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Cost-Effectiveness and Budget Impact of Lung Cancer Screening: A Systematic Review

Supplementary Material 1

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Appendix 1: PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Page 1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Page 2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Page 4
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Page 4
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Page 5
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Page 5
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Appendix 2
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Page 5
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Page 5
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Page 5
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	Page 5
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Page 6
	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	Page 5
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	Page 5
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Page 5
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Page 5
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	Page 5
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	N/A
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	N/A
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	Page 6
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	N/A
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Page 6, Figure 1
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Page 6, Appendix 3
Study characteristics	17	Cite each included study and present its characteristics.	Page 6, Supplementary Material 2
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Appendix 6&7
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g.	Table 3, Supplementary

Section and Topic	Item #	Checklist item	Location where item is reported
		confidence/credible interval), ideally using structured tables or plots.	Material 2
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Page 7-21, Table 1&2
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	Page 7-21, Table 1&2
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	N/A
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	N/A
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	Page 20&21, Appendix 6&7
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	N/A
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Page 21
	23b	Discuss any limitations of the evidence included in the review.	Page 28
	23c	Discuss any limitations of the review processes used.	Page 28
	23d	Discuss implications of the results for practice, policy, and future research.	Page 21-27
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	Page 5
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	Page 5
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	Page 5
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Page 29
Competing interests	26	Declare any competing interests of review authors.	Page 29
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	Page 29

Appendix 2: Search Strategy

(1) Search Strategy for Medline (Ovid)

1	exp Lung Neoplasms/ or (exp Lung/ and exp Neoplasms/)
2	((lung or pulmonary) and (cancer* or oncolog* or carcinoma* or neoplasm* or tumo?r*)).ti,ab.
3	1 or 2
4	exp Mass Screening/
5	(scan* or screen* or early detect* or checkup or check-up).ti,ab.
6	4 or 5
7	exp "Costs and Cost Analysis"/
8	exp Cost-Benefit Analysis/ or exp Cost-Effectiveness Analysis/
9	(cost* and (effect* or utilit* or benefit* or minimi* or analy* or outcome*)).ti,ab.
10	exp Budgets/
11	((budget* or financ*) and (impact analy* or assess* or evaluat* or model* or impact model*)).ti,ab.
12	economic evaluat*.ti,ab.
13	7 or 8 or 9 or 10 or 11 or 12
14	3 and 6 and 13
15	limit 14 to english language

(2) Search Strategy for Embase (Ovid)

1	exp lung carcinoma/ or exp lung tumor/ or exp lung cancer/
2	((lung or pulmonary) and (cancer* or oncolog* or carcinoma* or neoplasm* or tumo?r*)).ti,ab.
3	1 or 2
4	exp screening/ or exp cancer screening/ or exp mass screening/
5	(scan* or screen* or early detect* or checkup or check-up).ti,ab.
6	4 or 5
7	exp "cost utility analysis"/ or exp "cost benefit analysis"/ or exp "cost minimization analysis"/ or exp "cost"/ or exp "cost effectiveness analysis"/ or exp "cost of illness"/
8	(cost* and (effect* or utilit* or benefit* or minimi* or analy* or outcome*)).ti,ab.
9	exp budget/
10	((budget* or financ*) and (impact analy* or assess* or evaluat* or model* or impact model*)).ti,ab.
11	exp economic evaluation/
12	economic evaluat*.ti,ab.
13	7 or 8 or 9 or 10 or 11 or 12
14	3 and 6 and 13
15	limit 14 to english language

(3) Search Strategy for Web of Science

#1	TI=((lung OR pulmonary) and (cancer* OR oncolog* OR carcinoma* OR neoplasm* OR tumo$r*))
#2	AB=((lung OR pulmonary) and (cancer* OR oncolog* OR carcinoma* OR neoplasm* OR tumo$r*))
#3	#1 OR #2
#4	TI=(scan* OR screen* OR “early detect*” OR checkup OR check-up OR “check up”)
#5	AB=(scan* OR screen* OR “early detect*” OR checkup OR check-up OR “check up”)
#6	#4 OR #5
#7	TI=(“economic evaluat*” OR (cost AND (effect* or utilit* or benefit* or minimi* or analy* or outcome*)))
#8	AB=(“economic evaluat*” OR (cost AND (effect* or utilit* or benefit* or minimi* or analy* or outcome*)))
#9	TI=((budget* OR financ*) AND (“impact analy*” OR assess* OR evaluat* OR model* OR “impact model*”))
#10	AB= ((budget* OR financ*) AND (“impact analy*” OR assess* OR evaluat* OR model* OR “impact model*”))
#11	#7 OR #8 OR #9 OR #10
#12	#3 AND #6 AND #11
#13	#12 AND LA=(English)

(4) Search Strategy for Cochrane Library

#1	MeSH descriptor: [Lung Neoplasms] explode all trees
#2	MeSH descriptor: [Lung] explode all trees
#3	MeSH descriptor: [Neoplasms] explode all trees
#4	#2 AND #3
#5	((lung or pulmonary) and (cancer* or oncolog* or carcinoma* or neoplasm* or tumo?r*)):ti,ab
#6	#1 OR #4 OR #5
#7	MeSH descriptor: [Mass Screening] explode all trees
#8	(scan* or screen* or early detect* or checkup or check-up):ti,ab
#9	#7 OR #8
#10	MeSH descriptor: [Costs and Cost Analysis] explode all trees
#11	MeSH descriptor: [Cost-Effectiveness Analysis] explode all trees
#12	MeSH descriptor: [Cost-Benefit Analysis] explode all trees
#13	(cost* and (effect* or utilit* or benefit* or minimi* or analy* or outcome*)):ti,ab
#14	MeSH descriptor: [Budgets] explode all trees
#15	((budget* or financ*) and (impact analy* or assess* or evaluat* or model* or impact model*)):ti,ab
#16	economic evaluat*:ti,ab
#17	#10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16
#18	English:la
#19	#6 and #9 and #17 and #18

(5) Search Strategy for Econlit

(((TI ((lung OR pulmonary) AND (cancer* OR oncolog* OR carcinoma* OR neoplasm* OR tumo#r*))) OR (AB ((lung OR pulmonary) AND (cancer* OR oncolog* OR carcinoma* OR neoplasm* OR tumo#r*)))) AND ((TI (scan* OR screen* OR “early detect*” OR checkup OR check-up OR “check-up”)) OR (AB (scan* OR screen* OR “early detect*” OR checkup OR check-up OR “check-up”))) AND ((TI (“economic evaluat*” OR ((cost AND (effect* or utilit* or benefit* or minimi* or analy* or outcome*))) OR (AB (“economic evaluat*” OR ((cost AND (effect* or utilit* or benefit* or minimi* or analy* or outcome*))) OR (TI((budget* OR finance*) AND (“impact analy*” OR assess* or evaluat* or model* or “impact model*”))) OR (AB((budget* OR finance*) AND (“impact analy*” OR assess* or evaluat* or model* or “impact model*”))))) AND LA English

(6) Search Strategy for Scopus

(TITLE-ABS-KEY ((lung OR pulmonary) and (cancer* OR oncolog* OR carcinoma* OR neoplasm* OR tumor* OR tumour*))) AND (TITLE-ABS-KEY (scan* OR screen* OR "early detect*" OR checkup OR check-up OR "check up")) AND ((TITLE-ABS-KEY ((budget* OR financ*) and ("impact analy*" OR assess* OR evaluat* OR model* OR "impact model*"))) OR (TITLE-ABS-KEY ("economic evaluat*" OR (cost AND (effect* or utilit* or benefit* or minimi* or analy* or outcome*))))) AND (LIMIT-TO (LANGUAGE , "English"))

Appendix 3: Articles Excluded at Full Text Screening

	Study	Exclusion reason
1	Benefits, harms, and cost-effectiveness of risk model-based and risk factor-based low-dose computed tomography screening strategies for lung cancer: a systematic review.	wrong study design (review)
2	The Annual Cost of Cancer Screening in the United States.	wrong study design (cost analysis)
3	An Exploratory Analysis of the Cost-Effectiveness of a Multi-cancer Early Detection Blood Test Compared with Standard of Care Screening in Ontario, Canada.	wrong outcomes (no lung cancer specific outcomes)
4	Health Economic Evidence and Modeling Challenges for Liquid Biopsy Assays in Cancer Management: A Systematic Literature Review.	wrong study design (review)
5	Population-Based Screening Using Low-Dose Chest Computed Tomography: A Systematic Review of Health Economic Evaluations.	wrong study design (review)
6	Important parameters for cost-effective implementation of lung cancer screening.	wrong study design (review)
7	Lung cancer screening.	wrong study design (review)
8	Should we screen for lung cancer? A 10-country analysis identifying key decision-making factors.	wrong study design (review)
9	Systematic review of the cost-effectiveness of screening for lung cancer with low dose computed tomography.	wrong study design (review)
10	Variation in Model-Based Economic Evaluations of Low-Dose Computed Tomography Screening for Lung Cancer: A Methodological Review.	wrong study design (review)
11	Applying utility values in cost-effectiveness analyses of lung cancer screening: A review of methods.	wrong study design (review)
12	Low-dose computed tomography lung cancer screening: Clinical evidence and implementation research.	wrong study design (review)
13	Estimating the population health impact of a multi-cancer early detection genomic blood test to complement existing screening in the US and UK.	wrong study design (health impact analysis)
14	Cost-Effectiveness of Smoking Cessation Interventions in the Lung Cancer Screening Setting: A Simulation Study.	wrong study design (intervention, evaluate smoking cessation instead of lung cancer screening)
15	Development and Cost Analysis of a Lung Nodule Management Strategy Combining Artificial Intelligence and Lung-RADS for Baseline Lung Cancer Screening.	wrong study design (cost analysis)
16	Direct and indirect healthcare costs of lung cancer CT screening in Denmark: a registry study.	wrong study design (cost analysis)
17	The challenges of implementing low-dose computed tomography for lung cancer screening in low- and middle-income countries.	wrong study design (review)
18	Update on Lung Cancer Screening.	wrong study design (review)
19	Computed tomography screening for lung cancer.	wrong study design (review)
20	A bronchial-airway gene-expression classifier to improve the diagnosis of lung cancer: Clinical outcomes and cost-effectiveness analysis.	wrong population
21	A practical and adaptive approach to lung cancer screening: a review of international evidence and position on CT lung cancer screening in the Singaporean population by the College of Radiologists Singapore.	wrong study design (review)
22	Benefits, harms and cost-effectiveness of cancer screening in Australia: an overview of modelling estimates.	wrong study design (review)
23	Cost of screening for lung cancer in Australia.	wrong study design (cost analysis)
24	CT screening for lung cancer: Are we ready to implement in Europe?.	wrong study design (review)
25	Budget Impact Analysis of Cancer Screening: A Methodological Review.	wrong study design (review)
26	Early Results From the Implementation of a Lung Cancer Screening Program: The Beaumont Health System Experience.	wrong study design (cost analysis)
27	Cost-effectiveness of lung cancer screening and treatment methods: a systematic review of systematic reviews.	wrong study design (review)
28	What is the Optimum Screening Strategy for the Early Detection of Lung Cancer.	wrong study design (review)
29	Cost-Effectiveness Analyses of Lung Cancer Screening Strategies Using Low-Dose Computed Tomography: a Systematic Review.	wrong study design (review)
30	CT screening for lung cancer: Is the evidence strong enough?.	wrong study design (review)
31	Reviewing risks and benefits of low-dose computed tomography screening for lung cancer.	wrong study design (review)
32	Cost-effectiveness of screening for lung cancer with low-dose computed tomography: a systematic literature review.	wrong study design (review)
33	Understanding Cost-Effectiveness Analyses: An Explanation Using Three Different Analyses of Lung Cancer Screening.	wrong study design (review)
34	Projected Clinical, Resource Use, and Fiscal Impacts of Implementing Low-Dose Computed Tomography Lung Cancer Screening in Medicare.	wrong study design (cost analysis)
35	Current estimate of costs of lung cancer screening in the United States.	wrong study design (review)
36	Resource utilization and costs during the initial years of lung cancer screening with computed tomography in Canada.	wrong study design (cost analysis)
37	Low-dose chest computed tomography for lung cancer screening among Hodgkin lymphoma survivors: a cost-effectiveness analysis.	wrong population
38	Screening for lung cancer using low dose computed tomography.	wrong study design (review)
39	Lung cancer screening: review and performance comparison under different risk scenarios.	wrong study design (review)
40	Cost of a population-based programme of chest x-ray screening for lung cancer.	wrong study design (cost analysis)
41	Moving beyond the national lung screening trial: discussing strategies for implementation of lung cancer screening programs.	wrong study design (review)
42	Lung cancer screening: achieving a reduction in mortality.	wrong study design (review)
43	Lung cancer screening: an update, discussion, and look ahead.	wrong study design (review)
44	Feasibility of a screening programme for lung cancer in former asbestos workers.	wrong study design (cost analysis)

	Study	Exclusion reason
45	Screening for lung cancer: ACCP evidence-based clinical practice guidelines (2nd edition).	wrong study design (review)
46	Lung cancer screening.	wrong study design (review)
47	Computed tomography screening for lung cancer in Hodgkin's lymphoma survivors: decision analysis and cost-effectiveness analysis.	wrong population
48	The clinical effectiveness and cost-effectiveness of computed tomography screening for lung cancer: systematic reviews.	wrong study design (review)
49	CT screening for lung cancer: past and ongoing studies.	wrong study design (review)
50	Screening for lung cancer.	wrong study design (review)
51	Lung cancer screening: will the controversy extend to its cost-effectiveness?.	wrong study design (review)
52	Survey of the sputum cytology service in England and Wales.	wrong study design (cost analysis)
53	Modeling the Economic Impact of a CIZ1B Biomarker Blood Test for Lung Cancer Screening in High-Risk Populations	Wrong study design (preprint, cost analysis)
54	Lung Cancer Screening Can Be a Cost Saving Public Health Measure: A Cost-Consequences Assessment for Italy	Wrong study design (preprint)
55	Ethical Considerations and Implications of Multi-Cancer Early Detection Screening: Reliability, Access and Cost to Test and Treat	wrong study design (review)
56	Screening for lung cancer: A review of the current literature	wrong study design (review)
57	EE313 Model-Based Assessment of the Costs and Benefits of Lung Cancer Screening in the Czech Republic Before Introduction of the National Pilot Program	wrong study design (conference abstract)
58	EE605 Economic Evaluation of Lung Cancer Screening With Low-Dose Computed Tomography in Brazil	wrong study design (conference abstract)
59	Current Evidence for a Lung Cancer Screening Program	wrong study design (review)
60	P1.02-03 Budget Impact Analysis of Volume CT Lung Cancer Screening Based on NELSON Study Outcomes in Europe	wrong study design (conference abstract)
61	MA11.03 Updated Cost-Effectiveness Analysis of Lung Cancer Screening for Australia, Capturing Differences in the Impact of NELSON and NLST Outcomes	wrong study design (conference abstract)
62	EP01.03-009 Cost-effectiveness of Lung Cancer Screening in New Zealand Varies by Ethnicity	wrong study design (conference abstract)
63	Efficiency of the Annual CT Screening Interval for Those at a Lower Risk of Lung Cancer - A CISNET Comparative Modelling Study	wrong study design (conference abstract)
64	Cost-Effectiveness of Adaptive Schedules for Lung Cancer Screening: A Modeling Study	wrong study design (conference abstract)
65	Budget impact model of LungFlag, a predictive risk model for lung cancer screening	wrong study design (conference abstract)
66	Improved Lung Cancer Screening Outcomes Through Blood-Based Genomic Testing: Population and Payer Impact	wrong study design (conference abstract)
67	EE329 Budget Impact of Low-Dose Computed Tomography Screening for Lung Cancer in Argentina	wrong study design (conference abstract)
68	Cost effectiveness of a personalized approach for lung cancer screening with LDCT based on the use of blood-based biomarker test	wrong study design (conference abstract)
69	Pricing and cost-saving potential for deep-learning computer-aided lung nodule detection software in CT lung cancer screening	wrong study design (review)
70	Fiscal feasibility and implications of integrating lung cancer screening into Hong Kong's healthcare system	wrong study design (conference abstract)
71	EE505 Economic Analysis of the Screening Strategy for Lung Cancer with Liquid Biopsy from a Brazilian Perspective	wrong study design (conference abstract)
72	P1.17-03 Cost-effectiveness of Low-dose Computerized Tomography Lung Cancer Screening in High-risk Non-smokers and Smokers in Hong Kong	wrong study design (conference abstract)
73	P1.17-05 Cost-Effectiveness of LDCT Screening in Never Smokers at High Lung-Cancer Risk	wrong study design (conference abstract)
74	Lung Cancer Screening: New Perspective and Challenges in Europe	wrong study design (review)
75	Cost-Effectiveness Analyses of Lung Cancer Screening Using Low-Dose Computed Tomography: A Systematic Review Assessing Strategy Comparison and Risk Stratification	wrong study design (review)
76	HPR19 Tax Revenue Gains and Societal Net-Monetary Benefit Associated With Implementing Lung Cancer Screening in the United Kingdom	wrong study design (conference abstract)
77	POSC55 Model-Based Health Economic Evaluations of Screening Using Chest Computed Tomography: A Systematic Review	wrong study design (review)
78	EE325 Cost-Effectiveness of Lung Cancer Screening With Low Dose Computed Tomography in Hungary	wrong study design (conference abstract)
79	EE304 Cost-Effectiveness of Volume Computed Tomography in Lung Cancer Screening: A Cohort Simulation Based on Nelson Study Outcomes	wrong study design (conference abstract)
80	EE575 Cost-Effectiveness of Low-Dose Computed Tomography Screening for Lung Cancer	wrong study design (conference abstract)
81	Screening for Lung Cancer: CHEST Guideline and Expert Panel Report	wrong study design (review)
82	Implementation of lung cancer screening: what are the main issues?	wrong study design (review)
83	Lung cancer screening: who pays? Who receives? The European perspectives	wrong study design (review)
84	Cost-effectiveness of lung cancer screening with low-dose computed tomography in China: A modeling study	wrong study design (conference abstract)
85	PCN248 Lung cancer screening by low-dose computerised tomography: a cost effectiveness analysis of alternative programmes in the United Kingdom using a newly developed natural history based economic model	wrong study design (conference abstract)
86	An update on CT screening for lung cancer: The first major targeted cancer screening programme	wrong study design (review)
87	Implementation planning for lung cancer screening in China	wrong study design (review)
88	PCN197 Budget impact of lung cancer screening with low-dose computerized tomography for smoking groups	wrong study design (conference abstract)
89	Analysis Indicates Low Incremental Cost-Effectiveness Ratio for Implementation of Lung	wrong study design (conference abstract)

	Study	Exclusion reason
	Cancer Screening in Italy	
90	Implementing Lung Cancer Screening in Canada: Evidence on Adherence and Budget Impact from the Pan-Canadian Early Detection Study	wrong study design (conference abstract)
91	Economic evaluation of lung cancer screening with low-dose computerized tomography (LDCT) for smoking groups in Taiwan	wrong study design (conference abstract)
92	Economic impact of lung cancer screening in France: A modeling study	Non-English
93	Implementation of lung cancer CT screening in the Nordic countries	wrong study design (review)
94	UK lung screening trial cost effectiveness and current planning status of international lung cancer screening programs	wrong study design (conference abstract)
95	Cost effectiveness analysis of CT vs chest X-ray (CXR) vs no screening for lung cancer (LC) in the PLCO and NLST randomized population trials (RPTS)	wrong study design (conference abstract)
96	The clinical benefit and cost-effectiveness of adding a smoking cessation program to a simulated lung cancer screening program in Saskatchewan, Canada	wrong study design (conference abstract)
97	Cost-effectiveness of CT screening in the early detection of lung cancer	wrong study design (review)
98	The cost-effectiveness of lung cancer screening in Saskatchewan	wrong study design (conference abstract)
99	Lung cancer screening program is cost effective in french setting: A model based study	wrong study design (conference abstract)
100	Lung cancer screening: What is new since the NLST results? Topical Collection on Lung Cancer	wrong study design (review)
101	2016 reflections on the favorable cost-benefit of lung cancer screening	wrong study design (review)
102	Use of [^{18}F]Fluoro-2-deoxy-D-glucose Positron Emission Tomographic Imaging in the National Lung Screening Trial	wrong study design (cost analysis in discussion)
103	Recommendations on screening for lung cancerA1 - Anonymous.	wrong study design (review)
104	UK lung cancer screening trial (UKLS) cost effectiveness: Similarities with the NLST high-risk quintiles	wrong study design (conference abstract)
105	Results of the National Lung Cancer Screening Trial: Where Are We Now?	wrong study design (review)
106	Lung cancer screening - Why do it? Tobacco, the history of screening, and future challenges	wrong study design (review)
107	Lung cancer screening: Identifying the high risk cohort	wrong study design (review)
108	Cost-effectiveness analyses of lung cancer screening strategies using low dose computed tomography - A systematic review	wrong study design (review)
109	Assessing the benefits and harms of low-dose computed tomography screening for lung cancer	wrong study design (review)
110	Projected clinical, resource, and budget impact of implementing low-dose computed tomography lung cancer screening in the United States	wrong study design (conference abstract)
111	Low-dose computed tomography lung cancer screening in the Medicare program: Projected clinical, resource, and budget impact	wrong study design (conference abstract)
112	Cost-effectiveness of CT screening for lung cancer by risk and age	wrong study design (conference abstract)
113	Radiographic screening for lung cancer in Varese, Italy: Cost-effectiveness analysis	wrong study design (conference abstract)
114	Cost effectiveness of ct screening	wrong study design (conference abstract)
115	The Economic Burden of Incidentally Detected Findings	wrong study design (review)
116	Cost effectiveness of a lung cancer screening protocol based on 3D cell cytology antecedent to helical thoracic computed tomography (CT)	wrong study design (conference abstract)
117	Cost-effectiveness of screening older adult smokers for lung cancer with an autoantibody test (AABT)	wrong study design (conference abstract)
118	Lung cancer screening-contemporary issues: a narrative review	wrong study design (review)
119	Use of the predictive risk model LungFlagTM for lung cancer screening in screening in a Spanish reference center: A cost-effectiveness analysis	wrong study design (conference abstract)
120	Historical Perspective on Lung Cancer Screening	wrong study design (review)
121	Lung Cancer Screening The European Perspective	wrong study design (review)
122	Systematic Review of Lung Cancer Screening: Advancements and Strategies for Implementation	wrong study design (review)
123	Lung cancer screening in 2022: a narrative review	wrong study design (review)
124	Expected Cost Savings From Low-Dose Computed Tomography Scan Screening for Lung Cancer in Alberta, Canada	wrong study design (cost analysis)
125	Cost-effectiveness analysis of low-dose computed tomography screening for lung cancer in Hungary	wrong study design (conference abstract)
126	Cost-effectiveness evaluation of low-dose computed tomography screening for non-small cell lung cancer	wrong study design (conference abstract)
127	Low-Dose Computed Tomography for Lung Cancer Screening: A Review of the Clinical Effectiveness, Diagnostic Accuracy, Cost-Effectiveness, and Guidelines	wrong study design (review)
128	A cost minimization analysis of the implementation of the international lung screening trial in Catalonia (Spain).	wrong study design (although cost minimization analysis in Title, cost analysis according to text)
129	Computed tomography screening for lung cancer in the National Lung Screening Trial: a cost-effectiveness analysis.	wrong study design (review)
130	Could chest X-ray screening for lung cancer be cost-effective?.	wrong study design (conference paper)
131	UK Lung Cancer RCT Pilot Screening Trial: baseline findings from the screening arm provide evidence for the potential implementation of lung cancer screening.	report same study, include the most detailed one
132	Lung cancer screening by low-dose computed tomography: a cost-effectiveness analysis of alternative programmes in the UK using a newly developed natural history-based economic model.	report same study, include the most detailed one
133	Cost-effectiveness of a low-dose computed tomography screening programme for lung cancer in New Zealand.	An erratum was issued in 2020; therefore, the corrected 2020 version was used in this analysis.

	Study	Exclusion reason
134	Cost-effectiveness of a proposed feasibility study on the detection of early lung carcinoma in Germany.	wrong study design (conference paper)
135	Cost-effectiveness of lung cancer screening in Japan.	wrong study design (conference paper)

Appendix 4: Cost Effectiveness Evidence of Full Economic Evaluations stratified by Region, Screening Modality and Eligible Population

		Total (n = 93)	Cost-effective (n = 79)	Not Cost-effective (n = 5)	Mixed results (n = 9)
Region (n = 93)					
Europe		33	30	0	3
North America		28	24	2	2
Asia		22	20	0	2
Oceania		6	3	2	1
South America		2	1	1	0
Multiple countries		2	1	0	1
Screening modality (intervention) (n = 98)					
LDCT		81	71	4	6
LDCT + AI		5	5	0	0
LDCT + biomarker		4	3	1	0
LDCT + PRS		2	1	0	1
Biomarker		1	0	0	1
Chest X-ray		3	2	0	1
MRI		1	1	0	0
FCT (Full Chest CTCS)		1	1	0	0
Eligible population (n = 104)					
High-risk (smoker)	Smoking history: cumulative pack-years	53	44	4	5
	Smoking history: smoking duration and average daily cigarette consumption	18	17	0	1
	Risk model-based	11	9	1	1
	General smoker	3	2	1	0
High-risk (other eligibility)	Estimated from epidemiological data	5	5	0	0
	Risk model-based	3	3	0	0
	Asbestos-exposed	2	1	0	1
	Family history	1	1	0	0
	Suspected coronary artery disease	1	1	0	0
	Based on assumption	1	1	0	0
	Unspecified	2	2	0	0
General population		3	1	1	1
Nonsmoker		1	0	0	1

Appendix 5: Additional Study Characteristics of Full Economic Evaluations and BIAs

(1) Full economic evaluations

Regarding modeling software, 42 studies (45.2%) did not clearly report the software used. Among those that did, TreeAge was the most commonly used (n = 19) [1-18], followed by R (n = 16) [19-34], Microsoft Excel (n = 15) [34-48], Python (n = 1) [49], and STATISTICA (n = 1) [50].

Nearly half of the studies (n = 43; 46.2%) incorporated overdiagnosis into their models [1, 6, 8, 10, 11, 13, 18, 20-22, 25, 29-31, 34, 36, 38, 41-43, 47, 49, 51-71]. Among the 93 studies, all but one [48] involved imaging-based technologies for LC screening, which are associated with radiation exposure. However, only 13 studies incorporated the impact of radiation-related harms into the modeling [1, 7, 18, 21, 22, 30, 31, 64, 72-76].

Model validation was conducted in 24 studies (25.8%). Of these, three studies performed face validity [28, 77, 78], three conducted internal validation [29, 64, 74], and 16 reported external validation [2, 3, 15, 21, 22, 30, 40, 49, 51, 52, 54, 60, 61, 72, 73, 76]. Only two studies undertook all three types of validation—face, internal, and external validation [1, 33]. Among the studies that did not conduct or report model validation, nine relied on established models that had previously been validated [25, 31, 55, 57-59, 63, 75, 79]. A further six studies employed models that had been published in previous research but did not report any formal validation procedures [13, 16, 18, 35, 80, 81].

The most commonly reported limitations related to data inputs and evidence synthesis (n = 72), followed by modeling limitations (n = 70), issues concerning intervention and comparators (n = 46), and uncertainties in costs and resource use (n = 43).

(2) Budget impact analysis

Four studies reported the modeling software [16, 28, 49, 82].

Model validation was reported in five studies [28, 49, 54, 72, 82]. Of these, two studies assessed face validity through expert review [28, 82], and three conducted external validation [49, 54, 72]. Among the studies that did not conduct model validation, one adopted a model previously published in the literature [16], while another used an established model that had already undergone validation [83].

Appendix 6: Quality Assessment of Full Economic Evaluations

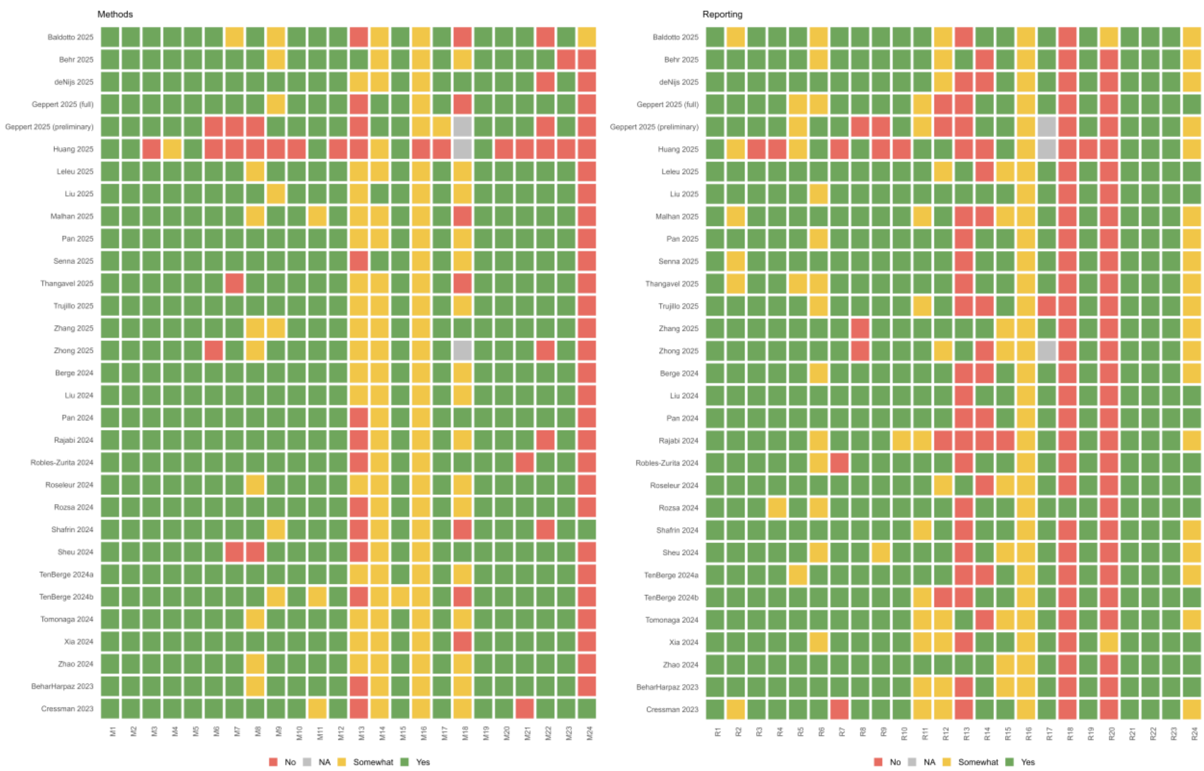
(1) Criteria for Health Economic Quality Evaluation (CHEQUE) tool

The Criteria for Health Economic Quality Evaluation (CHEQUE) tool was developed by Kim et al. [84]:

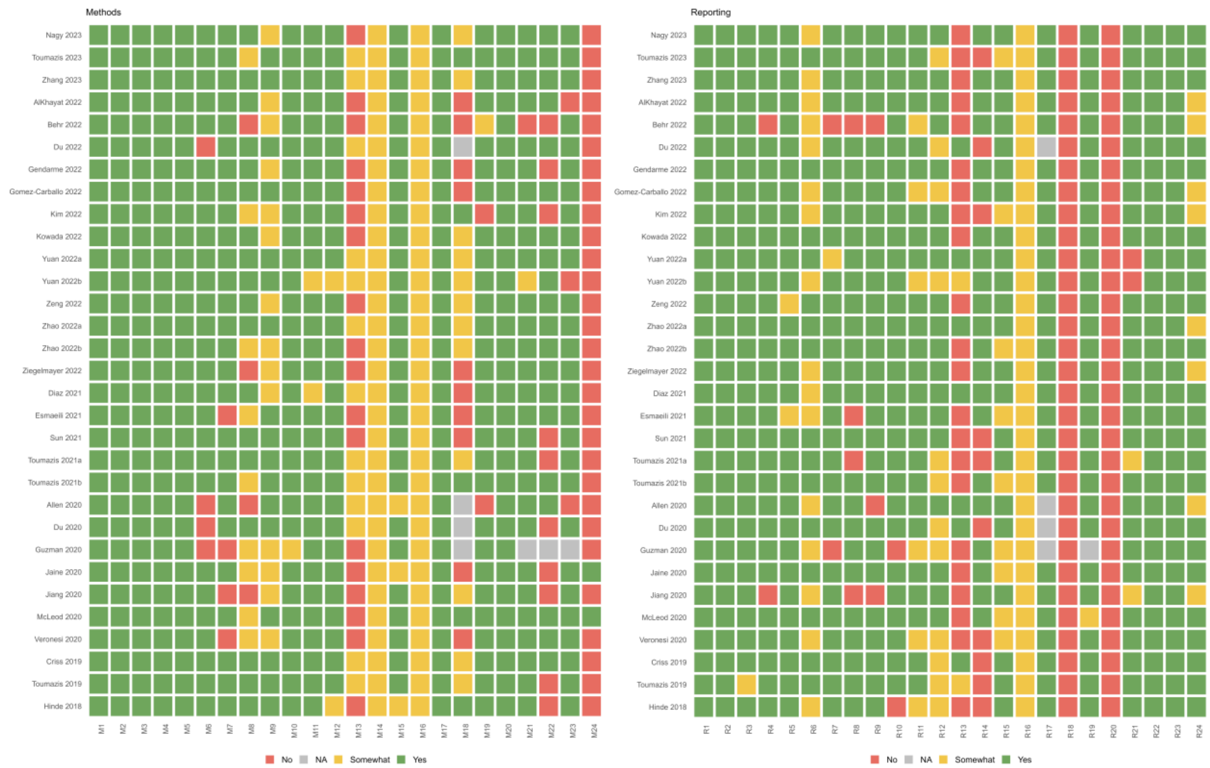
Decision Problem and Scope	
M1	The analysis answers an important question for decision-making
M2	The study objective (decision problem) is measurable
R1	The study objectives (or decision problems) are clearly stated
Intervention and Comparator(s)	
M3	Comparator is the best possible option that appropriately measures the opportunity cost of using the new treatment
R2	All aspects of the interventions that may affect their cost-effectiveness are defined (e.g., frequency of delivery, setting of delivery, specific technologies used)
R3	Comparator(s) are clearly stated
Perspective	
M4	Analytic perspective is appropriate to answer the research question posed
R4	Perspective is clearly stated
Population	
M5	The scope of the study encompasses all populations affected by the intervention
R5	Target population is clearly stated
Outcome Measures	
M6	Health outcomes are measured in health metrics that aggregate survival and health-related quality-of-life or disability (e.g., QALY or DALY).
R6	Primary outcome measure(s) are clearly stated.
R7	Incremental cost-effectiveness ratios (ICERs) are reported
Time Horizon	
M7	Time horizon is sufficient to reflect all important differences between intervention(s) and comparator(s)
R8	Time horizon is clearly stated
Discounting	
M8	Costs and health effects that occur in the future are discounted to their present value using a recommended discount rate
R9	Discount rate is clearly stated
Modeling	
M9	The chosen model type is appropriate to address study questions
M10	Structure of the model reflects the underlying health condition and the impact of interventions
M11	Modeling assumptions are reasonable given the underlying data
M12	Need for extrapolation and/or need to integrate multiple data sources are considered
M13	Model validation - including an assessment of the model structure, assumptions, data, and results - is conducted
R10	Type of model used is clearly stated
R11	Justification of modeling choices and assumptions are provided
R12	Model descriptions are detailed enough to allow for replication
R13	Description of how model was validated is provided
R14	Software used to develop the model is clearly stated
Data Inputs and Evidence Synthesis	
M14	A "best available evidence" approach is used to select data sources for model parameters (e.g., conducted or references systematic reviews/meta-analysis)
M15	Data inputs are generated by appropriate statistical and epidemiological techniques
M16	Quality of the data (e.g. sources of bias) are assessed appropriately
R15	All data sources are referenced
Consequences	
M17	Major consequences affected by the choice of interventions being compared are identified
R16	Comprehensive identification of consequences are summarized (e.g., using an Impact Inventory table in 2nd Panel's report)

Utilities (Preference Measures)	
M18	Health preferences reflect those of the jurisdiction(s) of interest (as specified in the decision problem)
R17	Sources for the utility weights are clearly stated
Costs and Resource Use	
M19	Resource use that is non-trivial in magnitude are included in the Reference Case analysis.
R18	Quantities of resources are reported separately from the prices (unit costs) of those resources.
Analysis	
M20	Incremental analyses are conducted (i.e., the additional costs generated by one alternative over another are compared to the additional effects generated)
M21	ICERs are obtained by comparing each intervention to the next most effective option, after eliminating dominated options
M22	Probabilistic sensitivity analysis is conducted to account for uncertainty in input parameters simultaneously
M23	Alternative modeling choices and assumptions (structural uncertainty) are explored through additional sensitivity analysis (i.e., scenario analysis)
R19	Approach to secondary analyses (e.g., sensitivity, scenario, or subgroup analysis) is reported
Equity Considerations	
M24	Relevant equity or distributional considerations are taken into account
R20	Discussion section includes a description of any significant ethical implications of the CEA results
Transparency and Reporting	
R21	Results are presented in a disaggregated format for transparency
R22	Relevance of study results to specific decision problems are discussed
R23	Implications of uncertainty for decision-making, including the need for future research, are explored
R24	Potential bias and limitations are discussed

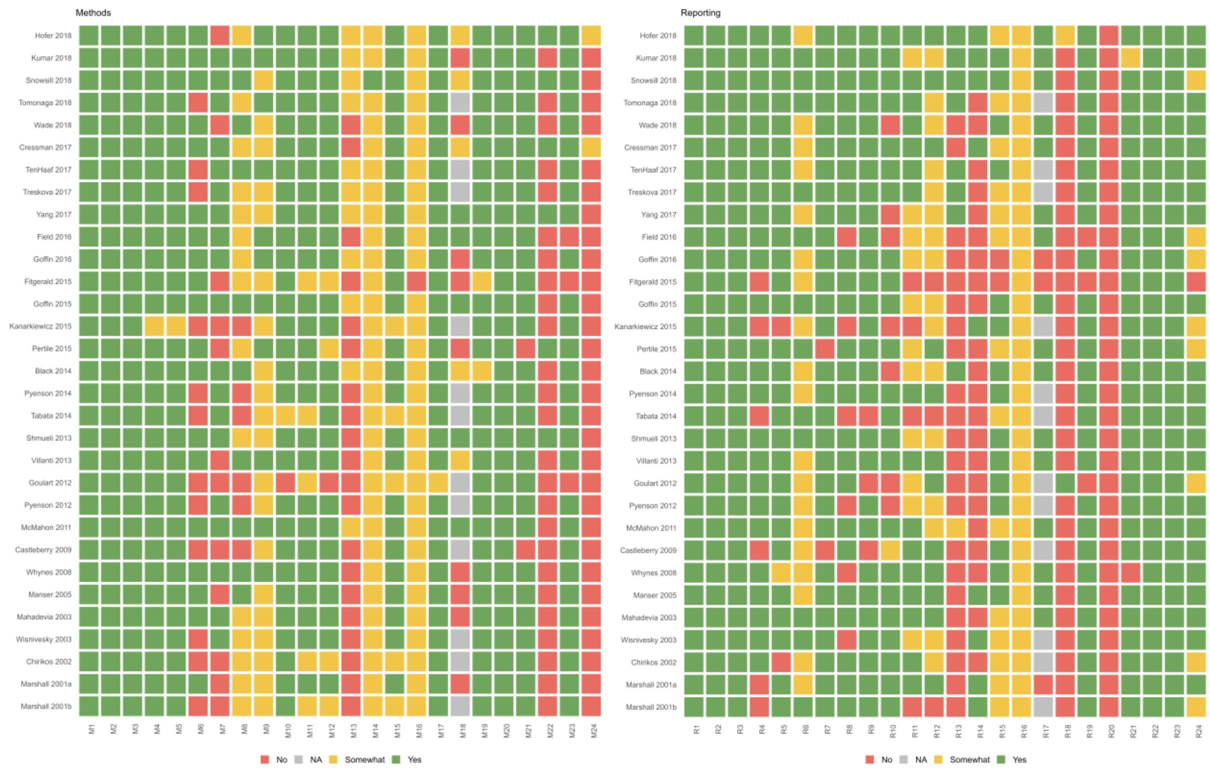
(2) Individual Study Scores by Methodological and Reporting Attributes



(a)



(b)



(c)

Figure: Individual Study Scores by Methodological and Reporting Attributes (a-c)

(3) Quality Scores of Full Economic Evaluations by Attribute

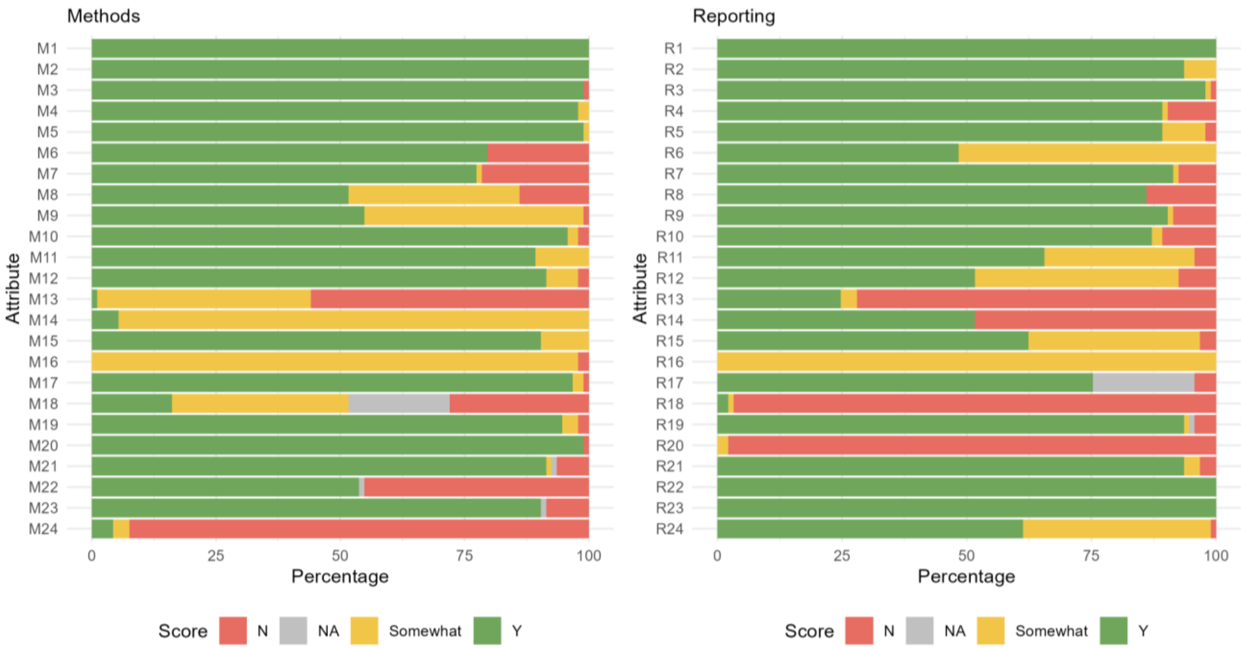


Figure: Quality Scores of Full Economic Evaluations by Attribute

(4) Total Scores of Each Full Economic Evaluation Study

Study ID	**Methodological quality (%) [a]**	**Reporting quality (%) [a]**
Baldotto 2025 [32]	75.50%	**81.00%**
Behr 2025 [33]	**85.00%**	**82.00%**
deNijs 2025 [51]	**86.00%**	**81.50%**
Geppert 2025 (full model) [17]	**83.00%**	75.50%
Geppert 2025 (preliminary model) [17]	72.96%	70.10%
Huang 2025 [85]	29.59%	56.19%
Leleu 2025 [52]	**87.00%**	**84.00%**
Liu 2025 [1]	**88.00%**	**93.50%**
Malhan 2025 [77]	**83.50%**	76.00%
Pan 2025 [35]	**88.00%**	**88.50%**
Senna 2025 [48]	**87.00%**	**87.50%**
Thangavel 2025[16]	**83.00%**	**83.00%**
Trujillo 2025 [78]	**88.00%**	76.50%
Zhang 2025 [15]	**85.00%**	**88.50%**
Zhong 2025 [72]	**81.63%**	78.35%
Berge 2024 [80]	**88.00%**	**83.50%**
Liu 2024 [18]	**88.00%**	**93.00%**
Pan 2024 [86]	**85.00%**	**88.00%**
Rajabi 2024 [53]	**81.00%**	63.50%
Robles-Zurita 2024 [19]	**82.00%**	**86.50%**
Roseleur 2024 [54]	**87.00%**	**84.00%**
Rozsa 2024 [36]	**84.00%**	**90.50%**
Shafrin 2024 [37]	78.00%	**87.00%**
Sheu 2024 [12]	79.00%	**85.00%**
TenBerge 2024a [81]	**88.00%**	**84.00%**
TenBerge 2024b [46]	75.00%	**80.00%**
Tomonaga 2024 [49]	**87.00%**	78.00%
Xia 2024 [31]	**87.00%**	**82.50%**
Zhao 2024 [3]	**87.00%**	**93.50%**

Study ID	**Methodological quality (%) [a]**	**Reporting quality (%) [a]**
BeharHarpaz 2023 [20]	**83.00%**	**82.00%**
Cressman 2023 [5]	79.50%	75.00%
Nagy 2023 [38]	**81.00%**	**90.50%**
Toumazis 2023 [55]	**88.00%**	**81.00%**
Zhang 2023 [13]	**88.00%**	**90.50%**
AlKhayat 2022 [23]	76.00%	**88.50%**
Behr 2022 [24]	71.00%	71.50%
Du 2022 [73]	**85.71%**	**83.51%**
Gendarme 2022 [34]	77.00%	**93.00%**
Gomez-Carballo 2022 [39]	**83.00%**	**80.00%**
Kim 2022 [87]	76.00%	**81.00%**
Kowada 2022 [7]	**81.00%**	**93.00%**
Yuan 2022a [22]	**88.00%**	**91.00%**
Yuan 2022b [21]	78.50%	**80.50%**
Zeng 2022 [6]	**81.00%**	**91.00%**
Zhao 2022a [2]	**88.00%**	**94.00%**
Zhao 2022b [4]	**80.00%**	**90.50%**
Ziegelmayer 2022 [14]	78.00%	**88.50%**
Diaz 2021 [26]	**81.50%**	**93.50%**
Esmaeili 2021 [8]	78.00%	**83.00%**
Sun 2021 [56]	**80.00%**	**88.00%**
Toumazis 2021a [57]	**85.00%**	79.00%
Toumazis 2021b [25]	**88.00%**	**86.00%**
Allen 2020 [40]	75.00%	**89.18%**
Du 2020 [76]	**82.65%**	**86.08%**
Guzman 2020 [27]	65.91%	69.68%
Jaine 2020 [47]	74.50%	**90.50%**
Jiang 2020 [9]	72.00%	78.00%
McLeod 2020 [41]	**85.00%**	**89.00%**
Veronesi 2020 [88]	75.00%	74.50%
Criss 2019 [58]	**88.00%**	**86.50%**
Toumazis 2019 [59]	**85.00%**	**82.00%**
Hinde 2018 [89]	78.00%	73.00%
Hofer 2018 [28]	**83.50%**	**92.00%**
Kumar 2018 [29]	**84.00%**	**86.00%**
Snowsill 2018 [42]	**88.00%**	**94.00%**
Tomonaga 2018 [60]	**81.63%**	**83.51%**
Wade 2018 [90]	73.00%	77.00%
Cressman 2017 [10]	**80.50%**	**88.00%**
TenHaaf 2017 [61]	**82.65%**	**83.51%**
Treskova 2017 [30]	78.57%	**83.51%**
Yang 2017 [74]	**85.00%**	73.50%
Field 2016 [91]	77.00%	65.00%
Goffin 2016 [79]	**83.00%**	67.00%
Fitgerald 2015 [62]	60.00%	49.50%
Goffin 2015 [63]	**86.00%**	79.50%
Kanarkiewicz 2015 [50]	64.29%	59.79%
Pertile 2015 [92]	73.50%	75.50%
Black 2014 [64]	**81.00%**	76.00%
Pyenson 2014 [65]	73.47%	**85.05%**
Tabata 2014 [66]	64.29%	58.25%
Shmueli 2013 [67]	**81.00%**	79.50%
Villanti 2013 [93]	77.00%	**85.50%**
Goulart 2012 [68]	46.43%	71.65%

Study ID	Methodological quality (%) [a]	Reporting quality (%) [a]
Pyenson 2012 [69]	73.47%	69.07%
McMahon 2011 [75]	**86.00%**	**80.00%**
Castleberry 2009 [70]	66.33%	72.68%
Whynes 2008 [94]	**80.00%**	79.90%
Manser 2005 [43]	73.00%	**90.50%**
Mahadevia 2003 [71]	76.00%	**85.50%**
Wisnivesky 2003 [11]	74.49%	78.35%
Chirikos 2002 [95]	63.78%	71.65%
Marshall 2001a [45]	72.00%	**81.00%**
Marshall 2001b [44]	63.78%	66.49%

[a] Total quality scores ≥80% were shown in bold.

Appendix 7: Quality Checklist for Budget Impact Analysis Studies

Study ID	Budget holder's perspective	Target population estimated	Costs of at least 3 years	Costs annual [a]	Costs screening	Costs diagnostic	Cost treatment	Comparator	Market share and participation rate stated	Validation	Uncertainty analyses	Uncertainty participation rate
Hernandez-Yumar 2025 [96]	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	Y
Silvestrini 2025 [82]	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N
Evans 2016 [83]	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	N	N
Thangavel 2025 [16]	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	N	N
Zhong 2025 [72]	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	N	N
Roseleur 2024 [54]	Y	N	Y	Somewhat	Y	Y	Y	Y	Y	Y	N	N
Tomonaga 2024 [49]	Y	N	Y	Somewhat	Y	Y	Y	Y	Y	Y	N	N
Hofer 2018 [28]	Y	N	Y	N	Y	Y	Y	Y	Y	Y	N	N
Goulart 2012 [68]	Y	Y	N	Y	Y	Y	Y	Y	Y	N	Y	Y

[a] somewhat for cost annual: Annual costs are presented in a graphical form without specific numbers.

Appendix 8: Overview of Current Strategies for Lung Cancer Screening Programs in Regions with National or Territory-wide Screening

Country/Region	Name of the Program (if applicable)	Screening Interval	Screen type	Eligibility
Australia [97]	National Lung Cancer Screening Program (NLCSP)	biennial	LDCT	50-70 years old, current or former (quit less than 10 years ago) smoker who smoked ≥30 pack-years
China (pilot areas [98]) (According to the 2024 guideline [99])	Cancer Screening Program in Rural Areas, Cancer Screening Program in Urban Areas	annual	LDCT	50-74 years old and meeting at least one of the following criteria: (1) smoking history ≥20 pack-years, including those who smoked ≥20 pack-years but quit less than 15 years ago. (2) exposed to passive smoking at home or in the workplace for ≥20 years. (3) a diagnosis of chronic obstructive pulmonary disease (COPD). (4) occupational exposure (e.g., asbestos, radon, beryllium, chromium, cadmium, nickel, silica, coal smoke, or coal dust) for >1 year. (5) having a first-degree relative (parents, children, or siblings) diagnosed with lung cancer.
Taiwan, China [100]	Lung Cancer Early Detection Program	biannual	LDCT	men aged 50-74 years old and women aged 45-74 years old with a family history (parents, children, or siblings) of lung cancer 50-74 years old, current or former (quit less than 15 years ago) smoker who smoked ≥30 pack-years
South Korea [101]	National Lung Cancer Screening Program (NLCSP)	biennial	LDCT	54-74 years old with a smoking history of ≥ 30 pack-years
Israel [102]	Screening for Early Detection of Lung Cancer Among Smokers	biennial	LDCT	65-75 years old, current or former (quit less than 15 years ago) smoker who smoked ≥20 pack-years
US (According to the USPSTF2021 recommendation [103])	Not a single program. Federal coverage by Medicare, Medicaid, and major commercial insurance	annual	LDCT	50-80 years old, current or former (quit less than 15 years ago) smoker who smoked ≥20 pack-years
Czech Republic (pilot) [104]	Lung Cancer Early Detection Program	Last five years, initially repeated after one year, then after 2 years	LDCT	55-74 years old and current smoker: ≥20 cigarettes/day for ≥20 years, or ≥40 cigarettes/day for ≥10 years former smoker: ≥20 cigarettes/day who quit <20 years ago, or ≥40 cigarettes/day who quit <10 years ago
Poland (pilot) [105]	National Program of Early Lung Cancer Detection	annual, last 2021-2025	LDCT	55-74 years old: current or former (quit less than 15 years ago) smoker who smoked ≥20 pack-years 50-74 years old: current or former (quit less than 15 years ago) smoker who smoked ≥20 pack-years and meeting at least one of the following criteria: (1) occupational exposure to silica, beryllium, nickel, chromium, cadmium, asbestos, arsenic compounds, diesel engine exhaust, coal smoke, or soot. (2) exposure to radon. (3) history of lung cancer, lymphoma, head and neck cancer, or other smoking-related cancers such as bladder cancer. (4) a close family member (first-degree relative) with lung cancer. (5) diagnosis of chronic obstructive pulmonary disease (COPD) or idiopathic pulmonary fibrosis (IPF).
Croatia [106]	National Lung Cancer Screening Program	annual	LDCT	50-75 years old, current or former (quit less than 15 years ago) smoker who smoked ≥30 pack-years
UK (phased rollout [107]) (According to NHS England protocol [108])	Lung Health Check	biennial	LDCT	55-74 years old, ever smoker meeting risk assessment (PLCOm2012 risk of ≥1.51% over six years or LLPv2 five-year risk of ≥2.5%)
Canada (regional) (According to CTFPHC2016 recommendation [109])	Province-level program	annual up to three consecutive times	LDCT	55-74 years old, current or former (quit less than 15 years ago) smoker who smoked ≥30 pack-years

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