Lung Cancer Screening and Its Impact on Surgical Volume

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KEYWORDS

- Lung cancer • Lung cancer screening • Thoracic surgery

KEY POINTS

- Screening for lung cancer in high-risk individuals with annual low-dose computed tomography examinations has been shown to reduce lung cancer mortality by 20%.
- Screening for lung cancer by chest radiography or in low-risk individuals is not recommended.
- Lung cancer screening is recommended by multiple health care organizations and is covered by Medicare and Medicaid.
- Lung cancer screening is projected to increase the case volume for the thoracic surgery workforce.

INTRODUCTION

Lung cancer is the leading cause of cancer-related death in the United States, with 1 out of 4 cancer deaths owing to lung cancer.[1] Each year, more people die of lung cancer than of colon, breast, and prostate cancers combined. For 2016, the American Cancer Society estimates about 224,390 new cases of lung cancer leading to about 158,080 deaths. Lung cancer mainly occurs in older people. Approximately 2 out of 3 people diagnosed with lung cancer are 65 years of age or older, and fewer than 2% are younger than 45 years. The average age at the time of diagnosis is about 70 years.

Cigarette smoking is the leading risk factor for developing lung cancer. Although reduced rates of cigarette smoking in the United States have resulted in a reduced incidence of lung cancer, the substantial burden of lung cancer will continue for many years. Smoking cessation has been the most important public health intervention that has reduced this burden. However, owing to its long preclinical phase and

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markedly improved outcomes for patients treated at an earlier stage, there is substantial rationale for screening asymptomatic, high-risk individuals to improve the morbidity and mortality from this disease.[2]

Lung cancer screening has been implemented since the early 1960s. Numerous large-scale clinical trials have evaluated the use of chest radiographs, sputum analyses, computed tomography (CT), and most recently low-dose CT (LDCT) scans as screening tools. Coincident with the improvements in imaging technology, there also have been the refinements in surgical techniques for lung resections. With the establishment of lung cancer screening guidelines, the impact on the workforce needed to implement these guidelines are beginning to be studied. This article reviews the lung cancer screening data and its impact on the thoracic surgical workforce.

LUNG CANCER SCREENING TRIALS

Early, large-scale, clinical trials published in the 1980s and 1990s used chest radiographs for lung cancer screening and were disappointing.[3–6] None of the 6 randomized, controlled trials demonstrated any mortality benefit.[3–8] In the PLCO Screening trial (Prostate, Lung, Colorectal, and Ovarian Cancer), 154,942 smokers and nonsmokers from the general population were randomized to the intervention arm with an annual chest radiographs versus the control arm with "usual care," which was standard care as determined by their general health care practitioners.[7] After 13 years of follow-up, only 20% of lung cancers in the screening group were detected by screening, and no mortality benefit was seen in either the general population or the subset determined to be at higher risk of lung cancer based on smoking history and age. The Mayo Clinic conducted a randomized trial of chest radiographs and sputum analysis versus usual care. In a 20-year follow-up of this Mayo Lung Project, significantly more cancers were detected in the screening group; however, there was a higher overall lung cancer death rate, attributed to biased documentation of lung cancer as a cause of death.[8] These studies, along with others, resulted in a recommendation by the US Preventive Services Task Force in 2004 against using chest radiographs for lung cancer screening.[9] With the failure of chest radiography-based screening, centers began evaluating CT-based screening for lung cancer.

Initial studies of LDCT screening were observational, including the ELCAP (Early Lung Cancer Action Project), International ELCAP, the Mayo Clinic CT study, and the COSMOS study (Continuous Observation of Smoking study).[10–13] Owing to the lack of randomization, the studies were subject to lead-time bias and overdiagnosis bias. However, they did demonstrate for the first time the ability of CT to detect lung cancer at an early stage.

The most important randomized, controlled trial to date is the National Lung Screening Trial (NLST) conducted by the National Cancer Institute of LDCT for lung cancer screening.[14,15] To date, it is the only large-scale, randomized trial of LDCT lung cancer screening. Other ongoing randomized trials exist, but may not be adequately powered to detect a mortality benefit. A total of 53,454 high-risk persons at 33 medical centers across the United States were enrolled. Determinants of high risk included age and smoking history: between 55 and 74 years of age with at least 30 pack-years of smoking, and subjects could not have quit smoking more than 15 years before enrollment. Excluded were subjects who had any prior history of lung cancer, unexplained weight loss or symptoms suggestive of lung cancer, other cancers within the past 5 years (other than a nonmelanoma skin cancer), a chest CT scan in the past 18 months, or a medical condition that posed a significant risk of mortality during the trial period.

Subjects were first enrolled in 2002 and randomized to either an annual chest radiographs or annual LDCT for 3 consecutive years. Imaging was completed in 2007, with continued follow-up until the trial was stopped in November 2010 when an interim analysis showed a significant benefit for LDCT screening. At median follow-up of 6.5 years, there were 1060 lung cancers and 247 lung cancer deaths in the LDCT group compared with 941 lung cancers and 309 lung cancer deaths in the chest radiography group. The data demonstrated a 20% reduction in lung cancer mortality and a 6.7% reduction in all-cause mortality. Positive findings were defined as any noncalcified nodule seen on chest radiographs and any nodule at least 4 mm in size seen on LDCT. A total of 24% of subjects in the LDCT arm had a positive result. Of these positive results, 96% ultimately were shown not to be lung cancer and considered false positives. These false positives had been determined based on additional imaging, but also with surgery in 297 subjects. The rate of complications from the evaluation of true or false-positive findings was only 1.4% in the LDCT group (**Table 1**).

Based largely on the strength of the results of the NLST, multiple organizations[16–21] involved in lung cancer and cancer screening now recommend annual lung cancer screening with LDCT for high-risk individuals using the aforementioned definitions or variations thereof. These organizations include the American Cancer Society, the American Association of Thoracic Surgeons, the American College of Chest Physicians, the American Society of Clinical Oncology and the American Thoracic Society, and the US Preventive Services Task Force. In 2015, the Centers for Medicare and Medicaid Services released a decision memorandum on coverage for LDCT and visits for counseling and shared decision making.[22]

A post hoc analysis of the NLST included an application of a lung cancer risk assessment model based on the PLCO screening trial cohort that included smoking history, age, race/ethnicity, education, obesity, chronic obstructive pulmonary disease, and personal or family history of cancer.[23,24] The NLST cohort was divided into quintiles of risk of death from lung cancer over 5 years (**Fig. 1**). Although the

Table 1
National Lung Screening Trial: Potential benefits and risks of low-dose computed tomography screening

Benefits	Events per 1000 Subjects Screened
Diagnosis of stage I or II lung cancer	16
Prevented lung cancer deaths	3
Harms	
False-positive CT	
Nodule size considered abnormal (mm)	
>4	263
>5	155
>6	93
>7	61
Invasive biopsy for benign lesion	41
Surgery for benign lesion	10
Major complication during evaluation of a benign lesion	3
Overdiagnosis of lung cancer	0.6–1.2

Adapted from Deffebach ME, Humphrey L. Lung cancer screening. Surg Clin North Am 2015;95(5):967–78; with permission.

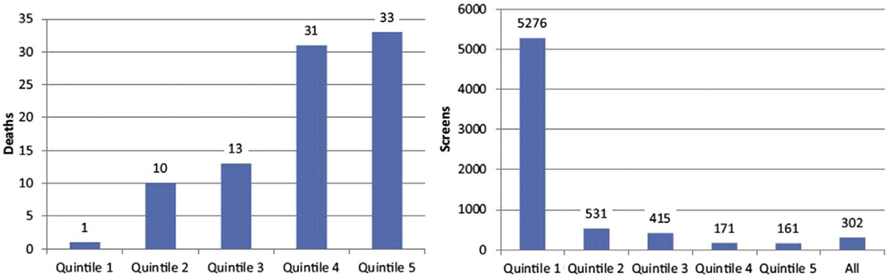


Fig. 1. From the National Lung Screening Trial, screened subjects divided into quintiles of risk of lung cancer death over 5 years. (*Left*) Lung cancer deaths prevented by low-dose computed tomography screening. (*Right*) Number needed to treat to prevent 1 lung cancer death. (*Data from* Kovalchik SA, Tammemagi M, Berg CD et al. Targeting of low-dose CT screening according to the risk of lung-cancer death. N Engl J Med 2013;369(3):245–54.)

20% decrease in lung cancer deaths was observed in all quintiles, only 1% of the prevented lung cancer deaths occurred in the lowest risk quintile. The number needed to screen to prevent 1 lung cancer death varied greatly with lung cancer risk. The lowest risk quintile required 5276 subjects to prevent 1 lung cancer death, whereas in the highest risk quintile, only 161. In addition, the proportion of false-positive results decreased with increasing risk of lung cancer.

There are several ongoing lung cancer screening studies that, although underpowered for determining the effect of LDCT on lung cancer screening mortality, are able to provide important information for the practice of lung cancer screening. The NELSON trial (Dutch-Belgian Lung Cancer Screening Trial) is a randomized trial of LDCT versus usual care (no screening) being conducted in Europe with 7557 subjects undergoing LDCT screening with a baseline CT followed by repeat LDCT at years 1 and 3.[25–29] Unlike the NLST, 5-year lung cancer survivors were eligible for inclusion. From published data thus far, the investigators have demonstrated that interval cancers (diagnosed outside of screening, between rounds of screening, and cancers detected at later rounds of screening) tend to be more aggressive.[30]

RISKS OF LUNG CANCER SCREENING

LDCT screening for lung cancer exposes individuals to radiation, which may include repeated exposure over 20 years. The risks of radiation are often extrapolated from environmental exposures, including atomic bomb survivors.[31] Analyses have suggested that serial imaging may add independently to the risk of developing a malignancy, and consideration of the risks of radiation need to include not only the screening LDCT, but also the radiation exposure from studies of positive (mostly false-positive) findings on follow-up imaging studies.[32] Restricting screening to the appropriate (older) age group, close attention to adherence and monitoring of an LDCT protocol, and judicious use of follow-up imaging are required to minimize the risks of radiation. The reported radiation dose for LDCT in screening studies ranges from 0.61 to 1.5 mSv, with 1 study documenting cumulative doses of up to 7 mSv for the screening and follow-up studies.[33]

Any abnormal finding that might indicate malignancy can cause anxiety, and this has been demonstrated in the context of lung cancer screening. Assessing the definition of abnormal and careful communication are important to reducing the stress and anxiety associated with screening for lung cancer.[34]

In the NLST, 96% of all positive findings were false-positive findings and required some evaluation, and 11% led to an invasive procedure. Many of the procedures carry substantial risks, such as image-guided biopsies, bronchoscopies, and surgery. Judicious use of these tests and expertise in their conduct are required to minimize associated risks.

Overdiagnosis occurs when there is a diagnosis of a cancer or other disease that would otherwise not go on to cause symptoms or death.[35] This result is not a false-positive diagnosis, because these individuals are diagnosed with tumors that meet pathologic criteria for cancer. The challenge is that one currently cannot determine which cancers will progress and which cancers will not progress; therefore, evaluation and treatment typically occur for all of them. However, when a patient is exposed to the risks of evaluation and treatment of disease that would not have become symptomatic during their lifetime, overdiagnosis has occurred with no benefit and undue harm may be incurred to the patient. Only randomized studies with long-term follow-up can determine the actual rate of overdiagnosis. Determinates of overdiagnosis include the aggressiveness of the cancer and the competing comorbidities in patients being diagnosed with cancer. Although lung cancer is generally an aggressive malignancy, it is heterogeneous with many subtypes that are very indolent. Studies have found that very indolent lung cancers, defined as having a doubling time greater than 400 days make up anywhere from 3% to 31% of detected lung cancers.[36] Furthermore, with smoking and age being the major lung cancer risks, patients at risk for developing lung cancer often have significant comorbidities, some of which result in death before development of symptoms.

Using a model of extended lifetime follow-up after LDCT screening in one study, the overdiagnosis rate of LDCT for non–small cell lung cancer was estimated to be less than 4%.[37] It has been suggested that lesions presenting as pure ground-glass nodules and typically associated with bronchoalveolar cell carcinoma or minimally invasive adenocarcinoma, although pathologically classified as cancers, may be candidates for overdiagnosis. Whether these lesions, when detected by screening, can be managed as truly indolent lesions, avoiding invasive procedures, is not yet known.

CHALLENGES FOR THE THORACIC SURGICAL WORKFORCE

As developments in imaging technology afforded the benefits seen in the lung cancer screening trials, similarly, refinements in surgical technique and instruments for lung resections led to improvements in outcomes for patients undergoing surgery.[38] Lung cancer surgery began with the first successful pneumonectomy reported by Graham and Singer in 1933.[39] Lobectomies and segmentectomies were reported in the 1940s and 1950s and the first successful sleeve lobectomy for carcinoma in 1952.[40,41] The introduction and development of surgical sutures and staplers made lung resections safer, faster, and less traumatic, while maintaining sound surgical oncologic principles. With surgeons gaining experience in lung resections and thoracic anesthesia, and intensive care progressing, specialized thoracic units developed in hospitals, and surgeons started extending cancer resections to the chest wall and great vessels.[42] The importance of lymph node involvement (hilar and mediastinal stations) in the prognosis of lung cancer was recognized.[43] The advent of video-assisted thoracic surgery in the 1990s considerably changed the approach to early stage lung cancer.[44–46] More recently, surgeons are gaining experience with robotic approaches to reduce the operative trauma, facilitate the surgical procedure, and reduce the duration of hospital stay.[47] Furthermore, new techniques, such as radiofrequency ablation and stereotactic body radiation therapy, are now offered as an alternative to surgery in patients unfit for lung resection, but are still being evaluated in prospective, randomized trials.[48,49]

Multiple publications have shown that the volume of lung cancer resections performed was associated positively with the survival of patients.[50] Patients operated on at high-volume centers have lower postoperative complication rates and lower 30-day mortality. Outcomes seem to be better in large teaching hospitals[51,52] and the surgeon's subspecialty—thoracic or cardiothoracic surgery versus general surgery—also influences in-hospital mortality.[53,54]

Despite a clear need for thoracic surgeons, the workforce is projected to decrease. A study by Williams and colleagues[55] in 2010 predicted a steady decrease in the number of practicing thoracic surgeons in the United States from about 4000 surgeons in 2000 to about 3000 surgeons in 2050, an approximate 25% decrease (**Fig. 2**). However, owing to continued population growth and increasing life expectancy, there will be an increasing need such that, by 2050, the number of practicing thoracic surgeons will be one-half the number that is needed. Furthermore, not accounting for this increase in the population is the potential impact of lung cancer screening programs throughout the country that will contribute to the increased workload for the thoracic surgery workforce.

CONSEQUENCES OF LUNG CANCER SCREENING IN RELATION TO SURGICAL VOLUME

To date, there has been only one published study examining the potential impact of the implementation of lung cancer screening programs on the thoracic surgery workforce.[56] The authors of this study by Edwards and colleagues[56,57] at the University of Calgary in Alberta, Canada, applied computer modeling techniques to forecast the "demand" for thoracic surgeons (the incidence of operable lung cancers in the Canadian population over time) and the "supply" of Canadian thoracic surgeons in the workforce, after the introduction of LDCT screening.[56,57] The demand component of the model used data from the annual Canadian Community Health Survey to determine smoking rates and smoking history (current, former, never, pack-years, quit time), controlling for age, sex, and location. The supply component of the model used data from the 2009 Canadian Thoracic Manpower and Education survey on the demographics, training history, practice characteristics, and estimated retirement age of thoracic surgeons in Canada.[58] The number of thoracic surgeons entering the workforce was calculated based on the number of Royal College of Physicians and

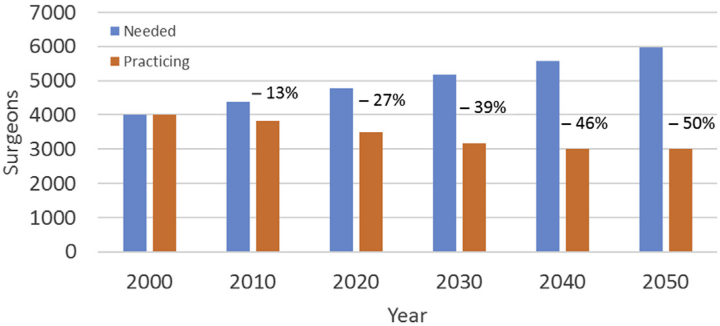


Fig. 2. Predicted number of surgeons practicing and number needed. (*Adapted from* Williams TE Jr, Satiani B, Thomas A, et al. The impending shortage and the estimated cost of training the future surgical workforce. Ann Surg 2009;250(4):590–7; with permission.)

Surgeons accredited programs in Canada (n = 8), with 4 to 8 graduates per year. A typical 7-year duration of training was assumed (5 years for general surgery, 2 years for thoracic surgery) with 0% attrition and emigration. This model was then advanced in 1-year cycles with the future year's projections based on present-day supply, clinical volume, retirement estimates, and the number of new surgeons entering the workforce. A national lung cancer screening program was then introduced into the model, phased in from 2014 to 2016, for the same population to predict changes in the number of operable lung cancers per surgeon.

In their model, the investigators forecasted an increase in the Canadian population from about 3.2 million (in 2006) to 4.6 million (in 2049). Those eligible for lung cancer screening (55–74 years old, >30 pack-years of current or former smoking) increased from 1,118,000 cases (in 2014) to 1,147,700 cases (in 2017) and then progressively decreased to 446,000 (in 2049) as lung cancer screening went into effect. Screening with chest radiographs was applied in 2014 to demonstrate lung cancer incidence and stage distribution in the absence of LDCT screening. With chest radiographs, the overall number of lung cancer diagnoses was forecasted to increase from 23,529 (in 2010) to 32,196 (in 2030) and then decrease to 28,585 cases (in 2040). With CT screening, the incidence of lung cancer diagnoses was projected to increase from 23,928 (in 2010) to 34,189 (in 2030) and then decrease to 30,681 cases (in 2040). When compared with chest radiographs, there was about a 7% increase in lung cancer diagnoses with LDCT for any given year.

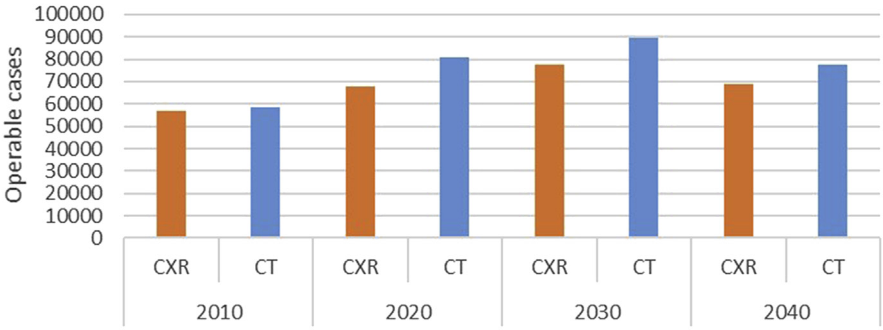
Examining by stage, their model forecasted an increase in early stage lung cancer diagnosed with LDCT versus chest radiographs. From 2010 to 2020, the proportion of stage IA lung cancer diagnosed by LDCT underwent a relative increase of 27.2%. For the same period, stage IB diagnosis increases by 2%, and stages II and IIIA remain stable. Stage IIIB lung cancer diagnoses decrease by 5.6% with LDCT screening, and stage IV decreases by 14.7%. Defining stage IA to IIIA as "operable lung cancer," the study also forecasted the incidence of operable lung cancer per surgeon to reach 114 cases per surgeon in 2030.

ESTIMATING THE IMPACT OF LUNG CANCER SCREENING IN THE UNITED STATES: SURGICAL VOLUME AND OTHER SEQUELAE

The American Cancer Society's 2016 estimate of new lung cancer cases (224,390) can be used to extrapolate the Canadian data in the study by Edwards and colleagues to the United States population and obtain estimates in a similar fashion. Assuming the same percentage of change as in the Canadian study, the number of operable (stages IA–IIIA) lung cancer cases in the United States each year steadily increases from 115,323 in 2010, to 148,454 in 2020, to 167,386 in 2030, and then decreases to 146,544 cases in 2040 (**Fig. 3**).

If one were to take into account the decreasing trend of US practicing thoracic surgeons according to the study from Williams and colleagues, the total number of lung cancer cases per surgeon would increase from 30 in 2010, to 42 in 2020, to 53 in 2030, to 49 cases per surgeon in 2040 (**Fig. 4**). However, if one were to assume a fixed number of practicing thoracic surgeons in the United States, the total number of lung cancer cases per surgeon would similarly increase and then decrease: 30 in 2010, to 39 in 2020, peak to 44 in 2030, then decrease to 38 in 2040. The difference at its peak in 2030 will be 9 additional cases per surgeon, followed by a greater difference of 11 additional cases per surgeon in 2040.

In addition to the increased workload for the foreseeable future, there may be a substantial downstream financial impact that may or may not affect the future workforce



Stage	CXR (%)	CT (%)	CXR (%)	CT (%)	CXR (%)	CT (%)	CXR (%)	CT (%)
IA	23883 (21.5)	24266 (21.4)	28403 (21.3)	39041 (27.1)	32559 (21.4)	42555 (26.3)	28649 (21.2)	35580 (24.5)
IB	11277 (10.1)	11594 (10.2)	13126 (9.8)	14374 (10.0)	15216 (10.0)	16530 (10.2)	13400 (9.9)	14563 (10.0)
IIA	3731 (3.4)	3901 (3.4)	4544 (3.4)	5045 (3.5)	5234 (3.4)	5570 (3.4)	4421 (3.3)	5055 (3.5)
IIB	4979 (4.5)	5244 (4.6)	5792 (4.3)	6057 (4.2)	6823 (4.5)	7040 (4.4)	6454 (4.8)	6270 (4.3)
IIIA	13031 (11.7)	13419 (11.9)	15882 (11.9)	16190 (11.3)	17774 (11.7)	18086 (11.2)	15835 (11.7)	16317 (11.2)
IIIB	14109 (12.7)	14478 (12.8)	17717 (13.3)	18114 (12.6)	19939 (13.1)	20081 (12.4)	17712 (13.1)	18663 (12.9)
IV	40242 (36.2)	40238 (35.6)	47893 (35.9)	44990 (31.3)	54683 (35.9)	51794 (32.0)	48692 (36.0)	48621 (33.5)
Total	111252	113138	133356	143811	152227	161655	135163	145068

Fig. 3. Absolute incidence of operable lung cancer (stages I, II, and IIIA) per year according to screening methodology. CT, computed tomography; CXR, chest radiography. (*Adapted from* Edwards JP, Datta I, Hunt JD, et al. The impact of computed tomographic screening for lung cancer on the thoracic surgery workforce. Ann Thorac Surg 2014;98(2):447–52; with permission.)

trajectory. Based on other publications estimating the hospital margin associated with anatomic resections for lung cancer to be approximately $20,000 per lobectomy,[59] it may be assumed that the gross financial impact of performing about 190 more cases per surgeon from 2010 to 2040 (estimated difference in area under the curves in Fig. 4) will be approximately $4,000,000 per surgeon from 2010 to 2040. A financially advantageous position as a result of higher margins may serve as an appealing factor in the pursuit of a career in thoracic surgery. In contrast, the inability to realize greater

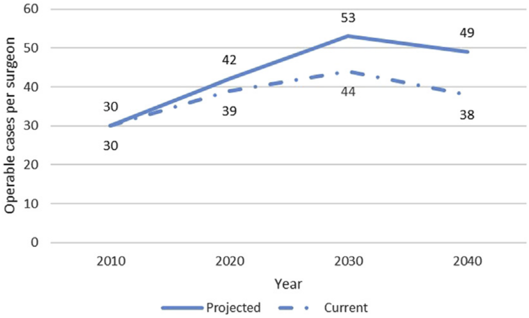


Fig. 4. Incidence of operable lung cancer (stages I, II, and IIIA) per US thoracic surgeon per year. "Projected" curve refers to the estimated cases per surgeon assuming the projected downtrend in thoracic surgeons.[55] "Current" refers to the estimated cases per surgeon assuming the current number of thoracic surgeons is maintained. (*Adapted from* Edwards JP, Datta I, Hunt JD, et al. The impact of computed tomographic screening for lung cancer on the thoracic surgery workforce. Ann Thorac Surg 2014;98(2):447–52; with permission.)

compensation despite increased volume and increased cumulative margin may result in a stagnation or even a continued decrease in the thoracic surgical workforce. Furthermore, health care systems must consider the increasing regionalization of surgical care toward high-volume centers.[60,61]

The Edwards and colleagues[56] Canadian simulation model forecasted that the operative caseload for thoracic surgeons will increase, even with the current number of trainees entering the workforce per year and retiring surgeons leaving the workforce per year. However, an important yet unaccounted consideration is the impact of body radiation therapy for the primary treatment of early stage lung cancer for high-risk surgical patients.[62] The outcomes of stereotactic body radiation therapy seem to be promising, and its impact on operable lung cancer cases and on workforce planning remains to be seen and will become an essential consideration. In the absence of randomized, controlled trials showing equivalence of this radiation therapy modality to surgical therapy, it could be argued that the proportion of patients actually undergoing a nonoperative form of therapy will have not changed.

SUMMARY

Lung cancer is an immense public health burden. Lung cancer screening has demonstrated a reduction in lung cancer mortality by 20%. Annual LDCT screening in high-risk individuals is now recommended by multiple national health care organizations and is covered under Medicare and Medicaid services. The impact of this public health intervention is projected to increase the case load for the thoracic surgery workforce and is incumbent upon the current workforce to continually improve outcomes in this patient population.

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