JAMA | US Preventive Services Task Force | MODELING STUDY

Evaluation of the Benefits and Harms of Lung Cancer Screening With Low-Dose Computed Tomography

Modeling Study for the US Preventive Services Task Force

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IMPORTANCE The US Preventive Services Task Force (USPSTF) is updating its 2013 lung cancer screening guidelines, which recommend annual screening for adults aged 55 through 80 years who have a smoking history of at least 30 pack-years and currently smoke or have quit within the past 15 years.

OBJECTIVE To inform the USPSTF guidelines by estimating the benefits and harms associated with various low-dose computed tomography (LDCT) screening strategies.

DESIGN, SETTING, AND PARTICIPANTS Comparative simulation modeling with 4 lung cancer natural history models for individuals from the 1950 and 1960 US birth cohorts who were followed up from aged 45 through 90 years.

EXPOSURES Screening with varying starting ages, stopping ages, and screening frequency. Eligibility criteria based on age, cumulative pack-years, and years since quitting smoking (risk factor–based) or on age and individual lung cancer risk estimation using risk prediction models with varying eligibility thresholds (risk model–based). A total of 1092 LDCT screening strategies were modeled. Full uptake and adherence were assumed for all scenarios.

MAIN OUTCOMES AND MEASURES Estimated lung cancer deaths averted and life-years gained (benefits) compared with no screening. Estimated lifetime number of LDCT screenings, false-positive results, biopsies, overdiagnosed cases, and radiation-related lung cancer deaths (harms).

RESULTS Efficient screening programs estimated to yield the most benefits for a given number of screenings were identified. Most of the efficient risk factor–based strategies started screening at aged 50 or 55 years and stopped at aged 80 years. The 2013 USPSTF-recommended criteria were not among the efficient strategies for the 1960 US birth cohort. Annual strategies with a minimum criterion of 20 pack-years of smoking were efficient and, compared with the 2013 USPSTF-recommended criteria, were estimated to increase screening eligibility (20.6%-23.6% vs 14.1% of the population ever eligible), lung cancer deaths averted (469-558 per 100 000 vs 381 per 100 000), and life-years gained (6018-7596 per 100 000 vs 4882 per 100 000). However, these strategies were estimated to result in more false-positive test results (1.9-2.5 per person screened vs 1.9 per person screened with the USPSTF strategy), overdiagnosed lung cancer cases (83-94 per 100 000 vs 69 per 100 000), and radiation-related lung cancer deaths (29.0-42.5 per 100 000 vs 20.6 per 100 000). Risk model–based vs risk factor–based strategies were estimated to be associated with more benefits and fewer radiation-related deaths but more overdiagnosed cases.

CONCLUSIONS AND RELEVANCE Microsimulation modeling studies suggested that LDCT screening for lung cancer compared with no screening may increase lung cancer deaths averted and life-years gained when optimally targeted and implemented. Screening individuals at aged 50 or 55 years through aged 80 years with 20 pack-years or more of smoking exposure was estimated to result in more benefits than the 2013 USPSTF-recommended criteria and less disparity in screening eligibility by sex and race/ethnicity.

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In 2013, the US Preventive Services Task Force (USPSTF) recommended annual screening for lung cancer with low-dose computed tomography (LDCT) for adults aged 55 through 80 years who have a smoking history of at least 30 pack-years and currently smoke or have quit within the past 15 years (B recommendation).[1] These recommendations were largely based on the results of the National Lung Screening Trial (NLST).[2-4] Since then, new clinical guidelines have emerged for classifying and managing screening-detected pulmonary nodules,[5] and new evidence has emerged on the benefits and harms of LDCT screening.[6,7]

Early reports of screening practices suggest that the implementation of LDCT screening in the US has not been optimal because less than 20% of eligible individuals have accessed screening, whereas some ineligible individuals with smoking exposure of less than 30 pack-years and some with severe comorbidities have been screened.[8-10] In addition, some groups, such as Black men, have been shown to be at high risk for lung cancer even when not meeting the 2013 USPSTF–recommended criteria and the criteria from other organizations.[11,12] Recognizing that simulation models provide an approach to extrapolate available evidence and predict long-term outcomes,[13-15] the USPSTF commissioned a simulation analysis to estimate the long-term benefits and harms associated with various LDCT screening strategies to inform its lung cancer screening recommendations update.

Methods

Four lung cancer simulation models developed within the Cancer Intervention and Surveillance Modeling Network (CISNET) were used to estimate the benefits and harms of 1092 LDCT screening strategies: the Microsimulation Screening Analysis-Lung Model from Erasmus University Medical Center, the Massachusetts General Hospital–Harvard Medical School model, the Lung Cancer Outcomes Simulation model from Stanford University, and the University of Michigan model. All 4 models were part of the 2013 lung cancer screening decision analysis conducted for the USPSTF.[1,13] The full collaborative modeling study technical report has been published.[16]

Model Descriptions

The simulation models differ in terms of parameters, assumptions, model structure, and approach; comparison of the results across models serves as an assessment of model specification uncertainty. Although they share common inputs, each modeling team developed its model independently. The models explicitly considered individual factors associated with lung cancer risk, including the number of cigarettes smoked per day at any given age, the age of smoking initiation, the duration of smoking, and the number of years since quitting.

A comparison of the model characteristics appears in eTable 1 in the Supplement. The models simulate the natural history of lung cancer given an individual's sex, birth year, and smoking history. The central component of each model is a dose-response module that predicts age- and sex-specific lung cancer incidence risk as a function of individual smoking history. A key component to all models is the shared Smoking History Generator, a validated microsimulator developed by the CISNET Lung Group that simulates individual smoking histories for the US population.[17,18] These smoking histories serve as the main inputs for the simulations.

Each model can simulate the effects associated with screening given an individual's smoking and lung cancer natural history. The models were calibrated to both the NLST and the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial.[13,19] Three of the models (Massachusetts General Hospital–Harvard Medical School, Lung Cancer Outcomes Simulation from Stanford University, and University of Michigan) were updated to reflect current practice and outcomes according to the Lung Imaging Reporting and Data System guidelines.[20] The other model (Microsimulation Screening Analysis-Lung Model from Erasmus University Medical Center) uses false-positive test results, sensitivity, and screening result rates based fully on the NLST, allowing for comparison of alternative protocols and assumptions. Additional details appear in the eMethods in the Supplement.

Screening Strategies

Risk Factor–Based Strategies

The primary analysis focused on risk factor–based strategies using criteria similar to the 2013 USPSTF recommendation, which determined eligibility as a function of age and smoking exposure (pack-years of smoking and years since quitting). These strategies varied by starting age of screening (45, 50, or 55 years), stopping age of screening (75, 77, or 80 years), frequency of screening (annual or biennial), minimum pack-years of smoking (20, 25, 30, or 40 pack-years), and maximum years since quitting smoking (10, 15, 20, or 25 years). A total of 288 risk factor–based screening scenarios (eTable 2 in the Supplement) were evaluated and compared with a reference scenario of no screening.

Various studies have suggested that reducing the minimum pack-year eligibility criterion to 20 pack-years would increase the number of lung cancer deaths that would be preventable by screening and also reduce sex and racial disparities in eligibility.[6,11,12,21] Motivated by these studies, risk factor–based strategies with 20 pack-years as the minimum pack-year criterion were further analyzed.

Risk Model–Based Strategies

The potential effects of screening with eligibility criteria based on multivariable risk prediction models (PLCOm2012 model,[22] Lung Cancer Death Risk Assessment Tool model,[23] and the Bach model[24]) that use smoking duration and intensity, sex, and age to estimate lung cancer risk (risk model–based strategies) also were assessed.

These risk prediction models were selected based on demonstrated ability to identify individuals at high probability of developing lung cancer,[23,25] practicality and ease of implementation, and use as risk calculators in current lung cancer screening recommendations and implementation strategies.[26] Simplified versions of these risk models considering only age, sex, and smoking covariates were used.[27] No other risk factors, such as race/ethnicity or chronic obstructive pulmonary disease, were considered because including these would require joint simulation of these factors with smoking, sex, and age at the population level and the availability of well calibrated and validated lung cancer natural history models incorporating all covariates.

The evaluated risk model–based strategies varied by risk prediction model, model-specific risk threshold (minimum level of risk

required for eligibility), lower age limits (50 or 55 years), and upper age limits (75, 77, or 80 years). A summary of the resulting 804 risk model–based screening strategies appears in eTable 2 in the Supplement.

Scenario Simulation and Analysis

The CISNET simulation models were used to estimate the benefits and harms of each strategy in the 1950 and 1960 US birth cohorts. These birth cohorts were selected because they are now in the middle of their screening eligibility according to current guidelines (70 years old for the 1950 cohort and 60 years old for the 1960 cohort) and are representative of different periods of the tobacco epidemic (higher smoking prevalence and intensity for the individuals in the 1950 cohort vs lower rates for the 1960 cohort). One million smoking histories per sex and cohort were simulated using the Smoking History Generator and used as common inputs by each model to simulate individual-level outcomes under the different screening scenarios. All simulations were performed assuming that all screening-eligible individuals would undergo screening and adhere to ongoing screening (annual or biennial) for the duration of their eligibility. Smoking cessation and the risk of competing causes of disease and death were assumed to be unaffected by the screening results. The risk model–based screening analysis was restricted to the 1960 birth cohort.

Outcomes

Simulated outcomes included counts of screening examinations, the number and percentage of persons screened given an eligibility criterion, the number of lung cancer cases and deaths, life-years gained relative to a scenario of no screening, the number of false-positive screening results, the number of biopsies, and the number of overdiagnosed cases (defined as lung cancer cases detected by screening that would not have been diagnosed nor caused death in the absence of screening). Two models (Massachusetts General Hospital–Harvard Medical School and University of Michigan) were used to estimate radiation-related lung cancer deaths. Outcomes are provided per 100 000 individuals alive at aged 45 years (including both screened and unscreened individuals), rather than per the screened population so that the outcomes are comparable across scenarios.

Selection of Consensus-Efficient Scenarios

Efficient scenarios estimated to provide the most lung cancer deaths averted and life-years gained for a given level of screening (number of LDCT screenings per 100 000 population) were identified via a data envelopment analysis.[13,28] The analysis ranks scenarios based on their distance to the model-specific efficient frontier of (1) LDCT screenings vs deaths averted and (2) LDCT screenings vs life-years gained. Model-specific efficient scenarios were those on the model's efficient frontier or in the top 30% for the model ranking (ie, those scenarios in which the model estimated the most or close to the most lung cancer deaths averted and life-years gained for a given level of screening). Scenarios that were deemed efficient by at least 3 of the 4 models were termed *consensus efficient* and were selected for further analysis. This approach ensured an equal weighting of the models. More details are provided in the full report.[16]

For each identified consensus-efficient scenario, sex-specific results were aggregated to derive the predicted population-level mean (across the 4 CISNET models) outcomes. Special attention was given to consensus-efficient scenarios leading to a mortality reduction of at least 9%.

Sensitivity Analysis

Additional sensitivity analyses were used to assess the effectiveness of different LDCT screening strategies in limiting screening to only those persons with more than 5 years of life expectancy, assuming a perfect assessment of life expectancy.

Results

The presented results focus on the 1960 US birth cohort. The results for the 1950 US birth cohort appear in the Supplement and in the full report.[16] Unless otherwise indicated, the results presented are for men and women combined.

Risk Factor–Based Strategies

Compared with no screening, risk factor–based screening strategies were estimated to result in lung cancer deaths averted and life-years gained, with variations according to the level of screening (number of LDCT screenings) and specific eligibility criteria for each scenario. The number of LDCT screenings and deaths averted relative to no screening for each risk factor–based strategy appears in **Figure 1**. In general, the scenarios that were on the model's efficient frontier had LDCT screening stopping at aged 80 years. Biennial strategies are concentrated on the lower-left side of each panel because they require fewer LDCT screenings and are estimated to avert fewer deaths. Annual strategies tend to be on the upper-right side because they require more LDCT screenings and are estimated to generally avert more deaths. Although the absolute range of predicted deaths averted varies by model, the general efficiency patterns were consistent across the CISNET models. The 2013 USPSTF-recommended strategy was on or among the closest to the efficient frontier for 3 of the 4 models.

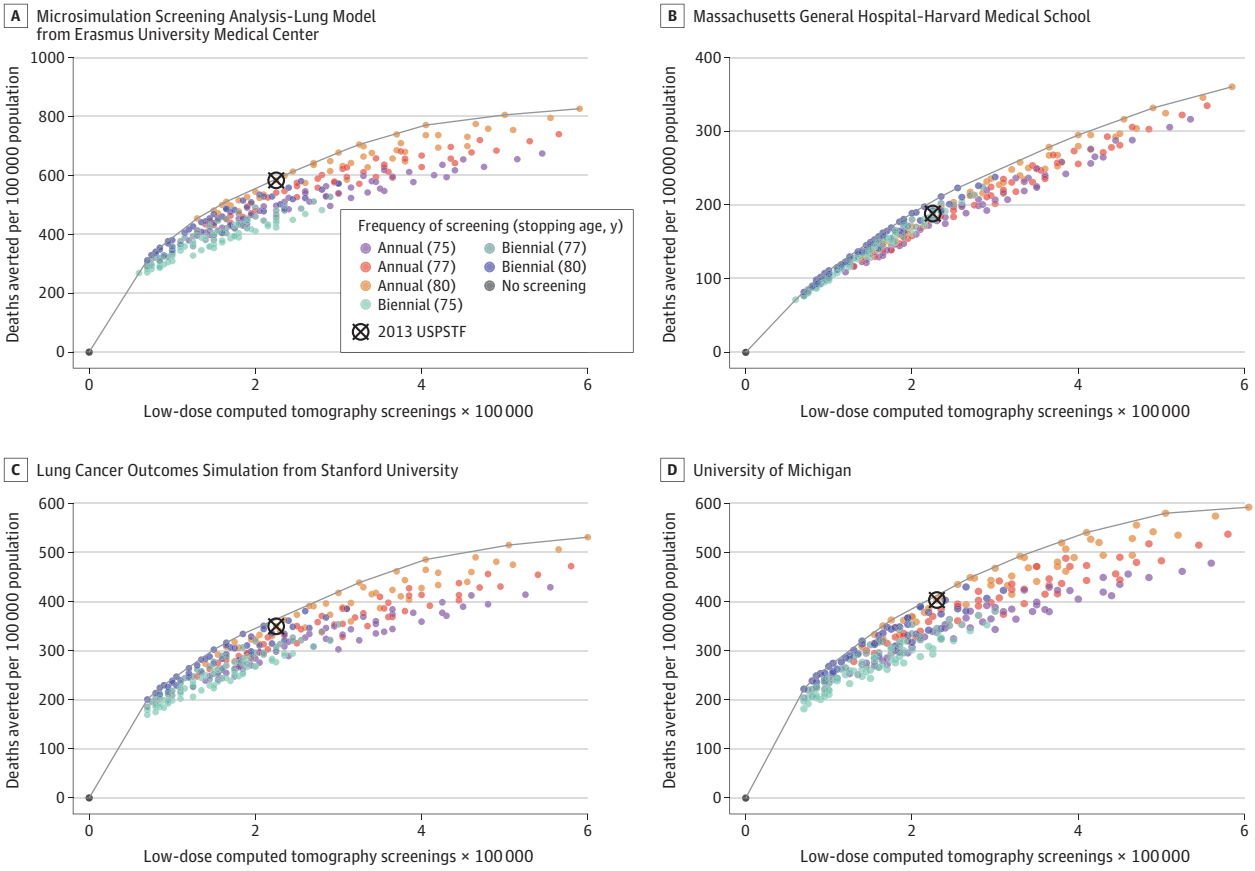
The corresponding efficient frontier curves using life-years gained as the benefit metric appear in **Figure 2**. The patterns were similar but show less variability among strategies than for deaths averted. In this case, the 2013 USPSTF-recommended strategy was only on (or among the closest to) the efficient frontier for 1 of the 4 models.

Risk Factor–Based Consensus-Efficient Scenarios

Fifty-seven consensus-efficient scenarios were identified. The 2013 USPSTF-recommended scenario was not 1 of the 57 consensus-efficient scenarios. The top of **Figure 3** shows the mean number of LDCT screenings (across CISNET models) compared with the number of deaths averted (left) and life-years gained (right) for all risk factor–based strategies, highlighting the consensus-efficient scenarios. Most of the consensus-efficient scenarios were on the efficient frontier or among the closest to the efficient frontier for both benefit metrics. Detailed outcomes for the 57 consensus-efficient scenarios appear in eTables 3 and 4 in the Supplement.

The estimated benefits of the consensus-efficient scenarios that were restricted to those leading to a lung cancer mortality reduction of at least 9% appear in **Table 1** along with the 2013 USPSTF-recommended scenario (a total of 26 scenarios). The scenarios are

Figure 1. Low-Dose Computed Tomography Screening Examinations vs Lung Cancer Deaths Averted in Each of the 288 Risk Factor–Based Strategies Evaluated by the 4 CISNET Models for the 1960 US Birth Cohort



Each point represents a different scenario and the line represents the estimated efficient frontier per model. Strategies vary by age at starting and stopping screening, frequency of screening, minimum pack-years of smoking, and maximum years since quitting smoking (eTable 2 in the Supplement). CISNET indicates Cancer Intervention and Surveillance Modeling Network; USPSTF, US Preventive Services Task Force.

estimated to result in a lung cancer mortality reduction close to or greater than that of the 2013 USPSTF–recommended strategy (9.8%). Of the 25 selected consensus-efficient scenarios, 5 were biennial and 20 were annual; all had 80 years as the stopping age of screening and ranged from 14.5% to 24.1% of eligible individuals. In terms of minimum pack-years of smoking exposure, 13 scenarios (52.0%) had 20 pack-years, 8 (32.0%) had 25 pack-years, 4 (16.0%) had 30 pack-years, and none had 40 pack-years. The estimated number of lung cancer deaths averted ranged from 348 to 578 per 100 000 population, corresponding to a population-level mortality reduction ranging from 9.0% to 14.9%. The estimated life-years gained ranged from 4490 to 8186 per 100 000 population and the number of persons needed to screen ranged from 34 to 63 (per 1 lung cancer death averted).

The corresponding estimated harms appear in **Table 2**. The mean number of false-positive results per screened individual ranged from 1.2 to 2.8, the number of biopsies ranged from 518 to 922 per 100 000 population, the mean number of LDCT examinations per person screened ranged from 8.6 to 24.9, and the overdiagnosis rate per 1 screening-detected case of lung cancer ranged from 5.6% to 6.3%. The estimated number of radiation-related lung cancer deaths ranged from 17.5 to 55.0 per 100 000 population.

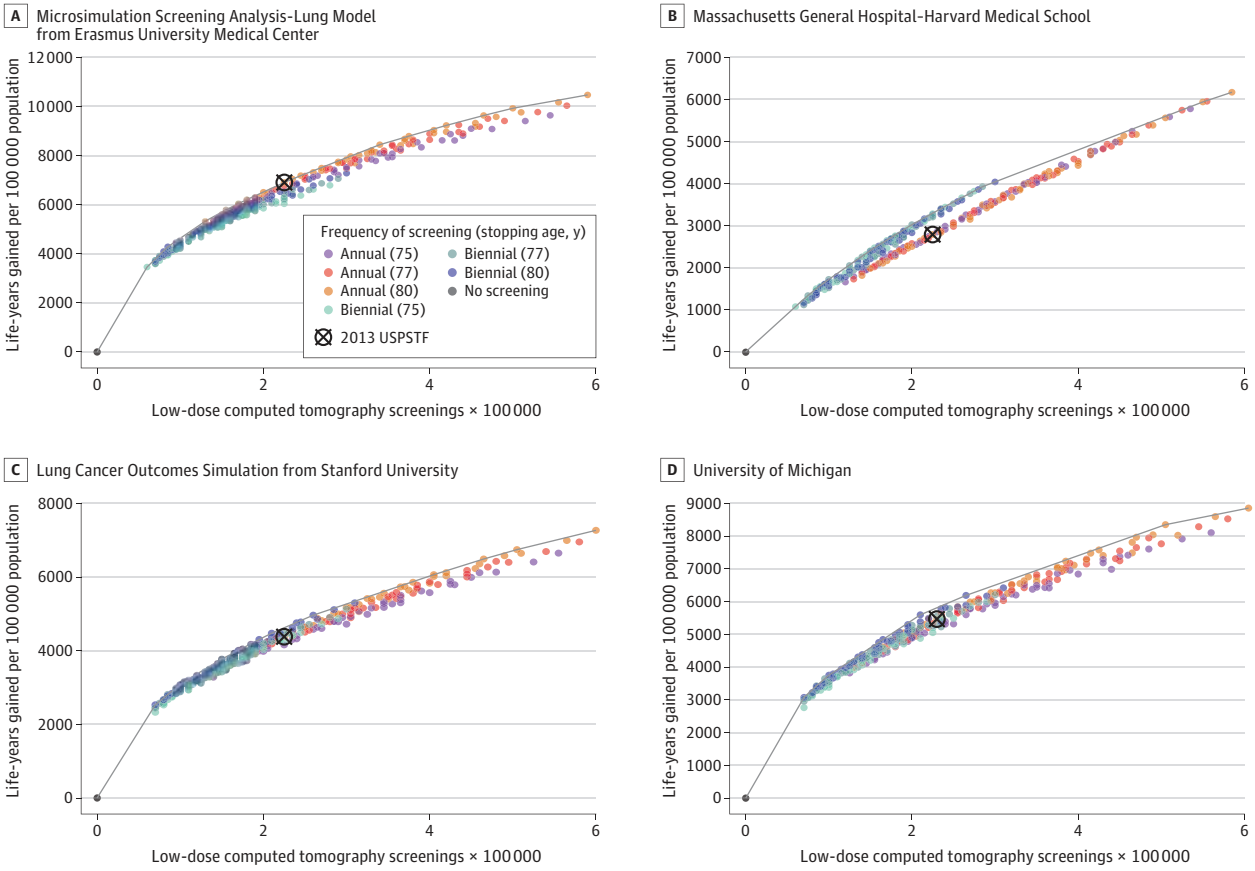
The estimates for the range of benefits and harms across the 4 CISNET models appear in eTables 5 and 6 in the Supplement.

Scenarios for 20 Pack-Years of Smoking

The consensus-efficient strategies with 20 pack-years of smoking and annual screening were examined further. There were 6 such strategies starting screening at aged 50 or 55 years and requiring at least 15 years since quitting smoking: A-55-80-20-15, A-55-80-20-20, A-55-80-20-25, A-50-80-20-15, A-50-80-20-20, and A-50-80-20-25 (Figure 3).

Expanding current screening eligibility to include individuals with 20 to 29 pack-years of smoking was estimated to increase the eligibility percentage from 14.1% for the population ever screened to between 20.6% and 23.6%, depending on the screening starting age and the number of years since quitting smoking. The mean number of LDCT screenings (across models) for these 20 pack-year scenarios ranged from 330 095 to 500 430 compared with 227 443 for the 2013 USPSTF–recommended strategy. The mean age at last screening ranged from 69.0 to 72.5 years compared with 71.3 years for the 2013 USPSTF–recommended criteria (eTable 7 in the Supplement). The mean age at first screening ranged from 51.5 years to 55.7 years (for all strategies with a starting age of 50 years)

Figure 2. Low-Dose Computed Tomography Screening Examinations vs Life-Years Gained in Each of the 288 Risk Factor–Based Strategies Evaluated by the 4 CISNET Models for the 1960 US Birth Cohort



Each point represents a different scenario and the line represents the estimated efficient frontier per model. Strategies vary by age at starting and stopping screening, frequency of screening, minimum pack-years of smoking, and maximum years since quitting smoking (eTable 2 in the Supplement). CISNET indicates Cancer Intervention and Surveillance Modeling Network; USPSTF, US Preventive Services Task Force.

vs 56.2 years for the 2013 USPSTF–recommended criteria (eTable 7 in Supplement).

The estimated number of lung cancer deaths averted for the 20 pack-year strategies ranged from 469 to 558 per 100 000 population, corresponding to a mortality reduction ranging from 12.1% to 14.4%. The estimated life-years gained for the selected 20 pack-year strategies ranged from 6018 to 7596 per 100 000 and the number needed to screen ranged from 42 to 45. In comparison, the 2013 USPSTF–recommended strategy was estimated to result in 381 per 100 000 deaths averted, a mortality reduction of 9.8%, 4882 life-years gained, and a number needed to screen of 37.

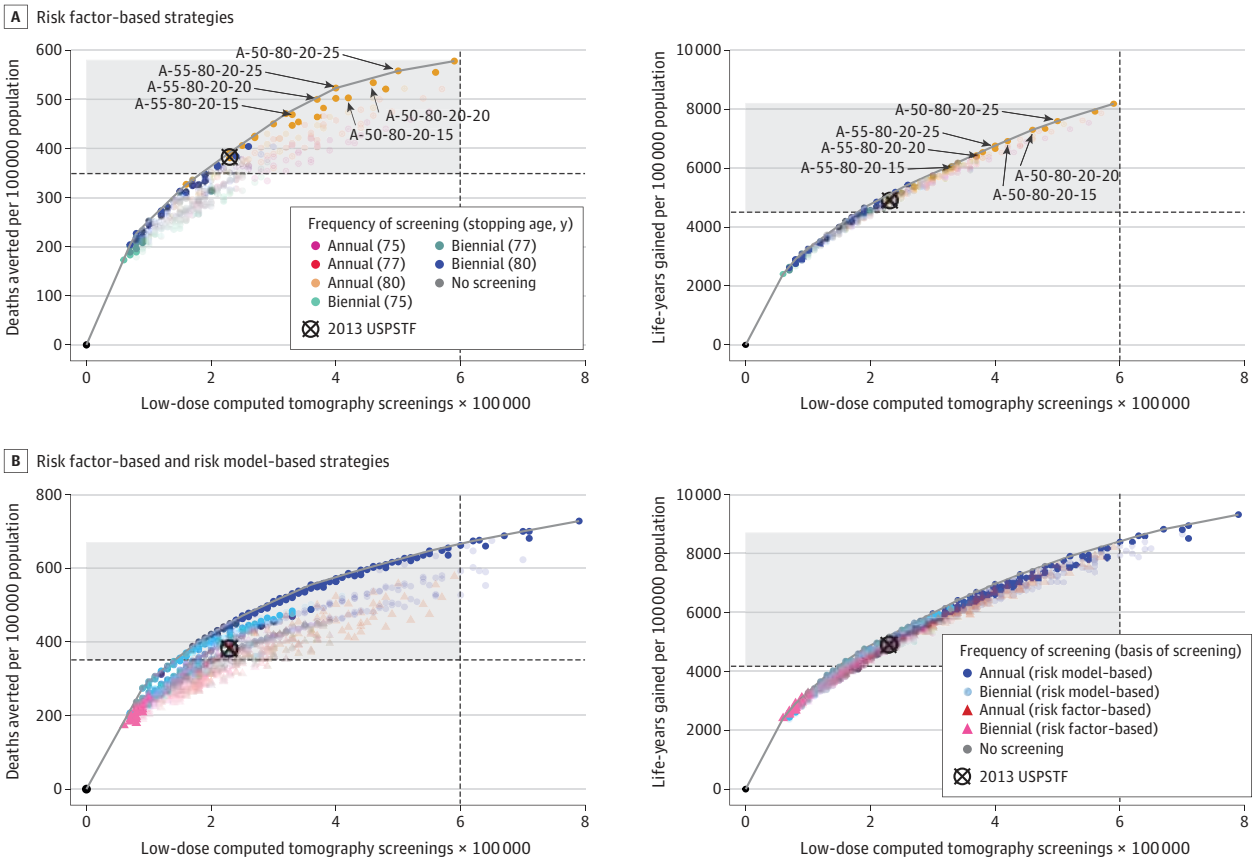
The estimated mean number of false-positive results per screened individual ranged from 1.9 to 2.5 for the selected 20 pack-year strategies vs 1.9 for the 2013 USPSTF–recommended strategy. The number of biopsies ranged from 526 to 849 per 100 000 vs 518 per 100 000 for the 2013 USPSTF–recommended criteria. The number of overdiagnosed lung cancer cases ranged from 83 to 94 per 100 000 population vs 69 per 100 000 for the 2013 USPSTF–recommended criteria. The rate of overdiagnosis per screening-detected lung cancer case ranged from 6.0% to 6.3% vs 6.3% for the 2013 USPSTF–recommended criteria. In addition, the number of radiation-related lung cancer deaths ranged from 29.0 to 42.5 per 100 000 population vs 20.6 per 100 000 population for the 2013 USPSTF–recommended criteria.

Comparisons by sex appear in eTables 8 and 9 in the Supplement. These estimates show similar patterns as those for the whole population; however, there were higher increases in eligibility, deaths averted, and life-years gained for women than men. Although the analysis did not consider different racial or ethnic groups, comparisons of the percentage of individuals eligible for screening in the US under the 2013 USPSTF–recommended strategy vs the selected 20 pack-year strategies by sex and race/ethnicity (non-Hispanic White, non-Hispanic Black, Hispanic, Asian, and American Indian/Alaska Native) appear in the full report[16] and in eTables 10 and 11 in the Supplement.

Risk Model–Based Strategies

Risk model–based strategies were estimated to result in considerably more lung cancer deaths averted for a given number of LDCT screenings than risk factor–based strategies. However, the differences in life-years gained were less pronounced. The mean (across the CISNET models) number of LDCT screenings appears

Figure 3. Low-Dose Computed Tomography Screening Examinations vs Lung Cancer Deaths Averted and Life-Years Gained Average Values Across the 4 CISNET Models for the 1960 US Birth Cohort



CISNET indicates Cancer Intervention and Surveillance Modeling Network; USPSTF, US Preventive Services Task Force.

A, The curve represents the estimated efficient frontier for the average model. Strategies vary by age at starting and stopping screening, frequency of screening, minimum pack-years of smoking, and maximum years since quitting smoking (eTable 2 in the Supplement). The panels show all 288 risk factor–based strategies and highlight the consensus-efficient scenarios (eTables 3-4 in the Supplement). The horizontal line divides strategies with a lung cancer mortality reduction of 9% or less. The shaded region includes those scenarios with a lung cancer mortality reduction of at least 9% (Table 1 and Table 2).

B, The curve represents the estimated overall efficient frontier for the average model. Risk factor–based strategies vary by age at starting and stopping screening, frequency of screening, minimum pack-years of smoking, and maximum years since quitting smoking (eTable 2 in the Supplement). Risk model-based strategies vary by risk model, risk thresholds, and frequency (eTable 2 in the Supplement). The vertical line represents 600 000 low-dose computed tomography screenings and the horizontal line divides strategies with a lung cancer mortality reduction of 9% or less. The shaded region includes those scenarios with fewer than 600 000 low-dose computed tomography screenings per 100 000 population and providing a lung cancer mortality reduction of at least 9% (eTables 12-13 in the Supplement).

in the bottom of Figure 3 compared with the number of deaths averted (left) and life-years gained (right) for all scenarios for each CISNET model (results for each CISNET model appear in eFigures 1 and 2 in the Supplement). The estimated benefits and harms of 144 consensus-efficient scenarios with a reduction in lung cancer mortality of at least 9% and requiring fewer than 600 000 LDCT screenings per 100 000 appear in eTables 12 and 13 in the Supplement.

Detailed comparisons of the 2013 USPSTF–recommended and the 6 selected 20 pack-year scenarios with corresponding risk model–based strategies and similar numbers of LDCT screenings appear in eTables 14 through 20 in the Supplement. These comparisons show that the age of screening shifts to older ages for the risk model–based screening strategies compared with the risk factor–based strategies. This shift leads to higher numbers of deaths averted and overdiagnosed lung cancer cases and to lower numbers of screenings per person and radiation-related lung cancer deaths for the risk model–based screening strategies.

Sensitivity Analyses

The general patterns observed for the 1960 US birth cohort held for the 1950 US birth cohort, with some variations in the absolute numbers due to the higher level of smoking in the 1950 birth cohort (eFigures 3 and 4 in the Supplement). In general, limiting screening to only those with more than 5 years of life expectancy (assuming a hypothetical perfect assessment of life expectancy) did not greatly affect the resulting estimated benefits (deaths averted or life-years gained) but was estimated to result in fewer harms and considerably fewer overdiagnosed cases. This finding was particularly true for screening strategies at older ages.

Table 1. Benefits of 25 Selected Consensus-Efficient Risk Factor–Based Screening Programs Plus the 2013 USPSTF–Recommended Criteria Ordered by Low-Dose Computed Tomography (LDCT) Screenings for the 1960 US Birth Cohort

	Mean estimate across 4 models per 100 000 population[b]									
Screening scenario[a]	Eligible, %	LDCT screenings	Screening-detected lung cancer cases	Lung cancer mortality reduction, %	Lung cancer deaths averted	Life-years gained	Life-years gained per lung cancer deaths averted	LDCT screenings per life-years gained	LDCT screenings per lung cancer deaths averted	NNS to prevent 1 lung cancer death
B-55-80-20-20	22.0	189 587	1134	9.0	348	4490	12.9	42	545	63
B-55-80-20-25	22.7	207 010	1189	9.5	366	4701	12.8	44	566	62
B-50-80-25-25	19.0	208 753	1169	9.4	363	4859	13.4	43	575	52
A-55-80-30-15[c]	14.1	227 443	1102	9.8	381	4882	12.8	47	597	37
A-55-80-25-10	16.0	234 030	1131	10.1	392	4969	12.7	47	597	41
B-50-80-20-20	23.3	239 223	1226	9.9	384	5194	13.5	46	623	61
A-55-80-30-20	14.5	250 592	1169	10.5	406	5170	12.7	48	617	36
B-50-80-20-25	23.6	258 024	1288	10.4	404	5436	13.5	47	639	58
A-55-80-25-15	17.2	267 471	1219	11.0	425	5387	12.7	50	629	40
A-55-80-30-25	14.8	269 096	1218	10.9	422	5333	12.6	50	638	35
A-55-80-25-20	18.0	298 016	1295	11.6	450	5690	12.6	52	662	40
A-55-80-25-25	18.3	324 008	1354	12.2	471	5930	12.6	55	688	39
A-55-80-20-15[d]	20.6	330 095	1334	12.1	469	6018	12.8	55	704	44
A-50-80-30-25	15.3	334 396	1273	11.5	447	6066	13.6	55	748	34
A-50-80-25-15	18.5	344 294	1282	11.7	454	6187	13.6	56	758	41
A-55-80-20-20[d]	22.0	369 610	1423	12.9	500	6379	12.8	58	739	44
A-50-80-20-10	21.2	369 742	1295	12.0	464	6435	13.9	57	797	46
A-50-80-25-20	18.9	377 405	1357	12.5	482	6542	13.6	58	783	39
A-50-80-25-25	19.0	404 469	1417	13.0	502	6764	13.5	60	806	38
A-55-80-20-25[d]	22.7	404 596	1492	13.5	523	6654	12.7	61	774	43
A-50-80-20-15[d]	22.6	419 030	1401	13.0	503	6918	13.8	61	833	45
A-50-80-20-20[d]	23.3	463 457	1487	13.8	534	7301	13.7	63	868	44
A-45-80-25-25	19.4	482 601	1448	13.5	521	7336	14.1	66	926	37
A-50-80-20-25[d]	23.6	500 430	1560	14.4	558	7596	13.6	66	897	42
A-45-80-20-20	24.0	557 453	1523	14.4	555	7919	14.3	70	1004	43
A-45-80-20-25	24.1	594 973	1592	14.9	578	8186	14.2	73	1029	42

Abbreviations: NNS, number needed to screen; USPSTF, US Preventive Services Task Force.

[a] The screening strategies have a lung cancer mortality reduction of at least 9% and correspond to frequency (A for annual or B for biennial)–age at start of screenings–age screenings should be stopped–minimum pack-years of smoking–maximum years since quitting smoking.

[b] Individuals were followed up from aged 45 to 90 years. The 4 models were the Microsimulation Screening Analysis-Lung Model from Erasmus University Medical Center, the Massachusetts General Hospital–Harvard Medical School model, the Lung Cancer Outcomes Simulation model from Stanford University, and the University of Michigan model.

[c] Recommended scenario by the 2013 USPSTF guidelines.

[d] Selected 20 pack-year consensus-efficient scenarios.

Discussion

The findings of this simulation analysis suggest that optimally targeted LDCT screening could lead to important reductions in lung cancer mortality and result in significant life-years gained. Although the analysis cannot identify a single optimal strategy, it identified a set of screening programs estimated to yield the most benefits for a given level of screening (consensus-efficient scenarios). The analysis estimates that screening strategies for individuals aged 50 or 55 years through aged 80 years with 20 or more pack-years of smoking exposure are efficient and would result in more benefits than the 2013 USPSTF–recommended criteria but also more harms.

Recent studies have suggested that expanding eligibility to include ever-smokers with 20 to 29 pack-years of exposure would increase the proportion of lung cancer deaths preventable by screening and reduce disparities in eligibility by race/ethnicity and sex.[11,12,21,29-31] Pinsky and Kramer[11] showed that reducing the minimum pack-years to 20 should increase the percentage of women and minorities who would be eligible for screening. They also found that the lung cancer risk for current smokers with 20 to 29 pack-years is comparable with that of former smokers eligible for screening based on the 2013 USPSTF–recommended criteria. Aldrich et al[12] found that proportionally fewer Black adults with lung cancer would have been eligible for screening vs White adults with lung cancer and that expanding the criteria to include 20 to 29 pack-year ever-smokers would considerably increase the screening sensitivity for Black adults. The Nederlands-Leuvens Longkanker Screenings Onderzoek trial[6] found a relative reduction of 24% for lung cancer mortality at 10 years after 4 rounds of LDCT screening vs a no screening group and included ever-smokers aged 50 to 74 years with lower smoking exposure criteria than the NLST and the 2013 USPSTF

Table 2. Harms of 25 Selected Consensus-Efficient Risk Factor–Based Screening Programs Plus the 2013 USPSTF–Recommended Criteria Ordered by Low-Dose Computed Tomography Screenings for the 1960 US Birth Cohort

	Mean estimate across 4 models per 100 000 population[b]								
	Low-dose computed tomography			False-positive results per person screened		Overdiagnosis			
Screening scenario[a]	Screenings	Scans	Examinations per person screened		Biopsies	Lung cancer cases	% of all lung cancer cases	% of screening-detected lung cancer cases	Radiation-related lung cancer deaths[c]
B-55-80-20-20	189 587	209 334	8.6	1.2	526	64	1.3	5.6	17.5
B-55-80-20-25	207 010	227 740	9.1	1.3	557	67	1.4	5.6	18.2
B-50-80-25-25	208 753	228 965	11.0	1.5	546	68	1.4	5.8	19.3
A-55-80-30-15[d]	227 443	247 644	16.1	1.9	518	69	1.4	6.3	20.6
A-55-80-25-10	234 030	254 870	14.6	1.8	536	71	1.4	6.3	21.5
B-50-80-20-20	239 223	261 627	10.3	1.4	593	70	1.4	5.7	22.8
A-55-80-30-20	250 592	272 008	17.3	2.0	554	73	1.5	6.2	21.5
B-50-80-20-25	258 024	281 421	10.9	1.5	626	74	1.5	5.7	23.6
A-55-80-25-15	267 471	290 163	15.6	1.9	586	77	1.5	6.3	23.4
A-55-80-30-25	269 096	291 461	18.2	2.1	580	76	1.5	6.2	22.1
A-55-80-25-20	298 016	322 330	16.6	2.0	630	82	1.6	6.3	24.7
A-55-80-25-25	324 008	349 657	17.7	2.1	664	84	1.7	6.2	25.6
A-55-80-20-15[e]	330 095	356 390	16.0	1.9	667	83	1.7	6.2	29.0
A-50-80-30-25	334 396	359 972	21.9	2.5	639	76	1.5	6.0	29.9
A-50-80-25-15	344 294	370 892	18.6	2.2	658	77	1.6	6.0	32.1
A-55-80-20-20[e]	369 610	398 094	16.8	2.0	722	89	1.8	6.3	30.6
A-50-80-20-10	369 742	397 994	17.4	2.1	684	77	1.5	5.9	36.5
A-50-80-25-20	377 405	405 682	20.0	2.3	701	82	1.6	6.0	33.5
A-50-80-25-25	404 469	434 104	21.3	2.5	735	85	1.7	6.0	34.9
A-55-80-20-25[e]	404 596	434 892	17.8	2.1	765	94	1.9	6.3	31.9
A-50-80-20-15[e]	419 030	449 947	18.5	2.2	750	84	1.7	6.0	38.6
A-50-80-20-20[e]	463 457	496 698	19.9	2.3	804	89	1.8	6.0	40.6
A-45-80-25-25	482 601	515 967	24.9	2.8	797	86	1.7	5.9	45.8
A-50-80-20-25[e]	500 430	535 519	21.2	2.5	849	94	1.9	6.0	42.5
A-45-80-20-20	557 453	595 203	23.2	2.7	879	91	1.8	6.0	53.1
A-45-80-20-25	594 973	634 568	24.7	2.8	922	95	1.9	6.0	55.0

Abbreviation: USPSTF, US Preventive Services Task Force.

[a] The screening scenarios have a lung cancer mortality reduction of at least 9% and correspond to frequency (A for annual or B for biennial)–age at start of screenings–age screenings should be stopped–minimum pack-years of smoking–maximum years since quitting smoking.

[b] Individuals were followed up from aged 45 to 90 years. The 4 models were the Microsimulation Screening Analysis-Lung Model from Erasmus University Medical Center, the Massachusetts General Hospital–Harvard Medical School (MGH-HMS) model, the Lung Cancer Outcomes Simulation model from Stanford University, and the University of Michigan (UM) model.

[c] Only 2 models (MGH-HMS and UM) used for the data in this column.

[d] Recommended scenario by the 2013 USPSTF guidelines.

[e] Selected 20 pack-year consensus-efficient scenarios.

recommendations, providing additional support to expanding the age and smoking eligibility criteria.

The comparisons made by sex and race/ethnicity suggest that the relative increase in eligibility for screening from reducing the pack-year criterion to 20 pack-years from the current criterion of 30 pack-years would be larger for women than for men and larger for non-Hispanic Black, Hispanic, and American Indian/Alaska Native persons than for non-Hispanic White and Asian persons.

The better performance of risk model–based screening vs risk factor–based strategies is largely because risk model–based strategies shift screening to older ages, which is when lung cancer risk is the highest. These findings are consistent with other recent studies in the literature.[27,32] The analysis shows that although the specific risk prediction model used for determining eligibility is an important consideration, an even more critical aspect is to determine eligibility risk thresholds specific to the corresponding risk prediction model.

The decision analysis used 4 established lung cancer natural history models that capture the complexity in smoking patterns and lung cancer risk and integrate and synthesize information from screening trials, large epidemiological prospective studies, and cancer surveillance data. The 4 CISNET models and the Smoking History Generator have been shown to reproduce the patterns of smoking and lung cancer incidence and mortality in the US[13,17,18] and thus provide a valid framework to extrapolate the potential effects of screening to the entire population. The relative performance of different scenarios according to their characteristics (starting and stopping age for screening, minimum pack-years of smoking, maximum years since quitting, and risk threshold) was consistent across the 4 CISNET models.

Limitations

This study has several limitations. First, the analysis assumed an idealized 100% screening uptake and adherence for eligible individuals; did not explicitly examine incidental findings or other potential harms, such as adverse events; and was based on models calibrated to lung screening trial outcomes, which might not be representative of screening in real-world settings. Thus, the estimations of the benefits should be interpreted as an upper boundary of what the actual effects could be.

Second, the analysis focused only on age, smoking history, and sex, ignoring other important risk factors, such as race/ethnicity, history of chronic obstructive pulmonary disease, exposure to occupational and environmental carcinogens, and family history of lung cancer.

Third, the analysis did not consider potential implementation challenges of risk model–based screening or whether those could vary by setting or among different demographic groups. Several ongoing implementation studies and trials are evaluating the feasibility and potential of risk model–based screening in clinical settings—so far with promising results.[20,33-36]

Fourth, the projections did not account for future improvements in lung cancer treatment and further changes in smoking trends. Recent developments in targeted therapies and immunotherapies could affect future lung cancer survival and screening efficacy.[37] In addition, the modeling did not consider the potential additional benefits of complementary smoking cessation programs within the context of lung cancer screening.[38-40]

Conclusions

Microsimulation modeling studies suggested that LDCT screening for lung cancer compared with no screening may increase lung cancer deaths averted and life-years gained when optimally targeted and implemented. Screening individuals at aged 50 or 55 years through aged 80 years with 20 pack-years or more of smoking exposure was estimated to result in more benefits than the 2013 USPSTF–recommended criteria and less disparity in screening eligibility by sex and race/ethnicity.

ARTICLE INFORMATION

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REFERENCES

1. Moyer VA; US Preventive Services Task Force. Screening for lung cancer: US Preventive Services Task Force recommendation statement. *Ann Intern Med*. 2014;160(5):330-338. doi:10.7326/M13-2771

2. Aberle DR, Adams AM, Berg CD, et al; National Lung Screening Trial Research Team. Reduced lung-cancer mortality with low-dose computed tomographic screening. *N Engl J Med*. 2011;365(5):395-409. doi:10.1056/NEJMoa1102873

3. Pinsky PF, Church TR, Izmirlian G, Kramer BS. The National Lung Screening Trial: results stratified by demographics, smoking history, and lung cancer histology. *Cancer*. 2013;119(22):3976-3983. doi:10.1002/cncr.28326

4. National Lung Screening Trial Research Team. Lung cancer incidence and mortality with extended follow-up in the National Lung Screening Trial. *J Thorac Oncol*. 2019;14(10):1732-1742. doi:10.1016/j.jtho.2019.05.044

5. Kazerooni EA, Armstrong MR, Amorosa JK, et al. ACR CT accreditation program and the lung cancer screening program designation. *J Am Coll Radiol*.

2016;13(2)(suppl):R30-R34. doi:10.1016/j.jacr.2015.12.010

6. de Koning HJ, van der Aalst CM, de Jong PA, et al. Reduced lung-cancer mortality with volume CT screening in a randomized trial. *N Engl J Med*. 2020;382(6):503-513. doi:10.1056/NEJMoa1911793

7. Becker N, Motsch E, Trotter A, et al. Lung cancer mortality reduction by LDCT screening—results from the randomized German LUSI trial. *Int J Cancer*. 2020;146(6):1503-1513. doi:10.1002/ijc.32486

8. Huo J, Shen C, Volk RJ, Shih YT. Use of CT and chest radiography for lung cancer screening before and after publication of screening guidelines: intended and unintended uptake. *JAMA Intern Med*. 2017;177(3):439-441. doi:10.1001/jamainternmed.2016.9016

9. Kinsinger LS, Anderson C, Kim J, et al. Implementation of lung cancer screening in the Veterans Health Administration. *JAMA Intern Med*. 2017;177(3):399-406. doi:10.1001/jamainternmed.2016.9022

10. Richards TB, Doria-Rose VP, Soman A, et al. Lung cancer screening inconsistent with US Preventive Services Task Force recommendations. *Am J Prev Med*. 2019;56(1):66-73. doi:10.1016/j.amepre.2018.07.030

11. Pinsky PF, Kramer BS. Lung cancer risk and demographic characteristics of current 20-29 pack-year smokers: implications for screening. *J Natl Cancer Inst*. 2015;107(11):djv226. doi:10.1093/jnci/djv226

12. Aldrich MC, Mercaldo SF, Sandler KL, et al. Evaluation of USPSTF lung cancer screening guidelines among African American adult smokers. *JAMA Oncol*. 2019;5(9):1318-1324. doi:10.1001/jamaoncol.2019.1402

13. de Koning HJ, Meza R, Plevritis SK, et al. Benefits and harms of computed tomography lung cancer screening strategies: a comparative modeling study for the US Preventive Services Task Force. *Ann Intern Med*. 2014;160(5):311-320. doi:10.7326/M13-2316

14. Knudsen AB, Zauber AG, Rutter CM, et al. Estimation of benefits, burden, and harms of colorectal cancer screening strategies: modeling study for the US Preventive Services Task Force. *JAMA*. 2016;315(23):2595-2609. doi:10.1001/jama.2016.6828

15. Mandelblatt JS, Stout NK, Schechter CB, et al. Collaborative modeling of the benefits and harms associated with different US breast cancer screening strategies. *Ann Intern Med*. 2016;164(4):215-225. doi:10.7326/M15-1536

16. Meza R, Jeon J, Toumazis I, et al. *Evaluation of the Benefits and Harms of Lung Cancer Screening With Low-Dose Computed Tomography: A Collaborative Modeling Study for the US Preventive Services Task Force*. Agency for Healthcare Research and Quality; 2021. AHRQ publication 20-05266-EF-2.

17. Moolgavkar SH, Holford TR, Levy DT, et al. Impact of reduced tobacco smoking on lung cancer mortality in the United States during 1975-2000. *J Natl Cancer Inst*. 2012;104(7):541-548. doi:10.1093/jnci/djs136

18. Jeon J, Holford TR, Levy DT, et al. Smoking and lung cancer mortality in the United States from 2015 to 2065: a comparative modeling approach. *Ann Intern Med*. 2018;169(10):684-693. doi:10.7326/M18-1250

19. Meza R, ten Haaf K, Kong CY, et al. Comparative analysis of 5 lung cancer natural history and screening models that reproduce outcomes of the NLST and PLCO trials. *Cancer*. 2014;120(11):1713-1724. doi:10.1002/cncr.28623

20. Pinsky PF, Gierada DS, Black W, et al. Performance of Lung-RADS in the National Lung Screening Trial: a retrospective assessment. *Ann Intern Med*. 2015;162(7):485-491. doi:10.7326/M14-2086

21. Holford TR, Levy DT, Meza R. Comparison of smoking history patterns among African American and white cohorts in the United States born 1890 to 1990. *Nicotine Tob Res*. 2016;18(suppl 1):S16-S29. doi:10.1093/ntr/ntv274

22. Tammemägi MC, Katki HA, Hocking WG, et al. Selection criteria for lung-cancer screening. *N Engl J Med*. 2013;368(8):728-736. doi:10.1056/NEJMoa1211776

23. Katki HA, Kovalchik SA, Petito LC, et al. Implications of nine risk prediction models for selecting ever-smokers for computed tomography lung cancer screening. *Ann Intern Med*. 2018;169(1):10-19. doi:10.7326/M17-2701

24. Bach PB, Kattan MW, Thornquist MD, et al. Variations in lung cancer risk among smokers. *J Natl Cancer Inst*. 2003;95(6):470-478. doi:10.1093/jnci/95.6.470

25. Ten Haaf K, Jeon J, Tammemägi MC, et al. Risk prediction models for selection of lung cancer screening candidates: a retrospective validation study. *PLoS Med*. 2017;14(4):e1002277. doi:10.1371/journal.pmed.1002277

26. National Comprehensive Cancer Network. Clinical practice guidelines in oncology: lung cancer screening: version 2. Accessed January 11, 2018. https://www.nccn.org/store/login/login.aspx?ReturnURL=https://www.nccn.org/professionals/physician_gls/pdf/lung_screening.pdf

27. Ten Haaf K, Bastani M, Cao P, et al. A comparative modeling analysis of risk-based lung cancer screening strategies. *J Natl Cancer Inst*. 2020;112(5):466-479. doi:10.1093/jnci/djz164

28. Charnes A, Cooper WW, Rhodes E. Measuring the efficiency of decision making units. *Eur J Operat Res*. 1978;2(6):429-444. doi:10.1016/0377-2217(78)90138-8

29. Wang Y, Midthun DE, Wampfler JA, et al. Trends in the proportion of patients with lung cancer meeting screening criteria. *JAMA*. 2015;313(8):853-855. doi:10.1001/jama.2015.413

30. Vu C, Lin S, Chang C-F. Gender gaps in care: lung cancer screening criteria in women. *Chest*. 2019;156(4 supp):A407. doi:10.1016/j.chest.2019.08.444

31. Han SS, Chow E, Ten Haaf K, et al. Disparities of national lung cancer screening guidelines in the US population. *J Natl Cancer Inst*. 2020;112(11):1136-1142. doi:10.1093/jnci/djaa013

32. Kumar V, Cohen JT, van Klaveren D, et al. Risk-targeted lung cancer screening: a cost-effectiveness analysis. *Ann Intern Med*. 2018;168(3):161-169. doi:10.7326/M17-1401

33. Crosbie PA, Balata H, Evison M, et al. Implementing lung cancer screening: baseline results from a community-based "Lung Health Check" pilot in deprived areas of Manchester. *Thorax*. 2019;74(4):405-409. doi:10.1136/thoraxjnl-2017-211377

34. Field JK, Duffy SW, Baldwin DR, et al. UK Lung Cancer RCT Pilot Screening Trial: baseline findings from the screening arm provide evidence for the potential implementation of lung cancer screening. *Thorax*. 2016;71(2):161-170. doi:10.1136/thoraxjnl-2015-207140

35. Tammemägi MC. Selecting lung cancer screenees using risk prediction models—where do we go from here. *Transl Lung Cancer Res*. 2018;7(3):243-253. doi:10.21037/tlcr.2018.06.03

36. Tammemagi MC, Schmidt H, Martel S, et al; PanCan Study Team. Participant selection for lung cancer screening by risk modelling (the Pan-Canadian Early Detection of Lung Cancer [PanCan] study): a single-arm, prospective study. *Lancet Oncol*. 2017;18(11):1523-1531. doi:10.1016/S1470-2045(17)30597-1

37. Howlader N, Forjaz G, Mooradian MJ, et al. The effect of advances in lung-cancer treatment on population mortality. *N Engl J Med*. 2020;383(7):640-649. doi:10.1056/NEJMoa1916623

38. Joseph AM, Rothman AJ, Almirall D, et al; SCALE (Smoking Cessation within the Context of Lung Cancer Screening) Collaboration. Lung cancer screening and smoking cessation clinical trials. *Am J Respir Crit Care Med*. 2018;197(2):172-182. doi:10.1164/rccm.201705-0909CI

39. Kathuria H, Detterbeck FC, Fathi JT, et al; ATS Assembly on Thoracic Oncology. Stakeholder research priorities for smoking cessation interventions within lung cancer screening programs: an official American Thoracic Society research statement. *Am J Respir Crit Care Med*. 2017;196(9):1202-1212. doi:10.1164/rccm.201709-1858ST

40. Cao P, Jeon J, Levy DT, et al. Potential impact of cessation interventions at the point of lung cancer screening on lung cancer and overall mortality in the United States. *J Thorac Oncol*. 2020;15(7):1160-1169. doi:10.1016/j.jtho.2020.02.008