Clinical Chemistry

Cancer Screening, Incidental Detection, and Overdiagnosis

Article:
H Gilbert Welch and Regan Bergmark.
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Clin Chem 2024; 70(1): 179–189. https://doi.org/10.1093/clinchem/hvad127

Guest: Dr. Gilbert Welch from the Center for Surgery and Public Health at Brigham & Women's Hospital in Boston, Massachusetts.

Bob Barrett: This is a podcast from *Clinical Chemistry*, a production of the Association for Diagnostics & Laboratory Medicine. I'm Bob Barrett. "Make a crucial catch. Cancer screening saves lives." The conventional wisdom, highlighted by the partnership between the National Football League and the American Cancer Society, is that cancer outcomes are improved when diagnosed in an early stage of disease. Expanded screening programs have led to a paradigm shift, increasing rates of cancer diagnosed in patients who do not show any symptoms. While this is generally viewed as a good thing, it also comes with a negative side effect, diagnosis of a cancer that will not go on to cause symptoms or death. This overdiagnosis has the potential to mislead by overestimating the true survival rate of certain cancers and falsely inflating the number of cancer survivors.

A review article appearing in the January 2024 issue of *Clinical Chemistry* summarizes the current approach to cancer screening, provides evidence that early detection has led to overdiagnosis, and challenges the assumption that the benefits of increased screening outweigh the undesirable side effects. In this podcast, we're pleased to welcome the review article's lead author. Dr. Gilbert Welch is a general internist, cancer epidemiologist, and Senior Researcher at the Center for Surgery and Public Health at Brigham & Women's Hospital in Boston. For more than three decades, he has been asking hard questions about his profession. His arguments are frequently counterintuitive, even heretical, and his most recent book is "Less Medicine, More Health: 7 Assumptions That Drive Too Much Medical Care." Dr. Welch, welcome to the podcast.

I noticed that the first table in your article was a glossary. I imagine some of the terms used may be unfamiliar to *Clinical Chemistry* readers, so maybe I should start by asking you to define and tie together the three terms in the title of your review article: screening, incidental detection, and cancer overdiagnosis.

Gilbert Welch: Sure. It's important to begin with the traditional diagnostic pathway for cancer. In the past, patients were only diagnosed with cancer because they had symptoms. Now, we are regularly looking for cancers in individuals who have no

signs or symptoms of cancer. That's screening. In addition, patients who have symptoms from illnesses or injuries that have nothing to do with cancer are being more intensively tested, particularly with advanced imaging, things like CT, MRI, PET scans, leading us to stumble onto some cancers. That's incidental detection.

For example, we evaluate shortness of breath and maybe consider a possible pulmonary embolism and we take a chest CT, which also identifies a mass in the kidney. Now the kidney mass has nothing do with the shortness of breath, but it turns out to be cancer. It was incidentally detected. In short, screening is purposeful, incidental detection is unintended, but they both lead to the same result--the diagnosis of cancer in patients who have no symptoms of the disease.

Now cancer overdiagnosis refers to the detection of abnormalities that meet the pathologic definition of cancer, yet are not destined to progress to cause either symptoms or death. Thus by definition, overdiagnosis cannot occur in a patient with symptoms from their cancer. Instead, cancer overdiagnosis is always the result of either screening or incidental detection.

Bob Barrett: In the article, you detail the evidence demonstrating that overdiagnosis can occur and is occurring in a variety of cancers, like breast cancer, thyroid, prostate, kidney, lung, and melanoma skin cancer. Why should we care about cancer overdiagnosis?

Gilbert Welch: Well first and foremost is that a cancer diagnosis regularly leads to cancer treatment and an overdiagnosed patient cannot be helped by treatment because there's nothing to fix. But they can be harmed, and we doctors don't want to be in the business of harming patients. Cancer overdiagnosis produces another more insidious problem, deceptive feedback. The harder we look for early cancer, the more overdiagnosis occurs, and the more overdiagnosis that occurs, the more people there are who feel they owe their life to early cancer detection. And more overdiagnosis, also creates skyrocketing five-year survival rates, leading people to conclude that the best way to deal with cancer is to test more people for it. It's a remarkably deceptive feedback loop.

Bob Barrett: That idea of cancer overdiagnosis can be challenging to wrap one's head around. It feels like we're all taught that anything called cancer is ultimately destined to cause death if left untreated, but the world is not that simple is what you're saying, right?

Gilbert Welch: No, it's not. Allow me to quote a Cleveland Clinic cancer surgeon by the name of George Crile. He wrote, "In clinical

practice, to say that a person has cancer gives us little information about the possible course of his disease as to say he has an infection. There are dangerous infections that may be fatal and there are harmless infections that are self-limited and may disappear. The same is true of cancers. Cancer is not a single entity. It is a broad spectrum of diseases related to each other only in name."

Now, Dr. Crile wrote that in 1955, the year I was born, and he was probably the originator of the barnyard pen analogy to communicate the tremendous heterogeneity in cancer growth. Here's the analogy. There are three animals in the barnyard, the birds, the rabbits, and the turtles. The goal of screening is to fence them in; you know, to catch them early. However, you see the problem with the birds. We can't catch the birds because they've already flown away and birds represent the most aggressive cancers; the fastest growing cancers, the cancers that have already spread by the time they're detectable. Screening doesn't help with the birds. The question is, can we treat them?

Now the rabbits are hopping around and you can catch them early if you build enough fences. So screening may help in these cases. But for screening to help however requires that treatment needs to be more effective early than it is late. Sometimes this is not true. In the case of hormone-responsive breast cancer for example, a two-centimeter tumor can be treated as well as a one-centimeter tumor.

And then there are the turtles, and here we don't need any fences because they're not going anywhere anyway. Turtles meet the pathologic definition of cancer. However, they're either not growing or growing so slowly that they will never cause problems until the patient dies from other causes, or they're regressing, they're getting smaller. That's right, some cancer start and may then disappear, perhaps recognized by a well-functioning immune system. The unfortunate reality is screening is very good at finding turtles, but doctors are not able to distinguish turtles from rabbits. Thus, we tend to treat everybody who's labeled as having cancer, creating the major harm of early detection, overdiagnosis and overtreatment.

Bob Barrett: Well finally, we'll conclude with the way you conclude the article with what many might consider a heretical statement. I'll quote you here, "Given the evolving understanding that tumor biology and host response are more relevant to prognosis than the time of diagnosis, it's time to challenge the assertion that early diagnosis is always the best approach to curing cancer." This leads me to ask, do you believe we've just overinvested in cancer screening?

Gilbert Welch: Absolutely. We do too much cancer screening. We have overstated the value of looking for early cancer in asymptomatic patients. The truth is, the most deadly cancer, the birds I was talking about a minute ago, they tend to be missed by cancer screening simply because they are so aggressive and become systemic so quickly. Now the good news is our cancer treatments are getting better, and ironically, the better we are able to treat cancers, the less important it is to find them before they cause symptoms. Consider this, why don't we screen people for pneumonia? Well, the answer is because we can treat pneumonia.

Furthermore, we have understated the harms of cancer screening, and the harms go well beyond cancer overdiagnosis. It's important to understand the dynamics of screening. Many, many people must be tested to potentially benefit a few. Ninety-nine percent of people screened cannot be helped by screening, but they can be hurt by it. False alarms are extraordinarily common. For example, mammography screening has made a breast cancer scare a rite of passage for American women.

Many are subjected to subsequent procedures and many are subjected to substantial out-of-pocket cost, and too many are told that while they don't have cancer, they are also not normal. Instead, they're told they are somehow at high risk. They have dysplasia, atypia, or some abnormal breasts. Screening has spread a great deal of fear, and that can't be good for your health.

And then finally, the promotion of early cancer detection has led the public and policymakers to believe that the path to health is through testing for disease, but instead that's a recipe for turning more people into patients. Recently, there's been a disturbing trend to promote cancer screening as a way to solve health disparities, but the health effects of poverty can't be cured by screening. Screening is about as likely to reduce health disparities as it is to reduce carbon emissions. Instead, screening tends to siphon resources away from interventions that can reduce health disparities like child tax credits, school lunches, affordable housing. It can only add to the rising cost of American medical care and amplify income disparities, which in turn are highly related to life expectancy. So yes, I think we've overinvested in cancer screening.

Bob Barrett: I imagine that this opinion hasn't made you many friends?

Gilbert Welch: Yeah. No, because there's a lot of money around in this business, great way to recruit patients, and on the surface, it seems to make so much sense. Of course, you want to be looking for cancer early until you realize, first it doesn't help that many people, if it does at all quite frankly and it leads a

lot of people to have a lot of problems that they otherwise wouldn't have.

Bob Barrett: That was Dr. Gilbert Welch from Brigham & Women's Hospital in Boston, Massachusetts. He served as lead author for a review article describing the unintended consequences of cancer screening in the January 2024 issue of *Clinical Chemistry* and he's been our guest in this podcast on that topic. I'm Bob Barrett. Thanks for listening.