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Contemporary Implications of U.S. Preventive Services Task Force and Risk-Based Guidelines for Lung Cancer Screening Eligibility in the United States

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Background:

U.S. Preventive Services Task Force (USPSTF) lung cancer screening guidelines recommend annual computed tomography (CT) screening for current or former smokers ("ever-smokers") aged 55 to 80 years with 30 or more pack-years of smoking and no more than 15 years since quitting (1). These criteria aim to improve the balance of benefits and harms of CT screening. However, using risk models to select ever-smokers for screening may be more effective and efficient (2). The USPSTF is considering recommending use of externally validated models (3) for screening. Although lung cancer risk models have been validated (4), their risk thresholds are based on historical data. Given large reductions in smoking over time, the current performance of these thresholds is unclear.

Note: The Lung Cancer Death Risk Assessment Tool was previously proposed in a manuscript coauthored by Drs. Cheung, Berg, Chaturvedi, and Katki.

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Three risk thresholds have been proposed to screen no more ever-smokers than would be screened according to the USPSTF guidelines yet potentially save more lives. National Comprehensive Cancer Network (NCCN) guidelines (version 1.2019) recommend screening ever-smokers with 6-year lung cancer risk of 1.3% or higher according to the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial Model 2012 ($PLCO_{M2012}$) (5). This threshold ("≥1.3%-NCCN") selects the same proportion of ever-smokers as application of the USPSTF criteria to the PLCO (5). The same authors (5) also proposed 6-year lung cancer risk of 1.51% or higher according to the $PLCO_{M2012}$ ("≥1.51%-$PLCO_{M2012}$") as being more efficient than the USPSTF criteria because this method limits screening to at least the 65th percentile of risk in PLCO ever-smokers and would screen fewer PLCO participants than the USPSTF criteria. Another proposal found that 5-year risk for lung cancer death of at least 1.2% according to the Lung Cancer Death Risk Assessment Tool (LCDRAT) ("≥1.2%-LCDRAT") (2) would allow screening of the same number of ever-smokers as application of the USPSTF guidelines to the U.S.-representative 2010-2012 NHIS (National Health Interview Survey) yet potentially save more lives.

Objective:

To evaluate these proposed risk-based thresholds for screening eligibility versus USPSTF guidelines on the number of ever-smokers selected, effectiveness (number of lung cancer deaths prevented), efficiency (number needed to screen [NNS] to prevent 1 death), and the number of false positive screening results per prevented death (FPPDs).

Methods and Findings:

We used the 2005 and 2015 NHIS to estimate the number of ever-smokers aged 50 to 80 years who were eligible for lung cancer screening according to the ≥1.3%-NCCN, ≥1.51%-$PLCO_{M2012}$, and ≥1.2%-LCDRAT risk thresholds. For each threshold, we used empirical modeling methods (2) to estimate screening effectiveness, screening efficiency, and FPPDs for a screening program akin to the NLST (National Lung Screening Trial) (3 annual CT lung screenings and 5 years of follow-up). We used the *survey* package in R, version 3.5.1 (R Foundation for Statistical Computing), for statistical analysis. Missing data were handled via multiple imputation (4).

We found that, in 2015, 8.0 million U.S. ever-smokers were eligible for screening according to the USPSTF guidelines. However, an additional 4.6 million (increase, 57% [95% CI, 49% to 64%]), 3.3 million (increase, 41% [CI, 34% to 47%]), and 1.0 million (increase, 12% [CI, 5% to 20%]) were eligible using the ≥1.3%-NCCN, ≥1.51%-$PLCO_{M2012}$, and >1.2%-LCDRAT thresholds, respectively (Table).

The increases are surprising because the ≥1.3%-NCCN threshold selected the same proportion (38%) of ever-smokers as the USPSTF guidelines in the PLCO (5), and the ≥1.51%-$PLCO_{M2012}$ threshold selected an even smaller proportion (35%). However, when applied to the 2015 NHIS, the USPSTF guidelines selected a smaller proportion of ever-smokers (18%) than either the ≥1.3%-NCCN (28%) or the ≥1.51%-$PLCO_{M2012}$ (25%) threshold. These decreases are due to changing demographic characteristics and smoking

histories since PLCO enrollment (1993 to 2001). Thus, the ≥1.3%-NCCN and ≥1.51%-$PLCO_{M2012}$ thresholds also chose substantially more ever-smokers (12.7 million and 11.2 million, respectively) than the USPSTF guidelines (8.7 million) in 2005. Even the ≥1.2%-LCDRAT threshold selected 1.0 million more ever-smokers in 2015 despite using data from 2010 to 2012 to select the threshold.

For the USPSTF guidelines, we estimated screening efficiency as an NNS of 194 and 133 FPPDs (Table). Compared with the USPSTF guidelines, estimated efficiency and FPPDs might be worse for the ≥1.3%-NCCN and ≥1.51%-$PLCO_{M2012}$ thresholds but might be improved for the ≥1.2%-LCDRAT threshold (Table). All 3 thresholds might prevent more deaths than the USPSTF guidelines (Table).

Recalibrating the risk thresholds to select 8.0 million ever-smokers in 2015 requires higher thresholds (≥2.19% for the $PLCO_{M2012}$ or ≥1.33% for the LCDRAT). At these thresholds, efficiency and FPPDs might be improved versus the USPSTF guidelines (Table). Although reducing the number of eligible ever-smokers also reduced the number of lung cancer deaths that could be prevented, they still exceeded USPSTF effectiveness (Table).

Discussion:

Compared with the USPSTF guidelines, the ≥1.3%-NCCN and ≥1.51%-$PLCO_{M2012}$ thresholds would screen millions more U.S. ever-smokers, possibly at lower efficiency and with more FPPDs. This is due to large reductions in smoking over time. These thresholds were based on selection of a set proportion of ever-smokers from an old data set (PLCO [1993 to 2001]), when a much larger proportion of ever-smokers were eligible for screening according to the USPSTF guidelines. Even the ≥1.2%-LCDRAT threshold chose 1 million more ever-smokers than the USPSTF guidelines, despite the threshold being selected using recent (2010 to 2012) data. Risk thresholds should be reevaluated regularly as population characteristics change to ensure they maximize the number of deaths prevented with acceptable efficiency and minimal harms.

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Table.

Projected Performance of Proposed Risk Thresholds for Selection of Ever-Smokers for CT Lung Cancer Screening Using NHIS 2015 Data [*]

Criteria	Risk Calculator	U.S. Ever-Smokers Aged 50-80 y		Screening Efficiency		Screening Harms		Screening Effectiveness[†]	
		Ever-Smokers Selected (Millions), *n* (%)	Increase vs. USPSTF Guidelines (95% CI[‡]), %	NNS to Prevent 1 Death	Improvement vs. USPSTF Guidelines (95% CI[‡]), %	False-Positive Results per Prevented Death, *n*	Improvement vs. USPSTF Guidelines (95% CI[‡]), %	Lung Cancer Deaths Prevented, *n*	Increase vs. USPSTF Guidelines (95% CI[‡]), %
USPSTF guidelines[§]	NA	8.0 (18.1)	NA	194	NA	133	NA	41 298	NA
NCCN guidelines (1.3% 6-y lung cancer risk)[‖]	$PLCO_{M2012}$[¶]	12.6 (28.4)	57 (49 to 64)	222	−14 (−20 to −9)	150	−13 (−18 to −8)	56 528	37 (32 to 41)
Other proposed thresholds									
1.51% 6-y lung cancer risk[**]	PLCO*M2012*[¶]	11.3 (25.5)	41 (34 to 47)	207	−7 (−12 to −1)	141	−6 (−12 to −1)	54 456	32 (28 to 36)
1.2% 5-y lung cancer death risk[††]	LCDRAT[‡‡]	9.0 (20.4)	12 (5 to 20)	168	14 (8 to 19)	119	10 (5 to 15)	53 732	30 (25 to 35)
Thresholds required to screen as many ever-smokers as USPSTF guidelines in 2015 (8.0 million)									
2.19% 6-y lung cancer risk	$PLCO_{M2012}$[¶]	8.0 (18.1)	0 (−6 to 6)	169	13 (7 to 19)	119	10 (5 to 15)	47 401	14(11 to 19)
1.33% 5-y lung cancer death risk	LCDRAT[‡‡]	8.0 (18.1)	−1 (−7 to 6)	156	20 (14 to 25)	112	15 (10 to 21)	51 019	24 (19 to 28)

CT = computed tomography; LCDRAT = Lung Cancer Death Risk Assessment Tool; NA = not applicable; NCCN = National Comprehensive Cancer Network; NHIS = National Health Interview Survey; NNS = number needed to screen; $PLCO_{M2012}$ = Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial Model 2012; USPSTF = U.S. Preventive Services Task Force.

[*] Multiple imputation was used to account for missing data (1.8% for race, 0.4% for education, 2.9% for body mass index, 0.4% for number of years since quitting, 7.3% for number of cigarettes smoked per day, 0.3% for number of years of smoking, 0.2% for presence of emphysema, and 12.1% for family history of lung cancer).

[†] We estimate there would be 202 442 lung cancer deaths without screening. The number prevented with each risk threshold/model combination was estimated using the LCDRAT.

[‡] Obtained using the delta method.

§ Guidelines recommend annual screening with low-dose CT for adults aged 55-80 y with a 30-pack-year smoking history and ≥15 y since quitting.

// 1.34% 6-y lung cancer risk according to the $PLCO_{M2012}$ was chosen to select the same proportion of ever-smokers as were eligible according to the USPSTF guidelines in the PLCO (1993-2001) cohort (38%) (4). The NCCN criterion is 1.3% (not 1.34%) 6-y lung cancer risk according to the $PLCO_{M2012}$.

¶ Reference 5.

** Chosen to select 35% of ever-smokers at highest risk in the PLCO (1993-2001) cohort (4).

†† Selects the same number of ever-smokers who were eligible according to the USPSTF guidelines in the 2010-2012 NHIS (9.0 million).

Reference 2.