LUNG CANCER SCREENING: SUMMARY OF THE EVIDENCE AND THE 2013 US PREVENTATIVE SERVICES TASK FORCE RECOMMENDATIONS

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Abstract

The United States Preventative Services Task Force is an independent panel of non-Federal experts in prevention and evidence-based medicine that reviews scientific studies and makes recommendations on screening and prevention interventions. The panel is widely respected for its rigour and basing its recommendations on the scientific evidence. In late 2013, the task force published a recommendation on screening for lung cancer using low-dose computerised tomography. They recommend annual screening in adults, aged 55 to 80 years, who have a 30 pack year smoking history and currently smoke or have quit within the past 15 years. They also recommend screening be discontinued once a person has not smoked for 15 years, or develops a health problem that substantially limits life expectancy or the ability or willingness to have curative lung surgery. The statement also stresses the need for rigorous quality controls to minimise the harms associated with lung screening and resultant diagnostic procedure.

The United States Preventative Services Task Force (USPSTF or task force) is an independent panel of non-Federal experts in prevention and evidence-based medicine. The task force is composed of primary care providers (such as internists, pediatricians, family physicians, gynecologists/obstetricians, nurses and health behavior specialists). They conduct scientific evidence reviews of a broad range of clinical preventive health care services (such as screening, counselling, and preventive medications). The task force has made recommendations on interventions as varied as screening for sexually transmitted diseases and vitamin D deficiency, to counselling on weight loss and screening for cancer of the breast.[1]

USPSTF recommendations are intended as information for primary care clinicians and health systems. By their very nature, these recommendations are for asymptomatic patients, meaning those without signs or symptoms related to the disease in question.

The task force bases its recommendations on the evidence of both the benefits and harms of the intervention and an assessment of the balance between these. Indeed they are known for their rigour and insistence on evidence. The process used involves an extensive structured, often systematic review of the medical literature. A group of experts, usually from a school of public health specialising in medical outcomes, is commissioned to do the review. The task force then digests that review. In recent years, the task force has also commissioned epidemiologists to do population modelling when assessing some interventions.

The results of the structured literature review are ultimately made available to the public, along with a draft recommendation.[3] Public comment is taken into account and discussed as the task force writes a final recommendation.

The task force does not consider the costs of a service in its assessment, even though a recommendation can have substantial financial impact. The US Patient Protection and Affordable Care Act, enacted in 2010 and commonly known as 'Obamacare' or 'Healthcare Reform,' requires private US health insurance organisations pay for screening tests that the task force deems should be offered to patients. Interestingly, the legislation does not require the US Medicare program to reimburse for these services. Medicare insures most Americans aged 65 and over. The Medicare program is allowed to make its own decision regarding insurance coverage.

USPSTF and lung cancer screening

In December 2013, the USPSTF published a final recommendation on the issue of lung cancer screening.[2] The statement recommends annual screening for lung cancer with low-dose computed tomography (LDCT) in adults aged 55 to 80 years who have a 30 pack-year smoking history and currently smoke or have quit within

the past 15 years. 'Pack-year' is a way to measure the amount a person has smoked over a long period of time. It is calculated by multiplying the number of packs of cigarettes smoked per day by the number of years the person has smoked.[3] They also recommend screening be discontinued once a person has not smoked for 15 years, or if a person develops a health problem that substantially limits life expectancy or the ability or willingness to have curative lung surgery.

The 2013 recommendation replaced a previous recommendation from 2004, which stated the evidence was insufficient to recommend for or against screening for lung cancer in asymptomatic persons with LDCT, chest radiography, sputum cytologic evaluation, or a combination of these tests.[4]

The task force grades recommendations.[1] They gave the 2013 recommendation a 'B', meaning they advise the test be offered to eligible patients as there is moderate certainty that the net benefit of screening is moderate to substantial in the target population.[4,5] Of note, an 'A' recommendation means there is high certainty that the net benefit is substantial. More specifically, it was the opinion of the task force that LDCT is of moderate net benefit in asymptomatic persons at high risk for lung cancer based on age, total cumulative exposure to tobacco smoke and years since quitting.[2]

The phrase 'moderate to substantial net benefit' was chosen because the US National Cancer Institute Lung Screening Trial (NLST) is the only prospective randomised trial to date showing a life-saving benefit.[6] Several smaller prospective randomised trials are underway in Europe. To date they have not shown a benefit, but these studies are much smaller and some involve patients with a lower risk of lung cancer.[4]

National lung screening trial

The recommendation was heavily influenced by the results of the NLST.[6] The NLST began in 2002 and was conducted in 33 academic centres throughout the US. It randomised approximately 53,000 persons to three annual LDCT scans or single-view posteroanterior chest X-rays. Eligible participants were between 55 and 74 years of age at the time of randomisation, with a history of cigarette smoking of at least 30 pack years, and if former smokers, had quit within the previous 15 years.

After a median follow-up of 6.5 years, there were 13% more lung cancers in the LDCT arm and a statistically significant relative reduction in lung cancer mortality of 20% (95% CI, 6.8 to 26.7) in the LDCT arm compared to the chest x-ray arm.[6] It is of note that the 20% mortality reduction among the more than 26,000 randomised to LDCT translates into 80 to 90 lung cancer deaths prevented, with more than 320 still dying of lung cancer. It is also noteworthy that the NLST LDCT group also demonstrated a 6.7% (95% CI, 1.2 to 13.6) decrease in all-cause mortality.

NLST participants were at very high risk for lung cancer. Indeed, 25% of all participant deaths during the study were due to lung cancer. Further analysis of the NLST shows that screening prevents the greatest number of lung cancer deaths among participants who were at highest risk and prevented very few deaths among participants at lowest risk.[7]

Limitations of low dose computerised tomography

NLST was well designed and well conducted. It showed there were some limitations to LDCT. After three annual screens, 39.1% of participants had at least one positive screening result. Of those who screened positive, the false-positive rate was 96.4%.[6] The most common positive finding was a single pulmonary nodule and after thorough evaluation, the most commonly diagnosed cause was a non-serious fungal or mycobacterial infection. A final diagnosis for most nodules was never obtained, but they failed to progress over time.

For every 1000 persons in the NLST, 391 had a positive screen, and most of these were false positives. For most of those with a positive LDCT, the work-up was a conventional CT with higher radiation dose, but 25 out of every 1000 had a false positive conventional CT scan leading to an invasive test such as a transthoracic needle biopsy, bronchoscopy or thoracic surgery. These diagnostic procedures can cause anxiety and complications (e.g. pneumo- or hemothorax after lung biopsy). Indeed, 3 per 1000 had a major complication from an invasive procedure and there were 16 deaths within 60 days of an invasive diagnostic procedure. Six of these 16 ultimately did not have cancer. While it is not known whether these deaths were directly caused by the invasive procedure, such findings do emphasise the importance of considering the harms, as well as the benefits, of screening.[6]

Overdiagnosis is a particular concern in cancer screening. It is the finding of a cancer that is indolent to the specific patient. It can be a tumour that fulfills the histologic requirements of malignancy, but if left alone will either never metastasise and cause harm or if a malignant tumour, will never progress to clinical significance within the patient's lifetime. In either case, treatment and cure is not necessary. An overdiagnosed cancer is by definition asymptomatic.

Initial assessment of NLST suggests 18.5% of screen-detected cancers are overdiagnosed tumours.[8] This is consistent with long-term follow-up of the Mayo Lung Study, which estimated overdiagnosis at 17% of

diagnosed tumours.[10] The Mayo Lung Study began in 1971 as a prospective study of chest X-ray and sputum cytology screening in 9211 smokers, and it last screened participants in 1983. The USPSTF commissioned some recent population modelling, which estimated overdiagnosis at less than 17% of screen-diagnosed cancers.[10]

The long-term risk of radiation-induced cancers is also a concern. Although the long-term risk cannot be measured directly, LDCT lung screening exposes a subject to between 0.61 to 1.5 mSv per scan. Putting this in proper context, annual background radiation exposure in the United States averages 2.4 mSv, radiation exposure from mammography is 0.7 mSv, and radiation exposure from computed tomography of the head is 1.7 mSv. Those screened patients with a false positive will have additional diagnostic imaging and additional radiation exposure.

USPSTF recommendation and the screening population

While the USPSTF relied heavily on the NLST in making its recommendation, there are important differences.[2] These differences reflect the influence of findings from population modelling. The NLST evaluated persons at high risk 55 to 75 years of age and gave three screens, each a year apart. The task force recommends screening persons at high risk, aged 55 to 80 years. The task force also recommends that annual screening continue until the person has not smoked for 15 years or develops a health problem that substantially limits life expectancy or the ability or willingness to have curative lung surgery.

The task force expanded the definition of high risk for lung cancer beyond age and smoking history, to include such risk factors as occupational exposure, family history, and history of other lung diseases. It also emphasised the need for screening to take place in a program that was carefully monitored to assure quality in diagnostic imaging and appropriate follow-up to replicate the benefits observed in the NLST in the general population. The task force also emphasised the importance of tobacco cessation as the primary way to prevent lung cancer deaths and noted that LDCT should not be used to discourage cessation efforts.

Applying LDCT to the US population

Recent estimates suggest that widespread high quality screening in the US has the potential to eventually prevent 12,000 lung cancer deaths per year.[11] However, there is uncertainty as to how many hospitals can provide the same high quality screening, diagnosis and treatment as was available in the NLST, which was performed at 33 centres with expertise in lung cancer diagnostics and treatment. Widespread screening may result in iatrogenic harm at rates significantly higher than in the NLST, and thus the balance of benefits and harms of screening on a widespread basis might be less favorable than suggested by the trial results.

Recommendations of other American organisations

The recent USPSTF recommendation is in general agreement with the recommendations of other American organisations. The American Cancer Society, the American College of Chest Physicians, the American Society of Clinical Oncology, and the National Comprehensive Cancer Network recommend that clinicians initiate a discussion about lung cancer screening with patients who would have qualified for the NLST, i.e. aged 55-74 years, at least a 30 pack-year smoking history, currently smoking or having quit within the past 15 years, and with relatively good health.[12,13]

Core elements of this discussion with the patient should include the benefits, uncertainties and harms associated with screening for lung cancer with LDCT. Adults who choose to be screened in the US setting should enter an organised screening program at an institution with expertise in LDCT screening, with access to a multidisciplinary team skilled in the evaluation, diagnosis and treatment of abnormal lung lesions. If such a program is not available, the risks of harm due to screening may be greater than the benefits.

All the above professional groups recommend annual screening, and the recommendations are not specific about when screening should cease.[12,13]

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