



Learning About New Ways to Prevent Cancer

Only ways to look at information on methods that are said to prevent cancer are addressed here, but some of the same principles can be used when looking at information on cancer treatment, symptom management, and other aspects of cancer detection and care. For more on learning about cancer treatments, see *Learning About New Cancer Treatments*.

Can cancer be prevented?

Sometimes cancer can be prevented. Looking at the whole country, it's quite possible that more than half of cancer deaths could be prevented – if everyone avoided tobacco, controlled their weight, got enough physical exercise, and took other steps to improve their health. Of course, that's a big “if.”

There's no guaranteed way to prevent cancer.

So far, nothing has been found that's proven to prevent every cancer. Right now we know there are ways to help prevent many cancers in large groups of people. And there are things you can do that might help reduce your personal chance of getting cancer. (See Appendix A at the end for the American Cancer Society's recommendations for reducing cancer risk.) But, as of today, even the best methods to try to reduce your cancer risk (called *cancer risk reduction*) cannot prevent all cancers.

Because certain methods and drugs can help prevent some cancers in large groups of people, we will still use the term *cancer prevention* here.

Early detection can help save lives

If cancer does develop, there are early detection tests that can improve the odds that some types of cancer will be found at an early stage (when they're small and easier to treat). To read about proven methods to find cancer before it causes symptoms, see our *American Cancer Society Guidelines for the Early Detection of Cancer*.

Although early detection alone rarely prevents cancer, it can often prevent cancer deaths.

When you hear about something new to prevent cancer

You've just heard about something new that might possibly reduce your risk of cancer, something you haven't heard about before. If you're worried about getting cancer, you may wonder if this might work for you. Even though your doctor might not have mentioned it, you want to find out more about this. You want every possible chance of never getting cancer.

But before you put your money, time, and energy on the line, you need to know more about the new prevention method so you can decide if it's worth it.. At this point, you probably don't know if it will actually reduce your risk of cancer, or if it could even harm you. Here are some of the things you may hear about:

FDA-approved drugs: The new method may be a medicine that your doctor recommends to reduce your cancer risk. It's pretty easy to find out more about FDA-approved drugs, since there are many trustworthy sources and careful scientific studies involved. We can help you find out more, and there are others who can help, too. (See the "To learn more" section at the end of this document.)

Methods being studied for FDA approval: Maybe the method you heard about hasn't been approved, but is "in the pipeline" to become a mainstream cancer prevention method in the future. It may be a pill, a treatment, or something else. It's usually not too hard to find information about these kinds of treatments. If the treatment has ever been approved by the FDA for any medical use, you can usually find good information on risks and side effects. But it may be harder to find out about how well it works for cancer prevention.

Non-prescription herbs, supplements, diets, and special treatments: Other methods you hear about may be herbs, vitamins, other dietary supplements, health tonics, "body cleansings," or special diets that are supposed to boost the immune system, among many other things. In the past, almost no studies were done to look at these methods, but researchers are now trying to study more of them in the same careful ways that they study other methods.

Lifestyle changes: You may hear about other things you can do that can help reduce your cancer risk. For instance, quitting tobacco, eating more fruits and vegetables, getting more exercise, cutting back on alcohol and red meats, and staying at a healthy weight have all been given more attention lately. Studies on some of these are fairly easy to find.

Whatever method you're thinking about, take the time to see what you can learn about it from sources you trust. Here we will give you some ideas to help you when you're searching for more information.

Look at where the information came from

To start, you'll want to consider the source of the information on the cancer prevention method.

- Was it a report in a newspaper or magazine?
- Was it discussed on a television or radio program?
- Did the news come from an Internet site, maybe one that also happens to be selling the treatment or is otherwise allied with the seller?
- Was it suggested by a health food store or nutrition center employee?
- Was there a study published in a respected, peer-reviewed medical journal such as the *Lancet* or the *Journal of the National Cancer Institute*?
- Did a friend tell you how well this new method is working for them or someone else?

Did it come from news reports?

If you see a report in a respected newspaper or magazine

Don't just look at the headlines – sometimes they can be overstated, confusing, or even misleading. Read the article carefully to find out where the reporters got their information. Look for these things:

- Is this a press release from a company announcing a new breakthrough in cancer prevention?
- Is it a report from a clinical study that was given at a scientific conference?
- Is it a report from a study that was published in a respected medical journal?
- Where was the study done? What do you know about the research center that conducted and sponsored the study?

If the report was on the TV or radio

You'll want to know if what you saw or heard can be trusted. Was the news reviewed and reported by a doctor, or was it a non-medical person such as a reporter or news anchor? Some news organizations hire medical reporters so that medical and health news can be reported more clearly to the public. Journalists without medical training don't usually understand all of the medical background and related research on the subject, so they may not be able to give a clear, unbiased view.

If it was a commercial or infomercial

Keep in mind that these are ads that tell you only what they want you to hear. You have to listen carefully to learn if studies have been done, and find other reliable sources to learn more. (See the section called “Was it from a promotion from a seller?”)

If you heard about a study on a reliable TV or radio news report

Try to remember the details. Look for the kind of information that you would try to get from a newspaper, including where the new information came from. Getting these facts from broadcasts can be much harder than from printed reports, because it’s hard to remember everything you hear on a short TV or radio spot. And you can’t always go back and search for the facts after the broadcast is over. Even if you can recall everything you heard, important details may have been left out because they have so little time to cover the subject.

Some news outlets post extra information or replay their newscasts online. If you’re unable to find more on their website, you may want to try contacting the TV or radio station to get your questions answered. It’s better to do this right away. Sometimes, a question that might be answered easily a day or two after the broadcast becomes impossible after a month or two. And, if it turns out that part of their report was wrong, you may find corrections or clarifications online soon after the report was aired.

In the section, “Consider the science,” we go into more depth about the important details you’ll want to get from a news report, no matter where it came from.

Was it anecdotal information?

If someone told you that he or she (or their friends or family) is healthy and feeling great using this method, it’s called *anecdotal* information. This is the personal report of one person or very few people. Really learning about cancer prevention involves looking at a lot of people over time.

Cancer happens much more often to older people. It’s pretty rare for younger people to develop cancer, whether or not they use some method to prevent it. This means it’s no surprise if a large number of people haven’t developed cancer while using a certain prevention method for a few years.

Still, if you’ve been told someone’s personal story, can you find out more? Keep in mind that a person may credit an herb or supplement with feeling better, even though there may be other factors involved. And sometimes, a person’s belief in a method may be enough to make a person feel better for at least a short time. (See our document called *Placebo Effect* for more on this.)

There are many other ways that people with good intentions can reach the wrong conclusion from a single person’s experience, or even the experiences of a group of people. This is why scientists look at cancer prevention methods under such careful conditions.

Was it a promotion from a seller?

If the report came from a seller on the internet, you may have lots of searching to do. Most of the cancer prevention methods sold online talk about the powers of herbs and supplements that have never been proven to reduce cancer risk or make people healthier. They often make vague claims about their product activating or strengthening the immune system, and other statements that are impossible to prove.

Some sellers have been caught using outright lies and fraud to make their websites look official. Some have written fake quotes from doctors. Others have reported on studies that were either never done or were misrepresented, saying they were from well-known cancer centers. There have been ads or websites with people dressed up as doctors who appeared to use or endorse the product.

Some marketers have implied their product was endorsed by the American Cancer Society. Some have even falsely said that their device or treatment was approved by the US Food and Drug Administration (FDA). Others note that their device is “registered” with the FDA. Even if that’s true, registration is not the same as approval. Registration doesn’t require proof that the device works or is safe. Another take on this is that a device is said to be FDA approved, and it is – but when you investigate, it’s not approved for the purpose they claim. You can find out more about these claims by calling the FDA. (See the “To learn more” section.)

Sometimes the staff at nutrition centers and herbal shops will suggest ideas or even prescribe “immune boosting” or “cleansing” herbs to help prevent cancer and other conditions. Studies on the accuracy of information from nutrition centers and herbal shops on cancer prevention methods are not available. But studies have been done on people who reported that they already had cancer, and asked nutrition center staffs about possible treatments. The research showed that treatments were often recommended that were not proven to help people with cancer. In fact, some of the suggested treatments could have caused harm. (For more information on these treatments, see our document called *Dietary Supplements: What Is Safe?*)

There are also commercials and infomercials that present new cancer preventives on TV. These are often set up to look like news interviews, and can be very misleading because they are carefully scripted by the sellers of the product. Some will cite studies without saying where they came from, or they’ll quote statistics from unreliable sources. Even worse, some will give glowing information and say it came from a reliable source – but when you go to look for it, the information isn’t there at all. In fact, you may learn that some of the people who sell prevention methods and other “secret cancer information” in these ways have been jailed for fraud. But when such reports are first aired, they can sound very promising.

What about press releases?

Sometimes a company will put out a press release about some promising substance or compound that claims to prevent cancer. Press releases are offered by many companies, including legitimate organizations and about matters that are important to the public.

Sometimes they're offered to generate good publicity for their company or organization. But those that are put out by a company that stands to make money from a product they're touting should be looked at in the same way as ads and infomercials. Some press releases appear on the company's website or online newsletters. After that, they may be and republished by magazines, bloggers, or others.

Some press releases offer preliminary details about a lab study, an animal study, or a small clinical trial (a type of study in humans). Even if the press release came out after a large study was done, the company or organization is only telling the press what they want the public to hear. This is not the same as putting out information after fellow scientists have taken a careful look at the study methods and outcome (the peer review process). You'll want to know more about the final study outcome after it's been evaluated by other experts in the field, not just the parts the company wants the public to know.

What about conference presentations?

Sometimes researchers will share information with other doctors and health professionals at scientific conferences. This information is often an early look at a study that can sometimes sound very dramatic and make headlines. News reporters go to these conferences looking for just this kind of story.

Again, it helps to know who is doing the study and where they work. Sometimes, the study is being done using all the careful methods of a well-run clinical trial, and the researcher is sharing early data with the audience. But the final outcomes of these studies are not complete at the time the findings are presented. And, in most cases, the science review (or peer review) that's needed before a study is published has not yet been done. You'll still want to look at the final report to find out what was done and how it turned out after the data was fully analyzed. By the time the study is published – if it gets published at all – the results may be quite a bit different from the conference presentation.

Look at the science behind the prevention method

To find a cancer prevention method with a proven track record, look at how the method was tested. The way tests are set up can affect the outcome, and sometimes can make it look like a method or substance prevents cancer when it really doesn't.

Pre-clinical tests

Studies in cells (laboratory studies)

Scientists usually start by testing a new prevention method or treatment on cells in a dish in the lab, to find out if it has any effect there. They may treat cells with a known cancer-causing agent and then add the compound they're testing to see if it stops pre-cancerous

changes in the cells. If it doesn't, they may change the formula or use different types of cells to try it again. Sometimes studies like this show some effect on the cells, and they're published. News broadcasters may then treat the study as proof that a cancer prevention method works. But just because a compound stops abnormal cell growth when it's added to cells in a lab dish does not mean that it will work in the human body.

This means that if you're looking at a report of a research study – even one that says a treatment “stops the growth of cancer cells” – you may notice that there's no mention of people. Some of these lab studies use human cancer cells, but others use cancer cells from animals. (Either way, studies done on cells alone are called *in vitro* studies.)

At this point, anything that stops cancer cells may sound like good news. But there are many compounds that can keep cancer cells from growing in a lab dish that don't work or aren't safe in people.

Some reasons a treatment might not work for people is that the substance also hurts or kills normal cells, or because the body can't absorb it and get it to the place where it's needed to stop cancer. Sometimes, even if the substance can be absorbed, can reach all the body tissues, and doesn't harm normal cells, the amount of the substance that gets to the tissues isn't enough to stop the cancer cells. There are many hurdles between lab studies and human ones.

Studies in animals

If the researchers find the effect they want in cells in a dish, they may move on to animal tests. This can help them find out if the substance can be absorbed from the stomach or intestine, and learn how it's distributed in the animal's body. They may look for good and bad effects. Because some of these reports are published, you may also hear about them on the news. These are called *in vivo* studies. This means that they were studied in living creatures.

If the study was done in animals, good outcomes may sound promising. But methods that work in animals don't always work when they are tested on people. Animal studies often help scientists know which drugs may be toxic to people, and which may have unexpected effects. Sometimes a drug or food supplement turns out to do almost the exact same things in people as animals, but many don't work for one or the other. And as any veterinarian can tell you, some foods and drugs that are safe for animals can hurt people, and some foods and drugs that are safe for people can hurt animals. So while animal tests can give researchers certain types of valuable information, they still may not show how the compound will affect people.

News stories on lab and animal studies can mislead

In both lab studies and animal studies, the research report may be published. Usually, the researcher's own report makes it clear that more studies need to be done to see if the substance makes a difference in people. But if a news group picks up the story and publishes it, they may not mention how the study was done or that more study is needed.

Often the headlines, and sometimes even the full story, do not clearly say what kind of study was done. Sometimes the news reports on this very early research may make it sound like the method will work in people, which can lead to confusion. This is why it helps to look at the whole printed story, and then see if you can find out more about the details of the research. Always keep in mind that there's a huge difference between positive results in lab or animal studies and good results in human studies.

Types of human studies on cancer risk

Many kinds of studies can be done in humans. Cancer prevention studies may observe people doing what they always do and compare certain activities to how many of the people get cancer. This helps them to find out if cancer risk might be linked to what they do. Or the study may offer something new (a drug, method, activity, etc.) for one group of people, and then compare them to a similar group that did nothing different.

Most human studies can be classed as either studies in which people are observed (watched), or studies in which something is done (called *intervention studies*).

- An *observation study* about cancer risk asks questions about habits and health and looks to see if there are differences in cancer risk that may be linked to these factors.
- A *clinical trial* on cancer risk is one in which the researchers ask healthy volunteers to do something to see if it makes a difference in their cancer risk. (This is different from a *clinical study*, a more general term that includes clinical trials as well as other less careful forms of research. Clinical studies can be medical reports describing a group of patients, or even one person's medical experience.)

Studies that observe humans

A study that simply looks at people is not really testing a method or compound to prevent cancer. The researchers are only looking at whether they can find differences in cancer risk that might be linked to something that the people already do.

They might observe that some of the people who did one thing (exercise and eat fruits and vegetables, for instance) were less likely to get cancer than those who didn't. Observation studies can also find out how strongly a factor is linked to a certain disease. But a study like this can't prove that a certain thing a person did caused them to get cancer, or that something else prevented cancer.

What's a population study?

Population studies look at large groups of people. Researchers may study how often a group gets certain types of cancer and compare their cancer risk to certain lifestyle factors. There's more than one way to do this: *cohort studies* follow the same group over time, and *cross-sectional studies* look at a group at a single point in time. Since cancer takes so long to grow, looking at the same group over time is often the best way to learn about cancer prevention methods.

Cohort studies: These studies take a group of people and watch them over time, testing them or asking them questions. (A cohort study may also be called a follow-up or *longitudinal* study.) A cohort study usually observes groups and compares people with different possible risk factors to see how these factors affect their outcomes.

Cohort studies can be *prospective*, meaning that the researchers select a group and follow them through time. They can also be *retrospective*, which means that the researchers find people (or often medical records) and look back at the group over time. For instance, a retrospective cohort study may look back at people who were exposed to radiation in Hiroshima to find out how many of them got cancer compared to similar people who were not exposed to radiation. A prospective cohort study looking at cancer risk may keep up with a healthy group of people over time and ask them about how much they exercise, what they eat, whether they take vitamins, or even take their blood to look at chemistries. They keep this information (and often collect more) while they wait and watch to see if there's a difference in their cancer rates that might be linked back to any of these factors.

Cross sectional studies: These studies look at people at just one point in time. They look at how certain factors might relate to each other, but there are some drawbacks. There's usually no way to find out what happened in the past without counting on a person's memory. And there's no way to find out what happens to the people after the study.

Cross sectional studies may observe people and look for links between their actions and cancer. They often give researchers ideas about what might be causing more cancers in some people, but these kinds of studies cannot show exactly what caused the cancers. Figuring out the cause requires further research, unless the link has already been proven.

For example, a cross sectional study that looks at the level of a certain vitamin and cancer may find that people with lower vitamin levels are more likely to have cancer than those people with higher vitamin levels. Can we assume just from this study that the vitamin protects against cancer? No, because we can't tell from this study which came first, the cancer or the low vitamin levels. We also don't know if the group had a high vitamin level because they ate healthy diets with lots of fruits and vegetables (which would contain many other things besides the vitamin). There are many other things that this kind of study can't tell us. But it does give researchers ideas about what to look at next, so this kind of information can be a good place to start.

Case control studies: These studies look at people who already have a disease or condition, like cancer, and compare them to an otherwise similar group of people who don't have the disease. Then, the researchers look at eating habits, exercise, drugs, or other factors to see if the groups are different in any ways that might explain why one group got cancer and the other didn't. Most case-control studies are *retrospective* (meaning that they look back at the group over time).

A common problem with these types of studies is that people often remember events or habits from years ago in different ways based on what has happened more recently. If a person has cancer, for instance, he or she may recall having had worse eating habits than those who are well – even if their habits were the same. A person who's still healthy may report better eating habits in the past than what actually happened, because there's no

reason to worry about them or try to remember the details. This is known as *recall bias*, which in this case is a type of *misclassification* error – it ends up putting people into the wrong groups.

In some studies, the poor recall of those being studied may be more random in its error. For instance, suppose you ask people whether they were exposed to high doses of a certain mineral, and they have trouble remembering. In this case, there may be nothing that pushes a number of people more toward one error than the other. This could mean that a number of people end up classified as having the exposure when they didn't, and others are classified as not having the exposure when they actually did. This can dilute the groups enough that there's no difference found between the groups, even though a difference would have been found if everyone was in the right group. This is another type of misclassification error. In this case, it's another way recall bias can cause false results.

When they are done well, case control studies can be helpful in producing ideas about cancer causes and risk reducers. But conclusions about cancer prevention methods, even when based on a number of case control studies, are not as strong as those based on clinical trials.

How are observation studies misunderstood?

A study that only observes people cannot prove what factor caused an illness, but that doesn't stop people from trying to guess at the cause and even writing about it as if the guess were fact. For instance, there were studies years ago that linked gum disease with heart attacks. News reports talked about this link, with many theories about how gum disease might cause heart attacks. The problem was that these were observational studies that could only show links, not find causes. The missing piece in many of the early study reports was that smokers are much more prone to gum disease. A lot of people with severe gum disease smoke; smoking causes both heart disease and gum disease. So the real culprit in some cases was smoking, not gum disease. Another explanation may be that people who don't care for their teeth are less likely to eat well or get good preventive health care. That's not to say that there's no other link between gum and heart disease, but studies that simply observe people have trouble controlling for all the differences between people with and without the disease being studied.

There are other kinds of statistical observation studies that may get a lot of attention and lead to confusion. For example, people from a country where fish is eaten 3 to 5 times a week may have a lower risk of certain diseases than people from another country. A person reading about such a study might believe that the oils found in fish are responsible, and take fish oil supplements. Or they may sell the supplements, and cite the statistics as evidence. But it may turn out that the reason the people in the study had lower disease risk is that they ate less red meat, that they walked more each day, that they weighed less, or some other factor that wasn't even discussed in the study. A closer look may even reveal that the people with the smallest cancer risk were not the ones who ate more fish.

As you can see, there are often many possible explanations for these types of findings in observation studies that the reader may not know about. It's no wonder that people – and even reporters – can be confused by the news reports on observation studies.

Human testing: Clinical trials

Clinical trials are research studies in which people volunteer to help doctors find ways to prevent or treat disease. When these kinds of studies are carefully designed and run, and are of sufficient size, they can begin to show whether a specific substance or method truly reduces cancer risk.

Clinical trials must be set up carefully and all the plans reviewed ahead of time, because they propose to change something that might affect a person's life. Cancer prevention clinical trials must always be approved by a group whose job it is to look after the safety of the volunteers in the clinical trial. This group is called an *Institutional Review Board* or IRB. It's an independent group of doctors, statisticians, and others who review human studies to be sure that the safety and well-being of the study volunteers are protected.

Researchers often design a clinical trial with a control group. That means, for example, they may give a test substance to one group of volunteers, and either a known cancer reducer or an inactive compound (called a *placebo*) to the other group. Or the researchers may test a method or activity in one group, like aerobic exercise 4 times a week, against a group that's offered a different type of activity, or perhaps no special exercise sessions. Then the groups are compared later to see if one group has more cancer than the other. There are several kinds of clinical trials that give us different kinds of information.

Safety first

Before tests of a substance that may prevent cancer can be done on humans, it's important to know if the compound or method being tested is safe. The results from any animal tests on the substance, and any human studies or observations, are reviewed along with other facts that are known about it.

If the substance is a known ingredient that's commonly found in food, it may be on the "generally recognized as safe" list, and be accepted for further testing. But if the amounts to be used are much higher than a person would usually get in food, further testing for safety may be needed. Other evidence may be weighed, too, such as the effects of related compounds, what's already known about the class of chemicals, and other such information. If the substance or method is thought to be safe to study in this group of volunteers, the researchers must convince an Institutional Review Board (IRB) that their methods have a chance of working, that the substance or method is safe, and that study volunteers are protected from harm.

If it's a compound that's a new substance, the company must tell the FDA why they think it will work in humans. They must also share research from any lab and animal studies that were already done, or human toxicology studies.

If the FDA and/or the IRB approve human testing, researchers must decide how to design clinical trials and find volunteers who are willing to take the compound or the control substance.

What is a cancer prevention clinical trial?

Clinical trials are most often thought of as research studies in which volunteers with certain illnesses or conditions help doctors find ways to treat disease or improve care. A cancer prevention clinical trial (or cancer prevention study) is a different kind of clinical trial. In these, healthy volunteers help doctors find ways to lower the risk of certain types of cancer. There are different types of cancer prevention studies.

All cancer prevention clinical trials are done to answer these questions:

- Does the medicine, supplement, or other cancer prevention method work to reduce the risk of cancer?
- How safe is it to take the study agent or use the cancer prevention method?
- Does it reduce the death rate in the group that uses the cancer prevention method by reducing the number of people who get cancer?

Some prevention studies may require the volunteer to do something, like exercise for a certain length of time each day, stop smoking, eat extra fruits and vegetables, or get tests to find and remove pre-cancers. The action may either be to avoid something thought to be harmful, or to do something thought to be helpful. These are called *action studies*, and they help researchers find out if the actions that are taken will reduce cancer risk.

In another type of study, the volunteer must take something, such as a drug, vitamin, mineral, or food supplement, to see if it reduces their cancer risk. Scientists who conduct these studies want to learn whether the medicine or supplement (often called a *study agent*) reduces cancer risk. They'll also look at the safety of the study agent. These are called *agent studies* or *chemoprevention* studies.

Cancer prevention clinical trials that involve a drug, supplement, vitamin, or mineral are set up something like the clinical trials that test new drugs. They are generally done in 3 phases, starting with phase I. Each phase is designed to answer different questions about the compound being tested:

- Phase I trials look for the best way to give the compound, the best dose, and check for any harmful side effects.
- Phase II trials look at whether the substance has an effect in preventing cancer.
- Phase III trials compare a promising new compound to one that's already in use by giving the new one to one group and the older one to the other group (see "Control group"). If there's no substance that's already being used for the same purpose, the control group may get a placebo (a sham pill or supplement; see our document, "Placebo Effect").

These phases build on each other. If, for instance, the side effects are severe in the phase I trial, a phase II trial is not likely to be done. If phase I shows no harmful effects, a phase II study may be carried out. But if the phase II study shows no effect, a phase III trial isn't planned, unless there's reason to doubt the phase II outcome. The phase I part of the clinical trial is usually the smallest of the study groups, and phase III the largest. If you can find only phase I studies on a cancer prevention method, it may mean that there's not yet good information about its use in humans.

A cancer prevention study may be done on different kinds of volunteers, depending on its purpose:

- Clinical trials that look for ways to reduce cancer risk in people who have never had cancer
- Clinical trials that look for ways reduce cancer risk in people who have already had cancer

Sometimes, a cancer prevention study may enroll volunteers from groups that are known to be at higher risk of cancer. Those at higher risk stand to benefit more from anything that helps to reduce risk. Also, if the method actually helps, it often takes less time to see if risk is lowered in those who are more likely to have cancer.

Controlled clinical trials of cancer prevention

A clinical trial is best done with at least 2 groups of people that are very much alike. This helps researchers know that any differences between the groups are actually due to the method being tested, rather than factors that the volunteers may have had when they came into the study. These 2 groups are called the *intervention group* and the *control group*. Sometimes, there are more than 2 groups, such as when 2 or more interventions are being tested against the control group. And sometimes, there are 2 control groups, one with a placebo or sham treatment, and one with no kind of intervention.

Intervention group: This is the group taking the study agent, or the group that does the action. It's also called the *test group* or *study group*.

Control groups: In the study of a compound to prevent cancer, or agent study, the control group takes either:

- A standard agent that's being compared with the study agent (the substance being tested)
- A look-alike pill or substance that contains no active ingredient, called a placebo

In an action study, the control group may:

- Get standard health promotion, such as information or instructions about eating or exercise
- Do something other than the action taken by the test group

- Do nothing or be put on a delayed treatment list (wait list)

No matter what the control group members do, they are watched in the same way the test group is during and after the intervention.

Protocols: Clinical trials follow strict guidelines that help make sure the science is sound and that volunteers who take part are protected. Each clinical trial has a *principal investigator* who is in charge of the study. Each study also has a detailed plan, called a *protocol*, which says what the study will do and how it will do it. The protocol explains the study design, who can and can't be in the study, what's being studied, what medical tests are needed and how often, and what other information will be gathered.

A closer look at the evidence

If you're able to find clinical trials that were done on the method you are looking at, it's important to notice what kind of study was done and see what was compared. You'll also want to look at some other factors in the study:

Study subjects: If you happened to get your information from a study done on people, this is a good start. But there are many stages a treatment must go through in human tests before it can be used by most doctors to prevent cancer. It's possible that the study is an early (*preliminary*) one, or a *pilot study*. These are small early studies, in which a drug or treatment is tested on a few people just to decide if it's worth testing on larger numbers of people. (See the "Human testing: Clinical trials" section.) These small studies don't have enough people in them to show whether a prevention method works.

Control group: A study that has a control group is called *controlled*. This might mean that the cancer prevention study was carefully planned, and that people who got the prevention method were compared to others who didn't get that prevention method.

Studies that do not have control groups may compare their disease rates with older studies or general information collected on other groups. But these may not offer good comparisons due to differences in the groups of people, which can affect how much cancer will be found. For instance, one group may span different ages, which affects how many people will get cancer during the study period. Different parts of the country have more cases of certain cancers. Some cancers affect one sex more than the other. Some regions (and even entire states) have a higher percentage of smokers than others. And certain subgroups get more exercise and eat healthier than others. These, and many more factors, make it a bad idea to compare a test group to others chosen in a different way or from a different pool of people than the test group.

The best control group is like the test group in every way other than the factor being studied. That's why better-planned studies start with one group of people and randomly divide them into 2 or more groups, as described below.

Randomization: This means that the prevention method is compared using similar groups of volunteers who were chosen completely by chance to be in one group or the other (they were *randomized* to a group). This reduces the risk, for instance, that the older

people who are at higher risk for cancer mostly end up in one group, which could change the study outcome.

Some of the benefits of randomization include helping to avoid situations which could bias results of a study. For instance, if more young people who start out healthier end up in the group getting the new prevention method, it may make the prevention method look better than it really is. If more people who started out with a higher risk of cancer (such as smokers) end up in the new cancer prevention group, that group may fare worse than the control group. This could make the prevention method look less effective, because it was tested on people who were more likely to get cancer. On the other hand, if more smokers end up in the control group, they may make the test method look better because the control group will likely get more cancer over the years.

To keep the groups balanced, researchers put people into one group or the other by choosing people for each group using methods along the lines of flipping a coin – usually with a computer program. Randomization lowers the odds that one group will be very different from the other. This is why you don't know, when you agree to take part in a randomized controlled cancer prevention trial, whether you'll get a standard prevention or the new one that's being tested. And since there aren't many known standard preventions for cancer, you may very well end up in a placebo group. When you're informed about the cancer prevention clinical trial, the study team will tell you if there's a chance you'll be in a placebo group.

Keep in mind that this is very different from clinical trials in which people already have cancer. When treatment clinical trials are randomized, current treatments (not placebos) are used in the control group. This lets the researchers know whether the new treatment works better than the one that's now being used.

Blinding: This means that the patients don't know which cancer prevention group they're in (test group, comparison group, or placebo group). If the patients do know what they're getting, the study is called an "open label" study. One advantage to a blinded study is that it can help the researchers learn more about side effects. For instance, if patients know that they're getting placebos, or that they're getting a vitamin or a known standard treatment, they might not bother to report health problems to the study coordinator. Those who know they may be getting the test drug or treatment are more likely to report nausea, headaches, and fever, even if the problems turn out to be from something else, like food poisoning or the flu. The same is true for serious illnesses, which also can happen with no known reason but may end up being blamed on whatever the person is taking.

You can see that if the treatment group mostly reports new health problems and the control group generally doesn't, it can make the treatment method look like it has a lot more side effects. This is just one of the ways a patient's knowledge about what they're taking can affect a study's outcome.

Double blinding: This means that neither the researchers nor the patient knows which treatment the patient is getting until after the prevention trial is completed and the observations are on record. This helps to avoid bias in which a researcher expects one group of patients to do better, which can affect the researcher's observations. In cancer prevention trials, observations are carefully measured and written up. After the study is

over, researchers break the code to find out who was in which group. Then the data is analyzed to find out which group (if any) did better than the other.

There is an exception to double blinding, however. In studies where there's a chance that some harm might take place, a Data and Safety Monitoring group follows the results of the study. They don't share this information with others unless it appears that harm is being done. For instance, if one group appears to be doing much better or worse than the other after an early review, they may require that the study be un-blinded so that a closer look can be taken at what may be going on. If the study is found to be causing harm (either to those getting the prevention or those not getting it), the study may be stopped before its scheduled ending time.

Statistical significance: The data are carefully looked at to see if the difference between the groups is likely to be due to chance. This is called a *test of statistical significance*. It means that if one group came out better than the other by a large enough margin, it's very unlikely that the differences were by chance, and the results are said to be "significant." Keep in mind this kind of test alone cannot prove that factors besides random chance didn't bias or confound the results. Careful study planning and precise measurements are used to avoid those factors.

Publication and peer review: Publishing the findings in a respected peer-reviewed journal means that the methods and information from the study were looked at by other doctors or scientists. When they look at the information, they want to be sure that the scientific procedures were properly followed. They also keep an eye out for any bias or other factors that would make one group do better than the other for some reason other than the treatment being studied.

The highest standard of proof that a cancer prevention method works is a double-blind randomized clinical trial on humans that has met the strictest standards of scientific method. If blinded studies are not possible, scientific procedures must still be carefully followed to be sure that any difference in outcomes are due to the treatment, and not other factors. This usually allows the study to be published in a respected, peer-reviewed medical journal.

It takes more than one study to prove something really works. Even breakthrough ideas take a lot of testing to show that they work. Since many good ideas don't pan out for cancer prevention, the failure rate can be high. One study with a good outcome doesn't mean a cancer prevention method works. Even if a study is done in the most careful manner, future studies that try the same thing sometimes find that they get different results. This can happen because the second clinical trial tests the method on a different group of people that doesn't respond the same way as the first group. Or the method may be used in a slightly different way, or with some other small difference that may have not even been noticed. Sometimes a treatment looks great on the first study, but then no other study gets the same outcome – meaning that real-life patients couldn't expect those great results either.

Science builds on the studies in the lab, and sometimes tests in animals. If the cancer prevention method seems to be safe, it's moved up to test in a small group of people. Getting to this point often takes years. If these results look promising, a phase I clinical

trial may be started. At any point, the researchers may find that the cancer prevention method really doesn't work the way they thought it would. But even if it does, good testing can take a long time.

Publication bias: There's another problem that can creep in as more studies are published. Sometimes, the studies that show no difference between the treatment and placebo, or the ones that show the placebo group doing better, are not published. After all, it isn't exactly exciting news when something doesn't work. But these kinds of studies could really help people who are trying to decide whether it's worthwhile to take the treatment. Worse, if the only clinical trials that are published are the ones that show the treatment helps, a person reviewing the published information might not be able to find studies that showed no difference. He or she might conclude that the treatment was helpful, because those are the only studies that were published. This is an example of what is called *publication bias*.

What if different clinical trials show different outcomes?

If you find clinical trials that show opposite outcomes, it can be very confusing. When there are just a few studies, as there may be on a compound that's generally thought to be safe, tests on humans may be the first type done. There may not be much understanding of how the compound might work from lab studies or animal studies. Even when the studies are set up well, these clinical trials often end up showing very little difference, if any, between the people who took it and those who didn't. When the compound really doesn't have any effect, chance will often tip the scales in one direction or another – sometimes even enough that the results look significant. This means that sometimes the placebo group will do a bit better than the test group, while at other times, the group that gets the new compound does a little better. When results conflict with one another like this, it often means that the treatment has very little effect. Publication bias can mean that you find more studies showing a method worked than studies showing it didn't work, because most of the studies showing it didn't work were never published. Or there can be study design problems, and other factors that affected the outcomes.

Other questions about studies on new ways to prevent cancer

Does the study make sense in light of what's known about the human body and the way the method affects it?

This question is often called *biological plausibility*. Does the effect on the body fit with what we already know? For instance, a substance that blocks female hormones may be expected to reduce the risk of cancers that use female hormones to grow. (Of course, whether it would really reduce cancer risk in people would still need to be tested.) But sometimes the researchers may not understand exactly how a substance may work in the body. In cases where little is known about how it may work, evidence from earlier studies may have a role in suggesting what the substance is likely to do in humans.

Does the study support or contradict past studies?

The more evidence there is for a prevention method, the more likely the results are to be true. Sometimes, a study or two will come out that encourages people to believe that a certain food or supplement will reduce cancer risk. Later on, more careful studies often find that the lower cancer risk was due to something else entirely – like chance, age, or healthy habits – and had nothing to do with the food or supplement. This kind of confusion starts most often with observation studies that try to guess the cause for different health outcomes.

Does the study promote something that's supposed to prevent all cancers?

This goes along with biological plausibility, discussed above. Since there are many different types of cancer, and many are known to be caused or affected by different factors, it's very unlikely that one method can address all of them. Claims that there's one method that prevents all kinds of cancer are highly suspect.

Why are most products that are advertised as immune boosters and cancer preventives not approved by the FDA?

There are many herbs and food extracts that are advertised as having an effect on cancer. As long as these food-related products are generally regarded as safe, there are relatively few restrictions on their sales. Many are simply packaged and sold. Because some of these supplements have been found not to contain what's listed on the label, and others have been found to include substances that were not on the label, the FDA set up rules for dietary supplements that took effect in 2010.

These rules were intended to help people be sure that the supplement contains what it says on the label, with no extra ingredients or impurities. The rules still don't require that those who make or sell the product offer any proof that the herb or supplement is safe or effective, and they do not address the supplements' effects on the body. They only address purity and manufacturing practices.

Still, a 2013 study done on herbal supplements in the US and Canada found that up to half of them didn't contain what was on the label. More than half the tested samples contained contaminants or substances that were not listed on the label. Since the 2010 rules went into effect, many supplements have been recalled due to impurities or extra ingredients that were not listed on the label.

Because there's growing interest in supplements, researchers have started studying some of them using the same methods used for cancer treatments and mainstream cancer prevention methods. Large sums of money are not usually available to study herbs and vitamins, so these studies tend to be smaller. But because the safety of the substance isn't usually called into question, there's less need for safety testing. When looking at studies

of these herbs or supplements in people, look at the same questions as you would for cancer prevention clinical trials.

On the Internet, in conferences, and in health food stores, those who sell herbs will sometimes try to use lab studies or animal studies showing that the substance blocks cancer cells as evidence that the herbs work. Some sellers will refer to studies that are not published in peer-reviewed journals. The studies may be written up in a “natural cures” book or posted on a website. These can leave you with no way to know that the studies were done as they are presented.

It also happens that science researchers will isolate a chemical from an herb and test it in the lab to find out if it affects cells. But the effects of the isolated chemical might be very different from the effects of the whole herb (especially in large doses). This is why researchers may have to prove that the extract is safe before testing it in humans. This type of study is usually published in scientific literature and can be found there.

There’s a down side to tests of specific herbal extracts. If sellers of an herb know about scientific studies done with herbal extracts, some of them may talk about the study’s findings as if the study’s success means the whole herb works the same way. Purified extracts are just one part of the herb and may have different effects from the whole herb, and these 2 types of studies cannot stand in for one another.

What does this mean to you?

After going over what all of these things mean, here are some questions about new treatments you’ll want answered:

- Was the new cancer prevention method tested in the lab (on cells in a dish, called *in vitro*), in animals, or in humans (*in vivo*)?
- Who did the study? Was it done by known researchers and cancer treatment centers?
- Are there other studies that support or contradict this outcome?
- If the study was done in humans, how many were involved? How long were they followed?
- Was there a control group (people who got placebo or another prevention method)?
- Were similar people chosen at random to be in either the test group or the control group (randomized)?
- Was the study blinded (were the patients and/or researchers kept from knowing who got which prevention method while the patient was being watched for the effects)?
- Was there a difference in outcome between the group getting the new method and the group getting the placebo/standard prevention?

- Was the difference in outcome measured in numbers of new cancer cases, survival, or both?
- Was the study published in a respected, peer-reviewed journal? Was it presented at a conference or sent out in a press release?
- Is the prevention method likely to be harmful to me? What's known about drawbacks or side effects?

What about heredity? How does it affect my cancer risk and prevention?

All cancers involve damage to genes that control the cell's growth (division). But only about 1 in 20 cancers are linked to a damaged gene that is inherited (passed on) from a parent. If you inherit certain damaged genes, you may have a very high risk of getting one or more types of cancer. If a certain type of cancer is common in your family, genetic testing can be done to find out if it's linked to an inherited problem. (See our document called *Genetic Testing: What You Need To Know* for more on how this works.)

If you think you are at high risk for certain types of cancer, talk with a doctor about whether earlier screening or extra testing is needed. In some cases, there are medicines that can reduce your risk, too. (See our document, *Medicines to Reduce Breast Cancer Risk*.)

Using unproven methods that might reduce your risk

For those who are still searching for a guarantee – or even a boost in the right direction – there's no shortage of other ideas as to how a person might be able to keep from getting cancer. Some ways have been studied, but most have not. Some methods have proven safe, but the safety of others is still unknown. Still, people want to be as healthy as possible, and if they find something that may help, they may want to try it even if there's no evidence to support it. With thousands of possibilities that take years to study, there will always be theories waiting to be checked out.

In the meantime, even if the evidence isn't there for a cancer prevention method, you may decide to use it anyway. The American Cancer Society supports the right of people to decide what's best for them. But we encourage people to discuss prevention methods or treatments they may be thinking about with their doctors and other health care providers. We also encourage people to consider using methods that have either been proven to work or are being studied in clinical trials.

If you choose to use unproven measures, talk with your doctor about it to get his or her opinion of the method. If it's a vitamin, herb, or supplement, see what you can find out about side effects, allergies, and other possible problems. You'll also need to let your doctor or pharmacist know about it in case it causes problems with other medicines you're taking. Often, studies of "natural remedies" don't collect this sort of information, and it can be hard to find.

We encourage you to learn all you can before you invest any time or money. You can always call your American Cancer Society, too. We can help you get more information on almost any treatment or method you're considering.

To learn more

More information from your American Cancer Society

Here is more information you might find helpful. You also can order free copies of our documents from our toll-free number, 1-800-227-2345, or read them on our website, www.cancer.org

More on understanding research and making decisions

Dietary Supplements: What Is Safe?

Clinical Trials: What You Need to Know (also in Spanish)

Placebo Effect

Known and Probable Human Carcinogens

Genetic Testing: What You Need to Know

More on reducing cancer risk

American Cancer Society Guidelines on Nutrition and Physical Activity for Cancer Prevention (also in Spanish)

American Cancer Society Guidelines for the Early Detection of Cancer (also in Spanish)

Medicines to Reduce Breast Cancer Risk (also in Spanish)

Skin Cancer Prevention and Early Detection (also in Spanish)

American Cancer Society Recommendations for Human Papillomavirus (HPV) Vaccine Use to Prevent Cervical Cancer and Pre-Cancers (also in Spanish)

Cervical Cancer Prevention and Early Detection (also in Spanish)

Colorectal Cancer Prevention and Early Detection (also in Spanish)

Lung Cancer Prevention and Early Detection

More on cancer and cancer treatment

What is Cancer? (also in Spanish)

Learning About New Cancer Treatments

Complementary and Alternative Methods and Cancer

We also have information on many herbs, supplements, and other treatments that may be marketed for cancer prevention. Please call us to find out more about any specific one you are thinking about trying, or visit us online at www.cancer.org/Treatment/TreatmentsandSideEffects/ComplementaryandAlternativeMedicine/index.

National organizations and websites*

Along with the American Cancer Society, other sources of information and support include:

Food and Drug Administration

Toll free number: 1-888-463-6332 (1-888-INFO FDA)

Website: www.fda.gov

Has information on FDA-approved cancer treatments. This sub-site links to reliable information on dietary supplements:

www.fda.gov/Food/DietarySupplements/default.htm

National Cancer Institute

Toll free number: 1-800-422-6237 (1-800-4-CANCER)

TTY: 1-800-332-8615

Website: www.cancer.gov

Has information on cancer, proven cancer treatments, living with cancer, and clinical trials of new drugs. This sub-site links directly to reliable information on complementary and alternative methods of cancer prevention and treatment:

www.cancer.gov/cancertopics/cam

National Institutes of Health – Clinical Trials Information

Website: www.clinicaltrials.gov

Has information on clinical trials for cancer prevention and treatment, as well as clinical trials looking at other health conditions

**Inclusion on this list does not imply endorsement by the American Cancer Society.*

No matter who you are, we can help. Contact us anytime, day or night, for information and support. Call us at **1-800-227-2345** or visit www.cancer.org.

References

American Cancer Society. *Cancer Facts and Figures 2014*. Atlanta, Ga: American Cancer Society; 2014.

Barnett ML, Hyman JJ. Challenges in interpreting study results: The conflict between appearance and reality. *J Am Dent Assoc*. 2006;137,Suppl 2,32S-36S.

Gotay CC, Dumitriu D. Health food store recommendations for breast cancer patients. *Arch Fam Med*. 2000;9:692-699.

Hoffer, LJ. Complementary or alternative medicine: the need for plausibility. *Canadian Med Assoc J*. 2003;168(2).

Kushi LH, Doyle C, McCullough M, et al. American Cancer Society Guidelines on Nutrition and Physical Activity for Cancer Prevention: Reducing the risk of cancer with healthy food choices and physical activity. *CA Cancer J Clin*. 2012;62:30-67.

Mills E, Ernst E, Singh R, Ross C, Wilson K. Health food store recommendations: implications for breast cancer patients. *Breast Cancer Res*. 2003;5(6):R170-174.

National Cancer Institute. Data and Safety Monitoring Guidelines. Accessed at www.cancer.gov/clinicaltrials/conducting/dsm-guidelines/allpages on October 9, 2014.

National Cancer Institute. Taking part in clinical trials: Cancer prevention studies. Accessed at www.cancer.gov/clinicaltrials/resources/taking-part-prevention-trials on March 11, 2008. Content no longer available.

Newmaster SG, Grguric M, Shanmughanandhan D, et al. DNA barcoding detects contamination and substitution in North American herbal products. *BMC Med*. 2013;11:222. Accessed at www.biomedcentral.com/1741-7015/11/222 on October 9, 2014.

Simon SD. *Statistical evidence in medical trials: What do the data really tell us?* 2006. Oxford: Oxford University Press.

Stampfer MJ, Skerrett PJ. Health for Life: Whom Can You Believe? 2006. *Newsweek*, Jan 16.

US District Attorney's Office, South District of Florida, Press Release. Arthur Vanmoor charged in superseding indictment for selling fake cancer cure, 2007. Accessed at www.usdoj.gov/usao/fls/PressReleases/070827-01.html on August 30, 2010. Content no longer available.

US Food and Drug Administration. Recalls, Market Withdrawals, & Safety Alerts. Accessed at www.fda.gov/Safety/Recalls/default.htm on October 9, 2014.

Weed DL, Gorelic LS. The practice of causal inference in cancer epidemiology. *Cancer Epidemiol Biomarkers Prev*. 1996;5:303-311.

Appendix A

Recommended ways to reduce your cancer risk

About 1 in 3 cancer deaths in the United States each year is related to diet, exercise, and overweight. Another 1 in 3 cancer deaths are due to tobacco exposure.

If you are looking for ways to reduce your cancer risk, and reduce your risk of dying from cancer, there's scientific evidence to support certain methods. Even though this document is focused on learning about unproven methods, your American Cancer Society has looked at the science and made the recommendations listed here. These methods are proven to help reduce the number of cancer cases and cancer deaths in large groups of people.

American Cancer Society recommendations for individual choices about nutrition and physical activity

Get to and stay at a healthy weight throughout life.

- Be as lean as possible throughout life without being underweight.
- Avoid excessive weight gain throughout life. For those who are overweight or obese, losing even a small amount of weight has health benefits and is a good place to start.
- Get regular physical activity and limit your intake of high-calorie foods and drinks as keys to help stay at a healthy weight.

Be physically active.

- **Adults:** Get at least 150 minutes of moderate intensity or 75 minutes of vigorous intensity activity each week (or a combination of these), preferably spread throughout the week.
- **Children and adolescents:** Get at least 1 hour of moderate or vigorous intensity activity each day, with vigorous activity on at least 3 days each week.

(Moderate activities are those that require about as much effort as a brisk walk. Vigorous activities generally use large muscle groups. They raise your heart rate, speed up your breathing, and make you sweat.)

- Limit sedentary behavior such as sitting, lying down, watching TV, and other forms of screen-based entertainment.
- Doing some physical activity above your usual activities, no matter what one's level of activity, can have many health benefits.

Eat a healthy diet, with an emphasis on plant foods.

- Choose foods and drinks in amounts that help you get to and stay at a healthy weight.
- Limit how much processed meat (like deli meats, hot dogs, and bacon) and red meat you eat.
- Eat at least 2½ cups of vegetables and fruits each day.
- Choose whole grains instead of refined grain products.

If you drink alcohol, limit your intake.

- Drink no more than 1 drink per day for women or 2 per day for men.

Avoid things that cause cancer

- Avoid smoking, second hand smoke, and all other forms of tobacco.
- Don't expose yourself to other known cancer causing agents (*carcinogens*). Learn more about chemicals or agents that you work with or use at home, and how to protect yourself. (See our document called *Known and Probable Human Carcinogens* to learn more.)
- Protect yourself from sunlight and other UV light sources (tanning beds and lamps).

Get the HPV vaccine if it will benefit you

- If you are female and between 11 and 18 years old, get the HPV vaccine series to reduce your risk of cancers caused by HPV infection. If you have daughters in this age range, talk to their pediatrician about the HPV vaccine.
- If you are a woman between 19 and 26 years old, talk with your doctor about whether the HPV vaccine might reduce your risk of HPV-related cancers.

Get tested for common cancers and pre-cancers

Use early detection methods that can find pre-cancerous changes in some parts of the body. Treating these pre-cancers can keep them from growing into cancer:

- Pap tests for women as recommended
- Colonoscopy, CT colonography, or sigmoidoscopy for people age 50 and over (or earlier if high risk)

Finding cancer early improves the chances of it being treated successfully. See the *American Cancer Society Guidelines for the Early Detection of Cancer* and talk with your doctor about the best plan for you.

Last Medical Review: 10/9/2014
Last Revised: 5/21/2015

2014 Copyright American Cancer Society

For additional assistance please contact your American Cancer Society
1-800-227-2345 or www.cancer.org