual. Skip the double cheeseburger and go for the grilled chicken sandwich with extra lettuce and tomato, using ketchup instead of dressing. It's rare that there are no smart choices available at all, but finding them might require some creativity and persistence — two qualities that are essential to achieving your goal of slowing the development and progression of prostate cancer.

It's rare that there are no smart food choices available, but finding them might require some creativity and persistence.

Nutritional Approaches and Therapeutic Strategies Going Hand in Hand

Dietary and lifestyle changes can play an important role in slowing the growth of prostate cancer, but they should *complement*, not replace, any drug therapy, surgery, and/or radiation treatments that might be recommended by your physician. Be sure to talk with your doctor before initiating any nutritional approaches, particularly if you have any medical conditions that affect your diet and lifestyle, such as diabetes or heart disease.

Remember, as with the foods that you put into your body, it's the *quality* of the effort that counts, not the *quantity*. A diagnosis of prostate cancer is the beginning of your journey, not the end. Every small step toward a healthier lifestyle is important and will ultimately contribute to your efforts in battling this disease.

References

- National Center for Health Statistics. Health, United States, 2004. Hyattsville, Maryland: 2004.
- Presti JC Jr. Obesity and prostate cancer. *Curr Opin Urol.* 2005;15:13-16.
- Key TJ, Allen N, Appleby P, et al. Fruits and vegetables and prostate cancer: no association among 1104 cases in a prospective study of 130544 men in the European Prospective Investigation into Cancer and Nutrition (EPIC). *Int J Cancer.* 2004;109:119-124.
- Giovannucci E, Rimm EB, Liu Y, Stampfer MJ, Willett WC. A prospective study of cruciferous vegetables and prostate cancer. *Cancer Epidemiol Biomarkers Prev.* 2003;12:1403-1409.
- Giovannucci E, Rimm EB, Liu Y, Stampfer MJ, Willett WC. A prospective study of tomato products, lycopene, and prostate cancer risk. *J Natl Cancer Inst.* 2002;94:391-398.
- Chan JM. Diet after diagnosis and the risk of prostate cancer progression. Presented at the Prostate Cancer Foundation 11th Annual Scientific Retreat; October 21-24, 2004; Lake Tahoe, Nevada. Abstract 6.
- Boileau TW, Liao Z, Kim S, Lemeshow S, Erdman JW Jr, Clinton SK. Prostate carcinogenesis in N-methyl-N-nitrosourea (NMU)-testosterone-treated rats fed tomato powder, lycopene, or energy-restricted diets. *J Natl Cancer Inst.* 2003; 95:1578-1586.
- Gann PH, Ma J, Giovannucci E, et al. Lower prostate cancer risk in men with elevated plasma lycopene levels: results of a prospective analysis. *Cancer Res.* 1999;59:1225-1230.
- Canene-Adams K, Clinton SK, King JL, et al. The impact of diets containing tomato, broccoli, or lycopene or receiving finasteride on the growth of Dunning R-3327-H transplantable prostate adenocarcinomas in rats. Presented at the International Research Conference on Food, Nutrition, and Cancer; July 15-16, 2004; Washington, DC. Abstract 47.
- Whittemore AS, Kolonel LN, Wu AH, et al. Prostate cancer in relation to diet, physical activity, and body size in blacks, whites, and Asians in the United States and Canada. *J Natl Cancer Inst.* 1995;87:652-661.
- Hou Z, Lambert JD, Chin KV, Yang CS. Effects of tea polyphenols on signal transduction pathways related to cancer chemoprevention. *Mutat Res.* 2004;555:3-19.
- Adhami VM, Siddiqui IA, Ahmad N, Gupta S, Mukhtar H. Oral consumption of green tea polyphenols inhibits insulin-like growth factor-I-induced signaling in an autochthonous mouse model of prostate cancer. *Cancer Res.* 2004;64: 8715-8722.
- Bettuzzi S, Brausi M, Rizzi F, Castagnetti G, Peracchia G, Corti A. Chemoprevention of human prostate cancer by oral administration of green tea catechins (GTCs) in high grade PIN subjects: a preliminary report from a 1 year proof of principle study. *Proc Amer Assoc Cancer Res* 2005;46:Abstract 4400.
- Platz EA, Leitzmann MF, Rimm EB, Willett WC, Giovannucci E. Alcohol intake, drinking patterns, and risk of prostate cancer in a large prospective cohort study. *Am J Epidemiol.* 2004;159:444-453.
- Schoonen WM, Salinas CA, Kiemeny LA, Stanford JL. Alcohol consumption and risk of prostate cancer in middle-aged men. *Int J Cancer.* 2005;113:133-140.
- Pantuck AJ, Leppert JT, Zomorodian N, et al. Phase II study of pomegranate juice for men with rising PSA following surgery or radiation for prostate cancer. *J Urol.* 2005;173 (4 suppl):225. Abstract 831.
- Holzbeierlein JM, McIntosh J, Thrasher JB. The role of soy phytoestrogens in prostate cancer. *Curr Opin Urol.* 2005;15:17-22.
- Strom SS, Yamamura Y, Duphorne CM, et al. Phytoestrogen intake and prostate cancer: a case-control study using a new database. *Nutr Cancer.* 1999;33:20-55.
- Lee MM, Gomez SL, Chang JS, Wey M, Wang RT, Hsing AW. Soy and isoflavone consumption in relation to prostate cancer risk in China. *Cancer Epidemiol Biomarkers Prev.* 2003; 12:665-668.
- Hussain M, Banerjee M, Sarkar FH, et al. Soy isoflavones in the treatment of prostate cancer. *Nutr Cancer.* 2003;47:111-117.
- Adams KF, Chen C, Newton KM, Potter JD, Lampe JW. Soy isoflavones do not modulate prostate-specific antigen concentrations in older men in a randomized controlled trial. *Cancer Epidemiol Biomarkers Prev.* 2004;13:644-648.
- Heinonen OP, Albanes D, Virtamo J, et al. Prostate cancer and supplementation with alpha-tocopherol and beta-carotene: incidence and mortality in a controlled trial. *J Natl Cancer Inst.* 1998;90:440-446.
- Cook NR, Stampfer MJ, Ma J, et al. Beta-carotene supplementation for patients with low baseline levels and decreased risks of total and prostate carcinoma. *Cancer.* 1999;86: 1783-1792.
- Rodriguez C, Jacobs EJ, Mondul AM, Calle EE, McCullough ML, Thun MJ. Vitamin E supplements and risk of prostate cancer in U.S. men. *Cancer Epidemiol Biomarkers Prev.* 2004; 13:378-382.
- Clark LC, Combs GF Jr, Turnbull BW, et al. Effects of selenium supplementation for cancer prevention in patients with carcinoma of the skin. A randomized controlled trial. Nutritional Prevention of Cancer Study Group. *JAMA.* 1996;276:1957-1963.
- Duffield-Lillico AJ, Reid ME, Turnbull BW, et al. Baseline characteristics and the effect of selenium supplementation on cancer incidence in a randomized clinical trial: a summary report of the nutritional prevention of cancer trial. *Cancer Epidemiol Biomarkers Prev.* 2002;11:630-639.
- Yoshizawa K, Willett WC, Morris SJ, et al. Study of prediagnostic selenium level in toenails and the risk of advanced prostate cancer. *J Natl Cancer Inst.* 1998;90: 1219-1224.
- Li H, Stampfer MJ, Giovannucci EL, et al. A prospective study of plasma selenium levels and prostate cancer risk. *J Natl Cancer Inst.* 2004;96:696-703.
- Weinstein SJ, Wright ME, Pietinen P, et al. Serum alpha-tocopherol and gamma-tocopherol in relation to prostate cancer risk in a prospective study. *J Natl Cancer Inst.* 2005; 97:396-369.
- Liang JY, Liu YY, Zou J, Franklin RB, Costello LC, Feng P. Inhibitory effect of zinc on human prostatic carcinoma cell growth. *Prostate.* 1999;40:200-207.
- Leitzmann MF, Stampfer MJ, Wu K, Colditz GA, Willett WC, Giovannucci EL. Zinc supplement use and risk of prostate cancer. *J Natl Cancer Inst.* 2003;95:1004-1007.
- Age-Related Eye Disease Study Research Group. A randomized, placebo-controlled, clinical trial of high-dose supplementation with vitamins C and E, beta carotene, and zinc for age-related macular degeneration and vision loss: AREDS report no. 8. *Arch Ophthalmol.* 2001;119:1417-1436.
- Jarrard DF. Does zinc supplementation increase the risk of prostate cancer? *Arch Ophthalmol.* 2005;123:102-103.
- Li H, Stampfer M, Giovannucci E, et al. Prediagnostic plasma vitamin D levels, vitamin D receptor gene polymorphisms, and susceptibility to prostate cancer. Presented at the 2005 Multidisciplinary Prostate Cancer Symposium; February 16-19, 2005; Orlando, Florida. Abstract 2.
- Giovannucci E, Rimm EB, Wolk A, et al. Calcium and fructose intake in relation to risk of prostate cancer. *Cancer Res.* 1998;58:442-447.
- Chan JM, Giovannucci E, Andersson SO, Yuen J, Adami HO, Wolk A. Dairy products, calcium, phosphorus, vitamin D, and risk of prostate cancer (Sweden). *Cancer Causes Control.* 1998;9:559-566.
- Chan JM, Stampfer MJ, Ma J, Gann PH, Gaziano JM, Giovannucci EL. Dairy products, calcium, and prostate cancer risk in the Physicians' Health Study. *Am J Clin Nutr.* 2001;74: 549-554.
- Krupski TL, Smith MR, Chan Lee W, et al. Natural history of bone complications in men with prostate carcinoma initiating androgen deprivation therapy. *Cancer.* 2004;101:541-549.
- Higano CS. Understanding treatments for bone loss and bone metastases in patients with prostate cancer: a practical review and guide for the clinician. *Urol Clin North Am.* 2004; 31:331-352.
- Locke FB, King H. Cancer mortality risk among Japanese in the United States. *J Natl Cancer Inst.* 1980;65:1149-1156.
- Gann PH, Hennekens CH, Sacks FM, Grodstein F, Giovannucci EL, Stampfer MJ. Prospective study of plasma fatty acids and risk of prostate cancer. *J Natl Cancer Inst.* 1994;86: 281-286.
- Leitzmann MF, Stampfer MJ, Michaud DS, et al. Dietary intake of n-3 and n-6 fatty acids and the risk of prostate cancer. *Am J Clin Nutr.* 2004;80:204-216.
- Terry P, Lichtenstein P, Feychting M, Ahlbom A, Wolk A. Fatty fish consumption and risk of prostate cancer. *Lancet.* 2001;357:1764-1766.
- Report on Carcinogens, Eleventh Edition; U.S. Department of Health and Human Services, Public Health Service, National Toxicology Program. Available at <http://ntp-server.niehs.nih.gov/ntp/roc/toc11.html>.
- Bogen KT, Keating GA. U.S. dietary exposures to heterocyclic amines. *J Expo Anal Environ Epidemiol.* 2001;11:155-168.
- Stuart GR, Holcroft J, de Boer JG, Glickman BW. Prostate mutations in rats induced by the suspected human carcinogen 2-amino-1-methyl-6-phenylimidazo[4,5-b]pyridine. *Cancer Res.* 2000;60:266-268.
- Norrish AE, Ferguson LR, Knize MG, Felton JS, Sharpe SJ, Jackson RT. Heterocyclic amine content of cooked meat and risk of prostate cancer. *J Natl Cancer Inst.* 1999;91:2038-2044.
- Keating GA, Sinha R, Layton D, et al. Comparison of heterocyclic amine levels in home-cooked meats with exposure indicators (United States). *Cancer Causes Control.* 2000;11: 731-739.
- Salmon CP, Knize MG, Panteleakos FN, Wu RW, Nelson DO, Felton JS. Minimization of heterocyclic amines and thermal inactivation of *Escherichia coli* in fried ground beef. *J Natl Cancer Inst.* 2000;92:1773-1778.
- Walters DG, Young PJ, Agus C, et al. Cruciferous vegetable consumption alters the metabolism of the dietary carcinogen 2-amino-1-methyl-6-phenylimidazo [4,5-b]pyridine (PhIP) in humans. *Carcinogenesis.* 2004;25:1659-1669.

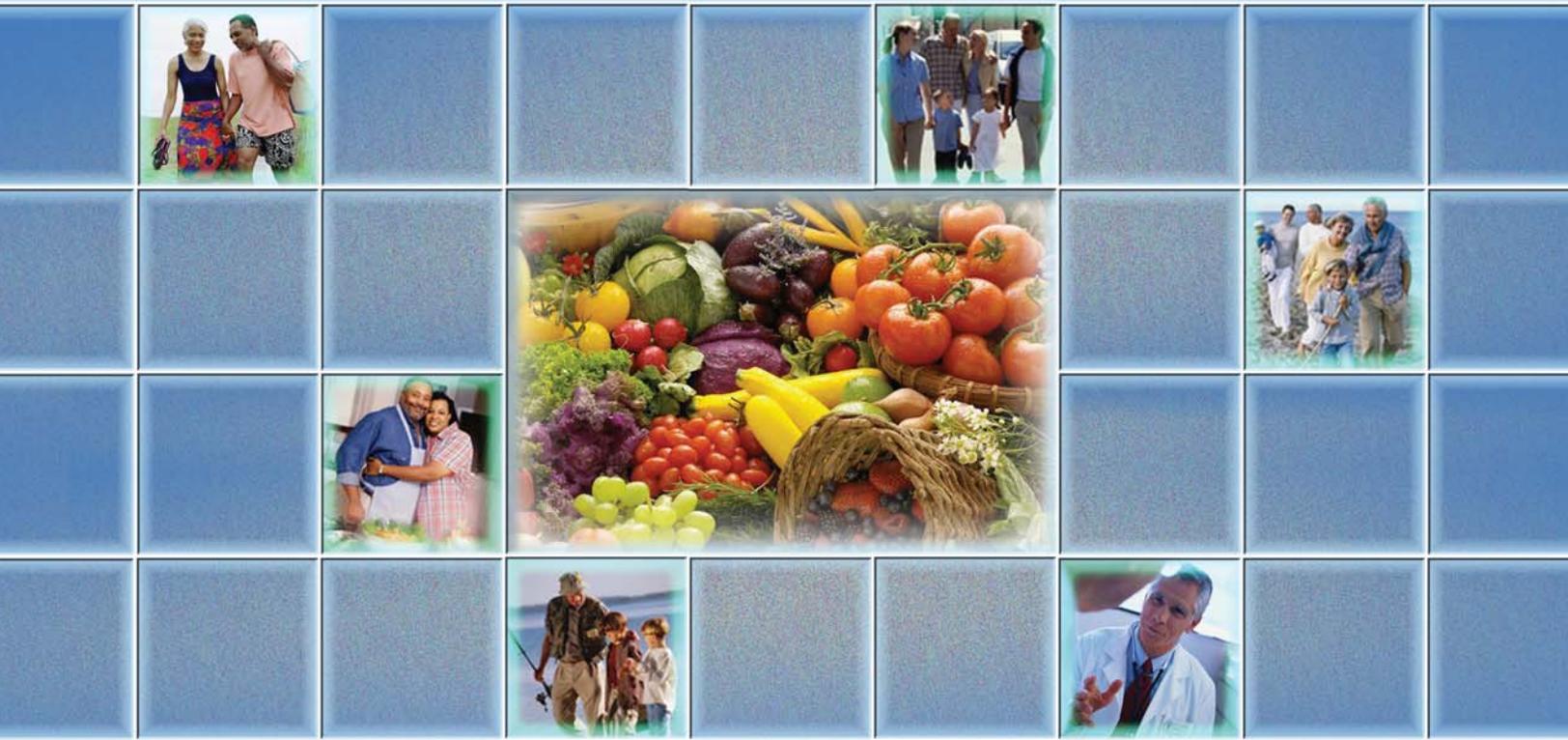


Join our Efforts: Your Role in the Future of Prostate Cancer Research

Over the past 12 years, the Prostate Cancer Foundation has provided financial support for many important advances in the field of prostate cancer research, including the discovery and early development of promising new treatments now in clinical trials, the development of gene therapy approaches to combat prostate cancer, and the development of vaccines that work with the body's immune system to kill prostate cancer cells. And because it's become clear that comprehensive therapeutic strategies must incorporate nutritional approaches, the PCF has moved foursquare behind the efforts of researchers in this area as well.

But finding better treatments and a cure for prostate cancer should not only be the mission of the PCF — it should be the mission of every man, woman, and child affected by prostate cancer. The future of prostate cancer research doesn't end in the lab. Even the most promising compounds have to be tested rigorously in the clinic to ensure that they're safe and effective in patients with prostate cancer. And we need your help to ensure that they can move from the clinic to the marketplace.

As you talk with your doctor about developing a comprehensive therapeutic strategy, find out if there is a clinical trial evaluating a new therapeutic and/or nutritional approach that might be right for you. Help us help you find better treatments and a cure for prostate cancer.



Prostate
Cancer
Foundation

1250 Fourth Street
Santa Monica, CA 90401

Tel: 800-757-CURE or 310-570-4700

Fax: 310-570-4701

Email: info@prostatecancerfoundation.org

Web: <http://www.prostatecancerfoundation.org>