BMJ Open

Evaluating the impacts of screening and smoking cessation programmes on lung cancer in a high-burden region of the USA: a simulation modelling study

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ABSTRACT

Objective: While the US Preventive Services Task Force has issued recommendations for lung cancer screening, its effectiveness at reducing lung cancer burden may vary at local levels due to regional variations in smoking behaviour. Our objective was to use an existing model to determine the impacts of lung cancer screening alone or in addition to increased smoking cessation in a US region with a relatively high smoking prevalence and lung cancer incidence.

Setting: Computer-based simulation model.

Participants: Simulated population of individuals 55 and older based on smoking prevalence and census data from Northeast Pennsylvania.

Interventions: Hypothetical lung cancer control from 2014 to 2050 through (1) screening with CT, (2) intensified smoking cessation or (3) a combination strategy.

Primary and secondary outcome measures: Primary outcomes were lung cancer mortality rates. Secondary outcomes included number of people eligible for screening and number of radiation-induced lung cancers.

Results: Combining lung cancer screening with increased smoking cessation would yield an estimated 8.1% reduction in cumulative lung cancer mortality by 2050. Our model estimated that the number of screening-eligible individuals would progressively decrease over time, indicating declining benefit of a screening-only programme. Lung cancer screening achieved a greater mortality reduction in earlier years, but was later surpassed by smoking cessation.

Conclusions: Combining smoking cessation programmes with lung cancer screening would provide the most benefit to a population, especially considering the growing proportion of patients ineligible for screening based on current recommendations.

Strengths and limitations of this study

- To our knowledge, this is the first study to model the impact of combining lung cancer screening and smoking cessation programmes in the USA.
- Our study demonstrates the use of simulation modelling as a critical resource to help translate national guidelines into local programmes, optimising cancer control efforts for a specific population.
- We assumed that current screening and treatment guidelines will remain the same; therefore, actual reduction rates may be different if future policies change. However, our results on the benefits of a long-term cessation programme are promising.

INTRODUCTION

Lung cancer is the leading cause of cancer-related death in the USA, resulting in approximately 150 000 deaths per year.[1] The National Lung Screening Trial (NLST), a randomised trial in the USA involving more than 53 000 current and former heavy smokers aged 55–74, found 20% fewer lung cancer deaths among trial participants screened with three annual low-dose CT versus three annual chest radiography examinations.[2 3] Based on the NLST results, the US Preventive Services Task Force (USPSTF) recommended annual CT screening for ever-smokers aged 55–80 with at least 30 pack-years of smoking history and no more than 15 years since quitting.[4] In early 2015, the Centers for Medicare and Medicaid Services (CMS) also released a decision memo in support of low-dose CT screening coverage for eligible individuals.[5] As a result, nationwide adoption of lung cancer screening is currently being implemented in the USA.

Although CT screening has been recommended by the USPSTF and CMS, the potential mortality reduction due to lung cancer

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screening as a stand-alone programme is limited. The 20% lung cancer mortality reduction seen in the NLST was estimated among people who were screened, and the lung cancer mortality reduction of screening with CT among the whole US population has yet to be established. The disease burden prevented by lung cancer screening with CT may also differ by geographical location because there exists much regional variation in smoking patterns and lung cancer rates.[1 6 7] For example, smoking prevalence is significantly higher in Northeast (NE) Pennsylvania compared with the USA as a whole, a finding typical of areas with low income and education.[8–10] In NE Pennsylvania, the incidence of lung and bronchus cancer is also higher in men and is increasing in women compared with rates among the US population.[11]

In this study, we utilised the Massachusetts General Hospital's Lung Cancer Policy Model (LCPM) to determine the optimal lung cancer control policy in NE Pennsylvania, where 29% of adults are current smokers.[12] We estimated the impacts of implementing lung cancer screening alone or incorporating an additional smoking cessation intervention on lung cancer mortality. Our results can aid policymakers' development of lung cancer control policy in NE Pennsylvania and in other areas with high prevalence of current and former smokers.

MATERIALS AND METHODS
Model overview
The LCPM is a state-transition microsimulation model that simulates an individual patient's lung cancer development, progression, detection, follow-up, treatment, and survival.[13 14] The LCPM has been used previously to evaluate the impact of tobacco control strategies on mortality reduction,[15 16] as well as the cost-effectiveness of imaging-based screening programmes for lung cancer.[17] Owing to concerns that chest CT examinations will detect incidental pulmonary nodules and result in invasive testing for benign or indolent disease, the LCPM explicitly models benign nodules and detailed clinical events. Each hypothetical individual in the LCPM can develop up to three cancers from any of the following five lung cancer cell types: adenocarcinoma (including adenocarcinoma in situ), large cell, squamous cell, small cell and other. The lung cancer risks, incidence rates and disease progression rates vary by histological type. Lung cancer risk and development in each simulated individual depends on a complete smoking history that includes length of time a person smoked and cigarettes smoked per day; both current and former smokers are at risk of developing lung cancer based on smoking history. The model outputs of the LCPM have been calibrated and validated using results from the NLST and the Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial (PLCO).[18]

The LCPM also incorporates the radiation risk equations specified in the Biological Effects of Ionizing Radiation (BEIR) VII report to account for the radiation exposure of screening.[16 17 19 20] The BEIR VII report derived a set of empirical radiation risk equations for multiple cancer sites primarily by fitting mathematical functions to data from Japanese atomic bomb survivors. This empirically derived model is also endorsed by the International Commission on Radiological Protection, and currently represents the most widely accepted approach to estimate cancer risks.

For additional details, the LCPM is described in an online technical appendix (http://www.cisnet.cancer.gov/lung/profiles.html).

NE Pennsylvania inputs
We developed a NE Pennsylvania version of the LCPM using data from regional surveys. The population of NE Pennsylvania is older in average age and has lower average household income and educational attainment than the general US population. Between 2005 and 2007, in Lackawanna and Luzerne counties, the two largest counties in the region, 18.1% and 18.3% of residents were over 65 years of age (compared with 12.5% in the USA) with median household incomes of $41 594 and $44 401, respectively (compared with $50 007 in the USA).

Regional smoking behaviour was derived from three separate sources. First, data on smoking prevalence—including tobacco use, the average number of cigarettes smoked per day, and cancer screening practices—was collected by the Northeast Regional Cancer Institute (NRCI) through a population-based study of health behaviours from 2002 to 2006, using a sampling protocol similar to that used by the Behavioral Risk Factor Surveillance System (BRFSS).[21] Tobacco use data in the region were also obtained from 800 NE Pennsylvania adults in the control arm of a 2007–2011 study of colorectal cancer.[22] The third data source was the Pennsylvania BRFSS, which includes regional aggregated data for three of six counties (Lackawanna, Luzerne and Wyoming counties) within the NE Pennsylvania region.[12 23] These three counties have a combined population of 563 631, representing 78.6% of the population of the greater NE Pennsylvania region. In the Pennsylvania BRFSS, 29% of adults in these counties aged 18 years or older were current smokers, compared with 20.4% of adults in the USA.[21] Additionally, 26% of adults in the region were former smokers.

Even with three data sources for smoking behaviour, the historical smoking data for the NE Pennsylvania region did not adequately span the entire age group and time horizon of interest and was therefore supplemented with 1965–2009 data from the National Health Interview Survey (NHIS) to create smoking histories beginning with the 1910 birth cohort and projected forward until 2050, using the methods described in Holford et al.[24] The probabilities of smoking initiation and cessation rates as functions of age observed in the NHIS were assumed to have similar shapes but differing

magnitudes in NE Pennsylvania, with the effect of age on smoking assumed to be the same in the NRCI population as in NHIS. Since periods were represented by a limited time span in NE Pennsylvania, they were assumed to remain constant. The birth cohort was systematically created to pick up differences over time. The data were then smoothed using constrained cubic splines for age, period and cohort to estimate the prevalence of current smokers, former smokers and never-smokers in cohorts beginning in 1910. An interaction between NRCI and NHIS was used to estimate possible differences in cohort trend between NE Pennsylvania and the USA.

Birth cohort-specific lung cancer incidence and mortality rates in NE Pennsylvania were used to ensure that the LCPM-generated outputs were consistent with local patterns. The NRCI manages a regional cancer registry that includes information on lung cancer incidence and initial treatment from nine community hospitals. The regional registry, which is part of the Pennsylvania Cancer Registry, captures more than 95% of lung cancer cases in the NE Pennsylvania region. Incidence and mortality data are aggregated from each of the six counties to obtain age-specific rates by sex and year for the region.

Lung cancer control scenarios

The effects of different cancer control scenarios on lung cancer incidence and mortality were evaluated. In the base case scenario, there was no lung cancer screening and no change in the current smoking cessation rate in NE Pennsylvania. We compared the base case with the following three scenarios: (1) screening based on the USPSTF recommendations with 100% adherence; (2) intensified smoking cessation—through programmes such as treatment provision and intervention by healthcare providers—resulting in a 50% increase in smoking cessation rates among all smokers; and (3) screening with 100% adherence plus intensified smoking cessation.

The screening programmes were implemented in the model in 2014 and the smoking cessation programmes were assumed to result in a 50% increase in cessation rates starting in 2014. Previous analyses have demonstrated increases in quit rates near 40% for programmes that expand cessation treatment coverage and encourage clinician intervention, with increases of over 76% when cessation strategies are combined with no-cost telephone quitlines.[25–27] Outcomes were projected until 2050 and results are presented for years 2020, 2030, 2040 and 2050.

We performed sensitivity analyses for screening scenarios assuming screening adherence rates of 40%, 60% and 80%, where adherence was defined as the proportion of the eligible screening population that was adherent during a given screen. Rates were chosen based on a NHIS study finding adherence rates of 54.6%, 69.3%, 85.8% and 46.4% in 2010 for colorectal, breast, cervical and prostate cancer screening, respectively.[28]

## RESULTS

Baseline lung cancer mortality

The projected lung cancer mortality rates in NE Pennsylvania compared with the USA, with no lung cancer screening programme and no change in current smoking cessation until 2050, are displayed in figure 1. Despite a decline in mortality rates in both NE Pennsylvania and the USA over the study period, the mortality rate in NE Pennsylvania remains higher than that of the USA, and the disparity between the two rates increases over time. In 2010, the lung cancer mortality rate in NE Pennsylvania was higher than the US average by 7.5 deaths per 100 000 person-years, a 5.3% increase. By 2050, the difference is projected to grow to 16.9 deaths per 100 000 person-years, a 44.1% increase.
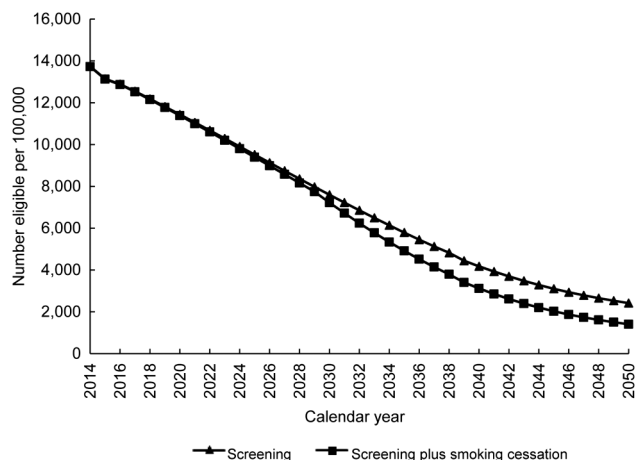
Eligibility for screening

The number of individuals eligible for lung cancer screening was comparable for the screening-only and the combined screening and cessation scenarios during the first 7 years of programme adoption, as shown in figure 2. If the current cessation programme is intensified, the number of people eligible for screening may not differ from the screening-only scenario because of the '15 years since quitting' criterion of the USPSTF screening guidelines, but should eventually decrease accordingly. However, our model results showed that the number of eligible individuals will progressively decrease in both scenarios after 2014.

Health outcomes of lung cancer control programmes

Health outcomes of the three lung cancer control scenarios and the base case scenario in 2020, 2030, 2040 and 2050 are presented in table 1. We estimate that in 2020 the screening-only scenario prevented 9.4 deaths per
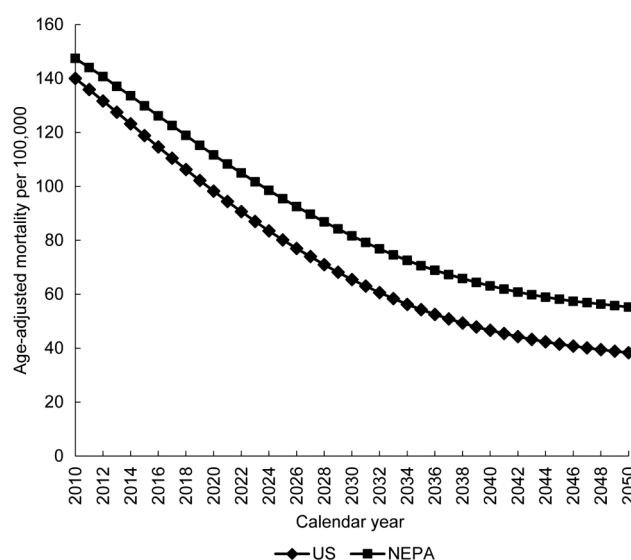
Figure 1 The projected lung cancer mortality rates for Northeast Pennsylvania (NEPA) and the USA for males and females ages 55 and older.

Figure 2 The number of people eligible for screening (per 100 000) as a function of calendar year, where triangles represent a screening-only scenario and squares represent combining screening with an intensive smoking cessation programme.

100 000 person-years (8.2% reduction in lung cancer death rate), the cessation-only scenario prevented 0.3 deaths per 100 000 person-years (0.3% reduction), and the combined screening and smoking cessation scenario prevented 9.7 deaths per 100 000 person-years (8.4% reduction). In 2050, we estimate that the rates of lung cancer deaths avoided were 1.0 deaths per 100 000 person-years (1.9% reduction) for screening-only, 4.0 deaths (7.1% reduction) for smoking cessation-only, and 4.6 deaths (8.2% reduction) for combined screening and cessation.

To quantify overall effectiveness of the scenarios, cumulative lung cancer mortality reduction, starting in 2014, is shown in figure 3. Our results showed that the cumulative lung cancer mortality reduction of the screening-only scenario will decrease from 2020 to 2050, while the mortality reduction of the cessation-only scenario will increase.

Since ionising radiation from screening CT has the potential to induce lung cancers, it is important to quantify the potential harms from lung cancer screening programmes. In 2020, the estimated additional number of lung cancers due to radiation exposure for screened males in the screening-only strategy was 0.78 per 100 000 person-years, which grew to 0.87 per 100 000 person-years by 2050.

Sensitivity analysis

We performed additional simulation runs to evaluate the impact of screening adherence on lung cancer mortality rates (table 2). In 2020, with screening adherence set at 40%, 60% and 80% for the screening-only scenario, the number of lung cancer deaths prevented per 100 000 person-years were 3.5, 5.4 and 7.2, respectively. In 2050, lung cancer deaths avoided for 40%, 60% and 80% adherence dropped to 0.2, 0.5 and 0.8 deaths per

Table 1 Screening and cessation scenario results (ages 55 and older)

	Lung cancer deaths per 100 K				Lung cancer deaths avoided per 100 K				Lung cancer diagnoses per 100 K				Number eligible for screening per 100 K				Radiation-induced cancers per 100 K			
	2020	2030	2040	2050	2020	2030	2040	2050	2020	2030	2040	2050	2020	2030	2040	2050	2020	2030	2040	2050
No intervention	115.2	84.2	64.4	55.8	NA	NA	NA	NA	200.9	151.2	119.0	105.8	NA	NA	NA	NA	NA	NA	NA	NA
Cessation-only	114.9	82.7	61.4	51.8	0.3	1.6	2.9	4.0	200.4	149.4	115.5	100.9	NA	NA	NA	NA	NA	NA	NA	NA
Screening-only	105.8	78.8	61.6	54.8	9.4	5.4	2.8	1.0	200.8	151.4	119.2	106.7	11 436	7597	4174	2416	0.78	1.12	1.11	0.86
Screening and cessation	105.5	77.3	59.3	51.2	9.8	7.0	5.1	4.6	200.4	149.1	115.6	101.7	11 385	7220	3117	1406	0.78	1.10	1.09	0.80

NA, not available.
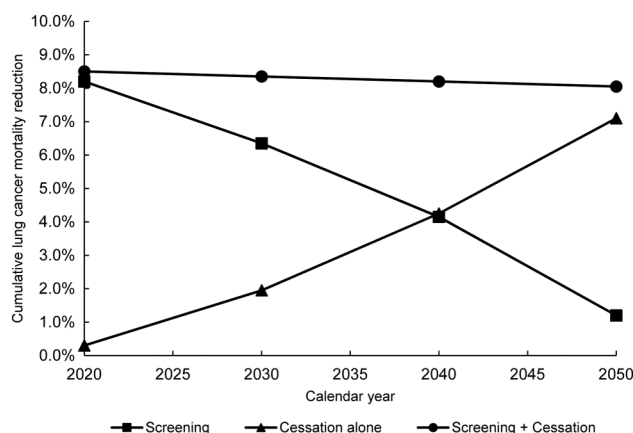
Figure 3 The cumulative lung cancer mortality reduction for screening-only, cessation-only, and combination of screening and cessation scenarios.

100 000 person-years, respectively. Our results indicate that even with 60% adherence, combined screening and smoking cessation resulted in a significant reduction of lung cancer deaths.

DISCUSSION

Our study applied an existing lung cancer model to evaluate screening and cessation programmes in NE Pennsylvania, a region with higher smoking prevalence and lung cancer incidence than the USA overall. By using region-specific data in a model, we were able to project and estimate the lung cancer mortality reduction under multiple potential lung cancer control policies. With higher baseline smoking rates in men and women, our results from the LCPM showed that the regional lung cancer mortality from the present through the year 2050 will be higher than national trends in lung cancer mortality. Thus, it is necessary to develop a comprehensive lung cancer control policy to minimise this disparity in health outcomes. Simulation modelling can serve as a critical resource to local cancer control planners to help translate national guidelines into programmes tailored for a specific geographic area and population.

Our results showed that the number of people eligible for screening will decrease in the future, which will reduce the benefits from a CT screening-only programme. Our model prediction is consistent with a recent study which showed a decrease in the proportion of patients with lung cancer meeting USPSTF screening eligibility criteria in a Midwestern region,[29] calling into question the potential long-term effectiveness of screening as a cancer control policy. A lung cancer control policy incorporating both CT screening and intensive smoking cessation may be the only option to achieve desired mortality reduction. Model predictions showed that the initial benefit of a screening-only programme compared with a cessation-only programme will eventually diminish as the number of people eligible for screening decreases. After 2040, a smoking

Table 2 Sensitivity analysis of screening adherence (ages 55 and older)

	Lung cancer deaths per 100 K				Lung cancer deaths avoided per 100 K				Lung cancer diagnoses per 100 K				Number screened per 100 K				Radiation-induced cancers per 100 K			
	2020	2030	2040	2050	2020	2030	2040	2050	2020	2030	2040	2050	2020	2030	2040	2050	2020	2030	2040	2050
40% adherence to screening	111.7	82.2	63.3	55.6	3.5	2.0	1.1	0.2	200.7	151.3	119.1	106.5	4268	2635	1460	836	0.8	0.8	0.7	0.6
60% adherence to screening	109.8	81.1	62.8	55.2	5.4	3.2	1.6	0.5	201.2	151.3	119.1	106.6	7007	4224	2341	1355	0.8	0.9	0.8	0.7
80% adherence to screening	108.0	80.1	62.2	55.0	7.2	4.2	2.2	0.8	200.9	151.4	119.3	106.6	9493	5829	3224	1856	0.8	1.0	1.0	0.8
60% adherence to screening plus cessation	109.5	79.5	60.2	51.6	5.7	4.7	4.3	4.2	200.7	149.0	115.5	101.6	6976	3953	1716	774	0.8	0.9	0.8	0.6

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cessation-only programme will reduce the number of lung cancer deaths more than a CT screening-only programme based on current screening guidelines. Our model also predicted a radiation-induced lung cancer rate associated with CT screening of less than 2 cases per 100 000 per year.

Our study reports reductions in mortality rates that are lower than the 20% observed in the NLST, because the mortality reduction in our study is based on the population of NE Pennsylvania, which includes both light smokers and non-smokers, whereas the NLST results are based on a population with restrictive eligibility criteria. The benefit of screening is diluted in the population that includes those eligible for screening as well as those at lower risk who are ineligible for screening. In addition, the NLST population was composed of healthy volunteers who knew they would be assigned to one of two screening arms. The participants were moderately younger and less likely to be current smokers, and thus were possibly healthier than the general US population.[30] So, the mortality reduction observed in the NLST cannot be directly compared with our model predictions for NE Pennsylvania.

Prior studies have found an important role for programmes that increase smoking cessation, for example, through brief interventions by healthcare providers, quit lines and by providing access to treatment.[25 31 32] The findings of our current study are consistent with those of prior studies, and extend those of prior studies by incorporating lung cancer screening. Health policy that does not integrate cessation, but instead is based solely on CT screening of individuals who meet the eligibility criteria recommended by the USPSTF, may be increasingly inadequate due to the decreasing number of people eligible for screening under these guidelines. To our knowledge, this is the first study to model the impact of combining lung cancer screening and smoking cessation programmes in the USA.

There are several limitations to this study. First is the paucity of county-level smoking pattern data. We used multiple sources of data to estimate the regional smoking pattern, and smoking rates were smoothed using constrained cubic splines that assumed current trends would continue into the future. Recent and future implementation of tobacco control policies, however, will influence the future prevalence of smoking and incidence of lung cancer. While the effects of tobacco control policies on lung cancer rates are delayed, these policies have the potential to affect a much larger percentage of the population in the long term. Second, we chose a hypothetical programme that results in a 50% increase in cessation to demonstrate the effect that increased cessation can potentially have on lung cancer mortality in NE Pennsylvania. Previous studies have demonstrated the potential for high rates of cessation after the implementation of cessation programmes, reporting increases in quit rates near 40% for programmes that expand cessation treatment coverage

and encourage clinician intervention, and increases of over 76% when cessation strategies are combined with no-cost telephone quitlines.[25–27 32] We did not consider recidivism in smokers and there are currently no trials to show that cessation reduces mortality in the long term. In addition, we assumed current screening and treatment guidelines will remain the same; therefore, actual reduction rates may be different if future policies change. However, our results on the benefits of a long-term cessation programme are promising.

In conclusion, a lung cancer control strategy that incorporates CT screening among eligible ever-smokers with intensified smoking cessation will decrease lung cancer mortality at a greater rate than screening-only or cessation-only programmes. This combination strategy may be the best option for achieving lung cancer mortality reduction in NE Pennsylvania that is comparable to mortality reduction in the USA. Our study demonstrates the ability for simulation models to translate national guidelines into local programmes, optimising cancer control efforts for a specific population. The lessons learned from this study will not only inform cancer control policy in NE Pennsylvania, but can inform other regional policymakers, who may benefit from using modelling for health economic evaluations before implementing national cancer control guidelines in their geographic area.

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