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Cost-effectiveness of Lung Cancer Screening: Insights from Risk Stratification, Guidelines, and Emerging Technologies—A Systematic Review

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## Abstract

Lung cancer is the leading cause of cancer-related mortality worldwide, with most patients diagnosed at advanced stages. Early detection through screening can significantly reduce mortality, making cost-effectiveness evidence crucial for guiding policy decisions. This systematic review aimed to evaluate the cost-effectiveness of lung cancer screening across various modalities, populations, and settings. A comprehensive search of PubMed, EMBASE, Web of Science, and Cochrane Library was conducted for studies up to March 18, 2025, adhering to PRISMA guidelines. A total of 79 studies from 21 countries were included, with model-based analyses prevalent and 89.9% rated as high quality. Low-dose computed tomography (LDCT) emerged as the primary screening modality, although evidence on artificial intelligence (AI) and biomarkers is limited. Fourteen studies comparing LDCT with no screening showed incremental cost-effectiveness ratios (ICERs) ranging from \$8,376 to \$200,921 per quality-adjusted life-year (QALY) gained. Notably, 90.3% of LDCT strategies were cost-effective by national thresholds, particularly in older adults and high-risk groups. Biennial screening often proved more cost-effective than annual in many scenarios. Overall, LDCT screening demonstrated favorable cost-effectiveness, necessitating further evaluation for emerging technologies in underserved regions.

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## Introduction

Lung cancer (LC) is the leading cause of cancer-related mortality worldwide, accounting for approximately 2 million new cases and 1.76 million deaths annually<sup>1</sup>. Alarmingly, nearly 75% of LC patients are diagnosed at an advanced stage, a factor strongly associated with poor prognosis<sup>2,3</sup>. This underscores the critical importance of early detection strategies to improve outcomes.

Screening for LC has been emerged as a pivotal strategy to identify disease at earlier, more treatable stages, thereby reducing LC morbidity and mortality<sup>4</sup>. Two large randomized controlled trials, the National Lung Screening Trial (NLST) and the Nederlands Leuven Screening Onderzoek (NELSON) trial, showed low-dose computed tomography (LDCT) screening reduces LC mortality by 20% compared to chest X-ray (CXR) and by 24% compared to no screening<sup>2,5,6</sup>.

Given the promising health benefits, Many economic studies have examined the cost-effectiveness of LC screening to guide large-scale implementation<sup>7-10</sup>. However, previous reviews focused only on LDCT screening, while other modalities like CXR are still commonly used for their lower cost and reduced radiation<sup>11,12</sup>. New advances, such as artificial intelligence (AI), also show promise for improving different LC screening methods<sup>3,13,14</sup>. To date, no reviews have comprehensively summarized and evaluated the cost-effectiveness of LC screening tools beyond LDCT, particularly with regard to emerging diagnostic approaches. Previous reviews have largely focused on LDCT, with literature searches conducted up to 2022, and limited databases<sup>7,10</sup>. Costing studies can provide valuable information on intervention costs that are essential for implementation. Given the scarcity of healthcare resources and the economic burden that scaling up LC screening may impose on individuals and society, a comprehensive and up-to-date review synthesizing the economic value of LC screening would help inform evidence-based policy and decision-making.

This systematic review aims to update and synthesis the evidence on cost-effectiveness of LC screening. We evaluated the methods and outcomes of existing economic studies, providing a comprehensive overview of the latest research to inform health policy decisions.

## Methods

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines<sup>15</sup>. The review protocol was prospectively registered in PROSPERO (CRD42024598581).

### Search Strategy

A structured search was performed using the following Boolean terms: “Lung Cancer” AND “Screening” AND “Economic Evaluations”. The complete and reproducible search strategies for each database are available in eTables 1–4. We searched the electronic databases EMBASE, PubMed, Web of Science, and Cochrane Library from their inception through 18 March 2025. We also reviewed the reference lists of included papers and pertinent systematic reviews for further eligible articles.

### Eligibility Criteria

We included both comprehensive (cost-effectiveness, cost-utility, and cost-benefit analysis) and partial (cost analysis) economic analyses of LC screening. Both trial-based and model-based economic analyses were eligible. Trial-based analyses were defined as those using data exclusively derived from clinical trials to estimate costs and effectiveness. Model-base studies incorporated external sources of data beyond trial parameters, even if trial data informed model inputs such as intervention duration and sample size. No restrictions were applied on language, publication date or country. We excluded commentaries, editorials, letters, protocol paper, conference abstract, and systematic reviews of economic analyses.

The population of interest comprised individuals undergoing LC screening regardless of the screening modality used. Studies focusing solely on clinically diagnosed LC cases (e.g., via biopsy and mediastinoscopy) were excluded. Outcomes of interest included any health-related measures such as quality-adjusted life-years (QALYs), life year gained (LYG), and mortality reduction due to screening.

### Study selection and data extraction

Following deduplication, two authors independently screened titles and abstracts, followed by full-text assessments to determine eligibility. Disagreements were resolved by consulting a third reviewer. All data extraction was performed independently and in a blinded fashion by the same two authors, with any discrepancies resolved by discussion.

Extracted information included: authors, publication year, country, type of economic analysis, risk prediction model used, cohort, screening tools, scenarios, study population, study design, type of economic analysis, cost year, time horizon, perspective of economic analysis, discount rate, measure of effectiveness, type of currency, detailed costs components (total costs, diagnosis and assessment costs, medical services and professional costs, treatment-related costs, and others), incremental cost-effectiveness ratio (ICER), sensitivity analysis. For studies lacking explicit cost years reporting, the cost year was calculated by subtracting two years from the publication year<sup>16,17</sup>.

### Risk of bias and quality appraisal

For model-based studies, the British Medical Journal checklist described by Drummond and Jefferson was used to assess the quality of the studies<sup>18</sup>. Studies were rated based on the presence of the following key elements: (1) description of the model type and analytic method; (2) transparency of data sources; (3) description of simulation components, including transition probabilities, health states utilities and costs, and related parameters and assumptions; and (4) assessment of uncertainty through appropriate sensitivity analysis. Studies satisfying all four criteria were classified as high quality; those failing to meet any single criterion were considered low quality<sup>17</sup>.

For trial-based studies, quality assessment was conducted using version 2 of the Cochrane Risk of Bias Tool for Randomized Trials<sup>19</sup>, the Newcastle - Ottawa Scale (NOS)<sup>20</sup>, and the Agency for Healthcare Research and Quality (AHRQ) for cross-sectional studies<sup>21,22</sup>. The Cochrane tool assessed bias across key domains including randomization, intervention adherence, missing data, outcome measurement, and selective reporting, categorizing studies as low risk, high

risk, or raising some concerns. The NOS evaluated cohort studies on population selection, comparability, and outcome measures, scoring quality as low (0–4), moderate (5 to 7), or high (>=8). The AHRQ assessed cross-sectional studies with 11 items scored dichotomously; total scores indicated low (0–3), moderate (4–7), or high quality (>7).

### Data synthesis

Results were not pooled due to heterogeneity in study population, intervention, methods, data and context. Instead, we presented a narrative synthesis of the findings from included studies. Summaries of cost-effectiveness and costs items were reported for each study. To facilitate comparability, costs reported in various base years and currency were converted to 2022 US dollars using Consumer Price Index (CPI) and Purchasing Power Parity (PPP) conversion factors from the Organization for Economic Co-operation and Development (OECD) database (<https://www.oecd.org/en.html>), including<sup>16</sup>. The formula used for this conversion is as follows:

$$\text{Cost in US\$} = \frac{\text{Cost}_{\text{original year}} * \left( \frac{\text{CPI}_{2022}}{\text{CPI}_{\text{Original Year}}} \right)}{\text{PPP Conversion Factor}_{2022}}$$

### Results

#### Study selection and quality assessment

The database search initially yielded 15,610 records, of which 3,348 duplicates were removed, resulting in 12,262 publications for title and abstract screening (detailed in eTable 1–4). After screening, 158 studies met inclusion criteria for full-text review; 12 could not be retrieved, leaving 146 full texts for evaluation. Of these, 67 were excluded after full text reading, leaving 79 for final inclusion (Figure 1)<sup>5,11,12,23–97</sup>. Reasons for exclusion are presented in eTable 5.

Among the included articles, 69 (69/79, 87.3%) were model-based studies. The majority (62/69, 89.9%) were rated as high quality<sup>11,23,26,27,29,30,32–39,41–48,50,53–64,66–82,84,85,87,89,91–93,95–97</sup>, while seven (7/69, 10.1%) were categorized as low quality but retained for their valuable contributions<sup>24,25,28,40,51,52,65</sup>. The remaining 10 trials–

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based studies (10/79, 12.7%) was distributed as follows: 50.0% (5/10) were high-quality cross-sectional studies<sup>31, 86, 88, 90, 94</sup>; 30.0% (3/10) were moderate-quality cross-sectional studies<sup>49, 83, 98</sup>; 10.0% (1/10) was a moderate-quality cohort study<sup>12</sup>; and 10.0% (1/10) was an RCT with some concerns<sup>5</sup> (eTable 6).

## Study characteristics

### *Study designs and perspectives*

The majority (69/79, 87.3%) used model-based evaluations, with 50 (63.3%) conducting cost-effectiveness or cost-utility analyses—28 (35.4%) were cost-effectiveness studies and only one cost-utility analysis (eTable 7).

Regarding cost perspectives, 20 studies (25.3%) did not specify any perspective. The most common perspectives reported were healthcare (26/79; 32.9%), followed by societal (13/79, 16.5%), health system (9/79, 11.4%), public payer (8/79, 10.1%), and one commercial payer perspective (eTable 7).

### *Study locations*

The included studies covered 21 countries or regions. China (18/79, 22.8%) had the highest number of publications, followed by the US (16/79, 20.3%). Canada, Japan, and the UK each contributed 5 studies (6.3%).

### *Screening tools*

LDCT was the most used tool, with usage steadily increasing since 2011. The integration of AI with LDCT emerged in 2022, and both the EarlyCDT-Lung test and polygenic risk score (PRS) were introduced alongside LDCT in 2024. Conventional CT and CXR usage remained low and stable after 2011. The diversity of screening tools increased substantially between 2014 and 2022, peaking in 2024 (Figure 2).

### *Economic analyses methodologies*

Almost all studies (78/79, 98.7%) reported their economic methods. Markov decision models were most common, used in 29 (37.2%) studies<sup>23, 28, 32, 38, 39, 41, 44, 48, 53, 54, 56, 57, 90</sup>. Algebraic models (10.3%)<sup>24, 31, 40, 47, 65, 74, 84, 87</sup>, decision tree models (10.3%)<sup>25, 26, 59, 60, 68, 69, 72, 85</sup>, and direct calculations (11.5%)<sup>11, 12, 49, 83, 86, 89, 90, 94, 98</sup> are similar represented (eFigure 1).

### *Cohort and populations*

A total of 31 studies (39.2%) reported cohort characteristics for economic analyses<sup>5, 11, 23, 30-34, 39-41, 43, 44, 47, 52, 53, 55, 56, 59, 60, 63, 64, 66, 98</sup>, encompassing 13 LC screening cohorts from eight countries, all focused on smokers. The NLST (USA) and NELSON (Netherlands) cohorts were most frequently cited. The earliest cohort was the Early Lung Cancer Action Project (ELCAP) in 1992 (USA), and the most recent was the International Lung Screening Trial (ILST) in 2017 (Canada). LDCT was the predominant screening tool; notably, the UK's Early Detection of Cancer of the Lung Scotland (ECLS) study incorporated LDCT with blood-based biomarker testing (See eTable 8 for more details).

### *Participation and adherence*

Nine studies have explored the impact of participation rates on the cost-effectiveness of LC screening, yet their findings are inconsistent<sup>28, 34, 36, 42, 56, 78, 79, 84, 96</sup>. Among them, two studies concluded that reduced adherence diminishes cost-effectiveness<sup>56, 96</sup>, while six reported that variations in adherence have minimal or no influence on cost-effectiveness<sup>28, 34, 42, 78, 79, 84</sup>. Additionally, one study suggested that lower participation rates may make screening more cost-effective for men<sup>36</sup>.

### *Risk prediction models*

Only 10 studies (12.7%) reported use of risk prediction models to identify high-risk populations for screening<sup>31-33, 41, 45, 47, 52, 56, 78, 90</sup>. The PLCO<sub>M2012</sub> model was most common (3 studies)<sup>33, 47, 78</sup>. Publicly available prediction tools, including Pan-Canadian Study web-based LC risk prediction tool<sup>31</sup> and the Liverpool Lung Project tool<sup>45</sup>, were used in two studies each. Two studies leveraged high-risk

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population prediction models developed based on Chinese LC screening cohorts<sup>41, 56</sup>.

#### *Cost items by perspective*

Cost items reported in evaluations from different perspectives were categorized into ten groups: invitation and promotion, equipment and operational, diagnosis and assessment, imaging examination, report interpretation, follow-up tests, advanced diagnostics, treatment, complications, and other related costs. The healthcare perspective included the most comprehensive range of cost components (eTable 9-14).

#### *Cost-effectiveness outcomes*

The included studies reported ICERs for three outcomes: QALY, LYG, death averted. Among the 79 studies included, 59 (74.7%) assessed the cost-effectiveness of LDCT versus no screening, while 8 (10.1%) compared LDCT to CXR. Two studies (2.5%) examined AI combined with LDCT (AI&LDCT) for LC screening (Figure 2). Notably, one study found that AI&LDCT was cost-saving, reporting a negative ICER of \$68/QALY versus LDCT alone<sup>97</sup>. Given the heterogeneity of the outcome measures, we synthesized only those studies comparing LDCT to no screening with reported ICERs.

Among studies comparing LDCT screening with no screening, 14 reported ICER, calculated as cost per QALY gained (in US\$) <sup>5, 23, 42, 47, 50, 66, 67, 70, 73, 75, 76</sup>. ICERs ranged from \$8,376 to \$200,921 per QALY across different age groups and smoking status, with 90.3% (28/31) of screening strategies showing cost-effective. Generally, older populations exhibit lower ICERs, suggesting greater cost-effectiveness. Higher-risk groups, characterized by longer or heavier smoking histories, tended to have lower ICERs (Table 1). Five studies reported ICERs, calculated as cost per LYG (in US\$) among smokers, with values varying between \$5,214 and \$364,763 per LYG <sup>5, 48, 67, 82, 90, 96</sup> (eTable 15).

Four studies reported variations in ICER across different age groups and screening frequencies<sup>39, 48, 50, 64</sup>. The most cost-effective screening frequency depended on population risk profiles. For example, among daily smokers aged 50–74, annual screening (\$12,613/QALY) was more cost-effective than biennial screening (\$23,374/QALY). In contrast, for individuals with high asbestos exposure in the same age group, biennial screening is favored over annual screening (Figure 3A).

Two studies reported ICER in US\$ per LYG by gender, reporting lower cost-effectiveness in women than men for equivalent population and screening frequencies. Biennial screening was more cost-effective than annual screening for the same screening age group. The ICER for annual screening in men aged 55–75 was \$656,019/LYG versus \$41,567/LYG for biennial screening (eFigure 2A). One study reported the economic analysis results of ICER in US\$ per death averted by gender<sup>36</sup>. Similar to the LYG results, LC screening is more cost-effective for men than for women within the same screening population and frequency. Additionally, biennial screening is more cost-effective than annual screening within the same age group. The ICER for annual screening in men aged 55–85 is \$604,658, while for biennial screening in the same age group, it is \$366,440 (eFigure 2B).

Four studies compared the cost-effectiveness of LC screening across guidelines, with ICER ranging from \$8,328/QALY to \$112,700/QALY<sup>34, 46, 77, 93</sup>. The NELSON and China guidelines consistently showed favorable cost-effective. In contrast, the Preventive Services Task Force (USPSTF) guideline had the highest ICER (Figure 3B). Three studies reporting ICER in US\$ per LYG similarly found NELSON more cost-effective than NLST (eFigure 3)<sup>34, 42, 46</sup>.

## Discussion

This systematic review synthesizes evidence from 79 studies across 21 countries, providing an updated and comprehensive assessment of the cost-effectiveness of LC screening strategies. We found that LDCT remains the primary and most cost-effective approach for LC screening, especially among older adults and high-risk smokers. Cost-effectiveness of LDCT varied by country, screening frequency, and risk criteria, with protocols based on the

NELSON and China guidelines yielding the most favorable results. Alternative screening tools such as chest X-ray was less frequently evaluated and generally less cost-effective. Economic evidence for emerging modalities, including AI-enhanced screening, remains limited. To support future research and policy, we compiled a comprehensive set of components essential for economic analyses of LC screening from multiple perspectives.

LC screening is generally more cost-effective among populations with elevated risk factors, such as a history of smoking, older age, and male sex, as evidenced by lower ICERs<sup>36,37</sup>. This trend is likely driven by the higher smoking prevalence and increased LC risk observed in men<sup>3</sup>. High-risk groups—including individuals with chronic obstructive pulmonary disease (COPD), longer smoking histories, greater smoking intensity, and current smokers as opposed to former smokers—derive the greatest economic benefit from screening<sup>7,82,93</sup>. Consequently, there is a growing emphasis on integrating smoking cessation interventions alongside screening programs in order to improve both health outcomes and overall cost-effectiveness, although the added costs of these interventions necessitate careful consideration in economic analyses<sup>3,99</sup>. However, evidence on the cost-effectiveness of LC screening for individuals with COPD is still lacking<sup>3,7,99</sup>. More recently, the use of risk prediction models and the implementation of tailored screening intervals have emerged as promising strategies for optimizing the targeting of high-risk individuals and enhancing cost-effectiveness<sup>34,56,78</sup>. However, the generalizability and external validity of these risk models, as well as risk-stratified screening approaches, remain to be fully established, particularly across diverse populations<sup>100-103</sup>. For example, while most studies report greater cost-effectiveness of screening among men, epidemiological evidence from East Asia indicates a higher incidence of LC among non-smoking women, and some analyses have reported lower ICERs in this group compared with men<sup>1,3</sup>. Whether LC screening consistently provides greater economic benefit among female non-smokers in East Asia remains unclear and warrants further investigation. Several studies have demonstrated that delaying the initiation age for LC screening generally reduces ICERs, thereby enhancing the economic efficiency of screening programs<sup>23,73,93,96</sup>. This improvement is primarily attributed to the increased LC risk with advancing age, which results in greater health benefits from screening<sup>1,104</sup>. However, extending the upper age limit for screening beyond 75 years yields limited marginal improvements in cost-effectiveness<sup>93</sup>. Evidence indicates that ICERs tend to increase when screening continues in populations older than 75, reflecting diminished marginal health benefits and

elevated healthcare costs<sup>93</sup>. These findings highlight the need for careful evaluation of the benefits and costs of LC screening in individuals over 75 years and suggest that more targeted approaches may be warranted to optimize resource utilization in this age group.

The impact of screening compliance on cost-effectiveness remains unclear due to inconsistent findings across studies. Most modeling studies suggest that low participation rates have limited influence on cost-effectiveness.<sup>28, 34, 42, 78, 79, 84</sup>. For example, Whynes et al., argue that if both costs and health gains fall with decreased participation, the ICER remain unchanged<sup>84</sup>. However, in scenarios where fixed costs for infrastructure and administration are substantial, reduced uptake can lead to diminished cost-effectiveness by increasing the average cost per screened participant. These considerations highlight the importance of maximizing program uptake and minimizing fixed overheads to ensure efficient allocation of resources in real-world screening projects.

This review emphasizes the emerging role of AI in LC screening and its potential to improve cost-effectiveness. AI integration can enhance various aspects of the screening workflow, including radiation dose reduction, improve lung nodule detection, personalized screening intervals, and the identification of incidental findings<sup>3, 105</sup>. Notably, one included study found that AI&LDCT was cost-saving compared to LDCT alone, underscoring its economic potential. The integration of AI into ultra-low-dose CT imaging has the potential to markedly reduce radiation exposure, thereby improving adherence to screening programs and ultimately influencing the economic evaluation of LC screening<sup>13</sup>. By improving sensitivity and accuracy of diagnosis, AI may reduce false positives and unnecessary interventions, thereby lowering costs and alleviating patient burden<sup>3, 13, 14</sup>. Additionally, AI has the capability to detect and classify incidental findings in LDCT examinations, such as coronary artery calcification and emphysema, can add additional health value to screening programs<sup>3</sup>. However, current economic analyses seldom account for the equipment and maintenance costs of AI systems. A reduction of these costs would likely lower total expenses and improve screening cost-effectiveness. However, as AI has not been widely implemented in practice, its real-world impact on cost-effectiveness is still uncertain. Given the limited evidence available—only two studies examined AI in this context—future comprehensive economic

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analyses are warranted to fully assess the cost-effectiveness of AI-assisted LC screening.

Unlike AI-assisted diagnosis, both blood tests and PRS identify individuals at high risk for LC through biomarkers, thereby impacting the cost-effectiveness of screening strategies<sup>69,96</sup>. Blood-based screening emerges as the most cost-effective alternative compared to either no screening or LDCT alone, and reducing its cost would further enhance its cost-effectiveness value<sup>69</sup>. In contrast, the PRS-based conjunctive strategy has not been found cost-effective, primarily because it may restricts screening to a smaller subgroup of high-risk individuals and therefore fails to yield additional life-years gained over LDCT screening alone<sup>96</sup>. Therefore, although lowering the cost of PRS testing may improve its economic profile, the prospect of achieving cost-effectiveness with PRS-based strategies remains uncertain and warrants further research.

Screening recommendations significantly influence the cost-effectiveness of LC screening<sup>1-3,7</sup>. Existing studies have compared the cost-effectiveness of various strategies, including NLST, NELSON, USPSTF and Centers for Medicare & Medicaid Services (CMS)<sup>34,46,77</sup>. Both Australian and Dutch studies have shown that the NELSON trial exhibits greater cost-effectiveness compared to the NLST<sup>46,77</sup>. This superiority is largely attributable to NELSON's use of volume doubling time (VDT) for nodule management, which yield a substantially lower false positive rate (1.2% for NELSON vs. 23.3% for NLST)<sup>77</sup>. The higher false positive rate in NLST leads to increased unnecessary diagnostic procedures, increasing costs and patient burden<sup>3,56,68,97</sup>. Additionally, NELSON identified a significantly higher proportion of early-stage lung cancers compared to NLST, which results in greater projected gains in QALYs and LYG<sup>2,6,77</sup>. These findings support the adoption of more precise nodule management strategies, as exemplified by NELSON, to enhance both clinical and economic outcomes in LC screening.

#### Strengths and limitations

To our knowledge, this is the most comprehensive systematic review of economic evaluations and costing studies of LC screening, and is the first to include research on screening tools beyond LDCT, including AI-assisted methods and

PRS. It also marks the first comprehensive synthesis comparing the cost-effectiveness of LC screening across populations recommended by different guidelines. Additionally, the review systematically categorizes potential cost items involved in LC screening from various cost perspectives for the first time. Summarizing cost items across different perspectives can assist policymakers in better managing expenses and making informed decisions. We acknowledge, however, that the field is rapidly evolving and continued updated reviews will remain important.

There are several limitations to this systematic review. Firstly, although we have made efforts to minimize heterogeneity across studies from different years and countries, methodological differences inevitably remain. Therefore, the results should be interpreted with caution. Specifically, variations in model types reflect differences in the underlying formulas, structural assumptions, and parameter choices used to estimate costs and outcomes. Analytic perspective influences which cost components are included in the analysis. The cost year accounts for adjustments related to inflation. The cost-effectiveness threshold represents the maximum expenditure a country is willing to make for additional health benefits, and this value typically varies according to a country's economic context. Secondly, most studies were conducted in high-income countries, the design of existing screening strategies, target populations, and associated costs can all vary by country, potentially limiting the generalizability of findings to specific settings. Thirdly, the review may be susceptible to publication bias, potentially leading to an overestimation of the benefits associated with LC screening. Further research is needed in low- and middle-income countries (LMICs) to address these gaps and enhance the applicability of evidence across diverse contexts.

## Conclusion

In this systematic review of, LDCT was the predominant modality and generally found to be cost-effective within national thresholds. However, its cost-effectiveness was strongly influenced by the population risk profile—including age, sex, and smoking history—as well as the choice of screening guidelines and research perspectives. Evidence for newer approaches, such as AI and biomarkers, is limited and needs further study. Few economic analyses exist for LMICs, where screening is not yet common. We strongly recommend that future work prioritize three critical areas: assessing the cost-effectiveness

of emerging technologies like AI and biomarkers; evaluating risk-based screening in real-world settings; and generating robust, context-specific economic analyses for LMICs. This is essential to guide effective and equitable global implementation of lung cancer screening.

#### DATA AVAILABILITY

All data generated or analyzed during this study are included in this published article.

#### AUTHOR CONTRIBUTIONS

ZJF and MQZ contributed equally as co-first authors. ZJF and MQZ conceptualized the study and developed the protocol. ZJF, ZYG and MQZ designed the search strategy and conducted the literature search. HTL, PYG, YZ, BZ, LYH and XQZ performed data screen and extraction. TTF, MTL, XRJ, NJR and CLZ assessed data quality. ZJF and MQZ conducted data analysis. WXW, CH and JHL provided expert supervision during data extraction and analysis. ZJF and MQZ drafted the initial manuscript. HTL, PYG, YZ, BZ, LYH, WXW, CH and JHL critically revised the manuscript for important intellectual content and supervised data interpretation.

#### COMPETING INTERESTS

All authors declare no financial or non-financial competing interests.

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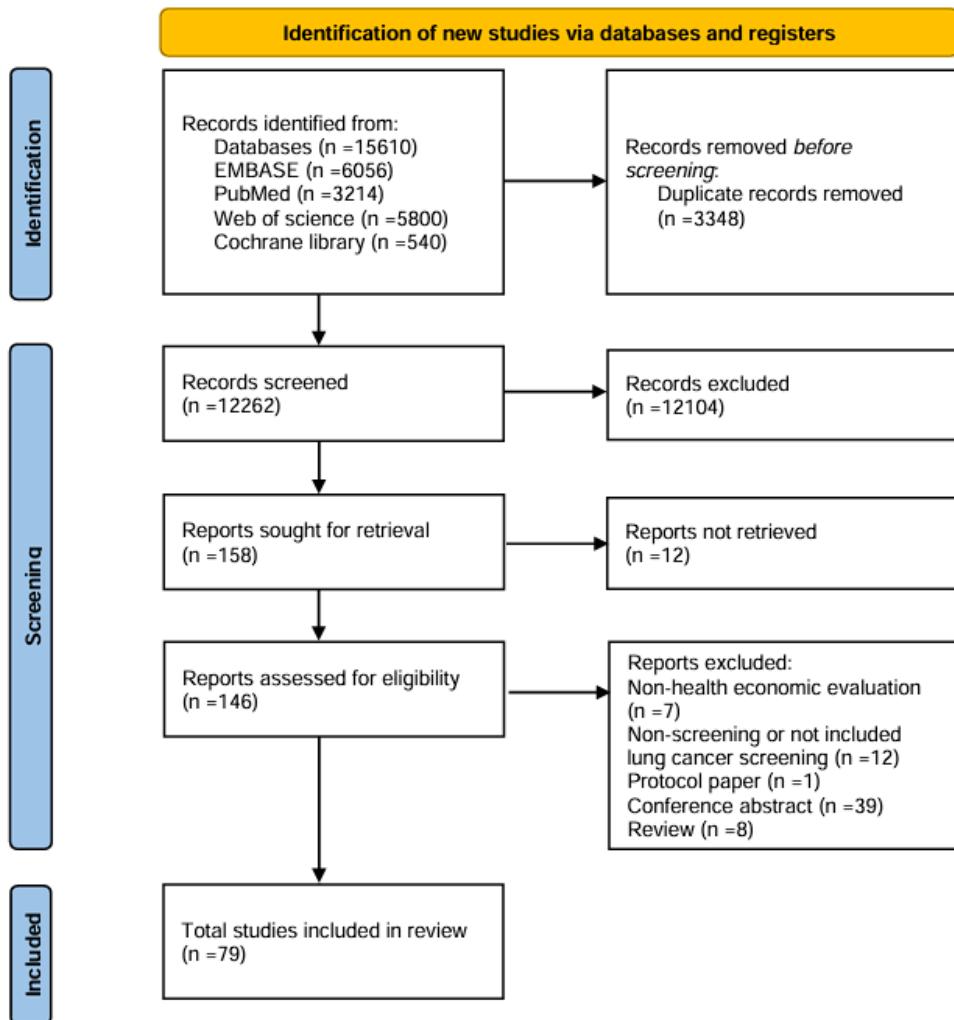


Figure 1 Flowchart of the literature search and exclusion of studies.

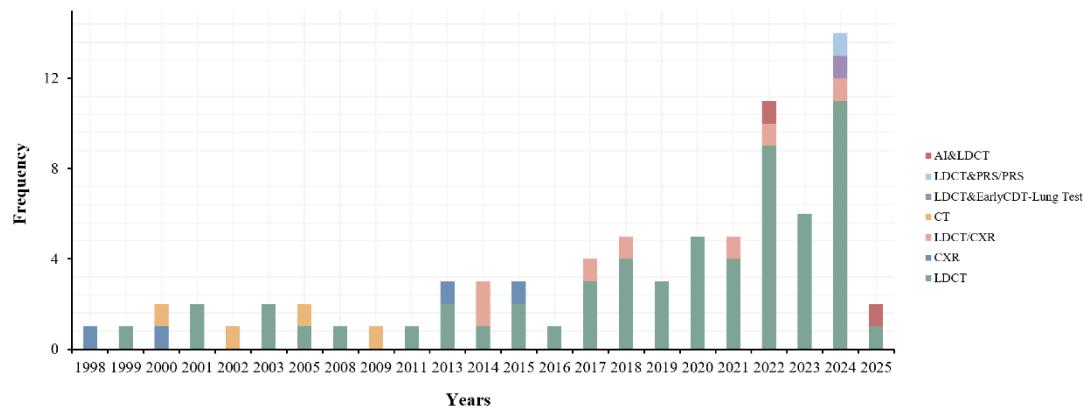
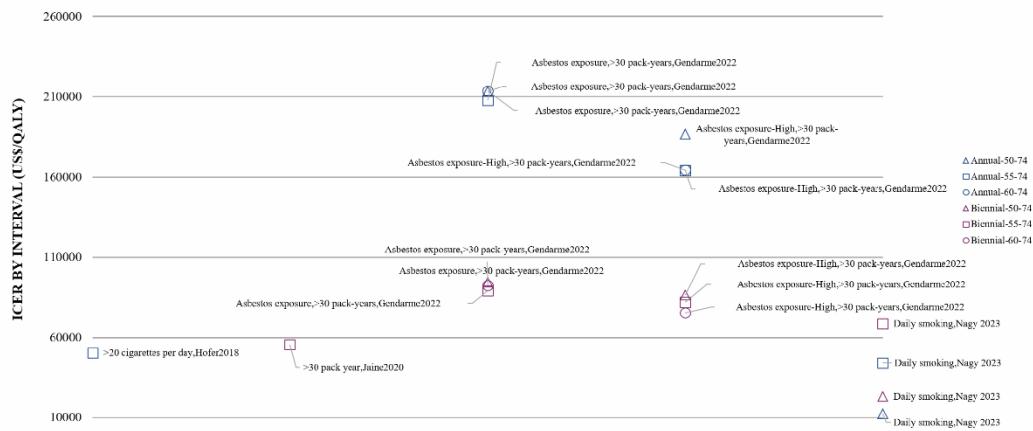


Figure 2 Frequency of lung cancer screening tools over time.

AI: artificial intelligence; LDCT: low-dose computed tomography; PRS: polygenic risk score; CT: computed tomography; CXR: chest X-ray.

A



B



Figure 3 Cost-effectiveness of lung cancer screening by age group in smokers (A) and guideline recommendations (B). ICER represents incremental cost-effectiveness ratio. Costs are reported in 2022 US\$. NLST: the National Lung Screening Trial; CMS: the Centers for Medicare & Medicaid Services; USPSTF: U.S. Preventive Services Task Force; NELSON: the Nederlands Leuven Screening Onderzoek.

Table 1 The cost-effectiveness of LDCT screening versus no screening as measured by ICER (US\$/QALY).

Author	Study design	Quorum	Study year	Country	Persons	Age	Smoking status	ICER (US\$/QALY)
					50			
					–			19, 55
AL2022	Mode 1-base d	Neth erland	Heal thca re	60	Smokers or ex-smokers who smoked more than 30 years at least 15 cigarettes per day, with no more than 10 years since smoking cessation	0		
				50				21, 05
				–				9
				70				
				*				
		So ns						
Bla ck2014	Triad	me nc d	Unit Stat er es ns	55				110, 4
				Soci etal	–	Smoking history of at least 30 pack-years	94	
				74				
				*				
Gof fin 5	Mode 1-base d	Canada	Heal thca re	55				59, 19
				–	30 pack-year smoking history			4
				74				
				*				
Hin de2018	Mode 1-base d	Unit King dom	Heal th syst em	55				18, 44
				–	Smoked and PLCO <sub>2012</sub> a 6- year lung cancer risk of $\geq 1.51\%$			6
				74				
				*				
Jai ne2020	Mode 1-base d	New Zeal and	Heal th syst em	55	With a smoking history of at least 30 pack years, and (if a former smoker) having quit within last 15 years	55, 65		
				–				4
				74				
Pan 2023	Mode 1-base d	Unit King dom	Heal thca re	50				8, 376
				–	With smoking history			
				74				
				*				

Pan	Mode				50		
202	1- base	4	Gree ce	Heal thca re	74	Heavy smokers	8, 869
5	d				*		
Róż	Mode				50		
sa2	1- base	4	Hung ary		74	Smoking exposure of at least 25 pack-years	50, 51 1
024	d				*		
					40		
					-		18, 34
					76		0
					*		
					45		
					-		17, 07
					76		1
					*		
Sun	Mode				50		
202	1- base	4	Chin a	Soci etal	- 76	>20 pack- years, where a pack- year refers to 20 cigarettes smoked every day for 1 year)	16, 02 2
1	d				*		
					55		
					-		15, 21
					76		7
					**#		
					60		
					-		15, 70
					76		2
					*		
Ten	Mode				50	Current or former smokers (those who had quit	
202	1- 4(1 ) d	4	Aust ria	Heal thca re	- 74	≤10 years ago) who had smoked >15 cigarettes a day for >25 years or >10 cigarettes a day for >30 years)	39, 67 8
Ten	Mode				50		
202	1- 4(2 ) d	4	Port ugal	Heal thca re	- 74	With a smoking history	10, 37 6
Wad	Mode				55		
e20	1- 18 d	4	Aust rali a	Heal th Syst em	- 74	Smoking history of at least 30 pack-years	200, 9 21

Zha	Mode	50					
o20	1- base	4	Chin	Soci	74	37, 61	
24	base	4	a	etal	74	4	
	d			*			
				55			
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				74	30, 07		
				*	9		
				60			
				—			
				74	24, 45		
				*	8		
				65			
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				74	21, 39		
				*	1		
				70			
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				74	20, 27		
				*	5		
				**#			
				65			
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				74	24, 70		
				*	6		
	Mode	74	Heal	74			
	1- base	4	Chin	thea	*		
	base	4	a	re	65		
	d			—			
				30	30 pack-years		
				79			
				*			
				40			
				—			
				79	24, 86		
				*	1		
				45			
				—			
				79	38, 65		
				*	4		
				50			
				—			
				79	32, 49		
				*	4		

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Mode				55	
1-	4	Chin	Heal	-	28, 58
base		a	thca	79	7
d			re		
				*#	
Mode				60	
1-	4	Chin	Heal	-	26, 37
base		a	thca	79	6
d			re	*	
Mode				65	
1-	4	Chin	Heal	-	25, 11
base		a	thca	74	1
d			re	*	
Mode				65	
1-	4	Chin	Heal	-	25, 34
base		a	thca	79	4
d			re	*	

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ICER: incremental cost-effectiveness ratio; QALY: quality-adjusted life year; PLCO: prostate, lung, colorectal, and ovarian cancer screening trial. Costs are reported in 2022 US\$.