Reviewing Lung Cancer Screening
The Who, Where, When, Why, and How

Brett C. Bade, MD[a], Paul B. Brasher, MD[b], Branden W. Luna, MD[b], Gerard A. Silvestri, MD, MS[b], Nichole T. Tanner, MD, MSCR[b,*]

KEYWORDS

• Lung cancer • Screening • Computed tomography • National Lung Screening Trial

KEY POINTS

- The goal of lung cancer screening is to improve lung cancer mortality by detecting early-stage disease in high-risk, asymptomatic individuals.
- Screening in the National Lung Screening Trial reduced lung cancer-associated mortality and overall mortality by 20% and 6.7%, respectively.
- Risks of lung cancer screening include overdiagnosis, anxiety regarding indeterminate nodules, and radiation exposure.
- Lung cancer screening is complex and requires individual risk assessment, shared-decision making, tobacco counseling, and a multi-disciplinary team that specializes in lung cancer.
- Specialty organizations have outlined both the components of high quality lung cancer screening programs and the proposed metrics that programs should track.

INTRODUCTION

Until recently, lung cancer was unique among the most common cancer types in that an effective screening test was unavailable. After more than 30 years of research, a large randomized controlled trial (RCT) established that low-dose computed tomography (LDCT) improves mortality in patients at high risk for lung cancer. Subsequently, most professional societies caring for patients with lung cancer support screening. Although lung cancer screening is not unanimously recommended, the value of identifying early lung cancers cannot be overemphasized. Most new cases of lung cancer present in advanced stages (III–IV) when cure is unlikely or unattainable. As a practical guide to those developing screening programs, this article is organized by addressing the basic clinical questions and summarizes pivotal lung cancer screening studies, discusses the benefits and harms of screening, reviews guideline-based recommendations, and outlines the recommended components of lung cancer screening programs.

WHY SCREEN FOR LUNG CANCER?

The overall 5-year survival of lung cancer (18%) is worse than any other cancer for which screening is available.[1] In 2012, the estimated number of new lung cancer cases and deaths worldwide were

Conflicts of Interest: None.
Funding Sources: None.
[a] Section of Pulmonary, Critical Care, and Sleep Medicine, Yale School of Medicine, New Haven, CT 206510, USA; [b] Division of Pulmonary, Critical Care, and Sleep Medicine, Medical University of South Carolina (MUSC), 96 Jonathan Lucas Street, Suite 816 CSB, MSC 630, Charleston, SC 29425-6300, USA
* Corresponding author.
E-mail address: tripici@musc.edu

Clin Chest Med 39 (2018) 31–43
https://doi.org/10.1016/j.ccm.2017.09.003
0272-5231/18/Published by Elsevier Inc.

1.8 million and 1.6 million, respectively.[1] Because of asymptomatic cancer growth, most lung cancers go undetected until reaching advanced stages. Between 2003 and 2009, 57% of new lung cancer cases were diagnosed with distant disease, whereas only 15% of cases were localized.[1] Because localized disease has the potential for resection and cure, the difference between 5-year survival of stage 1 disease (59.5%) and distant disease (5.2%) is significant (**Fig. 1**).[2] In the absence of symptoms to identify early lung cancers, screening high-risk individuals has the potential to shift diagnosis to earlier stages. The goal of lung cancer screening, therefore, is to improve lung cancer mortality by detecting early-stage disease in high-risk asymptomatic individuals.

HOW SHOULD SCREENING BE DONE?

In the 1970s the National Cancer Institute (NCI) funded several projects assessing lung cancer prevalence and screening via chest radiograph (CXR) and sputum cytology.[3–5] The initial results were encouraging; the dual screening group had more cancers detected and higher average survival. However, there was no improvement in lung cancer–associated mortality, suggesting the survival improvement was caused by lead-time bias, length-time bias, or overdiagnosis. Types of screening bias have been well described previously (**Fig. 2**). The Prostate, Lung, Colorectal, and Ovarian (PLCO) Trial (n = 154,901) confirmed that screening CXR did not reduce lung cancer mortality compared with usual care.[6]

In the Early Lung Cancer Action Project (ELCAP), chest computed tomography (CT) identified both noncalcified nodules (23%) and malignancy (2.7%) in higher rates in than CXR (7% and 0.7%, respectively).[7] The Lung Screening Study (LSS) and Depiscan were the first large feasibility trials for lung cancer screening comparing CXR and LDCT.[8,9] Both LSS and Depiscan showed that screening with LDCT was feasible and lung cancers were more frequently identified using LDCT compared with CXR. Although the false-positive rate was high, chest CT was established as a feasible and sensitive test for lung nodule identification.

WHO SHOULD BE SCREENED AND WHEN?

To date, 6 large RCTs evaluating LDCT for lung cancer screening have been performed. Only the National Lung Screening Trial (NLST) has shown positive results. Comparing the 5 negative trials with the NLST will help distinguish effective and ineffective screening strategies as well as providing a framework for understanding lung cancer screening guidelines. Notably, many of these trials were not powered to detect mortality and may be well suited for data pooling to assess combined efficacy.

The Italian Lung Trial (ITALUNG) (n = 3206) compared annual LDCT with a nonscreened control in active or former smokers (quitting within the last 10 years).[10] Although more stage I lung cancers were identified in the LDCT group, more overall lung cancers were identified in the control group (n = 71 vs n = 67). Reductions in overall

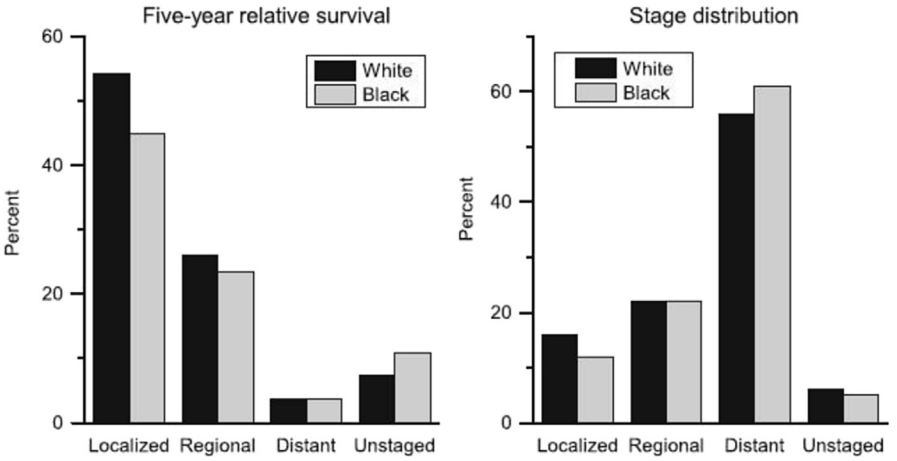

Fig. 1. Lung cancer survival and distribution by degree of spread. (*From* Howlader N, Noone AM, Krapcho M, et al, editors. SEER cancer statistics review, 1975–2010. Bethesda (MD): National Cancer Institute; 2013. Available at: http://seer.cancer.gov/csr/1975_2010/, based on November 2012 SEER data submission, posted to the SEER Web site, April 2013.)