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## Cancer Screening Has Not Been Shown to 'Save Lives'

Neil Osterweil

January 07, 2016

Debates about cancer screening programs tend to focus on when to start, who to screen, and the frequency of screening. But some investigators are asking a far more provocative question: Do screening programs actually save lives?

We do not know the answer to that question, and would need to conduct massive clinical trials to find out, said Vinay K. Prasad, MD, MPH, assistant professor of medicine at the Oregon Health Sciences University in Portland.

"Proponents of cancer screening say that screening tests have been shown to save lives. What we're trying to show is that, strictly speaking, that's sort of an overstatement," he told *Medscape Medical News*.

In an analysis [published online](#) January 6 in the *BMJ*, Dr Prasad and his colleagues argue that although cancer screening might reduce *cancer-specific* mortality, it has not conclusively been shown to have an effect on *overall* mortality.

The researchers go on to suggest that the harms of screening might actually contribute to overall mortality rates. These potential harms include false-positive results that lead to unnecessary biopsies or therapeutic interventions and overdiagnosis, in which treatment is delivered for a condition that is unlikely to affect patients during their natural lifespans.

"There are two chief reasons why cancer screening might reduce disease-specific mortality without significantly reducing overall mortality," the researchers write. "Firstly, studies may be underpowered to detect a small overall mortality benefit. Secondly, disease-specific mortality reductions may be offset by deaths due to the downstream effects of screening."

"The bar to say that screening saves lives should be overall mortality, and we haven't met that bar," Dr Prasad told *Medscape Medical News*.

### **Questionable Assumption?**

The rationale for cancer screening is based on the assumptions that screening will reduce deaths from cancer and that lowering cancer-specific deaths will decrease overall mortality. These assumptions remain unsupported by facts, Dr Prasad's team contends.

They illustrate this point with data from the National Lung Cancer Screening Trial (NLST). Although there was a 20% relative reduction in lung cancer deaths with low-dose CT screening, compared with chest x-ray, and a 6.7% relative reduction in overall mortality, the absolute reduction in risk for overall mortality was just 0.46%.

The researchers point out that the comparator in the NLST — chest x-ray — is no longer a standard of care, and might actually be associated with an increased risk for lung cancer death. Additionally, the overall mortality benefit with screening could not be explained by a reduction in lung-cancer-specific mortality.

The team also notes that "the benefit in lung cancer mortality of CT screening (estimated to avert over 12,000 lung cancer deaths in the United States annually) must be set against the 27,034 major complications (such as lung collapse, heart attack, stroke, and death) that follow a positive screening test."

### **Informed Discussion**

The decision to undergo screening should be part of an informed discussion between the patient and clinician that takes into account personal preferences and the risks and benefits of screening. Dr Prasad explained.

"Declining screening may be a reasonable and prudent choice for many people," the researchers write.

"Doctors should be comfortable with whatever choice people make when they hear about all the potential benefits and the known harms," Dr Prasad added.

To answer the mortality question would require pragmatic trials with millions of patients, but such trials could be practical if they are based on prospective registry data, the researchers say.

However, in an [accompanying editorial](#), Gerd Gigerenzer, PhD, from the Max Planck Institute for Human Development in Berlin, argues that "rather than pouring resources into 'megatrials' with a small chance of detecting a minimal overall mortality reduction, at the additional cost of harming large numbers of patients, we should invest in transparent information in the first place."

He explains that information about screening should be presented in a "fact box" that lays out the benefits and risks of mammography with numbers for how many women would be affected.

"It is time to change communication about cancer screening from dodgy persuasion into something straightforward," he concludes.

### **The Wrong Question?**

It would be impractical to conduct the trials necessary to get a definitive answer about whether screening offers a distinct overall survival benefit, said Robert Smith, PhD, senior director of cancer screening for the American Cancer Society.

However, he noted, reduction of cancer-related morbidity is a more meaningful way to frame the argument about screening.

If we focus on mortality, the question then becomes: "Is it worth doing something if it doesn't prevent you from dying of anything? That sets a very high bar for preventive health," he told *Medscape Medical News*.

"When you think about preventive health, you do things not to keep yourself from dying of anything, but to avoid dying from something specific and, in particular, dying *early* from something specific," he said.

### **"Imperfect Process"**

Richard L. Schilsky, MD, chief medical officer for the American Society of Clinical Oncology (ASCO), said that although, in general, ASCO supports cancer screening, "it's a very imperfect process."

The value of screening depends on the degree of risk for the condition being screened in the population of interest, the sensitivity and specificity of the screen, and the natural history of the disease detected by the screening test, Dr Schilsky told *Medscape Medical News*.

"It's the combination of these three factors that's getting all of us into so much difficulty in

interpreting screening data," he said.

The often high variability in the natural history of many cancers has been the source of particular confusion and uncertainty surrounding screening, he noted.

For example, there is little value in screening for aggressive cancers for which interventions are unlikely to make a difference in outcomes, no matter how early the disease can be detected.

Conversely, "if the cancer is never going to kill you, no matter what the doctors do, then screening won't help either," he said.

Additionally, there are some cancers for which treatments are sufficiently effective that they can be successfully managed whether they are diagnosed at an early or later stage.

"When you consider all these factors, the number of individuals who will actually benefit from detecting a screen-detected cancer is very small," Dr Schilsky said.

"These are highly complicated and highly nuanced issues," he continued. "Many doctors don't even fully understand many of these nuances, and certainly many, if not most, doctors don't have the time to really sit with the patient and work through all of these issues at the level of detail that's really necessary to communicate clearly what the potential risks and benefits are," he said.

Decision-making aids, such as the fact box to help women decide about mammography that Dr Gigerenzer describes, could help patients decide whether the risk–benefit equation falls in their favor, Dr Schilsky explained.

"ASCO continues to support screening as an important mechanism for reducing cancer-related deaths, but not everybody will benefit from screening, and we can't leave patients with the impression that somehow screening is completely harmless or that it's a guarantee that if the screening test is negative that they'll never get cancer, or if the screening test is positive that they'll be cured of cancer," he said.

"There are too many variables and too many unknowns," Dr Schilsky said.

*Dr Prasad reports receiving travel reimbursement from the Right Care Alliance of the Lown Institute. Dr Gigerenzer, Dr Smith, and Dr Schilsky have disclosed no relevant financial relationships..*

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