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Lung Cancer Screening Benefits and Harms Stratified by Patient Risk: Information to Improve Patient Decision Aids

To the Editor:

The landmark National Lung Screening Trial (NLST) demonstrated low-dose computed tomography (CT) scans in high-risk individuals can reduce lung cancer mortality by up to 20% (1, 2). In 2015, the Centers for Medicare and Medicaid Services approved coverage of lung cancer screening (LCS) for high-risk current or former smokers aged 55 to 77 years, with the caveat that patients first have a shared decision-making discussion with a healthcare provider that includes an overview of the benefits and harms of screening (3).

The potential benefits and harms of screening vary substantially according to an individual’s risk for developing lung cancer (4, 5). False positives in LCS can lead to anxiety, invasive procedures, and complications (2). Although several decision aids estimate the benefits of LCS according to an individual’s risk of lung cancer (6–8), no models exist for estimating the harms of screening according to personal risk factors. For example, the well-known shouldiscreen.com decision aid calculates a personalized risk of lung cancer but provides only the average harms (6). Caverly and colleagues (9) reported the harms of screening by risk quintile for a Veterans Affairs screening program, but the scans were interpreted before the release of currently used diagnostic criteria that have substantially decreased false positives (10). Therefore, we reanalyzed data from the NLST using current diagnostic criteria to estimate the harms and benefits of screening on the basis of individuals’ baseline risk for developing lung cancer (10).

Methods

We retrospectively analyzed data from the NLST, which was conducted from August 2002 through December 2009 at 33 sites

across the United States. The NLST randomized 53,452 persons at high risk for lung cancer on the basis of age and smoking history to either a low-dose CT scan or chest radiography (2). We assumed screened individuals would receive three annual CTs and be followed for 6.5 years to remain consistent with available decision aids.

Lung cancer risk calculation. We estimated each NLST participant’s risk of developing lung cancer using the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial Model 2012 (PLCO_{m2012}) (11), a validated risk-prediction model found to be well calibrated (12). Covariates in the model include age, race/ethnicity, education, body mass index, diagnosis of chronic obstructive pulmonary disease, personal history of cancer, family history of lung cancer, and smoking history.

Screening benefit calculation. At an average 6.5 years of follow-up in the NLST, the lung cancer death rate in the chest radiograph arm was 20.7 (552/26,730) versus 17.6 (496/26,722) in the CT arm, yielding a difference of 3.1 lives saved per 1,000 (1). Applying the PLCO_{m2012} (11) to the NLST participants, the mean 6-year risk of developing lung cancer was 3.29%. Therefore, we estimated the number of lives saved for a given risk level by dividing the corresponding PLCO_{m2012} risk score by the mean risk score of 3.29% and then multiplying the resulting quotient by 3.1 (the overall mean number of lives saved in the NLST). To illustrate, individuals at twice the mean risk of developing lung cancer (6.58% vs. 3.29%) would theoretically derive twice the benefit [$3.1 \times (6.58\%/3.29\%) = 6.2$ lives saved per 1,000 screened]. Because the main benefit of lung cancer screening is lives saved, we wanted to examine the harms of screening relative to this benefit. Therefore, we divided the NLST population into strata by selecting risk level ranges that result in the same number of lives saved per 1,000 individuals when rounded to the nearest whole number.

Screening risk calculation. We reinterpreted each NLST participant’s LCS as “positive” or “negative” using the Lung Imaging Reporting and Data System criteria, where a positive screen was any scan classified as Lung Imaging Reporting and Data System 3 or 4 (10, 12). We determined the proportions of

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Table 1. Characteristics of participants in lung cancer screening, by strata within the National Lung Screening Trial

6-yr Lung Cancer Risk	Lives Saved by Screening per 1,000*	No. in Strata in NLST	Mean Age (yr)	Median Pack-Years	Current Smoker (%)	Patients with COPD (%)
≤0.53	0	219	57	35	4	2
0.54–1.59	1	7,346	58	40	24	6
1.60–2.65	2	7,086	60	45	49	13
2.66–3.71	3	4,101	62	50	57	19
3.72–4.78	4	2,545	63	56	62	26
4.79–5.84	5	1,611	65	60	63	30
5.85–6.90	6	991	66	65	67	33
6.91–7.96	7	695	67	68	70	34
7.97–9.02	8	447	67	69	73	41
9.03–10.08	9	346	68	71	76	40
10.09–11.14	10	233	69	75	75	36
11.15–12.20	11	178	69	75	80	48
>12.20	≥12	511	70	86	82	58

Definition of abbreviations: COPD = chronic obstructive pulmonary disease; NLST = National Lung Screening Trial.

*Lives saved by screening per 1,000 patients screened for 3 consecutive years.

participants in each stratum who experienced at least one false-positive screen and who underwent an invasive procedure due to a false positive screen. Because of decreasing numbers of participants in higher-risk strata, we combined all strata resulting in more than 11 lives saved per 1,000 screened, and we combined rates for some outcomes with smaller cell sizes to obtain stable estimates.

Results

Table 1 displays the characteristics of patients stratified by the number of lives saved per 1,000 persons screened. Table 2 demonstrates the benefits (lives saved) and harms. The harms of lung cancer screening (false positives, invasive procedures, and complications) increase as an individual's risk of lung cancer increases.

Discussion

Our analysis demonstrates the complexity of estimating the risks and benefits of LCS. The likelihood of benefitting from screening is

higher for individuals at greater risk, as has been reported in other analyses (4, 10). In addition, as the risk of developing lung cancer increases, the likelihood of a false-positive result increases, explained in part by an increasing prevalence of pulmonary nodules with age and smoking intensity (13, 14). Caverly and colleagues showed differing results in their veteran population, where the rate of false-positive results remained stable across a quintile distribution of lung cancer risk; however, the finding of Caverly and colleagues is based on diagnostic criteria that are no longer used, which limits its extrapolation to current screening programs (9). How patients value these risks and benefits will impact their screening decisions. Therefore, decision aids that support values clarification related to such harms and benefits would be useful for clinicians and patients.

Our motivation for creating this new model arose from our desire to provide patients with personalized information about the expected benefits and harms of LCS. Static printable webpage decision aids are valuable, but they can only provide information

Table 2. Benefits and harms of lung cancer screening, by strata within the National Lung Screening Trial

6-yr Lung Cancer Risk	No. in Strata in NLST	Benefits	Harms per 1,000 Screened		
		No. Needed to Screen to Save 1 Life*	≥1 False-Positive Screen	≥1 Invasive Procedure	Major Complication from Procedure
≤0.53	219	>2,002	128	9	0.22
0.54–1.59	7,346	1,000	147	9	0.22
1.60–2.65	7,086	500	175	12	0.29
2.66–3.71	4,101	333	206	14	0.34
3.72–4.78	2,545	250	206	14	0.34
4.79–5.84	1,611	200	233	19	0.46
5.85–6.90	991	167	233	19	0.46
6.91–7.96	695	143	233	19	0.46
7.97–9.02	447	125	266	19	0.46
9.03–10.08	346	111	266	19	0.46
10.09–11.14	233	100	266	19	0.46
11.15–12.20	178	91	266	19	0.46
>12.20	511	<87	266	19	0.46

Definition of abbreviation: NLST = National Lung Screening Trial.

*Lives saved by screening per 1,000 patients screened for 3 consecutive years.

for the “average-risk” individual. Currently available interactive decision aids adjust the benefits of screening to the user’s risk factors but provide only average harm information. Incorporating our stratified results into current decision aids would fill a critical gap in the literature by listing the harms of screening for varying risk levels.

Shared decision-making visits improve patient understanding of the benefits and harms of screening (15, 16); however, some studies have shown that clinicians rarely use LCS decision aids, the quality of the shared decision-making discussions is poor and inconsistent, and they lack sufficient discussion on the harms of screening (17, 18). A recent review of more than 100 randomized clinical trials concluded that decision aids increase patients’ knowledge and result in decisions that are more likely to reflect their values (19). Future studies should examine strategies for incorporating decision aids in routine care. As we increase our attention to precision medicine, the ability to offer a more accurate portrayal of risk creates a greater opportunity for informed decisions about LCS.

Our analysis is based on data from the NLST, and the benefits and harms of screening could change over time. Our results should be validated as new data become available. In addition, we assume the relative risk reduction of screening remains constant across risk strata, which appears to be true for the majority of screening-eligible patients but could over- or underestimate benefits at very low or high risk for lung cancer (20).

In conclusion, current LCS decision aids are limited by their inability to provide patients with personalized estimates of the harms of screening. Our analysis can be incorporated into existing decision aids to provide personalized information and improve shared decision making as mandated by Medicare (3).

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Christina Bellinger, M.D.*
Wake Forest School of Medicine
Winston-Salem, North Carolina

Paul Pinsky, Ph.D.
Early Detection Research Branch of National Institute of Health
Bethesda, Maryland

Kristie Foley, Ph.D.
Douglas Case, Ph.D.
Ajay Dharod, M.D.
David Miller, M.D., M.S.
Wake Forest School of Medicine
Winston-Salem, North Carolina

*Corresponding author (e-mail: cbelling@wakehealth.edu).

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