HARVARD MEDICAL SCHOOL

Harvard Men's Health Watch

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Lifestyle prevention: Does it work? And why?

You started hearing it from your mom not long after you came into this world. In junior high school, your health education teacher took up the beat, and then passed the baton to your high school biology instructor. You caught a break in college (or, perhaps, you were too busy to notice), and your girlfriends had other things on their minds. But then everyone got into the act, from your wife and your doctor to your company's HR director, your insurance carrier, and the federal government. And if you've read *Harvard Men's Health Watch* for even a year or two, you've heard us preach the gospel of lifestyle prevention and therapy: live right to live well and live long.

We call it prudent advice, but you've heard it so often that it may come across as nagging. The concepts are so simple, even obvious, that they may seem trivial in a medical culture dominated by MRIs, gee-whiz surgery, and genetically engineered drugs. And although the precepts of prevention are simple, making the changes that count can be surprisingly hard. All in all, most men are tempted to drift along living like the guy next door, and many simply stay on the path of least resistance.

It's easy to wait for your doctor to roll out the latest drug or for your surgeon to stave off a crisis—but is it smart? Do lifestyle changes really work? And if so, how?

Simple but complex

Clean living sounds simple, but the devil is in the details. Only one guideline, avoiding tobacco, is simple and absolute. At the other extreme, dietary advice is rather complex, and the fine print seems to change with every new study. But even in an area as complex as nutrition, if you keep track of your overall pattern, you won't have to obsess about every morsel you eat.

At the risk of sounding like your mom, here are 10 lifestyle guidelines that matter:

1. Avoid tobacco in all its forms.
2. Eat well. That means eating more healthful foods and fewer harmful foods. *Eat more:* whole grains, fruits, vegetables and legumes, fish, low- or non-fat dairy products, and nuts and seeds. *Eat less:* red meat, whole-milk dairy products, skin of poultry, high-sodium (salt) processed foods, sweets, sugary drinks and refined carbohydrates, and trans fats.
3. Exercise regularly, including: 30 minutes of moderate exercise nearly every day, exercises for strength two to three times a week, and exercise for flexibility and balance according to need.
4. Stay lean. It's the hardest lifestyle change to achieve in our society, but even partial success will help.
5. If you choose to drink, limit yourself to one to two drinks a day, counting 5 ounces of wine, 12 ounces of beer, or 1.5 ounces of liquor as one drink.
6. Reduce stress. Get enough sleep. Build social ties and community support.
7. Avoid risky behavior, including drug abuse, unsafe sex, dangerous driving, unsafe firearm use, and household hazards.
8. Reduce exposure to toxins and radiation, including sunlight and medical x-rays.
9. Get regular medical check-ups, screening tests, and immunizations.
10. Have fun. Laughter is good medicine. Joy and optimism improve health as well as happiness. And if you make changes 1–9 slowly, steadily, and reasonably, you will enjoy your healthful lifestyle. ▸▸

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Does it work?

The short answer, of course, is yes. But a healthy lifestyle involves many variables, and it occurs in the context of genetic predispositions, socioeconomic imperatives, and biologic subtleties. Still, two studies published in 2008 demonstrate the enormous power of even a few lifestyle changes.

Living to 90

A Harvard study tracked 2,357 men who volunteered to participate in the Physicians' Health Study. Among the group, 970 men lived to age 90 or beyond. When researchers compared the men with exceptional longevity to their less fortunate peers, they identified five simple risk factors associated with a shorter life span. Three of these factors (smoking, lack of exercise, and obesity) can be corrected or modified by lifestyle changes, while the other two (high blood pressure and diabetes) can be prevented or modified by lifestyle changes, medical management, or both.

Men who were free of all five risk factors at age 70 enjoyed a 54% likelihood of living to age 90 or beyond. Even one risk factor reduced the chance of making it to 90; smoking was the most dangerous single risk factor (25% chance of survival to 90), lack of exercise the least (44% survival). Men with two risk factors at age 70 had a 22% to 36% chance of reaching age 90; three risk factors reduced the odds to between 14% and 22%; and four risk factors reduced the chance of survival even more, 9% to 11%. Men with all five risk factors had a nearly negligible 4% likelihood of living to age 90.

Living to 90 is a powerful incentive to live right. And there's more: the men with healthful behaviors also enjoyed superior physical function, mental function, and overall well-being later in life.

Gaining 14 years

A team of British scientists evaluated the relationship between health behaviors and mortality in a population of 20,244 men and women. The volunteers ranged in age from 45 to 79 years when the study began, and none had been diagnosed with cardiovascular disease or cancer.

The scientists focused on four health habits: not smoking, being physically active at work or in leisure time, eating at least five servings of fruits and vegetables a day, and consuming one to 14 alcoholic drinks a week. During a follow-up period that averaged 11 years, people with none of the four good habits were four times more likely to die than people who had all four healthy behaviors. That means a 74-year-old man with all four healthy habits had the same death rate as a 60-year-old with none of the desirable behaviors. In effect, having all four protective behaviors was equivalent to shaving 14 years off the calendar. And it doesn't have to be all or nothing: as compared to having none of the desirable traits, having even two cut the death rate by more than half. Most of the benefit came from protection against cardiovascular disease and cancer.

How does it work?

Virtue should be its own reward, but in the case of lifestyle prevention, the rewards depend on the many complex biological effects of health habits. The table on page 3 summarizes some of the ways that lifestyle can influence major risk factors. The range of improvements is remarkable, and there are additional benefits that are not covered by the table. For example, exercise improves sleep, reduces stress and depression, and lowers the risk of dementia; exercise and diet protect against osteoporosis and fractures; exercise and staying lean reduce the risk of erectile dysfunction; low-dose alcohol is associated with protection against stroke; and exercise improves bowel function and helps reduce the risk of colon cancer.

Most doctors perform medical tests to identify risk factors, and then prescribe medications to improve those factors. It's important, wise, and necessary, but it overlooks the fact that unhealthful lifestyle choices are behind many medical risk factors. In fact, more than 70% of

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cardiovascular events and 90% of new cases of diabetes can be attributed to just a handful of lifestyle failings. Doctors should spend more time on lifestyle prevention—but their success will depend on your ability to follow simple "prescriptions."

"But I'll never be thin"

Like many other studies, recent research from Boston, Mass., and Cambridge, England, shows that healthy habits pay big dividends and that half a loaf is better than none. But many people don't see it that way; if they are having trouble meeting some goals, they say, "Why bother?" and stop working toward improvements they can achieve. Most often, the sticking point is obesity.

A recent report from the Danish Diet, Cancer, and Health Study may convince overweight people to "bother" with good health habits. The subjects were 54,783 men and women age 50 to 64 who were free of coronary artery disease and cancer when they volunteered for the study between 1993 and 1997. During a follow-up period that averaged 7.7 years, excess body fat took a toll on health. Each extra point on the body mass index (BMI) scale boosted a man's risk of suffering an acute coronary event by 7%. But even among people who were overweight and obese, healthy choices about smoking, diet, and exercise lowered the risk of heart disease.

All in the genes?

A stubborn waistline is a common excuse for lifestyle laxity, and another is the belief that your genes determine your health, no matter how you live. The research reviewed here shows that is not true, and new studies suggest that in addition to improving risk factors (see table), wise lifestyle choices may actually improve your genes.

Each man comes into the world with some 20,000 to 25,000 genes passed down from his parents. These genes determine many physical attributes and some personality traits; some genes also increase or decrease the risk of disease. But genes don't stay static throughout life. As cells grow and divide, errors (mutations) crop up in the DNA that constitutes the genetic code. Fortunately, our cells have ways to detect and correct most genetic errors. But errors that slip through the body's defense mechanisms may start a cell down the path to disease, including the unrestrained growth that leads to cancer.

Lifestyle changes and risk factors

Risk factors that improve	Lifestyle change: Prudent dietary pattern	Regular exercise	Staying lean	Avoiding tobacco	Low-dose alcohol
LDL ("bad") cholesterol	+	+	+	+	
HDL ("good") cholesterol	+	+	+	+	+
Blood pressure	+	+	+	+	
Blood sugar	+	+	+		
Inflammatory markers		+	+		+
Blood clotting		+		+	+
Antioxidant status	+				
Endothelial (vascular) function	+	+		+	
Hormones and growth factors		+	+		

Many acquired mutations develop spontaneously, but others are triggered by harmful environmental influences. That's how smoking and radiation increase the risk of cancer. External influences can also turn down active genes and turn on dormant or sluggish ones. And while most genetic research has asked how bad things happen to good genes, a few scientists are starting to ask if good lifestyle choices can actually make good things happen to genes.

In one study, European researchers randomly assigned 21 men who were scheduled for clinically indicated prostate biopsies to supplement their usual diets with four servings of either broccoli or peas per week. At the end of the 12 months, the men who ate broccoli demonstrated genetic changes that might reduce the risk of prostate cancer.

In another study, scientists from California tracked 30 men who were undergoing periodic prostate biopsies as part of active surveillance for early prostate cancer (see *HMHW*, July 2007 and July 2008). The men made comprehensive lifestyle changes that included diet, exercise, and stress reduction. These changes produced improvements in weight, abdominal obesity, blood pressure, and blood lipids. In just three months, lifestyle changes also altered the activity of 501 genes in prostate tissue; 48 of the genes were ramped up, and 453 were turned down.

In a third experiment, researchers from Britain and the United States collaborated to study how exercise affects *telomeres*, repeating sequences of DNA located at the ends of chromosomes. Telomeres protect chromosomes from degradation, but as cells divide, their telomeres get shorter and shorter. Advancing age, oxidative stress, and obesity all contribute to telomere shortening; in turn, shortened telomeres have been linked to an increased risk of coronary artery disease, heart failure, diabetes, and osteoporosis. ▸▸

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In a study of 2,401 twins, regular exercise was associated with greater telomere length. The effect was substantial; the telomeres of the most active volunteers scored about 10 years "younger" than those from the least active subjects. The results remained valid even after the researchers took age, BMI, and smoking into account. And in the small number of identical twins who differed in their exercise habits, the exercising twins had longer telomeres than their sedentary siblings. The California study of men with prostate cancer also found that lifestyle changes protect telomeres. Perhaps, then, telomeres are one explanation for how regular exercise seems to slow the aging process.

When we come into the world, each of us has a unique genetic profile that has an important role in determining health and longevity. But if heredity deals us a hand of cards, lifestyle determines how we play those cards, and this also has a huge role in tipping the balance between health and disease. More than that, new research shows that lifestyle choices can actually reshuffle the deck, for worse or for better.

How are we doing?

American health is not what it should be. Diabetes and obesity are increasing at an alarming rate, and the prevalence of heart disease, cancer, stroke, and other devastating illnesses remains stubbornly—and unacceptably—high.

America spends far more on medical care than any other nation, yet America's health lags far behind most industrial countries. The reasons for the gap are many and complex, but an inconvenient truth is that we are simply not taking care of ourselves. According to the 2000 nationwide Behavioral Risk Factor Surveillance Survey, only 3% of Americans had all of four simple healthy lifestyle characteristics (not smoking, having a healthy weight, eating five servings of fruits and vegetables a day, and exercising regularly).

Although lifestyle changes seem simple, even obvious, they have enormous health benefits. Simple or not, they can be hard to achieve. It's worth your effort. Your health is too important to be left to your doctors.

Climate change and your health

The debate is over; nearly all scientists (and politicians) agree that climate change is real, is here, and is the result of human activity. Experts also agree that the consequences of global warming are serious and far reaching. All too often, though, these consequences are framed in terms of the threat to polar bears, exotic wildlife, and beautiful glaciers. Without minimizing the value of stately bears and snow-covered peaks, many people find it hard to make lifestyle changes and economic sacrifices to protect such distant assets. But climate change threatens more than the earth's vistas. It also threatens human health—and it's already causing problems here in the United States.

Our planetary greenhouse

Sunshine warms the earth. When solar radiation enters the atmosphere, a portion is bounced back into space, and another portion is absorbed by clouds and water vapor, but the majority strikes the planet's surface. This solar energy warms the earth, but it's also reflected back into the atmosphere in the form of infrared radiation. Some of the infrared penetrates through the atmosphere into space, but some bounces off atmospheric gases and heads back to earth, where it adds warmth (see figure, page 5).

The atmospheric gases that reflect infrared radiation back to earth are known as greenhouse gases. Without them, too much solar energy would be lost, and the earth would be ice cold. But since the industrial revolution, the concentration of atmospheric greenhouse gases has increased, and the increase has accelerated in the past 50 years. That means more infrared energy is reflected back to earth, where it produces global warming. Scientists report that the earth's temperature increased by 0.6° C (1.1° F) during the 20th century, and they project an additional rise by as much as 4.4° C (6.1° F) during this century.

Greenhouse gases

Heat-trapping greenhouse gases are formed on earth by natural processes and human activities and then enter the atmosphere. Here is a primer on the major gases:

Carbon dioxide (CO_2). A tiny amount of CO_2 enters the atmosphere every time you breathe out. But the CO_2 produced as a waste product of the body's metabolism is dwarfed by the CO_2 generated when wood and fossil fuels such as oil, natural gas, and coal burn. A variety of other industrial reactions also produce CO_2. Plants remove CO_2 from the air as part of the biological cycle. But as fossil fuel combustion has increased and the world's forests have shrunk, atmospheric CO_2 climbed from about 280 parts per million (ppm) in 1750 to 315 ppm in 1958, and then to today's level of nearly 380 ppm. Carbon dioxide bears much of the blame for global warming—and at the rate we're going, atmospheric CO_2 levels could double as early as 2050.

Methane. Like CO_2, methane is emitted during the production and transport of oil, gas, and coal. But methane also enters the air from the gastric emissions and "tailpipe" of cattle and from decomposing manure and organic wastes in solid-waste landfills. The concentration of methane in the atmosphere has more than doubled since the industrial revolution.

Nitrous oxide. This gas enters the atmosphere from agricultural and industrial activity, including fossil fuel combustion.

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Fluorinated gases (halocarbons). All fluorinated gases result strictly from human industrial activities, not natural sources. Although only tiny amounts are present in the atmosphere, they are very potent greenhouse gases.

While all of these gases contribute to worrisome global warming, CO_2 and methane are particularly concerning. And since CO_2 lingers in the atmosphere for 50 to 200 years and methane for 12 years, prompt action is needed to control gas emissions, mitigate global warming, and protect human health.

Health consequences of warming

Climate change can affect human health in many ways. The direct effect of exposure to extreme weather is the most obvious example. In the 1980s and '90s, heat stroke killed about 200 Americans a year, but the average toll is now close to 700 a year (see *Harvard Men's Health Watch*, August 2008). Heat-related illnesses and deaths will increase as the earth warms up. And climate change involves more than warming; hurricanes, cyclones, floods, and wildfires are expected to increase, causing injury, death, psychological trauma, and damage to the public health infrastructure.

Many insects thrive in warm weather. That means more insect-borne diseases, including West Nile virus and viral encephalitis (both carried by mosquitoes) and Lyme disease and Ehrlichiosis (both carried by ticks).

Tropical diseases may also spread to temperate zones, such as the United States. Examples include malaria, dengue, and yellow fever. These infections may seem exotic and remote, but a 2007 Italian epidemic of Chikungunya virus (a viral infection normally found in the Indian Ocean region) reminds us that warming can make our small world even smaller.

If unchecked, polar melting will have devastating effects on the earth and its peoples. The sea level will rise, displacing millions of people. Human suffering and economic stress are obvious consequences. In addition, disruptions in sanitation, the supply of fresh water, and food production may cause health problems that extend far beyond receding shorelines. Food- and water-borne infections and malnutrition are evident threats, but the combination of population shifts and socioeconomic hardships could also trigger political instability and international conflict.

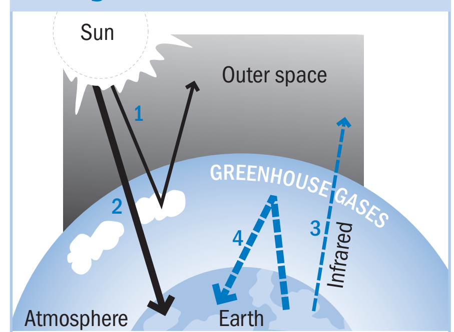
These worst-case scenarios may make the health consequences of global warming sound like science fiction or Al Gore's bad dream. But globalization means that America will suffer along with the rest of the world. And climate change has already produced health problems in the United States.

One example is depletion of the stratospheric ozone layer, which has increased exposure to UVB radiation, which contributes to skin cancer, cataracts, and immune suppression. Air pollution is another threat whose time has already come. Particulate emissions and noxious gases spewed from tailpipes, smokestacks, and burning forests contribute to heart and lung disease. Experts blame poor air quality for the fourfold increase in asthma since 1980 (see *HMHW*, July 2008).

Global warming may inhibit the growth of some important food crops, and it has already promoted the growth of some pesky plants. Ragweed plants now produce twice as much pollen as they did 100 years ago, and rising CO_2 levels will boost pollen even further in the years ahead. It's another reason for the increase in asthma, as well as hay fever and allergies. That's nothing to sneeze at—nor is the flourishing growth of *Toxicodendron radicans*, the CO_2-loving plant better known as poison ivy.

And just in case you still think climate change is just a problem for polar bears, consider this: the World Health Organization estimates that climate change is already responsible for 150,000 deaths a year worldwide, and the toll is expected to double by 2030.

The greenhouse effect



Some of the sun's energy bounces off the atmosphere (1) and is reflected back into space, but most penetrates (2) to warm the earth. Some of the earth's warmth radiates back into space (3), but much is trapped by greenhouse gases and is reflected back to earth (4), producing warming.

Cooling it

Climate change is a huge problem, so big that it may seem insolvable. But instead of throwing up our hands and continuing to turn fossil fuels into CO_2, we can take steps to control the problem. Like controlling tobacco (see *HMHW*, November 2008), success will depend on a combination of scientific research, new public policies, and informed personal choices.

Detailed policy proposals are beyond the scope of this humble health letter. Still, we should all encourage our government leaders to develop programs to:

- Promote efficient vehicles, buildings, power plants, factories, and farming.
- Promote renewable sources of energy, including solar, wind, and water power; geothermal energy; hydrogen; biomass fuels; and safe nuclear energy.
- Promote mass transit.
- Develop technologies to capture and store CO_2 and methane.
- Reduce deforestation and encourage new plantings.

Firm national and international commitments will be required to achieve these goals. But in addition to thinking globally, we should all act locally and do whatever we can to help. ▸▸

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Compact fluorescent bulbs

They look funny, but they use less electricity and generate less heat and carbon dioxide. Compact fluorescent bulbs are more expensive than old-fashioned incandescent bulbs, but since they last 10 times longer, they save money in the long run. A single bulb can shave more than $60 off your electric bill during its lifetime, while keeping 1,000 pounds of CO_2 out of the atmosphere.

But there are cautions. Compact fluorescents contain small amounts of mercury that can vaporize if a bulb breaks. Handle these bulbs with care, and when they burn out, recycle them at hazardous waste collection sites or at a retailer (such as Home Depot) that accepts them. If a bulb breaks at home, open windows, turn off forced-air heating or air conditioning, and keep people and pets away. After waiting 15 minutes, put on rubber gloves and use two pieces of cardboard or plastic to scoop up the glass and dust—avoid sweeping or vacuuming, which can spread mercury around. Place the debris into a sealed container that you can bring to a recycling center. Use a damp paper towel to finish the clean up, and then wash your hands and face. And it may be wise to limit very close (less than one foot) exposure to "single envelope" compacts, which emit ultraviolet radiation that might cause photodamage to sensitive skin; "double envelope" bulbs appear safe, even at close range.

Do it yourself

Small steps can add up to a long march to progress. Here are some things you can do:

Take steps. Walk (or bike) for transportation. You'll cut your gas bill and generate less CO_2. Of equal importance, you'll get exercise that will lower your risk of heart disease, high blood pressure, stroke, dementia, depression, colon cancer, and osteoporosis (see *HMHW*, May 2007).

Eat for a cooler planet. Cows are living smokestacks that generate methane and nitrous oxide, two powerful greenhouse gases. The world's farm animals make 18% of the emissions that produce global warming. Pound for pound, beef generates 11 times more greenhouse gases than chicken and 100 times more than carrots. If you eat less meat and dairy, you'll reduce the demand for cows, and you'll also take in less cholesterol-raising saturated fat and lower your risk of colon and prostate cancers (see *HMHW*, January 2008). Substitute healthful fruits, vegetables, whole grains, beans, and fish for the health of your planet and your body.

Become a "locavore." One pound of lettuce contains 80 calories of food energy—but it takes 4,600 calories of fossil fuel energy to grow and process it in California and transport it to an East Coast market. Choosing locally grown and organic foods will save energy used for fertilizer, pesticides, transportation, and storage—and you may also reduce your exposure to food-borne infections.

Ride right. Make your next car a high-mileage model. Keep your tires fully inflated, your car tuned, and your gas pedal off the floor. Drive less by carpooling or taking public transportation.

Dress right. Wear sweaters in winter, shorts in summer.

Make home improvements. Invest in insulation, weather stripping, and storm windows. Use a sealant or caulking to close cracks and plug leaks in and around doors and windows. Turn the heat down a few degrees in winter and at night, and set the air conditioner a few degrees warmer in summer. Adjust curtains and window shades to keep sunlight out on hot summer days, but to let it in when it's cool. Use fans to reduce air conditioner use in the summer. Switch to Energy Star appliances. Don't run your washer, dryer, or dishwasher until it's full. Switch to compact fluorescent light bulbs (see box). Turn off lights when you leave the room. Turn off your computer when it's not in use. Unplug TVs, printers, fax machines, and other electronics when you're away for more than a day or two; those little green lights mean you're using electricity and generating CO_2. Choose renewable energy if it's available to you. Reduce wasteful consumption, reuse whatever you can, and recycle whatever you can't reuse.

Use the Environmental Protection Agency's personal emission calculator (http://www.epa.gov/climatechange/emissions/ind_calculator.html) to calculate your carbon footprint, then do whatever you can to reduce or offset it.

Health is everyone's concern, and climate change is everyone's problem. Do what it takes to reduce your carbon footprint and to prod our leaders to reduce global warming. It's the cool thing to do.

Genetic screening for prostate cancer

Genes regulate the growth, multiplication, and death of all human cells. Cancer develops when cell growth escapes from the normal control that holds it in check. In a fundamental sense, then, all cancers depend on genetic abnormalities.

In some cases, abnormal genes are passed down from parent to child. In others, problems develop after birth as a result of environmental influences, including nutritional imbalances and exposure to tobacco, radiation, and toxins.

If genes are responsible for cancer, then therapies that target genetic abnormalities should be beneficial. That possibility lies in the future, but we are already at the point where genetic testing can predict the risk of certain cancers. The breast cancer genes BRCA1 and BRCA2 are the best-known examples.

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Prostate cancer is the most common internal malignancy in American men and the second leading cause of cancer death among males in the United States. Some men inherit an increased risk of prostate cancer. Men with fathers or brothers who've had prostate cancer are 1.5 to three times more likely to get the disease than men with no family history; if multiple relatives have been diagnosed before age 55, a man's risk rises even further. But most cases of prostate cancer occur in men without a family history of the disease; that's because anytime after birth, males can develop the genetic abnormalities that drive the disease later in life.

Gene screens

The first prostate cancer gene was identified by a team of scientists in the United States and Sweden in 1996. The gene was aptly named hereditary prostate cancer 1, or HPC1. It was an exciting discovery, but HPC1 accounts for just a tiny fraction of all prostate cancers.

In the past decade, genetic research has exploded. Numerous prostate cancer genes have been proposed; many have been confirmed, but some have not stood up to additional research. And even when particular genes have been implicated, their exact functions and roles in cancer have not been determined.

New techniques allow scientists to scan the entire human genome, the sum total of all the genetic material in human cells, for abnormalities. In brief, the idea is to recruit patients with a particular disease, scan their genes for *polymorphisms*, and compare the results with the genetic profiles of people who do not have the disease in question. Polymorphisms are naturally occurring variations in gene structure; it's normal to find some, but if the number is large, the statisticians weigh in to determine if the abnormalities occur often enough to suggest a link to the disease that's being investigated.

Staggering scientific advances have taken this research to a new level. In addition to looking for abnormal genes, researchers can now investigate the individual chemicals, called nucleotides, that come together to form DNA. So instead of studying "just" 20,000 to 25,000 genes, scientists can now investigate hundreds of thousands of individual nucleotides.

Abnormalities of individual nucleotides are known to the pros as *single nucleotide polymorphisms*, or SNPs. It's very sophisticated, complex research that usually depends on large teams of scientists from around the world. Few men will try to grapple with the details, but most will be interested to learn that many SNPs have been linked to prostate cancer. And even if you're not interested now, you may be later. That's because you could soon be invited to pay for a genetic test that screens for prostate cancer SNPs.

To test or not to test

To review the pros and cons of genetic screening, let's focus on one of the most widely publicized studies of prostate cancer. Scientists in the United States and Sweden compared the genetic profiles of 2,893 prostate cancer patients and 1,781 men who were free of the disease. They identified five individual SNPs that were linked to an increased risk of prostate cancer. Individually, the increased risk was modest; men with just one SNP were from 1.22 to 1.53 times more likely to develop prostate cancer than men who had none of the five SNPs. But men with four or five of the SNPs were 4.47 times more likely to get prostate cancer. And men who also had a family history of prostate cancer were a whopping 9.46 times more likely to develop the disease. That's a substantial risk indeed—but it doesn't necessarily mean the test is right for you.

One caution is based on the possibility of false-negative and false-positive results. Only 5.4% of the men with prostate cancer but no family history of the disease had four or five abnormal SNPs. That means the test failed to predict almost 95% of the cancers in these men. On the other hand, 2.2% of the men without cancer had four or five SNPs; they would worry about an increased risk when none was present.

Worry itself is another issue. Men with abnormal genetic scans might face years of anxiety. And privacy is also a concern since a positive test might affect insurance or even employment.

But the most important caution of all relates to the natural history of prostate cancer itself. Many prostate cancers are slow growing and indolent, even harmless, while some are aggressive, even lethal. This genetic test is not able to tell the good actors from the bad. Since positive genetic tests are likely to lead to aggressive prostate cancer screening with prostate-specific antigen (PSA) tests and prostate biopsies, it would lead to treatment (and side effects) that might never have been necessary. And there's a final hooker: even if the chain of events leads to early diagnosis, doctors don't know if that will lead to a better outcome.

What to do?

Genetic screening for prostate cancer is still experimental; it has not been approved by the FDA, and it's not available commercially. But if (or when) it's ready for prime time, the decision about testing will be up to you. Men with strong family histories of prostate cancer might choose genetic testing and aggressive prostate cancer screening, while men at average risk might decide to hold off. And all men will want to pay close attention to new research that may help answer some of these crucial but vexing questions.

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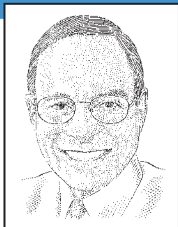

ON CALL

Statin therapy

Q I am 55 years old. My cholesterol counts are normal, but my wife clipped a newspaper article about a study that found statin drugs prevent heart attacks even in people with normal cholesterol. My golfing partners all take cholesterol medication—should I join them?

A Congratulations on being healthy, having normal cholesterol levels, and having a wife who watches over your health. Congratulations, too, on doing a little homework before you ask your doctor for a prescription.

Your newspaper was referring to the so-called JUPITER study, a multinational investigation headed by scientists at Harvard Medical School. The subjects were 17,802 apparently healthy people; nearly two-thirds were men older than 50 years of age. All the volunteers had LDL ("bad") cholesterol levels below 130 milligrams per deciliter (mg/dl), a level that is considered normal for healthy people (but high for patients with heart disease, diabetes, or high blood pressure). In addition, all the participants had elevated levels of C-reactive protein, or CRP, a marker of inflammation that suggests increased cardiovascular risk. The volunteers were randomly assigned to take either 20 mg of *rosuvastatin* (Crestor) or a placebo every day. The trial, which was funded by the drug's manufacturer, was scheduled to last four years but was halted after 1.9 years when a clear winner emerged. The winner was rosuvastatin, which reduced the occurrence of heart attacks, strokes, and cardiovascular deaths by 47%.

Newspapers summarized the JUPITER findings with a headline proclaiming that statins cut the risk of heart attacks in half in people with normal cholesterol levels. The headline is accurate, but it doesn't tell the whole story.

JUPITER researchers found that statin therapy produced a 47% reduction in *relative risk*; people who took the drug were 47% less likely to suffer cardiovascular events than people who took a placebo. That sounds great, and it is important. But it's just as important to consider *absolute* risk. Only 157 of the 8,901 people taking the placebo had major cardiovascular events; their absolute risk was just 1.8%. The 8,901 statin users had 83 events; their absolute risk was 0.9%. The difference represents a 47% lower relative risk, but it means that if you are like these subjects, two years of statin therapy would reduce your personal risk by only 0.9%. Put another way, 120 people would have to take daily medication for nearly two years to prevent one cardiovascular event.

In the trial, statin therapy was safe, though it did produce a slight rise in blood sugar levels. The drug reduced CRP levels, and it produced a dramatic fall in LDL cholesterol levels, to a median of 55 mg/dl; doctors don't yet know the long-term consequences of such low levels.

Although the JUPITER volunteers all appeared healthy, they had an average body mass index (BMI) of 28.3 (overweight) and an average systolic blood pressure of 134 mm Hg (prehypertensive). In addition, 41% had the metabolic syndrome, another important precursor of heart disease and stroke. Statin therapy does not address any of these abnormalities, but diet and exercise can improve all of them. Unfortunately, the study did not detail the diet and exercise habits of the subjects, nor did it comment on alcohol use, which is associated with a reduced risk of cardiovascular disease if the dose is right (one to two drinks a day for men). Only 17% of the subjects took aspirin, which can also reduce cardiovascular risk.

JUPITER is an important study, but people who are at low risk for heart problems to begin with don't have to rush to statin therapy. Instead, they should begin with diet and exercise to shed excess weight, lower blood pressure, and reduce risk. People with borderline cardiac risk factor profiles should ask their doctors if a CRP test would help decide if statin therapy is wise.

Should you take a statin? Perhaps; but first, be sure you are walking the course with your golfing buddies.

HBS

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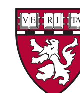

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