

Results of the National Lung Cancer Screening Trial: Where Are We Now?



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KEYWORDS

• Lung cancer • Screening • Low-dose CT • NLST

KEY POINTS

- In 2011, the National Lung Screening Trial (NLST) demonstrated a 20% reduction in disease-specific mortality using low-dose CT (LDCT) screening of a high-risk population compared with chest radiography (CXR).
- The United States Preventive Services Task Force (USPSTF) recommends screening high-risk individuals aged 55 to 80 years with annual LDCT.
- In November 2014, the Centers for Medicare & Medicaid Services (CMS) proposed to allow once-yearly screening for lung cancer with low dose computed tomography (LDCT) in appropriately selected patients.

INTRODUCTION

Screening for cancers in selected patient populations has become a well-established element of health care in the United States.¹ The most common cancers, in order of decreasing incidence, are prostate, breast, lung, and colorectal.² The treatment of breast and colorectal cancer has benefited from the widespread adoption of screening recommendations, whereas the treatment of prostate cancer, for which the USPSTF does not have screening recommendations (Table 1), has used the prostate-specific antigen test and digital rectal examination for screening for many years.³ As a result, 93% of prostate cancers are diagnosed at a local or regional stage, and 61% of breast cancers are diagnosed at a local stage. These screening practices contribute to

the high overall 5-year survival rates for prostate and breast cancer: 99.7% and 90.3%, respectively.⁴ The incidence of colorectal cancer has been decreasing by 2% to 3% per year during the past 15 years, whereas the rate of screening for colorectal cancer among average-risk patients has simultaneously grown to more than 60%.⁵

Lung cancer remains the leading cause of cancer death for both men and women in the United States, and it is expected to kill approximately 86,930 men and 72,330 women in 2014 in the United States alone.² Yet, there is no broadly adopted screening protocol for patients at high risk of developing lung cancer. More than 400,000 people in the United States have a history of lung cancer, and an estimated 224,210 new cases will be diagnosed in 2014.⁴ Early-stage lung cancers often develop asymptotically or

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| Cancer | Specified Population | Screening Recommendation | Grade |
|----------|---|---|-------|
| Prostate | NA | No screening recommended | D |
| Breast | Women aged ≥ 40 y | Mammography every 1–2 y, with or without BSE | B |
| Colon | Adults aged 50–75 y | FOBT annually OR flexible sigmoidoscopy with FOBT every 3 y OR colonoscopy every 10 y | A |
| Cervical | Women aged 21–65 y Women aged 30–65 y wanting to lengthen screening interval | Papanicolaou smear every 3 y Papanicolaou smear and HPV testing every 5 y | A |

Grade A: the USPSTF recommends the service. There is high certainty that the net benefit is substantial.

Grade B: the USPSTF recommends the service. There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.

Grade D: the USPSTF recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits.

Abbreviations: BSE, breast self-examination; FOBT, fecal occult blood testing; HPV, human papilloma virus; NA, not applicable.

Data from Recommendations. U.S. Preventive Services Task Force. 2014. Available at: <http://www.uspreventiveservices.org/Page/Name/recommendations>. Accessed November 19, 2014.

with nonspecific symptoms. This feature, combined with the lack of an established screening protocol, plays a role in 57% of non-small cell lung cancers diagnosed at an advanced stage,⁴ which carry a dismal 5-year survival rate of only 4%.² Alternatively, lung cancers diagnosed at an early stage have a much better 5-year survival rate, of 53.5%, with 68% of early-stage lung cancers amenable to surgical resection.⁴ Comparatively, only 8% of stage III and IV tumors were operatively managed in 2011.⁴ Thus, there is great potential to reduce mortality by establishing an early detection program for lung cancer.

Several previous initiatives to assess the feasibility of early detection in individuals with the highest risk of developing lung cancer have been completed. Early trials investigating the utility of CXR and sputum cytology as screening modalities were unable to demonstrate a mortality benefit.^{6–9}

As imaging technologies have advanced, attention has turned to CT as a modality for lung cancer screening.^{10–13} The Early Lung Cancer Action Project, for instance, published a series of 1000 patients who underwent LDCT screening and suggested that this modality was superior to CXR for detecting malignant nodules at early stages (Fig. 1). Although these initial findings were promising, this study was not designed to include a control arm for comparison, necessitating further research.¹⁰ In 2011, a NLST research group published results from the largest-to-date, randomized, multicenter study, which included more than 50,000 patients and tested the utility of LDCT versus conventional CXR for lung cancer screening in high-risk patients. This well-developed and rigorous study observed a 20% decrease in disease-specific mortality in the LDCT group.^{14,15} Stated differently, 3 deaths were averted for every

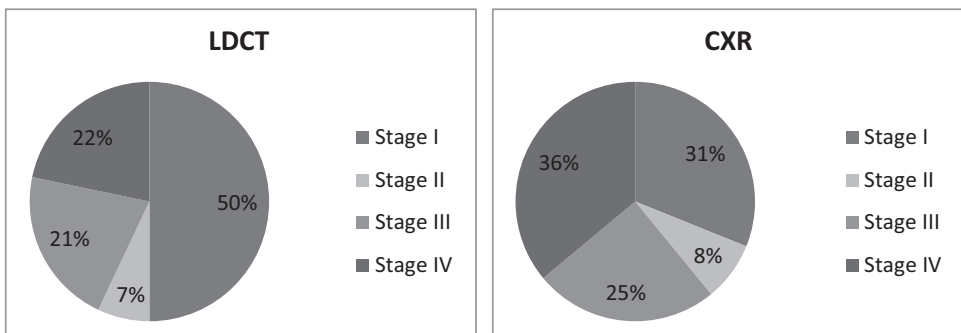


Fig. 1. Diagnoses, by stage, for LDCT and CXR. (Data from Aberle DR, Adams AM, Berg CD, et al. Reduced lung-cancer mortality with low-dose computed tomographic screening. *N Engl J Med* 2011;365(5):395–409.)

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