

Letters to the Editor

Identify Patients Likely to Benefit from Lung Cancer Screening

Original Article: Lung Cancer Screening: Pros and Cons [Lown Right Care]

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To the Editor: As researchers studying lung cancer screening, we recognize the associated uncertainties. Dr. Leishman recently discussed lung cancer screening with more than 200 primary care clinicians and found that the concerns Drs. Lazris and Roth raised in their article are shared by many frontline clinicians. However, reports from recently completed European lung cancer screening trials affirm the benefit of screening. The current strategy used for interpreting nodules on lung cancer screening examinations (American College of Radiology Lung Imaging Reporting and Data System) is more conservative than the strategy used in the National Lung Screening Trial and may significantly reduce false-positive rates compared with the National Lung Screening Trial. Weighing the balance of benefit and harm is challenging, especially for individual patients whose lung cancer risk and general health may not reflect that of the average trial participant.

Although clinicians have reservations about the generalizability of the National Lung Screening Trial, almost all acknowledge that the evidence cannot be totally discounted, and most feel some obligation to offer screening. We have often heard these clinicians say things like, “I’ve been meaning to get around to lung cancer screening.” Most acknowledge that screening might be

a good idea for some patients, saying things like, “if a patient is a very heavy smoker with a very high lung cancer risk but no major health issues, then I might recommend screening.” There is an important insight embedded in this line of thinking: some patients can likely expect a much larger than average benefit from lung cancer screening.

How can clinicians identify patients who are more likely to benefit from lung cancer screening? If an eligible patient is reasonably healthy, clinicians could consider calculating individualized lung cancer risk using one of several well-validated risk models.¹ We and others have developed web-based tools to help clinicians incorporate individualized risk calculations into decision-making.² Individualized risk assessment can be helpful because patients at higher risk of developing lung cancer are also more likely to benefit from early detection through screening.³ When lung cancer risk increases, uncertainty about whether to recommend screening decreases when the person has a reasonable life expectancy.⁴

At a time when screening uptake is so low (i.e., 2% to 6% of eligible patients get screened),⁵ making an effort to identify patients at high risk who are in otherwise good health for whom screening is likely to be highly advantageous might be an idea that primary care clinicians can agree on.

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- Caverly TJ, Cao P, Hayward RA, et al. Identifying patients for whom lung cancer screening is preference-sensitive: a microsimulation study. *Ann Intern Med.* 2018;169(1):1-9.
- Huo J, Shen C, Volk RJ, et al. Use of CT and chest radiography for lung cancer screening before and after publication of screening guidelines: intended and unintended uptake. *JAMA Intern Med.* 2017;177(3):439-441.

In Reply: We appreciate the response to our article. The authors state correctly that recent European studies confirm the benefit of the National Lung Screening Trial, with similar survival benefits of three to six people out of 1,000 screened avoiding lung cancer death over five to 10 years of screening. However, doubt about the net benefit of lung cancer screening persists, which may be why few doctors are implementing lung cancer screening.

False-positive rates for low-dose computed tomography scans are high. In the German Lung Cancer Screening Intervention Trial, women inexplicably had a survival advantage with screening, but men did not; it is possible that other ongoing studies will continue to introduce uncertainty about who benefits and who does not. In older studies, the survival rate is not significant, and those studies need to be factored into our knowledge base.¹ There are still many questions left unanswered, especially as to who benefits the most from screening (e.g., active vs. distant smokers, high pack-year history vs. lower pack-year) and whether we can reduce the risk of false-positive screenings without compromising the benefit of screening.

The use of web-based methods to identify high-risk patients who may benefit from lung cancer screening seems potentially valuable and may, after being verified, help reduce unnecessary screenings while enhancing the benefit to risk ratio of screening. Until then, we hope our article provides physicians and patients with sufficient information about the risks and benefits of screening to help them make a shared decision.

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Lung Cancer Screening Effective for Reducing Cancer Deaths

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To the Editor: We read with interest the article by Drs. Lazris and Roth. They report that no other study besides the National Lung Screening Trial (NLST) has shown a benefit from lung cancer screening. Two other randomized trials (Multicentric Italian Lung Detection [MILD], Dutch-Belgian Randomized Lung Cancer Screening Trial) have reported lung cancer mortality reductions greater than were found in the NLST.^{1,2} A third trial (German Lung Cancer Screening Intervention Trial) demonstrated the same finding in women. The greater reduction in lung cancer mortality found in these studies may be because of the longer screening protocols compared with the 24 months in the NLST. The MILD trial continued screening for up to 10 years and showed the largest reduction in lung cancer (39%) and overall mortality (20%).¹

The authors highlight important risks including false-positive findings and overdiagnosis. Compared with the NLST, the widely implemented American College of Radiology Lung Imaging Reporting and Data System (Lung-RADS) has lowered false-positive rates to 10% to 12% on the initial screening examination and 5% on subsequent scans.³ Using the original Lung-RADS system would have reduced the number of false-positive findings in the NLST by more than 50% and corresponding invasive procedures by 23%. The Veterans Health Administration study cited in the Lazris and Roth article used liberal criteria for positive examinations (i.e., any nodule larger than 2 mm), which contributed to the high false-positive rate.⁴

Long-term follow-up in the NLST suggests that overdiagnosis does not occur other than for carcinoma in situ. Under the current standard of care, these patients return to annual surveillance with no further interventions unless the lesion grows aggressively.⁵ The recent update to Lung-RADS increased the size threshold for such lesions from 20 mm to 30 mm, further reducing the risk of overdiagnosis.⁵

Real-world evidence highlights the effectiveness of well-organized screening programs. A

survey of 165 lung cancer screening programs in the United States, most in community settings, demonstrated similar outcomes as those in academic centers.⁶ Lung cancer screening can successfully take place in the real world and is increasingly being performed, with a survey of 10 states finding that 14.4% of eligible patients had a low-dose computed tomography scan within the past 12 months.

Lung cancer screening is effective for reducing the number one cause of cancer deaths for men and women. The time has come to make lung cancer screening part of routine primary care for patients who are at risk.

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In Reply: We appreciate the letter from Drs. Lim, Kitts, and Tremblay. After our article was sent to press, several new studies were published that further illuminated the potential benefits of annual screening. However, these new studies do not fundamentally alter our conclusion that there are both risks and benefits to low-dose computed

tomography screening, and persistent uncertainty around how effective screening is for different populations.

The authors cite a 39% reduction in lung cancer death among participants screened for 10 years in the MILD trial. Although technically correct, relative numbers (39%) do not help physicians and patients make shared decisions because these numbers do not tell us the absolute benefit of screening. In the MILD trial, 1.7% of participants died of lung cancer over 10 years in the screened arm, and 2.3% died in the control arm, leading to a reduction of six lung cancer deaths out of 1,000 people screened. This is similar to the NLST findings, showing that long-term screening can slightly improve benefits, with persistently high false-positive rates. The German Lung Cancer Screening Intervention Trial did show reduced lung cancer mortality in women (seven out of 1,000 fewer lung cancer deaths after five years of screening), but no survival advantage for men. Finally, Lung-RADS does reduce the false-positive rate; however, the authors noted a decrease in sensitivity of lung cancer detection, which may lead to a lower survival advantage of screening.¹

There are still many questions left unanswered. Why do men have improved survival in some studies and not others? Do survival advantages vary based on other characteristics? The Centers for Medicare and Medicaid Services is organizing a real-world survey to assess the prevalence, survival advantage, and risks of screening in the community, and many physicians and organizations are waiting for those data before pursuing an organized screening program. Until then, the results from the NLST and the newer trials do provide some information that will help physicians and patients reach a decision as to whether to pursue lung cancer screening.

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