Targeted lung cancer screening in the age of immunotherapies and targeted therapies – an economic evaluation for Australia

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Summary

Background The cost-effectiveness of different lung cancer screening strategies has been evaluated from an Australian public health system perspective using static models. In addition, the impact of novel therapies, including immunotherapies and targeted therapies, on the cost-effectiveness of lung cancer screening has not yet been evaluated comprehensively. We evaluated the benefits, harms and cost-effectiveness of a targeted national lung screening program in Australia, accounting for the increasing uptake of novel therapies, which informed the lung cancer screening recommendations of the Australian Medical Services Advisory Committee (MSAC).

Methods Australia-specific data on lung cancer epidemiology, smoking behaviour and care costs were used to adapt the MIcrosimulation SCreening ANalysis (MISCAN)-Lung model. Benefits, harms and cost-effectiveness of different targeted lung cancer screening scenarios were evaluated for individuals born between 1945 and 1969. The scenarios considered various screening age ranges, intervals and eligibility criteria (minimum accumulated smoking history and PLCOm2012 risk thresholds).

Findings The MSAC-recommended scenario was cost-effective at AUD62,754 per quality-adjusted life-year compared to no screening. This scenario biennially screens current and former smokers (quit ≤10 years ago) who smoked ≥30 pack-years between ages 50 and 70, preventing 62 lung cancer deaths per 100,000 and yielding 8.4 quality-adjusted life-years per prevented lung cancer death. Using novel therapies reduced the incremental costs of screening compared to no-screening by 14.8% but yielded 11.3% fewer incremental quality-adjusted life-years compared to traditional anti-cancer therapies, due to the improved survival yielded by novel therapies. Overall, the cost-effectiveness of screening was better when costs and effects of novel therapies were applied (AUD62,754 vs AUD65,340 per quality-adjusted life-year gained; 4% difference).

Interpretation Targeted lung cancer screening is more cost-effective when costs and effects of novel therapies are applied, although impacts on cost-effectiveness are likely to be marginal.

Funding Cancer Australia.

Keywords: Personalised lung cancer screening; Australia; Cost-effectiveness; Immunotherapy; Population-based screening

Introduction

The National Lung Screening Trial (NLST) and Dutch–Belgian lung cancer screening trial (NELSON) have shown that low-dose computed tomography (LDCT) screening reduces lung cancer mortality.[1,2] Current U.S. guidelines recommend screening based on an individual's accumulated pack-year smoking history and years since smoking cessation (generally referred to as "pack-year criteria").[3] In contrast, ongoing pilot screening programs and trials are evaluating screening based on risk assessments through risk-prediction models.[4] Risk-based lung cancer screening models may enhance performance and reduce socioeconomic or ethnic disparities compared to pack-year criteria.[5–7] Yet, limited assessments exist on the cost-effectiveness of such screening programs.

The effects of the increased uptake of novel therapies on the cost-effectiveness of lung cancer screening have

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Research in context

Evidence before this study

Lung cancer screening trials have demonstrated the efficacy of low-dose computed tomography (LDCT) screening in reducing lung cancer mortality. The impact of the increased adoption of novel therapies for lung cancer, including immunotherapies and targeted therapies, on the cost-effectiveness of lung cancer screening has not been comprehensively assessed. The integration of novel therapies has substantially improved lung cancer survival rates, as shown in the United States, potentially affecting the incremental effectiveness of screening programs. As novel therapies primarily target advanced disease, early detection through screening is anticipated to reduce both lung cancer mortality and the costs associated with novel therapies.

Added value of this study

This economic evaluation is the first study to comprehensively evaluate the costs and effects of novel therapies using natural-history modelling in investigating the cost-effectiveness of a national lung cancer screening program. Although the application of novel therapies improves the cost-effectiveness of lung cancer screening, we found the difference in cost-effectiveness compared to analyses that did not apply the costs and effects of novel therapies to be modest. Overall, accounting for novel therapies reduced the incremental costs of screening by 14.8% but also yielded 11.3% fewer incremental quality-adjusted life-years compared to a situation without novel therapies. The reduction in incremental quality-adjusted life-years due to screening after accounting for novel therapies is due to the lower relative benefit in life-years due to screening. This is because the overall survival in the scenario without screening is greater in scenarios with novel therapy, compared to scenarios without novel therapy use.

Implications of all the available evidence

Targeted screening has been demonstrated to be an effective and cost-effective strategy to reduce morbidity and mortality from lung cancer. The impact of novel therapies on the cost-effectiveness of lung cancer screening may be more modest than anticipated.

also not yet been evaluated comprehensively. Adopting novel therapies has substantially improved lung cancer survival, as demonstrated in the U.S., which may reduce the incremental effectiveness of lung cancer screening in quality-adjusted life-years gained.[8] However, as novel therapies are predominantly used for prolonging survival of advanced disease, early detection through lung cancer screening is expected to both reduce lung cancer mortality and offset the significant costs of novel therapies.[9] Previous analyses were either performed before the widespread implementation of novel therapies or did not apply natural-history modelling, which can directly evaluate the effects and costs of lead-time and overdiagnosis.

Recently, Cancer Australia conducted an enquiry into the prospects and delivery of a national lung cancer screening program in Australia, incorporating an integrated pathway for risk assessment, screening and treatment.[10] This paper describes the economic and financial modelling undertaken for the enquiry.

The Australian Medical Services Advisory Committee (MSAC), an independent non-statutory committee that uses health technology assessment to appraise medical services proposed for public funding and provides advice to the Australian Government, supported the introduction of a national lung cancer screening program. Specifically, MSAC recommended as part of its support for the program that eligibility for the program be targeted at individuals aged 50–70 years who have a history of cigarette smoking of ≥30 pack-years and, if former smokers, had quit within the previous 10 years.[11] Based on MSAC's recommendation, the Australian Government recently announced an AUD263.8 million investment to support implementing a national lung cancer screening program by 2025.[12]

The aim of our study was twofold: firstly, we investigated the cost-effectiveness of alternative lung cancer screening strategies from an Australian public health system perspective. Secondly, we investigated the impact on costs and health effects of novel therapies for the eligibility criteria identified as most cost-effective. We present an evaluation of the benefits, harms and cost-effectiveness of potential targeted national lung screening program scenarios in Australia using the MISCAN-Lung model. The MISCAN-Lung model has been previously used to inform screening recommendations in the United States, Canada and Switzerland.[13–16] MISCAN-Lung was adapted to reflect the population (population structure, life expectancy and smoking behaviour) and lung cancer epidemiology (occurrence of different histologies and stage distribution) in Australia. Data on lung cancer survival in Australia was only available by overall stage and histology. However, overall survival rates in Australia and the United States Surveillance, Epidemiology, and End Results Program (SEER) were similar (data not shown). Therefore, the more detailed survival by stage and the survival data from SEER, which provides stage-specific survival by histology, were used. The evaluated screening program scenarios include integrated risk assessment, screening and diagnosis pathways and

analyses reflecting scenarios in which novel therapies are and are not available.

Methods

MISCAN-lung

The analysis was based on the MIcrosimulation SCreening ANalysis (MISCAN) Lung model, which was one of the models that informed the United States Preventive Services Task Force (USPSTF) lung cancer screening recommendations in 2013 and 2021.[17,18] MISCAN-Lung was calibrated to individual-level data from NLST and the Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial, from which information on the preclinical duration of lung cancer and LDCT effectiveness were derived.[19] MISCAN-Lung has previously evaluated the cost-effectiveness of lung cancer screening in the United States, Canada and Switzerland.[13–16] More details on MISCAN-Lung are provided in Appendix 1 pp 3–9.[15,16,19]

In brief, MISCAN-Lung simulates life histories for each individual from birth until death, in the presence and absence of screening. By comparing life histories in the presence of screening with the corresponding life histories in the absence of screening, MISCAN-Lung estimates the benefits, harms and costs of screening scenarios.

Characteristics of modelled population

Five birth cohorts were investigated: 1945–1949 (ages 74–78 in 2023), 1950–1954 (ages 69–73 in 2023), 1955–1959 (ages 64–68 in 2023), 1960–1964 (ages 59–63 in 2023), 1965–1969 (ages 54–58 in 2023). These cohorts represent approximately 6.7 million individuals in Australia in 2021.

Australia-specific smoking behaviour data were used to model smoking behaviour by age, sex and cohort, as described in the Appendix 1 pp 10–18. In brief, smoking initiation and cessation probabilities were calibrated to match observed current/former/never smoking prevalence. The observed number of cigarettes smoked per day (CPD) were evaluated and divided into five quintiles; linear interpolation was used to fit the average number of CPD by age and quintile between observed CPD values while future values were obtained through extrapolation. Data on CPD were obtained from the National Campaign Against Drug Abuse Social Issue surveys, the National Drug Strategy Household surveys and published literature. The products included in CPD were manufactured and self-rolled cigarettes. Smokers were divided into five smoking-intensity quintiles, ranging from the lightest to heaviest smokers by the reported average number of CPD at each age, similar to Anderson et al.[20] For surveys in which numbers of cigarettes were provided as a continuous outcome, means per quintile were determined based on the absolute number of cigarettes per day. For surveys in which numbers of cigarettes were provided as a categorical outcome, the mid-point of the category was assumed as the absolute number of cigarettes per day. Australia-specific life tables by birth-year, age and sex were obtained from the Human Mortality Database. Mortality probabilities for never- and ever-smokers were derived by adjusting their mortality probabilities to reflect smoking-related comorbidities and match these life tables after adjustment for smoking behaviour (Appendix 1 pp 18–23). Our estimated smoking prevalence rates were consistent with previous analyses by Vaneckova et al.[21] Furthermore, we expand on these previous analyses by explicitly and jointly modelling smoking initiation and cessation rates, cigarettes per day patterns and smoking-related mortality.

The Australian-specific smoking behaviour data were integrated in MISCAN-Lung to replicate the age- and sex-specific lung cancer incidence, histology proportions, and stage proportions observed in data from the Australian Institute of Health and Welfare from 2015,[22] in which screening did not occur (Appendix 1 pp 24–26).

Lung cancer survival was based on sex-, stage-, and histology-specific survival estimates from SEER-18 2004–2010, before the implementation of novel therapies. Survival curves were consequently adapted to reflect current care pathways by considering the uptake rate of novel therapies by stage and type of lung cancer. For stage III and IV cancers, novel therapy use was integrated based on their use as first- and second-line treatments. For stages I and II, the use of novel therapies was integrated based on their application in treating recurrent cancers. More detail is provided in Appendix 1 pp 26–36.

Screening scenarios

Overall, we evaluated 432 scenarios (Appendix 1 Table 15). 216 scenarios considered pack-year criteria ("NLST-like approaches"), which determined eligibility based on smoking intensity, duration and time since quitting. Furthermore, 216 scenarios considered risk-based approaches using the reduced PLCOm2012 model (Appendix 1 pp 37–38).[4,23–25] Screening eligibility for each scenario was not a model input; instead, screening eligibility for each individual at each age was assessed by evaluating their smoking history up to each age. Both types of screening strategies considered different combinations of: screening starting ages (50, 55, 60), stopping ages (70, 75, 80, 85) and intervals (annual, biennial).

Recent studies from the United Kingdom's Targeted Lung Health Checks suggest uptake rates have increased since their initial introduction, ranging from 35 to 48% with an average of 42%.[26–28] Therefore, a 65% uptake rate (modelled as a 50% chance to attend the first invited screening, followed by an 81% chance to attend the next screening if the person attended the previous screening, and a 35% chance if the person did not attend) was assumed for the base-case investigation.

MISCAN-Lung was adjusted to incorporate the screening and assessment pathway proposed by Cancer Australia (Appendix 1 pp 39–44).[15] In particular, MISCAN-Lung was adjusted to incorporate adjustments in nodule management guidelines compared to those used in the National Lung Screening Trial. Given the low occurrence of invasive procedures and major complications reported in NLST and NELSON, morbidity and death due to screening-related follow-up procedures were not considered.[15,29] The health outcomes and costs for each scenario were determined by comparing the scenario to the no-screening scenario.

Costs

Costs were analysed from an Australian public healthcare system perspective. Costs associated with the 1) overall program management (program costs), 2) provision of screening and subsequent diagnostic costs, and 3) lung cancer treatment were considered. Program costs were derived through consultation with Cancer Australia and included annual ongoing program costs and initial program establishment costs. Risk assessment and screening costs were based on existing Medicare Benefits Schedule (MBS) item numbers.[30] Diagnostic procedure costs were estimated from existing MBS item numbers for services provided in the private system and public hospital costing data (Appendix 1 pp 45–48).[30,31] We weighted the costs for the private and public hospital systems by the proportion of Australians who have private health insurance (43.8%).[32]

Lung cancer treatment costs by phase of care (initial, continuing, and terminal care), histology (small cell and non-small cell lung cancer) and stage at diagnosis (localised, regional, distant metastases, unknown) were available from the Australian 45 and Up Study cohort.[33] These costs were adapted to reflect novel therapy costs by using data on clinical treatment pathways for immunotherapies and targeted therapies and treatment duration distributions from Pharmaceutical Benefits Scheme (PBS) data provided by Cancer Australia. Continuing care phase costs for stage I/II cancers were based on protocol-informed estimates of the frequency of follow-up imaging and specialist visits for patients remaining progression-free.

The estimated costs for the screening program, lung cancer treatment by phase of care and quality of life assumptions are presented in Table 1.

All costs are reported in Australian dollars, using 2020 as reference year. A lifetime horizon for the costs and effects was applied to each simulated person. Annual discount rates of 5% were applied to both costs and effects.

Utilities

Age-specific general population-based utility values representative of Australia were applied to individuals without lung cancer.[34] Separate utility values were applied to individuals with lung cancer diagnosed in stages I/II and III/IV, with separate utility weights applied to the terminal 12-month phase for patients who died of lung cancer.[35] No disutility was assumed with screening itself due to its minor impact on quality of life in both the short and long term.[36,37] No disutility was applied in the continuing care phase for patients diagnosed in stage I/II to reflect their disease-free state after treatment with (assumed) curative intent.

Benefits, harms and cost-effectiveness of screening scenarios

The main outcomes assessed for each scenario were: proportion of individuals ever screened, number of LDCT examinations, lung cancer mortality reduction, lung cancer deaths prevented, life-years gained (LYG), quality-adjusted life-years gained (QALYs), overdiagnosis (defined as cancers detected through screening that would never have been clinically detected if screening had not occurred), false positives and costs. Outcomes were standardised to 100,000 individuals alive across all cohorts in 2023.

Under the QALY maximisation scenario, screening scenarios that were more expensive but less or equally effective (i.e. fewer QALYs gained) than other scenarios were excluded due to dominance. Extendedly dominated scenarios, i.e. scenarios that were more costly and less effective than a combination of other scenarios, were also ruled out. The remaining scenarios constitute the efficient frontier. The incremental cost-effectiveness ratio (ICER) was determined for each efficient screening scenario, calculated as the incremental net costs per incremental QALY gained compared to the previous efficient screening scenario. This analysis was applied to all 432 screening programs and separately to the 216 biennial screening programs to reflect concerns about the budget impact of annual screening.

Budget impact analysis

The budget impact of selected screening programs was analysed over the period 2023–2033, inclusive. The budget impact analysis includes individuals from birth cohorts outside of the modelled birth cohorts that age into the program i.e., 1970 onwards, depending on starting age eligibility. Projected population estimates for the year that different birth years became eligible for screening were used.

Sensitivity analyses

The sensitivity of the base-case cost-effectiveness results was investigated by deterministically varying cost and utility parameter values, the uptake rate, the proportion of those screened with significant incidental findings, the discount rate and applying a life-expectancy threshold of at least 5-years (with perfect information on other-cause mortality) to be eligible for screening.

Screening and treatment costs were varied by 20% compared to base-case values. We varied utilities by applying the upper limit for stage I/II utilities in the initial phase and the lower limit for stage III/IV utilities in the initial and continuing care phases. Furthermore, we evaluated the effects of the screening-eligible population to have an overall lower quality of life (5% lower), similar to Ngo et al.[38] Uptake rates of 42% and 20% were modelled (Appendix 1 Table 28). Incidental findings of 5%, 10% and 20% (base case = 15%) were also evaluated. A 3% discount rate was also modelled. In addition, we reduced the impact of novel therapies on the survival rates by 30% (reflecting an arbitrary but considerable reduction in the impact of these therapies). Selected multi-way sensitivity analyses are reported. To evaluate the impact of novel therapies, we also evaluated scenarios in which screening (with either PLCOm2012 or pack-years) was compared to a no-screening scenario without including the costs and effects of novel therapies. We also undertook a probabilistic sensitivity analysis, for which statistical distributions are reported in Table 1. In brief, the standard deviation of the costs was assumed to be 20% (similar to the variation used for the univariate analyses) and the distribution from utility estimates were derived from the original publication.

Role of the funding source

Cancer Australia commissioned the research and defined its scope. Cancer Australia supported access to data and contributed to interpretation of the results and obtained approval from the Australian Department of Health and Aging for submission.

Results

Effects of screening scenario characteristics on cost-effectiveness

No clear distinction was evident between the cost-effectiveness of pack-year-based screening scenarios and risk-based screening scenarios (Appendix 2 Fig. S1), and younger starting ages dominate screening scenarios (Appendix 2 Fig. S2). Scenarios with younger stopping ages have lower costs compared with scenarios that stop at older ages but also yield fewer QALYs gained (Appendix 2 Fig. S3).

Cumulative smoking is an important factor for cost-effectiveness. Screening scenarios with higher cumulative smoking criteria have lower costs but gain fewer QALYs than those with lower cumulative smoking criteria (Appendix 2 Fig. S4). Compared to the 30-pack-year and 40-pack-year scenarios, the 20-pack-year scenarios yielded 15.6% and 44.6% more QALYs but incurred 19.7% and 50.2% higher costs, respectively. A similar pattern is seen when comparing strategies using the PLCOm2012 risk prediction model. Screening strategies with higher risk thresholds gain fewer QALYs than those with lower risk thresholds and are less costly (Appendix 2 Fig. S6). Increasing the maximum number of years since smoking cessation increases costs and QALYs gained (Appendix 2 Fig. S5).

Appendix 2 Fig. S7 shows the effects of annual screening compared with biennial screening. Biennial screening scenarios have lower costs and gain fewer QALYs than annual screening scenarios.

Program costs		**Probabilistic sensitivity analysis distribution mean and SD**
Description	Annual costs	
Annual program costs (Annual screening)	$27,475,501	N ($27,475,501, $5,495,100)
Annual program costs (Biennial screening)	$22,498,654	N ($22,498,654, $4,499,731)
Additional annual program costs incurred in years 1 and 2	$47,800,000	N ($47,800,000, $9,560,000)

Screening and subsequent diagnostic costs		
Description	Unit costs	
Risk Assessment	$35	N ($35, $7)
Screening LDCT examination	$295	N ($295, $59)
Interval screening	$333	N ($333, $67)
Incidental findings[a]	$303	N ($303, $61)
Diagnosis (false positive)[a]	$1548	N ($1549, $310)
Diagnosis (true positive)[a]	$3344	N ($3344, $669)

Excess treatment costs[b]			
Stage at diagnosis and phase of care	Costs per person-year (novel treatments)	Costs per person-year (without novel treatments)	
Localised			
Initial treatment phase	$36,057	$36,057	N ($36,057, $7211)
Continuing care phase	$652	$652	N ($652, $130)
Terminal care phase	$143,808	$69,927	N ($143,808, $28,762)
Regional			
Initial treatment phase	$64,271	$40,369	N ($64,271, $12,854)
Continuing care phase	$7810	$7810	N ($7,810, $1562)
Terminal care phase	$79,179	$55,648	N ($79,179, $15,836)
Distant Metastases			
Initial treatment phase	$77,012	$42,803	N ($77,012, $15,402)
Continuing care phase	$24,398	$24,398	N ($24,398, $4880)
Terminal care phase	$92,827	$59,013	N ($92,872, $18,565)

Quality of life assumptions		
State	Utility value	
General population	0.87[34]	N (0.87, 0.004)
Stage I/II lung cancer	0.78 (95% CI 0.70–0.86)[35]	N (0.78, 0.04)
Stage III/IV cancer	0.69 (95% CI 0.65–0.73)[35]	N (0.69, 0.02)
Terminal lung cancer	0.59[35]	N (0.59, 0.10)

[a]Appendix 1 pp 45-49 shows a detailed breakdown of these costs. [b]Costs were allocated to the different phases of care using the following set of assumptions: Terminal phase costs: costs incurred in the final year up to and including the death date defined the terminal phase or from diagnosis to death for individuals surviving less than 1 year from diagnosis; initial phase costs: the first year after diagnosis or the period from diagnosis until the start of the 12-month terminal phase for individuals surviving more than 1 year but less than 2 years; continuing phase costs: the period between the end of the initial phase and the start of the terminal phase.

Table 1: **Program costs, costs of screening-related events, treatment costs and utilities used in the MISCAN-Lung model (in 2020 Australian dollars).**

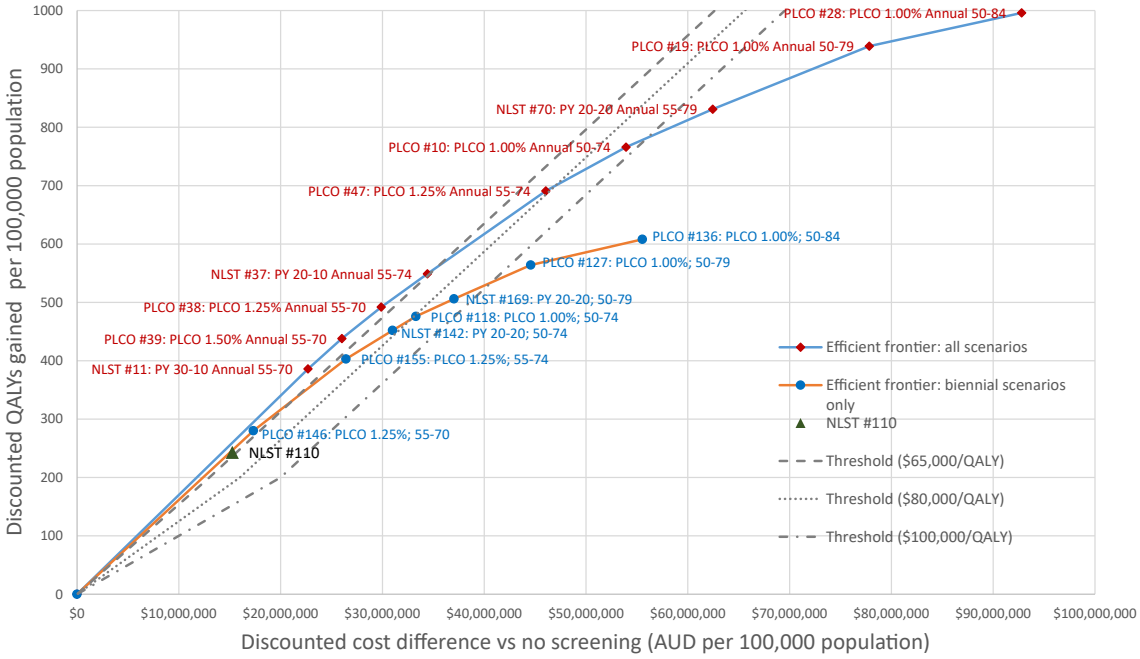

Fig. 1: The cost-effectiveness of the lung cancer screening scenarios on the efficient frontier for the combined analysis (blue line) and the biennial-only analysis (orange line). Results are presented per 100,000 individuals alive in 2023 and are discounted by 5% annually. NLST #110 is the MSAC-recommended screening scenario.

Screening scenarios on the efficient frontier

Fig. 1 shows the efficient frontier for the combined analysis of all screening scenarios (annual and biennial) and the analysis of biennial screening scenarios only. Fig. 1 also shows the MSAC recommended screening scenario (NLST #110) located just beneath both efficient frontiers. All scenarios on the efficient frontier for the combined analysis were annual screening scenarios. The screening scenario with the lowest ICER (AUD58,774) compared to no screening was a pack-year-based screening scenario: current and former smokers (who quit ≤10 years ago) who smoked ≥30 pack-years aged between ages 55 and 70 screened annually (NLST #11). In the biennial-only analysis, the screening scenario with the lowest ICER (AUD61,859) compared to no screening was the risk-based screening scenario for current and former smokers aged between 55 and 70 with a 1.25% 6-year risk of developing lung cancer (PLCO #146). Regarding screening outcomes, NLST #11 involves 27,261 LDCT screens, resulting in a gain of 386 QALYs per 100,000 individuals, 37 overdiagnosed lung cancer cases, and a 4.3% reduction in lung cancer mortality (Table 2). PLCO #146 requires 18,791 LDCT screens, yields 280 QALYs, leads to 27 overdiagnosed cases, and achieves a 3.2% reduction in lung cancer mortality (Table 2). The MSAC recommended scenario, NLST #110, requires 13,727 LDCT screens, achieves a gain of 243 QALYs, leads to 25 overdiagnosed cases, and results in a 2.8% reduction in lung cancer mortality (Table 2). The number of screens per death prevented was 288, 265 and 222 for NLST #11, PLCO #146 and NLST #110 respectively. Non-discounted life-years gained and non-discounted QALYs gained for NLST #11, PLCO #146 and NLST #110 were 905, 681 and 585, and 811, 608 and 521, respectively.

Costs and health effects of novel therapies compared to results with traditional anti-cancer therapies

Table 3 compares selected screening programs from analyses with and without the representation of the costs and effects of novel therapies. The incremental costs of screening compared to no-screening were lower when accounting for novel therapies, reflecting the high costs of these medications: 16.3%, 15.0% and 14.8% for NLST #11, PLCO #146 and NLST #110, respectively. However, the improved survival yielded by novel therapies does result in fewer incremental QALYs compared to the implementation of screening in a setting without novel therapies: 11.1%, 10.8% and 11.3% for NLST #11, PLCO #146 and NLST #110, respectively. Furthermore, overall screening was more cost-effective in a setting with novel therapies compared to a setting with traditional anti-cancer therapies, demonstrated by the ICERs being 5.9%, 4.7% and 4.0% lower for NLST #11, PLCO #146 and NLST #110 respectively.

Scenario	Scenario characteristics	Discounted costs compared to no screening (in AUD) per 100,000	Discounted QALYs gained per 100,000	Discounted costs (in AUD) per QALY gained compared to no screening	ICER compared to the previous efficient scenario	Percentage of the population ever screened	Number of performed LDCT screens (per 100,000)	Lung cancer mortality reduction (%)	Lung cancer deaths prevented (per 100,000)	Non-discounted life-years gained (per 100,000)	Non-discounted QALYs gained (per 100,000)	Non-discounted life-years gained per lung cancer death prevented	Non-discounted QALYs gained per lung cancer death prevented	Over-diagnosed lung cancers (per 100,000)	Percentage of screen-detected cancers that is over-diagnosed	Lung cancer deaths prevented per over-diagnosed case	False positive screens (per 100,000)
Combined analysis of annual and biennial screening scenarios																	
NLST #11	PY 30-10 Annual 55-70	22,686,911	386	58,774	–	6.1%	27,261	4.3%	95	905	811	9.55	8.56	37	13.6%	2.54	959
PLCO #39	PLCO 1.50% Annual 55-70	26,016,959	438	59,399	64,039	8.2%	33,730	5.0%	112	1043	934	9.30	8.33	46	14.0%	2.42	1174
PLCO #38	PLCO 1.25% Annual 55-70	29,880,658	492	60,733	71,550	10.0%	42,386	5.6%	125	1178	1055	9.42	8.43	50	13.8%	2.48	1484
NLST #37	PY 20–10 Annual 55-74	34,421,149	549	62,698	79,658	9.2%	45,375	6.8%	151	1301	1162	8.61	7.69	80	17.0%	1.88	1615
PLCO #47	PLCO 1.25% Annual 55-74	46,056,605	691	66,652	81,940	14.0%	68,999	9.1%	204	1685	1504	8.28	7.39	113	17.4%	1.81	2459
PLCO #10	PLCO 1.00% Annual 50-74	53,934,605	766	70,411	105,040	16.9%	87,106	10.0%	223	1874	1674	8.42	7.52	121	17.2%	1.84	3123
NLST #70	PY 20-20 Annual 55-79	62,446,782	831	75,147	130,957	16.1%	94,907	11.6%	259	2027	1800	7.83	6.95	187	21.1%	1.38	3445
PLCO #19	PLCO 1.00% Annual 50-79	77,831,020	939	82,887	142,447	21.8%	129,502	14.5%	323	2367	2101	7.33	6.51	247	21.9%	1.31	4706
PLCO #28	PLCO 1.00% Annual 50-84	92,798,230	996	93,171	262,583	22.5%	157,737	17.0%	379	2578	2272	6.81	6.00	371	25.7%	1.02	5808
Analysis of biennial screening scenarios only																	
PLCO #146	PLCO 1.25% Biennial 55-70	17,320,419	280	61,859	–	7.7%	18,791	3.2%	71	681	608	9.61	8.59	27	12.6%	2.62	590
PLCO #155	PLCO 1.25% Biennial 55-74	26,422,346	403	65,564	73,999	11.3%	31,419	5.3%	119	1003	890	8.44	7.49	63	16.0%	1.88	1019
NLST #142	PY 20-20 Biennial 50-74	30,996,706	452	68,577	93,354	12.9%	39,984	5.8%	130	1121	993	8.64	7.65	70	16.1%	1.85	1328
PLCO #118	PLCO 1.00% Biennial 50-74	33,291,071	476	69,939	95,599	14.9%	44,049	6.5%	145	1197	1060	8.27	7.32	82	16.6%	1.76	1450
NLST #169	PY 20-20 Biennial 50-79	37,034,095	506	73,190	124,767	13.9%	45,818	7.2%	161	1264	1115	7.86	6.93	114	19.5%	1.41	1536
PLCO #127	PLCO 1.00% Biennial 50-79	44,578,043	564	79,039	130,068	18.7%	60,825	8.8%	197	1456	1280	7.38	6.49	149	20.4%	1.32	2037
PLCO #136	PLCO 1.00% Biennial 50-84	55,536,493	608	91,343	249,056	20.1%	77,623	10.9%	243	1626	1415	6.70	5.83	252	25.0%	0.96	2670
MSAC recommended screening scenario																	
NLST #110	PY 30-10 Biennial 50-70	15,249,290	243	62,754[a]	–	5.3%	13,727	2.8%	62	585	521	9.47	8.43	25	13.1%	2.48	438

LDCT: Low-Dose Computed Tomography; MSAC: Medical Services Advisory Committee; NLST: National Lung Screening Trial; PLCO: Prostate, Lung, Colorectal and Ovarian Cancer Screening trial; QALY: Quality-adjusted life year. [a]MSAC relied on the ICER estimates of the different scenarios supplied by the Health Technology Assessment group contracted by Cancer Australia, which includes the authors of this article, and subsequently chose one of these scenarios with an estimated ICER of $65,663. In writing this paper, these authors revised these estimates to correct for errors in the estimated fixed costs. Because the fixed costs were revised, the costs of all scenarios were revised by the same magnitude; consequently, the incremental cost differences (and thus the incremental cost-effectiveness ratios) between the scenarios remain the same. The corrected average cost-effectiveness ratios (comparing alternative screening scenarios to a no-screening strategy) decreased by around $1000 to $2,000, amounts that are unlikely to affect decision-making.

Table 2: **Overview of costs and health outcomes (per 100,000 individuals alive in 2023) of the risk-based and pack-year-based screening scenarios on the efficient frontiers.**

Scenario	3% Discounted costs compared to no screening (in AUD) per 100,000	3% Discounted QALYs gained per 100,000	3% Discounted costs (in AUD) per QALY gained compared to no screening	Reduction in discounted costs per QALY gained compared to no screening	5% Discounted costs compared to no screening (in AUD) per 100,000	5% Discounted QALYs gained per 100,000	5% Discounted costs (in AUD) per QALY gained compared to no screening	Reduction in discounted costs per QALY gained compared to no screening	Percentage of the population ever screened	Number of performed LDCT screens (per 100,000)	Lung cancer mortality reduction (%)	Lung cancer deaths prevented (per 100,000)	Non-discounted life-years gained (per 100,000)	Non-discounted QALYs gained (per 100,000)	Life-years gained per lung cancer death prevented	Non-discounted QALYs gained per lung cancer death prevented	Lung cancer deaths prevented per over-diagnosed case
NLST #11																	
Traditional	28,757,861	574	50,101		27,112,948	434	62,472		6.16%	27,295	4.27%	108	1048	905	9.68	8.36	2.90
Novel	23,166,766	512	45,248	9.7%	22,686,911	386	58,774	5.9%	6.15%	27,261	4.25%	95	905	811	9.55	8.56	2.542
PLCO #146																	
Traditional	21,765,580	421	51,700		20,383,999	314	64,917		7.75%	18,814	3.18%	81	786	676	9.75	8.39	2.97
Novel	17,820,974	376	47,396	8.3%	17,320,419	280	61,859	4.7%	7.74%	18,791	3.18%	71	681	608	9.61	8.59	2.62
NLST #110																	
Traditional	19,083,776	364	52,428		17,903,249	274	65,340		5.26%	13,744	2.79%	71	676	581	9.58	8.23	2.83
Novel	15,678,670	325	48,242	8.0%	15,249,290	243	62,754[a]	4.0%	5.25%	13,727	2.77%	62	585	521	9.47	8.43	2.48

Overdiagnosed lung cancers (per 100,000), percentage of screen-detected cancers that is over-diagnosed and false positive screens (per 100,000) did not change from those presented in Table 2. LDCT: Low-Dose Computed Tomography. [a]MSAC relied on the ICER estimates of the different scenarios supplied by the Health Technology Assessment group contracted by Cancer Australia, which includes the authors of this article, and subsequently chose one of these scenarios with an estimated ICER of $65,663. In writing this paper, these authors revised these estimates to correct for errors in the estimated fixed costs. Because the fixed costs were revised by the same magnitude; consequently, the incremental cost differences (and thus the incremental cost-effectiveness ratios) between the scenarios remain the same. The corrected average cost-effectiveness ratios (comparing alternative screening scenarios to a no-screening strategy) decreased by around $1000 to $2,000, amounts that are unlikely to affect decision-making.

Table 3: **Comparison of selected outcomes (per 100,000 individuals alive in 2023) for costs and effects of novel therapies and traditional anti-cancer therapies for selected screening scenarios (3% and 5% discount rate).**

Budget impact analysis

Fig. 2 presents the budget impact analysis for scenarios with the lowest cost per QALY gained for the combined annual and biennial analyses (NLST #11) and biennial-only (PLCO #146) analyses, as well as the MSAC recommended scenario (NLST #110). The costs for the first ten years of a national screening program were AUD2.2 billion, AUD1.6 billion and AUD1.7 billion for NLST #11, PLCO #146 and NLST #110, respectively. Appendix 2 Figs. S8–S10 presents costs by stage at diagnosis and phase of care.

Sensitivity analyses

Table 4 presents the sensitivity analyses results, reporting the ICERs compared to a no-screening strategy for the two screening scenarios with the lowest ICERs for the combined annual and biennial analyses (NLST #11), the biennial-only analyses (PLCO #146) and the MSAC recommended scenario (NLST #110). The results show cost-effectiveness is relatively insensitive to uncertainty around most input parameter values except the discount and uptake rates. Scenario NLST #11 has an ICER of AUD58,774 in the base case. In the one-way sensitivity analyses, decreasing the discount rate to 3% generated an ICER of AUD45,248, while decreasing the uptake rate to 20% increased the ICER to AUD78,940. Similarly, the ICER decreased from AUD61,859 to AUD47,396 for the most cost-effective biennial screening scenario (PLCO #146) and from AUD62,754 to AUD48,242 for the MSAC recommended scenario (NLST #110) when applying a 3% discount rate. An uptake rate of 20% increased the ICER from AUD61,859 to AUD91,976 and from AUD62,754 to AUD98,732 for PLCO #146 and NLST #110, respectively. In the multi-way sensitivity analysis, applying a life-expectancy threshold for screening eligibility of at least five years, decreasing the stage I/II initial phase costs by 20%, using a 3% discount rate and increasing novel therapy costs by 20% resulted in ICERs of AUD34,655, AUD37,727 and AUD38,233 for scenarios NLST #11, PLCO #146 and NLST #110 respectively. In the probabilistic sensitivity analyses, the ICER ranged from $36,907 to $85,815 for NLST #11, from $38,947 to $91,402 for PLCO #146 and from $39,314 to $93,079 for NLST #110 (see Figs. S11–S13 in Appendix 2).

Discussion

This economic evaluation is the first study to evaluate the cost-effectiveness of an organised, targeted national lung cancer screening program, including the application of risk-prediction models and the costs and effects of novel therapies. Base-case results indicate that in Australia, the lowest ICER for a targeted lung cancer screening program is AUD62,754 per QALY gained compared to no screening (see footnote in Table 2).

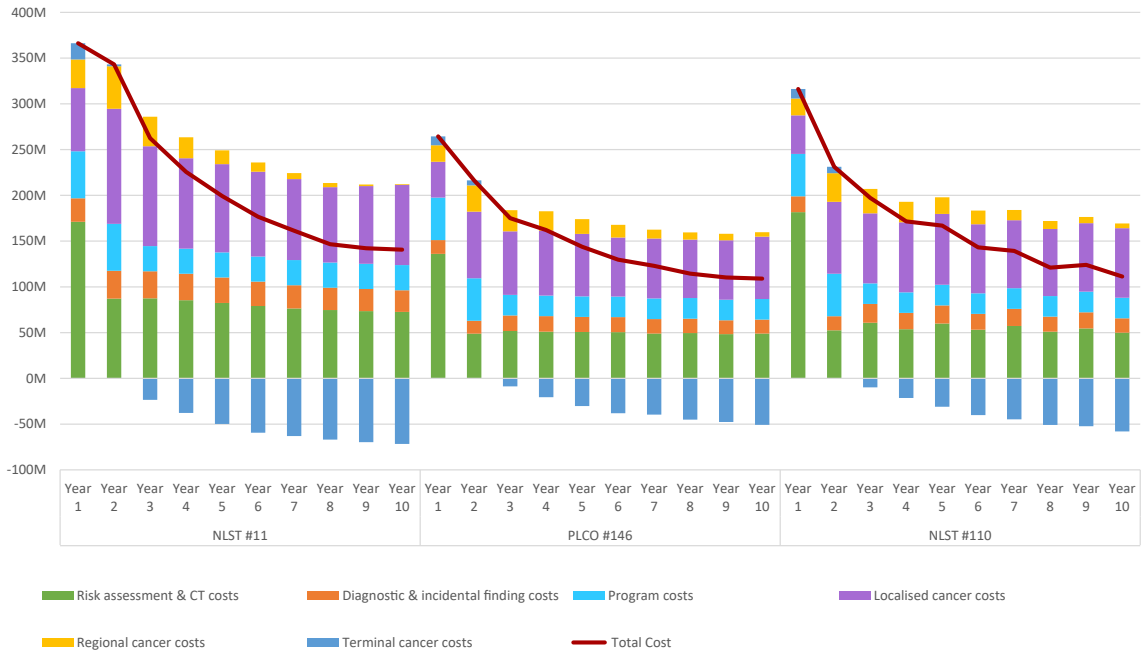

Fig. 2: Budget impact analysis: costs for the first ten years (2023–2032) of a national lung cancer screening program for the Australian population (non-discounted) in Australian dollars.

The reported modelling analyses informed MSAC's recommendation to the Minister for Health, as reported in their Public Summary Document.[11] MSAC preferred biennial screening as it was consistent with other cancer screening programs in Australia, more feasible and acceptable for the screened population, aligned with the NELSON trial design, and was associated with significantly lower total costs.[11] They also preferred the pack-year eligibility criteria as it aligned with all relevant trials assessing the benefits of lung cancer screening, simplified risk assessment and reflected international programs such as the USPSTF recommendations.[11] However, analyses from the International Lung Screening Trial suggest that the use of risk-prediction models could mitigate socioeconomic and sex-based disparities. In addition, studies in the U.S. demonstrate that the use of such models may also aid in mitigating race/ethnicity-based disparities. Consequently, future evaluations using natural-history models should investigate the impact of using risk-prediction models on mitigating disparities.[39–41]

MSAC did not have a pre-defined cost-effectiveness threshold, rather they observed the estimated ICERs and then assessed value for money. An ICER of around $65,000 per QALY gained was estimated for a group of screening strategies that met the above criteria. MSAC made the recommendation that an ICER of $65,000 per QALY gained represented value for money for a targeted lung cancer screening program from a public health system perspective. If the estimated ICERs had been higher, MSAC may still have assessed screening to be cost-effective. Whilst $65,000 per QALY was assessed as being cost-effective, $65,000 was not a defined threshold.

Across the selected group of screening strategies, expected outcomes for numbers of overdiagnosed cases, LDCT screens and false positive test results were reviewed to select the other parameters of the preferred screening program (e.g. stopping age of screening, number of pack years and number of years since smoking cessation), alongside a preference for a starting age of 50 years to align with current Australian breast and colorectal cancer screening programs. This resulted in the recommendation to implement a national screening program targeted at individuals aged 50–70 years who have a history of cigarette smoking of ≥30 pack-years who had not quit more than 10 years previously.

An important finding from this study is the impact of incorporating novel therapies on the cost-effectiveness of lung cancer screening. Although the application of novel therapies improves the cost-effectiveness of lung cancer screening, we find the difference in cost-effectiveness compared to analyses that do not represent the costs and effects of novel therapies to be modest (4% lower costs per QALY). This contrasts with some expectations that the high costs of novel therapies may render lung cancer screening cost-saving.[9] However, this finding can be explained by the following three effects of screening.

Scenario	NLST #11	PLCO #146	NLST #110
Base-case	$58,774	$61,859	$62,754[a]
One-way analyses			
LDCT costs increased by 20%	$62,517 (6.37%)	$65,357 (5.65%)	$65,748 (4.77%)
LDCT costs decreased by 20%	$55,032 (−6.37%)	$58,361 (−5.65%)	$59,760 (−4.77%)
Initial care costs (all stages) increased by 20%	$62,905 (7.03%)	$66,226 (7.06%)	$67,301 (7.24%)
Initial care costs (all stages) decreased by 20%	$54,644 (−7.03%)	$57,492 (−7.06%)	$58,208 (−7.24%)
Terminal care costs (all stages) increased by 20%	$57,752 (−1.74%)	$60,951 (−1.47%)	$61,848 (−1.44%)
Terminal care costs (all stages) decreased by 20%	$59,797 (1.74%)	$62,766 (1.47%)	$63,661 (1.44%)
Initial care phase costs for stage I/II increased by 20%	$63,774 (8.51%)	$66,834 (8.04%)	$67,874 (8.16%)
Initial care phase costs for stage I/II decreased by 20%	$53,774 (−8.51%)	$56,883 (−8.04%)	$57,635 (−8.16%)
Upper limit for stage I/II initial phase utilities	$55,742 (−5.16%)	$58,713 (−5.08%)	$59,336 (−5.45%)
Lower limit for stage III/IV initial and continuing care phase utilities	$58,471 (−0.52%)	$61,639 (−0.36%)	$62,497 (−0.41%)
General population utilities set to 0.83	$60,498 (2.93%)	$63,678 (2.94%)	$64,343 (2.53%)
Incidental findings set to 5%	$56,949 (−3.11%)	$60,160 (−2.75%)	$61,303 (−2.31%)
Incidental findings set to 20%	$59,687 (1.55%)	$62,708 (1.37%)	$63,480 (1.16%)
20% Uptake rate	$78,940 (34.31%)	$91,976 (48.69%)	$98,732 (57.33%)
42% Uptake rate	$62,290 (5.98%)	$67,341 (8.86%)	$71,024 (13.18%)
30% Reduction of novel therapy impact on survival rates	$59,929 (1.97%)	$63,033 (1.90%)	$63,783 (1.64%)
Discount rate of 3% instead of 5%	$45,248 (−23.01%)	$47,396 (−23.38%)	$48,242 (−23.13%)
Life-expectancy threshold of at least 5-years (with perfect information on other-cause mortality) to be eligible for screening	$52,660 (−10.40%)	$56,716 (−8.31%)	$57,130 (−8.96%)
Multi-way analyses			
Life-expectancy threshold of at least 5-years (with perfect information on other-cause mortality) to be eligible for screening AND 3% discount rate	$40,265 (−31.49%)	$43,070 (−30.37%)	$43,663 (−30.42%)
Initial care phase costs for stage I/II increased by 20% AND 3% discount rate	$49,331 (−16.07%)	$51,452 (−16.82%)	$52,420 (−16.47%)
Initial care phase costs for stage I/II decreased by 20% AND 3% discount rate	$41,164 (−29.96%)	$43,340 (−29.94%)	$44,064 (−29.78%)
Life expectancy threshold of 5 years AND stage I/II initial phase costs decreased by 20% AND 3% discount rate AND novel costs increased by 20%	$34,655 (−41.04%)	$37,727 (−39.01%)	$38,233 (−39.08%)

[a]MSAC relied on the ICER estimates of the different scenarios supplied by the Health Technology Assessment group contracted by Cancer Australia, which includes the authors of this article, and subsequently chose one of these scenarios with an estimated ICER of $65,663. In writing this paper, these authors revised these estimates to correct for errors in the estimated fixed costs. Because the fixed costs were revised, the costs of all scenarios were revised by the same magnitude; consequently, the incremental cost differences (and thus the incremental cost-effectiveness ratios) between the scenarios remain the same. The corrected average cost-effectiveness ratios (comparing alternative screening scenarios to a no-screening strategy) decreased by around $1000 to $2,000, amounts that are unlikely to affect decision-making.

Table 4: **Sensitivity analyses for the screening scenarios with the lowest cost per QALY gained for the combined analysis (NLST #11), the biennial-only analysis (PLCO #146) and the MSAC recommended screening scenario (NSLT #110) in Australian dollars.**

First, screening aims to shift stage at diagnosis from later (stage III/IV) to earlier (stage I/II). Comparing novel therapies to the non-use of novel therapies, screening is expected to reduce treatment costs for cancers whose stage at diagnosis is shifted due to screening. Curative treatment in stage I/II is significantly less costly, and novel therapies are avoided if these patients are successfully cured. However, curative treatment will be unsuccessful for some individuals who are screen-detected in stage I/II and will progress to more advanced stages of lung cancer. Consequently, these individuals are expected to incur more novel therapy costs than people diagnosed in stage IV, because they will, on average, have a longer survival time where they are treated with novel therapies compared to clinical detection at a late stage.

Second, screening will not always facilitate a stage shift but will detect some cancers earlier within the same stage. Consequently, cancers detected earlier within stages III/IV will undergo treatment with novel therapies for longer, leading to an overall increase in treatment costs.

Finally, although the degree of overdiagnosis in lung cancer screening is modest, some cancers detected in stages III/IV will still be overdiagnosed; that is, the person may die of other causes, and the cancer would not have been found had it not been for screening.[42,43] However, these patients may still be treated with novel therapies, thus leading to increased costs.

The aggregate effects of the representation of novel therapies on the ICERs for screening depend on the relative frequencies and magnitudes of effects of these three screening effects. Overall, we find that the use of novel therapies improves the cost-effectiveness of screening, although more modestly than some had previously anticipated.[9] But, this study assumed the use of novel therapies would lead to greater increases in

treatment costs (ten-fold) whereas our study suggests a doubling in costs which is in line with other, more contemporary, studies for Australia.[44,45]

Previous studies evaluated the cost-effectiveness of lung cancer screening in Australia. Wade et al.[46] evaluated lung cancer screening using pack-year-based selection criteria, finding it unlikely to be cost-effective at $138,000 per life-year gained and $233,000 per QALY gained with wide confidence intervals. A more recent analysis by Behar Harpaz et al.[44] evaluated screening according to the NELSON and NLST criteria and found NELSON-based screening to be cost-effective at AUD39,250 per QALY compared to NLST's AUD76,300/QALY. However, these studies only considered individuals meeting the NLST, NELSON or USPSTF2021 criteria or a PLCOm2012 risk of 1.51% rather than a range of scenarios, even though it is essential to provide a sufficient number of comparator scenarios to yield appropriate ICERs. Furthermore, these studies did not consider screening periods beyond those observed in the NLST or NELSON trials. Finally, they did not include a natural history component in their model, which is essential to evaluate the impact of lead-time and overdiagnosis on screening outcomes. In contrast, we evaluated a wide range of scenarios, considered long-term screening periods, and applied a well-validated natural-history model to evaluate the impact of lead-time and overdiagnosis on the costs and effects of novel therapies in a screening context. In addition, previous studies evaluated specific populations (e.g. heavy smokers within a specific age-range) or applied screening eligibility derived from cohort studies at a singular moment in time as an input. We added to the knowledge of previous studies by modelling a variety of age ranges and smoking behaviours across different birth-cohorts. In addition, we specifically modelled lifetime smoking behaviours, consistent with population-based estimates from nationally representative health surveys. Consequently, we were able to evaluate screening eligibility over time as an output, providing information on individuals becoming eligible later in life (through accumulating additional risk/pack-years) and those becoming ineligible later in life (through no longer meeting the years since smoking cessation criteria).

Toumazis[14] recently found that annual screening at a 1.2% PLCOm2012 risk threshold was cost-effective in the United States at an ICER of USD94,659 (AUD145,000). Our analysis estimated the ICER for this strategy to be AUD79,089. Overall, we found a greater variety in the cost per QALY among risk-based scenarios compared to previous studies in other countries. Consequently, this highlights the importance of country-specific cost-effectiveness analyses.

Our study assumed novel therapies are mostly applied for advanced-stage disease. However, the application of novel therapies in the treatment of early-stage disease is now being considered. Consequently, the impact of screening may further change if the application of novel therapies becomes more common for early-stage disease. Given the potential for heterogeneity in model assumptions on the impact of novel therapies and their interaction with screening, future studies should consider collaborative modelling approaches such as those of the Cancer Intervention and Surveillance Modelling Network (CISNET).[4,47]

Limitations

This study has several limitations. We applied a reduced version of the PLCOm2012 risk assessment tool that only considered age, sex and smoking-related risk factors. If additional risk factors were presented in the model and the full PLCOm2012 risk calculator was applied, more individuals may be identified as eligible for screening. However, the reduced version of the PLCOm2012 model has shown good performance in previous studies.[25] Some risk factors such as chronic obstructive pulmonary disease not only increase the risk of lung cancer, but also affect other-cause mortality risk. Those at risk for lung cancer are more likely to be from lower socioeconomic backgrounds and have reduced life expectancy. However, we accounted for the effects of smoking-related comorbidities on life expectancies in our analyses. Furthermore, we evaluated the impact of reduced overall quality of life in populations eligible for screening.

Smoking histories were based on self-reported data from retrospective surveys. Although retrospective surveys are subject to response and recall biases, the surveys used in our study represent the best available and nationally representative data. Furthermore, both pack-year criteria and PLCOm2012-based approaches have shown good performance in Australian cohorts that used self-reported smoking behaviour.[23]

Although our estimated relative risks for smoking-related mortality are lower than those observed in an Australian cohort study,[48] their overall mortality rate was lower compared to the general Australian population, suggesting it included a healthier population. Overall, our mortality estimates, after accounting for smoking-related mortality, replicate those of the overall population. Furthermore, our estimates for the number of life-years gained per lung cancer death prevented are consistent with previous studies.[13,15,17,18] Consequently, we believe our evaluation appropriately accounts for smoking-related mortality.

Our study utilised costs from the 45 and Up study, with a median follow-up of 5.4 years after diagnosis. However, in the 45 and Up study, 74% of cases died within three years, suggesting the costs for most individuals are captured. Furthermore, we account for the costs of lung cancer death in individuals with survival longer than three years through the incorporation of the continuous care phase and terminal care phase costs.

Although the model was calibrated and was consistent with both randomised clinical trial data and Australian national data, long-term extrapolations inherently introduce uncertainty in the estimates. However, evaluating many different screening scenarios provides sufficient comparator scenarios to yield appropriate ICERs.[49] Furthermore, the cost-effectiveness of Scenario #NLST 110 was robust across various sensitivity analyses.

Another limitation is that to estimate the budget impact of selected screening programs over the period 2023–2033, inclusive, we included individuals from birth cohorts outside of the modelled birth cohorts that age into the program. Given declining rates of smoking in more recent birth cohorts, applying the smoking behaviour data from the 1965–1969 birth cohort will overestimate eligibility for screening and the average risk of lung cancer in eligible individuals, resulting in an overestimate in the budget.

In conclusion, targeted lung cancer screening in Australia was suggested to be of acceptable cost-effectiveness by MSAC, whose recommendations were accepted by the Minister for Health and Aged Care. To inform the recommendations, cost-effectiveness modelling with and without the representation of the costs and effects of novel therapies was undertaken. While this study confirms the expectation that novel therapies improve the cost-effectiveness of lung cancer screening, the impact may be more modest than previously anticipated.

Contributors

Kevin ten Haaf had access to raw data underlying the MISCAN model. Kevin ten Haaf, Jacqueline Roseleur and Jonathan Karnon had access to data used as inputs and verified the data. All authors had final responsibility for the decision to submit for publication.

Jacqueline Roseleur: Data curation, Formal analysis, Investigation, Project administration, Visualization, Writing–original draft, Writing–review & editing.

Jonathan Karnon: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Supervision, Writing–original draft, Writing–review & editing.

Harry de Koning: Conceptualization, Funding acquisition, Investigation, Writing–review & editing.

Vivienne Milch: Conceptualization, Data curation, Writing–review & editing.

Katrina Anderson: Data curation, Project administration, Writing–review & editing.

Jacqui Real: Data curation, Project administration, Writing–review & editing.

Dorothy Keefe: Conceptualization, Writing–review & editing.

Kevin ten Haaf: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Software, Supervision, Validation, Writing–original draft, Writing–review & editing.

Data sharing statement

Data used as input for the MISCAN-Lung model can be requested from the primary sources.

Declaration of interests

Jacqueline Roseleur and Jonathan Karnon report funding from Cancer Australia. Harry de Koning reports funding from Cancer Australia, consulting fees from Bayer and speaking fees from Teva, Monarin and Astra Zeneca. Vivienne Milch, Katrina Anderson and Jacqui Real report no other interests. Dorothy Keefe reports personal stock options from Entrinsic Bioscience. Kevin ten Haaf reports funding from Cancer Australia, grants from the NIH, the European Union and the Dutch Research Council, speaking fees from Johnson&Johnson and travel support for speaking at the Rescue Lung Society.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.lanwpc.2024.101241.

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