The advent of widely accessible lung cancer screening using low-dose computed tomography

“We need to continually reassess the screening population, the screening interval and the screening technology.”

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On 10 November 2014, the Centers for Medicare and Medicaid Services (CMS) published a draft statement for public comment in favor of screening for lung cancer using low-dose computed tomography (LDCT). In the decision summary, CMS stated that the “evidence is sufficient to add a lung cancer screening counseling and shared decision making visit, and for appropriate beneficiaries, screening for lung cancer with LDCT, once per year, as an additional preventive service benefit under Medicare” [1]. This benefit is for smokers with at least 30 pack-years, between 55 and 74 years of age, who were asymptomatic and were either still smoking or had quit within less than 15 years. With this decision, the transition from a successful prospective randomized clinical trial to public policy has been advanced.

The debates over insurance coverage for LDCT screening over the past 3 years have highlighted the many variables that can influence screening. These include the prevalence of the disease, the public health impact of the disease, the ability to positively intervene in the disease if screened, a safe and accurate technology to screen, the cost of screening and the

ability to significantly reduce the disease burden. Furthermore, each of these variables can change. Diseases can become more prevalent, as lung cancer has from the 1980s to the current time. Technology can improve, such as the development of LDCT to detect lung nodules. Technology could advance still further, to the future development of a breath test to screen for lung cancer. This is why it is important to understand the influences of each of these variables in order to properly judge the strengths and potential pitfalls of screening for lung cancer at this point in history.

A quick historical review of how we arrived to the November CMS decision is warranted. Small trials of lung cancer screening with chest x-ray started in the 1950s [2]. Large, prospective, randomized controlled trials comparing chest x-ray and sputum cytology were run in the 1970s and 1980s. The lack of success of these screening methods led many to conclude that lung cancer screening would never be practical, but things changed. The number of newly diagnosed cases of lung cancer doubled to 228,190 from the 1980s to 2013 [1]. Competing causes of lung nodules became less common. The technological

KEYWORDS

- LDCT • low-dose CT scan
- lung cancer screening
- lung cancer screening the elderly • lung cancer screening risk

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development of LDCT scans allowed sufficient image resolution at an acceptable cost and radiation dose to be considered for its use as a screening tool.

A nonrandomized, single-arm, prospective trial of using LDCT to screen for lung cancer in smokers was started in New York in the 1990s [3]. The early success of this program led to a multicenter trial called I-ELCAP in 1993. The success of this program [4] yielded significant detection of early-stage disease (85% compared with the contemporary statistics of 15% in nonscreened patients) and showed an amazing 10-year survival of 88% in pathologically proven NSCLC patients. Thus, the lead time in detection led to cure.

The largest randomized prospective clinical trial in the world for lung cancer screening was the National Cancer Institute-sponsored National Lung Screening Trial (NLST). The trial accrued 53,454 participants from August 2002 to April 2004 [5]. The entry age was limited to 55–74 years of age, smoking history was raised to 30 pack-years and an arbitrary decision was made that if the patient had quit, they must have smoked within the last 15 years. Screened patients were randomized to either annual chest x-ray or annual LDCT for 3 consecutive years, followed by 4 years of observation. The trial was stopped early when it achieved a 20% reduction in lung cancer-specific mortality. This clinical trial provided level 1 evidence in favor of LDCT screening.

The US Preventive Services Task Force (USPSTF) endorsed LDCT screening for lung cancer in their position statement of December 2013 [6]. The USPSTF recommendation, however, endorsed screening up to 80 years of age based on clinical models. This recommendation had previously been made by the American Association of Thoracic Surgery [7] and the National Cancer Care Network [8]. Due to the USPSTF recommendation, private insurance companies are required by the Affordable Care Act to provide insurance coverage for LDCT screening as of 1 January 2015. The CMS recommendation now extends that coverage to 74 years of age within the Medicare population.

The review in this volume entitled ‘Assessing the benefits and harms of low-dose computed tomography screening for lung cancer’ is timely. The authors provide a lot of data in their review. However, I find that I disagree with what appears to be two underlying premises: that the benefits

of LDCT screening are likely to be less than expected and that the harms may be substantial. Both of these premises can be challenged.

First, let us examine the expected benefits. The NLST was stopped early upon achieving a 20% mortality reduction. This is not a modest reduction in lung cancer-specific mortality; it is a game changer. The authors try to minimize the impact of the NLST by pointing out that the results have not been confirmed by ongoing European trials. The three European randomized controlled trials are much smaller and lack sufficient statistical power to add to the conversation [6]. Furthermore, it is important to remember that the eligibility criteria for the NLST excluded smokers over 74 years of age, yet the peak incidence in American men occurs between 75 and 80 years of age [9], and the age-specific lung cancer mortality for US smokers, which accounts for competing causes of death, increases exponentially after 50 years of age and peaks at 80 years of age [10]. Thus, more benefit could be expected if the screening covered Americans between 75 and 80 years of age, as recommended by USPSTF. In addition, the NLST had not reached a ‘steady state’. That is, only three annual scans were performed, followed by 4 years of observation during which there was no screening. If annual scans had been ongoing, the lung cancer-specific mortality may have exceeded 20%. The goal of screening, after all, is to gain lead time, diagnose at an early stage and thus increase the cure rate.

Let us address the potential harms. The NLST trial was designed to measure harms and benefits. The harms of repeat scans, radiation exposure and adverse events following invasive interventions were exceedingly low. Claims that these harms could be greater outside the large randomized clinical trial can only be viewed as conjecture.

Concern is raised over the distress that a patient may experience when told that the scan is abnormal, but the patient does not have a lung cancer. Is this harmful? Distress can lead to a teaching moment. After all, the participant is between 55 and 74 years of age and has accumulated 30 pack-years of smoking with no previous indication of disease. Suddenly finding out that there is an abnormality on the chest CT scan may lead to tobacco cessation.

I believe that the insurance coverage for LDCT screening for lung cancer is the most important US public health improvement in

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the past two decades. A double-digit improvement in lung cancer-specific mortality is sorely needed in this deadly disease, in which only 15% present with early-stage cancer, 56% present with metastatic disease and the number of new cases continues to increase every year. Yet, this optimistic future could be even better. If the CMS draft proposal is unchanged after public comment, certain high-risk groups will remain excluded from coverage. These include previous lung cancer survivors (including many women who were never smokers), 30 pack-year smokers between 75 and 80 years of age (excluded from participation in the NLST) and those with less than 30 pack-years of smoking but strong additional risk factors, such as lung cancer in a first-degree relative under 65 years of age [7]. Essentially, the CMS proposal

is extending the NLST to all accredited centers in the USA. This may be the next logical step, but we must remember that screening indications change through history. We need to continually reassess the screening population, the screening interval and the screening technology.

Financial & competing interests disclosure

The author has no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

No writing assistance was utilized in the production of this manuscript.

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