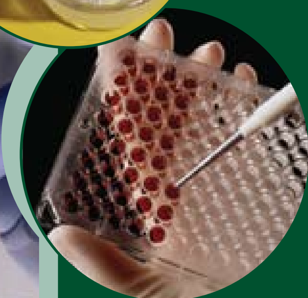
Solving the Diet-Cancer Mystery:

Scientific Studies Provide Clues



World Cancer Research Fund

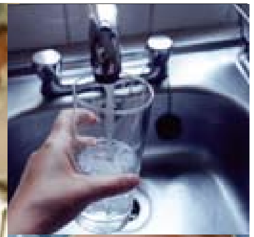
Scientific studies provide clues

If you have an interest in the link between diet and cancer, it helps to understand how we have come to learn what we know today, and how to interpret what we'll learn in the future.

Over the years, researchers have conducted thousands of studies of many different types. It's not the latest or most talked-about study that matters, but what all of the research collectively indicates. WCRF UK's advice is always based on the research as a whole, never on one single study, so the public can be confident in our message.

In preparing the landmark WCRF/AICR second expert report, *Food, Nutrition, Physical Activity and the Prevention of Cancer: A Global Perspective*, to be published in November 2007, thousands of studies from many different sources were evaluated in detail by a group of independent international researchers, who made up our expert Panel.

This brochure explains the different kinds of scientific investigation they examined and notes the strengths and weaknesses of each type. It will give you a better understanding of the range of research included in the second expert report and how the Panel went about preparing the most comprehensive scientific assessment of the diet-cancer link ever undertaken.



The diet-cancer mystery

It sounds like a simple question: can what we eat influence our risk of cancer? In fact, finding the answer is a complex puzzle worthy of Sherlock Holmes.

Do you eat exactly the same thing every day? Probably not. Most people's diets are complex, and they change over weeks, months and years. To pinpoint associations between diet and cancer, researchers must analyse this mass of information to isolate the specific effects of individual foods, or their constituents such as nutrients, vitamins and minerals, as well as combinations of foods – dietary patterns.

Each scientific study provides another clue to the evolving mystery of how diet affects cancer. But as with any good mystery, some clues hold more weight than others. Cancer is a complex disease and no single piece of research can give us all the answers. The 'body of evidence' formed by many studies together must be considered as a whole as we investigate the diet-cancer connection.

Each kind of study has its pluses and minuses. Let's consider the following: epidemiological studies, laboratory studies and controlled trials.

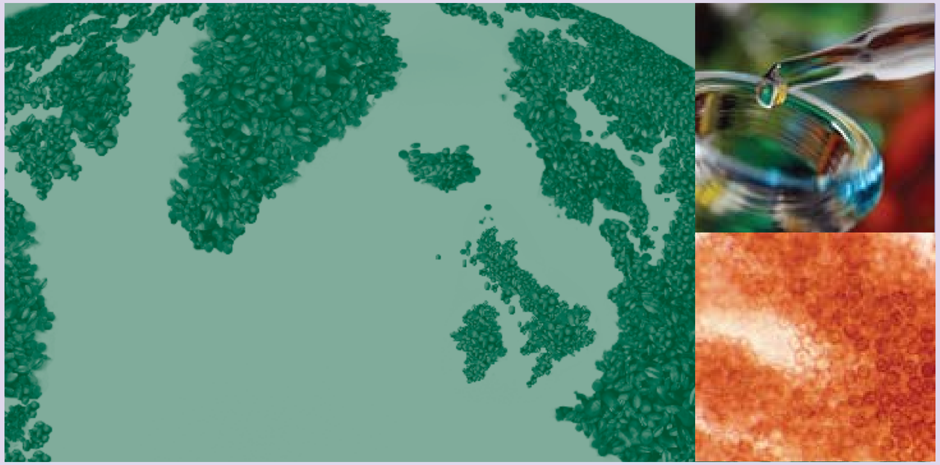
Epidemiological studies

What are they?

Epidemiological studies observe groups of people over time and relate their characteristics, such as their diet or physical activity levels, to their later risk of disease.

For example, an epidemiological study might investigate how diet affects the risk of breast cancer in African-American women who live in rural areas. These studies are observational: scientists watch what's going on, but they don't try to change it. Strong evidence can and does arise from epidemiological studies, but remember, detectives can't build a complete case out of this evidence alone.

There are three main types of epidemiological studies: ecologic studies, cohort studies and case-control studies.



Ecologic studies

Ecologic studies look at diet and cancer at the population level. Think of this as the view from 30,000 feet. For example, you've probably heard about studies that found lower cancer rates in Asian communities that consume a lot of fish. These are ecologic studies.

Strengths of ecologic studies

Ecologic studies can provide powerful clues pointing in a particular direction, especially when they compare large populations with different diets.

Weaknesses of ecologic studies

Ecologic studies can't prove cause and effect. If a detective keeps noticing a certain person near the scene of a series of burglaries, he may consider the person a suspect.

But the person could just be a nosy neighbour or a reporter. The detective would need more evidence to prove that the person committed the crimes. Similarly, scientists need more evidence – other studies to help prove the connection that ecologic studies point to.

Cohort studies

Cohort studies gather data on a large group of healthy people and then follow the group over many years. Study participants may keep daily food diaries or fill out questionnaires about what they eat.

As some people in the study develop cancer, researchers focus on how their diets differed from the people who remained healthy. For example, did the people who stayed cancer-free eat more fruit and vegetables or soy products than the people who developed cancer? Their diet may provide a clue.

Strengths of cohort studies

Cohort studies let researchers study people over a long period of time, which is important as cancer can take many years to develop. They have an advantage over case-control studies (page 6) because they ask people to keep track of what they're eating while they're still healthy. This is more accurate than waiting until people develop cancer and then asking them to remember what they ate in the past. Another strength of cohort studies is that many different types of cancer (or other diseases) can be studied using the same group of people.

Weaknesses of cohort studies

As in any kind of dietary investigation, to have real scientific and statistical significance, cohort studies need to be extremely large and participants need to be followed over a long period of time. In addition, cohort studies, like ecological studies, can't prove cause and effect.

Case-control studies

Case-control studies differ from cohort studies because they include people who already have cancer when the study starts (‘cases’). These people are then compared to a group of people who don’t have cancer (‘controls’).

Strengths of case-control studies

With enough participants in the study and careful selection of controls, case-control studies can provide a cost-effective way to study cancer.

Weaknesses of case-control studies

Imagine trying to list the kinds of foods you ate most often 10 years ago. Like eyewitness testimony in a courtroom, case-control studies depend on our unreliable memories. In case-control studies, cases and controls may remember their past diets differently or actually change their diets because they have the disease. However, some new scientific developments, such as biomarkers of dietary intake, act like fingerprints of the foods we eat regularly and can help to avoid this problem. This is also very useful for cohort studies.

Laboratory studies

What are they?

Just as forensic scientists use advanced crime labs to sift through the many confusing clues found at crime scenes, cancer researchers also examine complex dietary evidence in controlled laboratory environments.

Laboratory studies involve more than observing and gathering data. Scientists make small, defined changes in one or more sets of test subjects – such as animals, cells or tissues. They then compare the various outcomes.

There are two main types of laboratory studies: in vitro studies and in vivo studies.



In vitro studies

In vitro studies help researchers work out precisely how and why certain foods or food substances might protect against cancer. They examine animal or human cells or tissues removed from the body to seek clues as to the mysterious array of chain reactions that happen after we consume a particular nutrient.

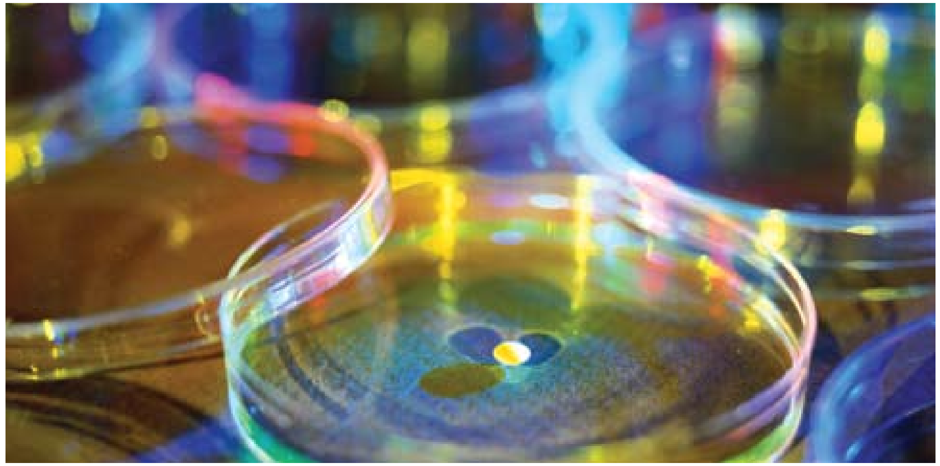
An epidemiological study can suggest that eating green beans protects against cancer. But that's only a correlation. With in vitro studies, scientists can look at what happens in cells when they are exposed to constituents from the beans. Put those two types of studies together, and you're closer to solving the mystery than with either type of study alone.

Strengths of in vitro studies

In vitro studies are tightly focused, which means that scientists can control the many different variables. Once an in vitro study finds a 'suspect' – a biological mechanism that might protect against or increase your risk of cancer – they can test their suspicions in an animal model.

Weaknesses of in vitro studies

In vitro studies can't tell us if an anti-cancer effect that happens at the cell level also occurs in the 'real world' of the complex human body. They also can't tell us how much we might have to eat of a particular food to gain the anti-cancer benefits, and they only involve food components, not whole foods – you can't feed a cell an apple.



In vivo studies

In vivo studies put diets to the test in complex living organisms. If cell or tissue studies (in vitro) provide evidence that a certain nutrient protects against cancer, an in vivo study can give researchers the next clue.

Strengths of in vivo studies

Testing diets in animal models allows scientists much stricter control than with humans. A mouse eats what it's fed – so researchers know exactly what's going in and what's going out.

Weaknesses of in vivo studies

Humans aren't mice. While a surprising number of our biological processes may be similar – including the cancer process – many things that happen in mice don't happen the same way in humans, and vice versa.

Controlled trials

What are they?

In controlled trials, scientists don't just observe what happens to study subjects as they eat what they would usually eat. They make specific changes, for instance to the participants' diets, to see how those changes affect them.

One group of study participants, the 'intervention group', consumes foods or nutrients scientists think may protect against cancer. Other participants, the 'control group', get a different 'food prescription' – often just a placebo (a substance that has no physical effects).

Most controlled trials are randomised and double-blind. 'Randomised' means that study subjects in the two groups don't differ in any major way other than in what they've been asked to eat, so the results aren't affected by unrelated things. 'Double-blind' means that neither the scientists nor the people in the study know who's in which group.

Strengths of controlled trials

Controlled trials avoid many of the types of bias that can be found in other studies. They also let scientists keep tight control over the enormous complexity of our daily diets.

Weaknesses of controlled trials

Controlled trials are often called the scientific 'gold standard'. This can be true in many situations, but for unraveling the diet-cancer mystery, this investigation method may not be perfect. It's difficult to disguise dietary modifications. In controlled trials, the particpants know what they are eating and they'll be aware if someone changes it. That's why many controlled trials involving diet and cancer give the nutrients in the form of a supplement. But even if scientists prove that an isolated supplement produces no anti-cancer effects, this wouldn't tell us anything conclusive about how whole foods or diets made up of many different foods affect cancer risk. Since cancer can take decades to develop, it's hard to know if a study has lasted long enough. Nevertheless, a positive result from a controlled trial can constitute strong evidence that a particular nutrient has a protective effect against cancer.

Putting the evidence together

Meta-analysis

Meta-analysis is about putting different studies together in a scientific way. It combines the findings of many studies on the same issue, using statistical methods. It increases our ability to detect links and see how big the effects are.

The bigger picture

Another way of approaching the evidence is to stand back and assess the research as a whole. Rather than using a complex mathematical model, this means stacking up all the related studies and figuring out what they say overall. This requires expertise and discussion. Think of our fictional detective looking at fingerprints, eyewitness testimony, DNA evidence and circumstantial evidence, and putting them all together to see what kind of case they form.

Drawing conclusions

The most compelling evidence demonstrating an association between a particular food and lowered cancer risk only emerges when several different kinds of studies say the same thing. Now that you know what those kinds of studies are and what their strengths and weaknesses might be, you'll be better able to evaluate new pieces of evidence about diet and cancer, and what they mean for your health.

The portfolio approach

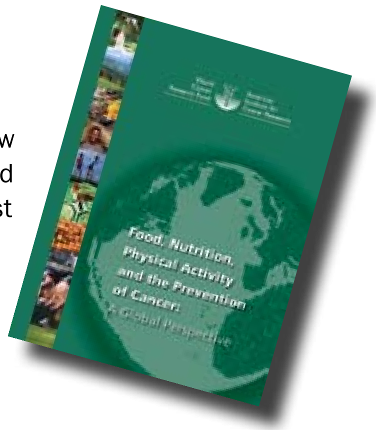
When it comes to mapping the complex links between diet and cancer, no single study can tell us everything. The portfolio approach incorporates all the methods described on the previous page to bring together scientific evidence from which we can draw conclusions.

As we've explained, each of the different kinds of study used to explore diet and cancer can only answer specific sets of questions. Even when all the different types are put together, some gaps in our understanding remain – some questions go unanswered.

To try to fill those gaps, and answer those questions, scientists must look to the assembled research – all of the assembled research – and draw out the findings. They do this by looking at where the majority of evidence is pointing.

That's where the portfolio approach comes into its own. Instead of imposing a fixed hierarchy, the portfolio approach tries to account for the strengths and weaknesses particular to each study type. Some types still carry more weight than others, but none are simply dismissed. If a cohort study finds an association for which there is no laboratory evidence, it's noted and discussed. Likewise, if strong laboratory results link a specific food or nutrient to fighting tumours in an animal model, but the amount necessary for protection is far outside what's feasible for human intake, that finding is taken into account.

The portfolio approach allows researchers a comprehensive overview of how the relevant evidence is stacking up. It takes time and patience. Ultimately, researchers are able to draw conclusions through well-informed discussion and debate that balances all the evidence from a vast array of sources. This is the approach used to compile our expert report – upon which all WCRF UK advice is based – as it is the most reliable method of putting together science-based guidelines for cancer prevention.



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