Finding the causes of cancer is the first step to prevention

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Credit: AI-generated image (disclaimer)

Big Tobacco is the poster child for how an industry can confuse the experts and the public on the dangers of its product. It delayed any smoking restrictions for decades by employing the subterfuge of demanding "perfect knowledge" for proof of harm. This would mean complete and quantitative definitions of all aspects of human exposure,

disease outcomes, biomolecular mechanisms of how smoking can cause cancer and effects of smoking on cancer in rats and mice.

But the evidence that smoking caused cancer came only from studies that looked at large numbers of people over time that showed associations, and association is not causation, Big Tobacco argued. Therefore, they claimed there was no proof that smoking caused cancer.

This tactic worked for far too long, until finally, scientists and policy makers realized that decisions had to be made on the basis of the available evidence. (Years later it became clear that Big Tobacco knew all along that their product was deadly.)

Lawyers understand the concept well: In the absence of perfect knowledge we must still seek justice; a jury evaluates the evidence and renders a verdict. That verdict may be overturned on appeal based on newer evidence, or it may not. In fact, the International Agency for Research on Cancer has been convening "juries" of experts to make cause-and-effect evaluations for suspected carcinogens since 1971.

The verdict, based on available evidence, is that smoking causes lung cancer. The IARC recently confirmed this finding and extended it to passive smoking.

Perfect knowledge wasn't needed to prove that smoking causes cancer. What was needed was epidemiology – the study of the distribution and determinants of disease in human populations – which lets us identify cancer hazards, which then forms the basis for prevention. In fact, epidemiology is the primary tool to identify causes of cancer.

What is cancer and how can it be prevented?

Cancer is a disease in which some of our own cells begin to grow

uncontrollably. If untreated, it will often kill us.

Even with no toxic exposures, some cancers will still happen spontaneously. Gene mutations happen at a predictable rate in almost all cells of the body spontaneously. This mutation rate can, however, be increased by exposures to carcinogens like cigarette smoke and ionizing radiation. So, the word "prevention" really means "reduction of risk." And the word "causes" means "increases risk."

The first step in discovering whether something is a carcinogen – that is, causes cancer – is epidemiology. I'll describe some different ways epidemiologists do this.

Once an exposure that causes cancer has been identified, understanding the biological mechanism can also help develop effective prevention strategies. But in many cases we don't actually need to understand how an exposure causes cancer to develop those strategies.

Smoking and lung cancer

So what is the evidence that smoking causes lung cancer?

In one type of epidemiological study, called case-control, people with cancer are compared to those without cancer for differences in personal habits, diet, environmental exposures and so on.

Beginning as early as 1939, it was found that men with lung cancer were much more likely to have been long-term smokers than men in the general population. Since then, many studies have also shown this.

This knowledge led to education and interventions that have in turn led to lower smoking rates among men and consequently lower lung cancer death rates in America. (Women started smoking later in history.)

Understanding how smoking causes lung cancer is not needed to effectively intervene and lower risk. The strategy is to discourage young people from starting to smoke, and help current smokers to quit.

Hepatitis B virus and liver cancer

In another type of epidemiological study, called a cohort study, a large number of healthy people are enrolled, blood samples are taken and they are asked questions about personal habits and exposures. They are then followed for many years to see who gets cancer.

For example, the primary causes of liver cancer were not understood until epidemiologist R. Palmer Beasley began a large cohort study in Taiwan in 1975. He enrolled 22,707 otherwise healthy men and followed them for several years. Of the sample, 3,454 were chronically infected with hepatitis B virus (HBV). After several years of follow-up, there were 40 new cases of liver cancer in the HBV carrier men and only one in the much larger noncarrier group.

The cohort study clearly showed that HBV can cause liver cancer. And in this case, understanding the biology of HBV and how it is transmitted has led to prevention of liver cancer by making a vaccine against the virus.

This knowledge has also greatly improved treatment because now chronic HBV carriers are tested annually for alfa fetoprotein in the blood to screen for the presence of cancer. As a result, liver cancer is caught much earlier than in the past.

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Electric light and breast cancer

A newer idea is that excess exposure to electric light during the night might increase risk of breast cancer. In the 1980s, I started working on the idea because at the time there was no good answer to explain why breast cancer risk was so much higher in the industrialized world than in developing countries.

It's an easy idea to state but difficult to assess. So I and others had to make testable predictions from the theory, the first of which was that women who work at night would be at increased risk.

Based on a series of epidemiological studies of shift workers, the IARC has now classified shift work as a probable human carcinogen. This is

consistent with the theory but does not by itself prove it.

Since then, I have collaborated on studies of blind women who tend to have lower risk, as predicted. There is also growing evidence that exposure to light at night has a range of physiological effects. For instance, intense evening light exposure can lower the blood level of the hormone melatonin in people. There is also some biological evidence, primarily in lab rats, that melatonin fights breast tumors. In this case, both epidemiological and biological evidence may be needed to make the case.

Not enough evidence has accumulated to convince a jury of experts that exposure to electric light at night is a carcinogen. However, the evidence is mounting, and the American Medical Association has warned of potential health risks from "white" LED street lighting based on what we do know.

Unless and until convincing evidence from epidemiological studies surpasses the threshold for a panel of experts to conclude causality, preventive measures will remain modest.

Cancer prevention using best available evidence

In the absence of perfect knowledge, we must still evaluate the available evidence and make policy decisions to safeguard the public's health. This might be a decision to take no action at present, and wait for further evidence to clarify a fuzzy picture.

First and foremost, it should be recognized that in science, the term "proof" can be defined only as a "consensus of experts." This is true from physics to bird-watching, and every discipline in between, including public health.