

# Benefits and harms of lung cancer screening strategies in Argentina: a modeling study



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## Summary

**Background** Argentina lacks formal recommendations for lung cancer screening (LCS). We modeled the potential benefits and harms of different national LCS strategies with low-dose computed tomography in Argentina.

**Methods** We adapted one of the Cancer Intervention and Surveillance Modeling Network (CISNET) LCS models to Argentina's epidemiologic and demographic context. Using inputs from Argentina's version of the Smoking History Generator, a microsimulation model that generates cohort-specific smoking histories by age and sex, we modeled 26 annual screening scenarios for the 1960 birth cohort, including the US Preventive Services Task Force (USPSTF) 2021 criteria (ages 50–80,  $\geq 20$  pack-years, currently smoke or  $\leq 15$  years since quitting (YSQ)) and the US National Lung Screening Trial (NLST) criteria (ages 55–74,  $\geq 30$  pack-years, currently smoke or  $\leq 15$  YSQ).

**Findings** For any given number of screens, scenarios with an upper screening age limit of 80 years yielded the greatest number of lung cancer deaths (LCD) averted, followed by those that relax the YSQ criterion. Under the USPSTF 2021 recommendation, 25.2% of the population would be eligible for LCS, resulting in 547 LCD averted and 7618 life-years gained (LYG) per 100,000 population; the expected relative reduction in LC mortality is 14.6%. Under the NLST criteria, 14.2% would be eligible for LCS, resulting in 289 LCD averted and 4466 LYG per 100,000 population, with a relative reduction in lung cancer mortality of 7.7%.

**Interpretation** Approaches extending the upper age limit and relaxing YSQ criteria are the most effective.

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## Introduction

Lung cancer remains the leading cause of cancer mortality worldwide, with the majority of lung cancer cases diagnosed at advanced stages, particularly in low- and middle-income countries (LMICs).<sup>1</sup> This late detection limits therapeutic options and is associated with poorer clinical outcomes. Argentina, a middle-income country in South America, mirrors this global pattern. With

adult smoking prevalence still exceeding 20%,<sup>2</sup> lung cancer remains the leading cause of cancer mortality in the country, accounting for 14.6% of all cancer-related deaths in 2021, and representing approximately 1.4% of total national healthcare expenditures.<sup>3</sup>

Earlier diagnosis through screening could alleviate some of the lung cancer-related burden by shifting treatment toward less advanced disease. Landmark

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### Research in context

#### Evidence before this study

Lung cancer is the leading cause of cancer mortality worldwide. For this study, we first conducted a literature search in MEDLINE and Lilacs databases between August and December 2024 for synonyms of “Argentina”, “lung cancer”, and “lung cancer screening”. These were supplemented with Google searches, and the authors’ own knowledge. Landmark trials, such as the U.S. National Lung Screening Trial (NLST) and the Dutch-Belgian lung cancer screening trial (NELSON), have demonstrated that low-dose computed tomography (LDCT) can detect lung cancer at earlier stages and significantly reduce mortality from lung cancer. While many high-income countries recommend lung cancer screening (LCS) for high-risk populations, the potential impact of LCS with LDCT has been poorly studied in low- and middle-income countries (LMICs). In Argentina, lung cancer experts have issued a position statement recommending annual LDCT screening for high-risk individuals based on NLST eligibility criteria. However, there is currently no national screening plan or recommendation from Argentina’s Ministry of Health. For this simulation study, we adapted one of the Cancer Intervention and Surveillance Modeling Network (CISNET) lung cancer screening models to Argentina’s epidemiologic and demographic context. Model inputs included smoking patterns from three nationally representative surveys conducted between 2004 and 2018, lung cancer stage distributions from the RITA hospital registry, lung cancer and other-cause mortality from national vital statistics, and population projections from the United Nations Statistics Division.

trials, such as the U.S. National Lung Screening Trial (NLST)<sup>4</sup> and the Dutch-Belgian lung cancer screening trial (NELSON),<sup>5</sup> have demonstrated that low-dose computed tomography (LDCT) can detect lung cancer at earlier stages and significantly reduce mortality from lung cancer. While many high-income countries recommend lung cancer screening (LCS) for high-risk populations, the potential impact of LCS with LDCT has been poorly studied in LMICs, with no current guidelines for implementation.<sup>6</sup> Argentine lung cancer experts published a position statement recommending annual screening with LDCT for high-risk populations based on the eligibility criteria of the NLST.<sup>4,7</sup> Additionally, the National Commission for the Assessment of Health Technologies and Clinical Excellence (CONETEC) has recently issued a recommendation for conditional health coverage (provided certain conditions are met, such as implementing the screening within a comprehensive patient monitoring program, which has not yet been defined) for LDCT screening using the same eligibility criteria.<sup>8</sup> Nevertheless, there is currently no national screening plan

#### Added value of this study

This study provides a comprehensive evaluation of 26 different lung cancer screening strategies with LDCT for Argentina using a validated simulation framework from the CISNET Lung Working Group, adapted to the country’s specific epidemiological, demographic, and smoking context. By generating cohort-specific projections for benefits and harms, we identify strategies that maximize mortality reduction while considering screening burden. Notably, we show that extending the screening stopping age to 80 years and relaxing the years-since-quitting criterion outperform more restrictive approaches.

#### Implications of all the available evidence

Our results suggest that a lung cancer screening program in Argentina could substantially reduce lung cancer mortality. Screening strategies that extend the stopping age to 80 years and relax years-since-quitting requirements may provide better mortality benefits without disproportionate increases in screening volume, supporting a reconsideration of current recommendations in Argentina based on the NLST eligibility criteria, which propose stopping at age 74. These findings provide policymakers with evidence to guide discussions on optimal planning and implementation of an LCS program in Argentina, as well as a valuable framework for other LMICs considering lung cancer screening implementation.

or recommendation from Argentina’s Ministry of Health.

Here, we evaluate the potential benefits and harms of different LCS strategies with LDCT in Argentina using the simulation modeling framework developed by the US Cancer Intervention and Surveillance Modeling Network (CISNET) Lung Working Group (LWG).<sup>9–11</sup> CISNET LWG modeling supported both the U.S. Preventive Services Task Force (USPSTF)<sup>9–11</sup> and American Cancer Society (ACS)<sup>12</sup> lung cancer screening recommendations. We adapt the CISNET approach to Argentina and use this model to evaluate the potential impacts of screening in the country.

## Methods

### Argentina Smoking History Generator

The model’s population inputs needed for the LCS model are based on the Argentina-specific adaptation of CISNET’s Smoking History Generator (SHG), a precursor microsimulation model that produces cohort-specific smoking histories and other-cause mortality

rates (i.e., deaths from causes other than lung cancer).<sup>13</sup> The SHG simulates individual life histories of smoking initiation, cessation, intensity in terms of cigarettes per day (CPD), and mortality rates. Argentina's adaptation of the SHG was developed using data from three nationally representative surveys conducted between 2004 and 2018.<sup>14</sup> These inputs allow the model to simulate Argentine individual smoking histories,<sup>15</sup> national smoking prevalence, lung cancer incidence and mortality projections, and ultimately to evaluate the benefits and harms of LDCT screening under various scenarios. A more detailed description of Argentina's SHG can be found in the [Supplementary Material](#), as well as in previous publications.<sup>14,15</sup>

### Lung cancer natural history and screening model

We adapted the Lung Cancer Interventions and Decision Simulation (LuCID-Sim) model (previously known as BCCRI-LungCan or Michigan Lung model) to Argentina's epidemiological and demographic context to assess the effectiveness of LDCT screening in the Argentine population. This model is one of the CISNET simulation models used in the US to inform the USPSTF and ACS guidelines on lung cancer screening.<sup>9–12</sup>

The LuCID-Sim model combines a natural history model of lung cancer progression and a screening module. The natural history component simulates lung cancer onset, progression, and mortality in the absence of screening, conditional on individual smoking histories. Lung cancer risk is modeled using the Two-Stage Clonal Expansion (TSCE) model.<sup>16</sup> If an individual develops clinically diagnosed lung cancer, the natural history model simulates the age at lung cancer onset, histology, stage at diagnosis, preclinical sojourn time for each stage, and age at lung cancer death. Lung cancer histology is categorized into four primary histological groups: adenocarcinoma, squamous cell carcinoma, small-cell lung cancer, and other non-small cell types. Histology is assigned using a multinomial logistic regression model derived from the Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial data, accounting for age, sex, and smoking exposure.<sup>9,17</sup> Preclinical sojourn times for each stage follow a Weibull distribution with shape and scale parameters depending on sex, stage, and histology. Tumor stages are aggregated into commonly used clinical groupings: IA, IB, II, IIIA, IIIB (including IIIC), and IV. Lung cancer-specific survival was simulated using cure models with lognormal survival distributions.

The outputs from the natural history component serve as inputs for the screening component to simulate the effect of screening on lung cancer incidence, stage, and survival. The model uses sensitivity and specificity rates to simulate screening results: true positive, false positive, or negative. The screening

component estimates the effect of LDCT screening on lung cancer outcomes under varying screening eligibility and frequency criteria. Screening sensitivity and specificity are based on data from the NLST trial and adjusted for the Lung-RADS screening protocol.<sup>18,19</sup> The rates of potential screening harms, including false-positive results and overdiagnosed cases are also based on the NLST. The U.S. version of the model was calibrated to reproduce lung cancer incidence, mortality, and screening outcomes from the PLCO and NLST trials.<sup>10</sup>

For Argentina's version, we incorporated lung cancer stage distributions from the RITA hospital registry (for cases diagnosed between 2022 and 2024),<sup>20</sup> lung cancer mortality and other cause mortality (non-lung cancer mortality) from DEIS,<sup>21</sup> and population projections from the United Nations Statistics Division.<sup>22</sup> Therefore, in our adaptation, the model has been recalibrated using Argentina-specific data on smoking patterns (from adapted SHG), lung cancer staging, mortality, and survival from lung cancer. Parameters for tumor initiation and promotion in the TSCE model were also calibrated to match national lung cancer mortality trends by age in Argentina.

This simulation study used publicly available, de-identified secondary data sources and did not include individual-level identifiable information. Because the data posed no risk of identifying specific individuals, institutional review board/ethics committee approval and informed consent were not required. A more detailed description of the LuCID-Sim model, as well as a schematic representation of Argentina's adaptation, can be found in the [Supplementary Material](#).

### Modeled scenarios

We used Argentina's SHG to simulate individual smoking and life histories from Argentina's 1950, 1960, and 1970 birth cohorts by sex. Consistent with previous work by the CISNET LWG,<sup>9,23</sup> we simulated 1 million males and 1 million females for the no screening scenario. For each lung cancer screening scenario, outcomes were estimated on this same underlying cohort, and the simulation was repeated five times to confirm numerical stability of the outcomes. We restricted to simulated individuals who were alive at age 45 (we assume lung cancer does not occur before this age) and followed them until death or age 90, whichever comes first. Assuming annual screening, we modeled 26 scenarios for each sex; [Table 1](#) lists the parameters that define each scenario. These scenarios include the US Preventive Services Task Force (USPSTF) LCS 2021 criteria (individuals aged 50–80 who have smoked at least 20 pack-years and currently smoke or have quit within the past 15 years),<sup>11</sup> the NLST eligibility criteria (individuals aged 55–74 who have smoked at least 30 pack-years and currently smoke or have quit within the past 15 years),<sup>4</sup> the ACS current LCS criteria

Parameters whose combinations generate 24 of the 26 screening scenarios	
Age at screening initiation (years)	50 or 55
Age at screening cessation (years)	75 or 80
Minimum pack-years smoked	20 or 30
Maximum YSQ (for former smokers) (years)	15, 25, or no YSQ criteria
NLST eligibility criteria	
Age at screening initiation (years)	55
Age at screening cessation (years)	74
Minimum pack-years smoked	30
Maximum YSQ (for former smokers) (years)	15
NELSON study eligibility criteria	
Age at screening initiation (years)	50
Age at screening cessation (years)	74
Smoking intensity	>15 CPD for >25 years or >10 CPD for >30 years
Maximum YSQ (for former smokers) (years)	10

Abbreviations: YSQ: years since quit; CPD: cigarettes per day.

**Table 1: Parameters used to develop 26 lung cancer screening scenarios.**

(individuals aged 50–80 who currently smoke or formerly smoked and have a  $\geq 20$  pack-year history; similar to the USPSTF 2021 recommendation except that removes the years since quit criterion),<sup>12</sup> and the NELSON study eligibility criteria (50–74 years of age; current or former smokers who had quit  $\leq 10$  years ago, who had smoked >15 CPD for >25 years or >10 CPD for >30 years).<sup>5</sup>

We assumed perfect screening uptake and adherence among those eligible for screening to focus exclusively on the impact of varying the screening eligibility criteria. Smoking cessation and the risk of competing causes of death were assumed to be unaffected by screening.

All analyses were performed using R software (versions 4.4 and 4.5).

**Outcomes**

Modeled outcomes include the percentage of individuals eligible for screening and the number of LDCT screens; measures of benefit, such as lung cancer deaths (LCD) averted, lung cancer mortality reduction, and life-years gained (LYG) versus a no-screening scenario; and measures of harm, including the mean false-positive screens per person screened and the number of overdiagnosed cases. All count outcomes are reported per 100,000 individuals in the general population alive at age 45 years. We also estimated the number of individuals needed to screen (NNS) to prevent one lung cancer death, assuming screening occurs throughout the lifetime as long as the individual remains eligible. In addition, we estimated the lung cancer detection rate per screen (expressed as a percentage), defined as  $100 \times$  (screen-detected lung cancer cases/LDCT screens).

Screening scenarios are presented as: frequency of screening (A = annual)–age at start of screenings–age at stopping screenings–minimum pack-years of smoking–maximum years since quitting (YSQ). For example: A\_50\_80\_20\_15 means annual LCS starting at age 50, stopping at age 80, with a 20 pack-years minimum and 15 or less YSQ (for former smokers). Scenario A\_50\_74\_x\_10 refers to the NELSON study eligibility criteria (in which the minimum pack-years is variable).

**Role of the funding source**

The funders had no role in study design; in the collection, analysis, and interpretation of data; in the writing of the report; or in the decision to submit the paper for publication.

**Results**

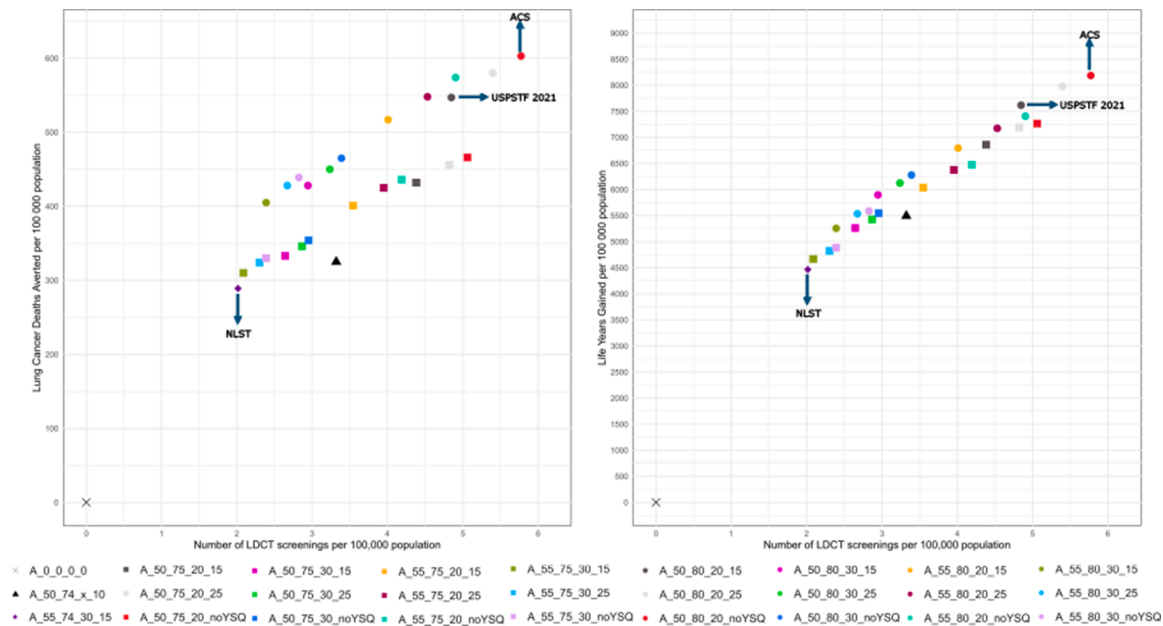
As the eligibility criteria are expanded (in terms of age range, minimum pack-years, or maximum years since quitting), the number of LDCT screens increases, along with both the benefits of screening (measured as LCD averted and LYG) and the potential harms (measured as false positives and overdiagnosis). For all three birth cohorts, the scenario with the maximum LCD averted and LYG corresponds to the broader one (current ACS recommendation: scenario 50\_80\_20\_noYSQ); inversely, the smallest absolute benefit is observed under the more restrictive NLST eligibility criteria (scenario 55\_74\_30\_15). For any given number of screens, the upper boundary (representing the scenario with the highest number of LCD averted) is consistently defined by the scenario in which the upper age limit for screening is 80 years. Among scenarios with screening ending at age 80, relaxing the YSQ criterion (e.g., allowing YSQ = 25 or removing the restriction) appears to prevent more LCD than lowering the starting age of screening to 50. However, this advantage is not as evident when LYG is considered (Fig. 1, and Figures S3 and S4).

When comparing screening scenarios to each other (rather than to the no-screening scenario), we use scenario A\_50\_80\_20\_15, which aligns with the current USPSTF 2021 recommendation, as the reference.

**1960 birth cohort**

The 1960 birth cohort is currently in the middle of its screening eligibility age range. Fig. 1 illustrates the number of LCD averted (left panel) and the LYG (right panel) by the number of LDCT screens per 100,000 population for all evaluated scenarios; Table 2 shows the benefits of screening, and Table 3, the corresponding harms.

Under the current USPSTF recommendation (scenario A\_50\_80\_20\_15), 25.2% of the population would be eligible for screening during their lifetime, resulting



**Fig. 1:** Number of LDCT screens versus number of lung cancer deaths averted (left panel) and number of LDCT screens versus the life-years gained (right panel) for the 1960 birth cohort. LDCT: low-dose computed tomography; NLST: US National Lung Screening Trial eligibility criteria; USPSTF 2021: US Preventive Services Task Force 2021 criteria; ACS: American Cancer Society criteria. Scenarios represented as: A = annual screening; Age at screening initiation; Age at screening cessation; Minimum pack-years smoked to be eligible for screening; Maximum years since quitting smoking. A\_0\_0\_0\_0\_ No screening scenario; A\_50\_74\_x\_10: NELSON study eligibility criteria.

in 484,697 screening examinations, 547 LCD averted, and 7618 LYG per 100,000 population, with an NNS of 46 (Fig. 1 and Table 2). The expected relative reduction in lung cancer mortality under these eligibility criteria is 14.6% (Table 2). Under the scenario A\_50\_80\_20\_noYSQ (ACS recommendation), 25.6% of this birth cohort would be eligible for screening during their lifetime. This would result in 577,334 screening examinations, 603 LCD averted, and 8187 LYG per 100,000 population, with an NNS of 42, which results in a 10.2% increase in LCD averted and a 19.1% increase in the number of LDCT screens when compared to the current USPSTF recommendation. Conversely, the scenario A\_55\_74\_30\_15 (NLST criteria) would result in 201,618 screening examinations, 289 LCD averted, and 4466 LYG per 100,000 population, and an NNS of 49. This would lead to a 58.4% reduction in the number of LDCT screens compared to the current USPSTF 2021 recommendation, but at the expense of a 47.2% decrease in LCD averted. The scenario that gives the lowest number of LDCT screens per lung cancer death averted is the USPSTF 2013 criteria, A\_55\_80\_30\_15 (Table 2).

In terms of harms, screening according to the current USPSTF 2021 criteria would result in 1.1 false-positive screens per person screened and 95 overdiagnosed lung cancer cases per 100,000 population (Table 3). Removing the YSQ criterion (ACS eligibility

criteria) would result in 107 overdiagnosed cases per 100,000 population, and the NLST criteria are projected to produce 38 overdiagnosed cases per 100,000 population.

### 1950 and 1970 birth cohorts

Patterns for these birth cohorts are similar to those described for the 1960 cohort (Figures S3 and S4 in the Supplementary Material), although the absolute benefit of LCS is lower for the 1970 cohort. Under the USPSTF 2021 recommendation, the projected relative reduction in lung cancer mortality is 15.5% for the 1950 birth cohort and 12.2% for the 1970 cohort (Tables S2 and S4, respectively). Expanded results for these two cohorts are provided in the Supplementary Material.

### Discussion

In this study, we found that a lung cancer screening program in Argentina could substantially reduce lung cancer mortality and increase life-years gained. Although the benefits appear to decline for the 1970 birth cohort (due to lower smoking prevalence in more recent generations<sup>14</sup>), a reduction of more than 10% in lung cancer mortality can still be expected if screening were implemented under the current USPSTF criteria. Because we assume perfect uptake/adherence and no screening-induced changes in competing mortality or

Scenario	% Eligible	LDCT screens	Screen-detected lung cancer cases	Lung cancer mortality reduction (%)	Lung cancer deaths averted	Life-years gained	Life-years gained per lung cancer deaths averted	LDCT screens per lung cancer deaths averted	LDCT screens per life-years gained	NNS	Lung cancer detection rate (%)
A_50_75_20_15	25-1	438,244	1347	11-5	432	6860	15-9	1014	64	58	0-3
A_50_75_20_25	25-5	482,081	1404	12-2	456	7193	15-8	1057	67	56	0-3
A_50_75_20_noYSQ	25-5	506,077	1435	12-5	466	7265	15-6	1086	70	55	0-3
A_50_75_30_15	15-2	264,237	1044	8-9	333	5262	15-8	794	50	45	0-4
A_50_75_30_25	15-3	286,658	1089	9-3	346	5427	15-7	828	53	44	0-4
A_50_75_30_noYSQ	15-3	295,383	1101	9-5	354	5547	15-7	834	53	43	0-4
A_50_80_20_15	25-2	484,697	1724	14-6	547	7618	13-9	886	64	46	0-4
A_50_80_20_25	25-6	539,727	1828	15-5	580	7976	13-8	931	68	44	0-3
A_50_80_20_noYSQ	25-6	577,334	1886	16-1	603	8187	13-6	957	71	42	0-3
A_50_80_30_15	15-9	294,465	1368	11-4	428	5897	13-8	688	50	37	0-5
A_50_80_30_25	16	323,629	1439	12	450	6125	13-6	719	53	36	0-4
A_50_80_30_noYSQ	16	339,033	1476	12-4	465	6278	13-5	729	54	34	0-4
A_55_74_30_15	14-2	201,618	918	7-7	289	4466	15-5	698	45	49	0-5
A_55_75_20_15	23-8	354,597	1272	10-7	401	6037	15-1	884	59	59	0-4
A_55_75_20_25	24-8	395,314	1333	11-4	425	6376	15	930	62	58	0-3
A_55_75_20_noYSQ	24-9	419,102	1365	11-7	436	6476	14-9	961	65	57	0-3
A_55_75_30_15	14-5	208,748	988	8-3	310	4667	15-1	673	45	47	0-5
A_55_75_30_25	14-8	230,153	1034	8-7	324	4823	14-9	710	48	46	0-4
A_55_75_30_noYSQ	14-9	238,824	1047	8-8	330	4887	14-8	724	49	45	0-4
A_55_80_20_15	23-8	401,055	1652	13-8	517	6794	13-1	776	59	46	0-4
A_55_80_20_25	24-9	452,963	1753	14-7	548	7174	13-1	827	63	45	0-4
A_55_80_20_noYSQ	25	490,348	1814	15-3	574	7406	12-9	854	66	44	0-4
A_55_80_30_15	15-2	238,970	1314	10-8	405	5256	13	590	45	38	0-5
A_55_80_30_25	15-5	267,129	1382	11-4	428	5535	12-9	624	48	36	0-5
A_55_80_30_noYSQ	15-6	282,481	1418	11-7	439	5587	12-7	643	51	35	0-5
A_50_74_x_10	20-8	332,118	1005	8-7	325	5494	16-9	1022	60	64	0-3

Numbers are per 100,000 individuals in the general population alive at age 45. Abbreviations: NNS: number needed to screen; YSQ: years since quit; LDCT: low-dose computed tomography. The screening strategies correspond to annual screening for: age at start-age at stopping-minimum pack-years-maximum YSQ. A\_50\_74\_x\_10: NELSON study eligibility criteria.

Table 2: Benefits of 26 screening programs for the 1960 Argentina birth cohort.

smoking behavior, our estimates should be interpreted as upper-bound projections under full participation, representing the maximum potential benefit under these idealized conditions.

The decision to implement lung cancer screening in a country, and if so, under which eligibility criteria, must consider factors not addressed here (such as costs and health system capacity). In Argentina, LCS lacks formal national clinical guidelines. The existing expert consensus<sup>7</sup> and the CONETEC assessment<sup>8</sup> function as recommendations rather than binding protocols, limiting their impact on clinical practice. Consequently, LCS is not recognized as a quality-of-care metric. In addition, Argentina currently lacks an organized national LCS program, a coordinated network of cancer centers for program delivery, and publicly available monitoring indicators (e.g., screening uptake and downstream diagnostic and treatment capacity) to support a robust assessment of implementation readiness. As a result, LCS activity, where it occurs, appears fragmented and largely confined to the private sector.

These systemic gaps underscore the need for the results presented here, which aim to identify the most suitable LCS strategies for the Argentine context, and they motivate future work to quantify the health care resources required to implement LCS in Argentina.

Our results suggest that extending the screening stopping age to 80 years performs better than stopping earlier, without a significant increase in the number of LDCT scans. This supports revisiting current recommendations in Argentina based on the NLST eligibility criteria, which propose stopping at age 74, as has been done in the US. Additionally, relaxing the years-since-quit criterion appears more effective in reducing lung cancer deaths than lowering the starting age. The superior performance of scenarios that extend the screening end age (when lung cancer risk is highest) aligns with findings from other studies.<sup>9,24</sup> Similarly, including individuals with more than 15 years since smoking cessation compensates for the decline in lung cancer risk from smoking cessation by accounting for the increased risk due to aging. This shift moves

Scenario	LDCT screens	Mean LDCT screens per person screened	Mean false-positive results per person screened	Overdiagnosed cases	Overdiagnosis: Percentage of all lung cancer cases	Overdiagnosis: Percentage of screen-detected lung cancer cases
A_50_75_20_15	438,244	17.4	1	58	1	4
A_50_75_20_25	482,081	18.9	1.1	60	1	4
A_50_75_20_noYSQ	506,077	19.8	1.1	62	2	4
A_50_75_30_15	264,237	17.4	1	45	1	4
A_50_75_30_25	286,658	18.8	1.1	46	1	4
A_50_75_30_noYSQ	295,383	19.3	1.1	49	1	4
A_50_80_20_15	484,697	19.2	1.1	95	2	6
A_50_80_20_25	539,727	21.1	1.2	103	3	6
A_50_80_20_noYSQ	577,334	22.5	1.3	107	3	6
A_50_80_30_15	294,465	18.6	1	77	2	6
A_50_80_30_25	323,629	20.2	1.1	83	2	6
A_50_80_30_noYSQ	339,033	21.2	1.2	85	2	6
A_55_74_30_15	201,618	14.2	0.8	38	1	4
A_55_75_20_15	354,597	14.9	0.9	56	1	4
A_55_75_20_25	395,314	15.9	0.9	60	1	5
A_55_75_20_noYSQ	419,102	16.8	1	62	2	5
A_55_75_30_15	208,748	14.4	0.8	45	1	5
A_55_75_30_25	230,153	15.5	0.9	47	1	5
A_55_75_30_noYSQ	238,824	16.1	0.9	49	1	5
A_55_80_20_15	401,055	16.8	1	96	2	6
A_55_80_20_25	452,963	18.2	1	103	3	6
A_55_80_20_noYSQ	490,348	19.6	1.1	107	3	6
A_55_80_30_15	238,970	15.7	0.9	78	2	6
A_55_80_30_25	267,129	17.2	1	82	2	6
A_55_80_30_noYSQ	282,481	18.1	1	84	2	6
A_50_74_x_10	332,118	15.9	0.9	40	1	4

Numbers are per 100,000 individuals in the general population alive at age 45. Abbreviations: YSQ: years since quit; LDCT: low-dose computed tomography. The screening strategies correspond to annual screening for: age at start-age at stopping-minimum pack-years-maximum YSQ. A\_50\_74\_x\_10: NELSON study eligibility criteria.

**Table 3: Harms of 26 screening programs for the 1960 Argentina birth cohort.**

screening focus from younger to older adults while also expanding eligibility among younger high-risk individuals who currently become ineligible after reaching 15 YSQ. These findings reinforce the potential benefits of expanding eligibility criteria in terms of both age and YSQ, i.e., increasing the screening stopping age to 80 and relaxing the YSQ criterion to 25 or without the YSQ criterion. However, these strategies are not only more resource-intensive; they will also result in increases in overdiagnosis, because competing causes of death are also more prevalent at older ages, concern that can be moderated if screening is restricted to those with reasonable life expectancy.<sup>23</sup>

In addition to benefits and harms, we report the lung cancer detection rate per LDCT examination. Under NLST-like eligibility, the modeled detection rate was 0.5% per LDCT examination. This is lower than the observed NLST baseline detection rate (~1.1%),<sup>4</sup> but our estimate represents an average across all annual screening rounds over a lifetime screening horizon for a given birth-cohort, rather than 1 to 3 screening

rounds with 6–7 years of follow-up as in NLST. Because Argentina currently lacks national screening program data, our modeled detection rates should be interpreted as projections that can be refined as local screening evidence becomes available.

Our results are aligned with similar findings reported for the US population. A modeling analysis that informed the revision of the previous USPSTF 2013 recommendation estimated that screening starting at age 50 or 55 and continuing through age 80, with a minimum of 20 pack-years of smoking exposure, would result in greater benefits.<sup>9</sup> Although there is a scarcity of local data, two different modeling studies conducted in Argentina estimated that between 0.7 and 0.8 million individuals were eligible for annual LCS in 2023 based on the NLST eligibility.<sup>25,26</sup> Even though this estimate is not directly comparable to our findings, since it reports eligibility for a single calendar year rather than by birth cohort, both the 1950 and 1960 birth cohorts would have been eligible in that year. Under the NLST criteria (A\_55\_74\_30\_15), our results are consistent in scale

with those previous estimates, despite methodological differences.

Our study has notable strengths. In the absence of local clinical trials and while awaiting results from observational studies, we applied a modeling framework developed by the CISNET Lung Working Group and adapted to the Argentinian context to simulate the potential impact of different lung cancer screening schedules in the Argentine population. The Argentinian SHG reproduces national smoking patterns, and its lung cancer natural history model replicates observed age-specific mortality,<sup>14,26</sup> supporting the validity of our projections. Using this well-established model, we compared the benefits and harms of LCS across strategies and identified those offering the greatest benefit relative to the number of screenings required.

Our study also has some limitations. First, because this is the first Argentina-specific implementation of this modeling framework, we could not benchmark results against other independent Argentina models; nevertheless, comparative interpretation is supported by prior comparative modeling analyses indicating that relative strategy performance is more consistent than absolute outcome magnitudes.<sup>9</sup> Second, our analysis focused on smoking history by age and sex, the major determinants of lung cancer risk<sup>16,27</sup>; however, it did not account for other important risk factors such as history of chronic obstructive pulmonary disease, exposure to occupational and environmental carcinogens, and family history of lung cancer. Third, updated smoking prevalence estimates in Argentina remain limited, as they rely primarily on self-reported surveys. Similarly, lung cancer burden is assessed mainly through mortality data from national vital statistics due to the lack of high-quality national incidence data and reliance on subnational sources for prevalence and stage distribution. Because the validity of modeling studies depends on the quality of the input data, these constraints limit our ability to directly assess the relationship between smoking prevalence and lung cancer incidence, underscoring the need for improved population-based surveillance and cancer registration in the country. Fourth, we only modeled an annual screening frequency; yet, biennial screening could be as effective as annual screening, or at least provide a reasonable balance between benefits, harms, and resource requirements, particularly in resource-limited settings.<sup>6</sup> We will explore these trade-offs as well as adaptive screening strategies in future work.<sup>28</sup> Fifth, in settings where granulomatous lung disease is more prevalent (e.g., prior tuberculosis), LDCT screening may identify a higher number of benign nodules, potentially increasing false-positive findings and downstream diagnostic evaluation; however, this does not preclude the implementation of LDCT lung cancer screening in such settings.<sup>29</sup> Sixth, for the 1970 birth cohort, we had

only limited data on lung cancer mortality to calibrate the model to national trends, which may have contributed to the reduced benefit observed in this cohort. Finally, this study assumed a 100% screening uptake and adherence rate to focus on the differences found in the distinct eligibility scenarios; however, recent studies have shown that uptake to annual lung cancer screening varies widely (12%–91%), depending on population and program characteristics, with the highest values representing uncommon, highly selected or intensively supported program settings rather than typical real-world practice.<sup>30</sup> Considering the effects of uptake and adherence on the projected impacts of screening will be the focus of future work.

Despite these limitations, our study helps address a gap in local data regarding optimal lung cancer prevention in a middle-income country. Systemic barriers restrict the broader adoption of LDCT screening in countries like Argentina, where there is a critical lack of country-specific data on clinical outcomes and healthcare system demands. Here, we present results that can help identify the most suitable LCS strategies for Argentina. The choice of screening strategy carries important implications for healthcare planning. Strategies that extend the screening age while maintaining or modestly increasing the number of LDCT scans may offer better returns on investment compared to those that significantly broaden eligibility without proportional gains in mortality reduction. Future work incorporating Argentina-specific cost data could further refine these assessments and support informed resource allocation. Integrating risk prediction tools beyond smoking history, as explored in recent international studies, could also improve efficiency by identifying high-risk individuals who do not meet traditional eligibility criteria.<sup>31</sup> Additionally, while this study focuses on screening strategies, any national lung cancer control program must integrate strong tobacco control policies and cessation services. The projected benefits of LDCT screening are magnified when paired with sustained reductions in smoking prevalence. Expanding cessation support alongside screening may enhance program effectiveness and long-term sustainability.<sup>32</sup>

While focused on Argentina, our work has broader relevance for other LMICs, particularly for Latin American countries, with similar resource constraints and health system challenges. Although Latin American experience with LDCT screening is limited but growing, local evidence to date has largely come from pilot studies and emerging health technology assessments rather than established national programs.<sup>33–35</sup> Because smoking prevalence and smoking-history distributions vary across the region, these differences will materially affect the size of the screening-eligible population, the absolute benefits of LDCT screening, and the required screening and downstream diagnostic

capacity. Therefore, our Argentina-specific projections should not be directly extrapolated to other settings without adapting the model to local smoking patterns and competing mortality risks. Nonetheless, given that many LMICs currently rely on evidence from high-income countries that may not reflect their epidemiology or infrastructure, this study provides a first practical, context-specific modeling framework that can be tailored to inform lung cancer screening planning and implementation in comparable settings.

In conclusion, our analysis of various screening strategies for Argentina suggests that approaches extending the upper age limit and relaxing years-since-quitting requirements yield the highest number of lung cancer deaths averted and life-years gained, for any given number of LDCT screens, but result in more overdiagnosed cases and would require more resources. These findings provide policymakers with evidence to guide discussions on optimal planning and implementation of an LCS program in Argentina.

#### Contributors

MVS: Conceptualization; Data curation; Formal analysis; Funding acquisition; Investigation; Methodology; Project administration; Resources; Writing—original draft; and Writing—review & editing.

PC: Conceptualization; Formal analysis; Funding acquisition; Methodology; Resources; Software; Supervision; Validation; Writing—review & editing.

JJ: Conceptualization; Formal analysis; Funding acquisition; Methodology; Supervision; Validation; Writing—review & editing.

IB: Conceptualization; Investigation; Resources; Validation; Writing—review & editing.

RauM: Conceptualization; Formal analysis; Funding acquisition; Investigation; Methodology; Supervision; Validation; Writing—original draft; and Writing—review & editing. MVS accessed and verified the data.

RafM: Conceptualization; Funding acquisition; Investigation; Methodology; Project administration; Resources; Supervision; Validation; Writing—original draft; and Writing—review & editing.

#### Data sharing statement

This study utilized publicly accessible, de-identified data from surveys such as Argentina's National Census and the Argentinian Vital Statistics (DEIS). The databases can be found on their respective websites. Smoking model parameters are available at: <https://sph-umich.shinyapps.io/shgdisplayappargentina/>.

#### Declaration of interests

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#### Appendix A. Supplementary data

Supplementary data related to this article can be found at <https://doi.org/10.1016/j.lana.2026.101476>.

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