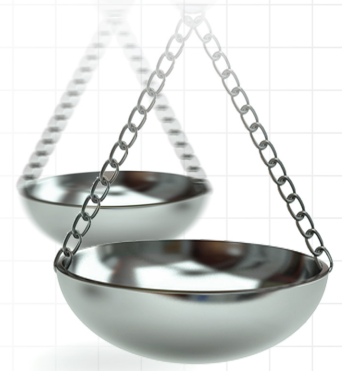




Lung cancer screening in Lithuania: a cost-effectiveness analysis

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Aim: This study aimed to assess the cost-effectiveness of the annual volumetric-enabled low-dose computed tomography (LDCT) lung cancer screening (LCS), based on the NELSON screening outcomes, versus no screening for the asymptomatic high-risk population in Lithuania. **Materials & methods:** The previously established model with a decision tree with an integrated state-transition Markov trace was adapted to assess the health benefits and the financial consequences of LCS from the Lithuanian healthcare system perspective. Individuals aged 50–74 years and with a smoking history underwent LCS with LDCT in the screening arm, and it was compared with the absence of screening across a lifetime horizon. The primary outcomes included the clinical benefits (lung cancer cases detected per stage and premature lung cancer deaths averted), direct costs (recruitment, diagnostic and treatment costs) of LCS implementation, quality-adjusted life years, life-years and the incremental cost-effectiveness ratio. One-way sensitivity analysis and probabilistic sensitivity analysis were conducted to ascertain the result's robustness. **Results:** Annual LCS with volumetric-enabled LDCT for 170,808 eligible individuals in Lithuania resulted in 6117 additional early-stage (I and II) lung cancers detected and 1874 averted late-stage (III and IV) lung cancers, leading to 2606 premature lung cancer deaths averted and 21,639 life-years gained at an uptake rate of 46.5%. The incremental cost-effectiveness ratio was €1372 per quality-adjusted life year with incremental costs of €21.1 million and 15,391 quality-adjusted life years gained. The results were robust based on sensitivity and scenario analyses. **Conclusion:** This study demonstrated that annual LCS with volumetric-enabled LDCT for a high-risk population could be cost-effective compared with no screening in Lithuania.

Plain language summary

What is this article about? Several lung cancer screening (LCS) studies have been carried out worldwide, with the two largest studies showing that screening people at high risk can reduce deaths from lung cancer. In 2024, Lithuania launched a pilot LCS study to assess feasibility, organization and clinical effectiveness in 2024. In evaluating the introduction of a new screening program, cost-effectiveness analysis plays a central role in informing national screening decisions. Therefore, our study assessed both the health benefits and the economic impact of the LCS program in Lithuania by conducting a cost-effectiveness analysis.

What were the results? The study found that LCS leads to better health outcomes for high-risk individuals. Although screening increases healthcare costs, these additional costs are considered acceptable. Overall, LCS was shown to be cost-effective compared with no screening. The incremental cost-effectiveness ratio was €1372 per quality-adjusted life year gained.

What do the results mean? These results suggest that implementing LCS in Lithuania could be a better approach for diagnosing lung cancer than the current clinical pathway without screening. The findings provide valuable evidence for policymakers and healthcare decision-makers and support the consideration of launching a LCS program in Lithuania.

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Keywords: computed tomography • cost-effectiveness • early detection • lung cancer screening • Markov model

Lung cancer is the most diagnosed cancer worldwide and the leading cause of cancer-related mortality, with 1.8 million deaths in 2022 [1]. In Lithuania, lung cancer is the fourth most prevalent cancer accounting for approximately 9% of all new cancer cases [1]. Tobacco smoking is the most relevant risk factor related to lung cancer [2]. In Lithuania, the prevalence of smoking among men significantly exceeds that of women, with male smoking rates being more than three-times higher (29% vs 9.5%) [3]. This disparity is reflected in lung cancer incidence rates, which are markedly higher in men (53.5 per 100,000) compared with women (7.3 per 100,000) [2].

Cancer mortality in Lithuania is above the European average [4]. Lung cancer stands as the leading cause of cancer-related mortality in Lithuania, with low overall survival (OS) [5]. This is primarily attributable to the high proportion of patients diagnosed at an advanced stage, in fact the 5-year relative survival rate for advanced stage lung cancer remains below 10% compared with 43% in case of early diagnoses [5]. Lithuania's preventable and treatable mortality rates are above the Europe average but have decreased in the last decade [4], due to improved public health policies, such as prevention and screening programs. Screening with low-dose computed tomography (LDCT) for high-risk individuals can facilitate the detection of lung cancer at earlier stages, subsequently improving the prospects for successful treatment and reducing lung cancer-specific mortality. This is supported by two large randomized controlled trials, the National Lung Screening Trial (NLST) conducted in the US [6] and the Dutch–Belgian Lung Cancer Screening Study (NELSON [NEderlands-Leuven Longkanker Screenings ONderzoek]) in Europe [7]. Both the NLST and NELSON studies demonstrated significant reductions in lung cancer-specific mortality attributable to LDCT screening. The NLST reported a 20% reduction in lung cancer mortality, while the NELSON trial showed a 24% reduction in men [6,7]. Additionally, early-stage lung cancer detection using CT screening is corroborated by other smaller randomized European trials [8–13].

The European Council has advised Member States to explore the (financial) feasibility and effectiveness of quality-controlled lung cancer screening (LCS) with LDCT in 2022 [14]. The implementation of an LCS program in Lithuania has been initiated, engaging pulmonary specialists, the National HealthCare System, and representatives from the National Health Insurance Fund (NHIF) [2] and the first results of the Lithuanian LCS pilot have been published [15]. The NHIF currently provides reimbursement for several cancer screening programs. However, LCS is not encompassed within the current reimbursement scheme. This study evaluates the cost-effectiveness of implementing a population-based LCS program using volumetric-enabled LDCT compared with no screening for an asymptomatic, high-risk population in Lithuania, from a healthcare system perspective. Cost-effectiveness analysis is a key tool for informing national screening decisions and has become standard for assessing healthcare interventions [16], and this study provides to our knowledge the first country-specific assessment for Lithuania. For this analysis, we build on our group's previous LCS evaluations in the UK [17]. The Lithuanian analysis applies the original UK modeling structure to a Lithuanian context. The novelty of this study lies in applying an established LCS modeling framework to Lithuania to assess its policy relevance in a new national setting. Conducting a country-specific cost-effectiveness analysis is essential because differences in demographics, epidemiology, healthcare systems and costs can substantially alter the feasibility of implementing a screening program for national decision-makers.

Materials & methods

This study was based on a previously established and validated model, developed in Microsoft Excel Microsoft Corporation (2018), consisting of a decision tree and a state-transition Markov model [17]. The decision tree simulated the identification and diagnosis of lung cancer patients, while the state-transition Markov model demonstrated the transition of lung cancer patients between health states over time, based on the natural history of lung cancer. Detailed figures illustrating the decision tree and Markov model used in this analysis are available in the previous publication [17], providing a detailed visual representation of the model structure and transitions. Given the com-

prehensive publication of core model specifications elsewhere [17], the subsequent section provided a condensed overview of the methods, primarily emphasizing the localized Lithuanian data inputs utilized in this analysis.

Model structure & design

A validated decision tree and state-transitioned Markov model were used to simulate a no screening and a screening scenario [17]. The no screening scenario reflected the current clinical pathway for Lithuanian lung cancer patients. In a Markov model, individuals are evenly assigned to health states at the start to ensure a balanced comparison of transitions, costs and health outcomes across different strategies. However, it was observed in the model that LCS detected more lung cancer patients compared with the no screening arm where lung cancer patients were diagnosed after clinical presentation, as previously explained by Pan *et al.* [17]. Therefore, a branch named ‘missed individuals’ was added to the no screening arm. This branch consisted of an asymptomatic cohort defined as the ‘missed individuals’. These individuals were asymptomatic patients with preclinical disease. For the missed individuals, it was assumed that they followed the OS rates of patients with lung cancer stage II. This approach applies a conservative assumption for undiagnosed cases in the no-screening arm, avoiding survival overestimation while preventing underestimation of the benefits of LCS. However, no direct costs would be applied to them, as they were not diagnosed (yet), and therefore did not undergo any diagnostic procedures or treatment. For the screening scenario, the NELSON study volumetric protocol and screening outcomes were used to stimulate the detection of lung cancer for LCS participants. Additionally, in the screening scenario, a branch of nonparticipants, who were diagnosed through clinical presentation, was included. The analysis utilized one screening cohort, wherein individuals eligible for screening in a given year were followed throughout their lifetime. Individuals without a lung cancer diagnosis would enter the next screening round in the following year, as annual screening is the recommended method [18]. Individuals diagnosed with lung cancer and the missed individuals would enter the state-transition Markov model. The Markov model included three health states: preprogression, postprogression and death. The preprogression state represented the phase following diagnosis, during which patients remained until disease progression occurred. Individuals transitioned to the postprogression state upon disease progression, as they were not cured by the initial treatment. Additionally, individuals from the pre- and post-progression state transitioned to the death health state (lung cancer mortality and all-cause mortality). The Markov model was based on the natural history of lung cancer, and used to stimulate disease progression, long-term survival, and treatment costs for lung cancer patients by stage at diagnosis [17]. Therefore, the Markov trace was designed with a 3-month cycle to correspond with the lung cancer treatment and follow-up timeline [19]. The model included 17 annual screening rounds, starting from the mean age of participants in the NELSON study (58 years), and stopped at the upper boundary of the age inclusion criteria for a scan (74 years) [20].

The study followed the Lithuanian and Baltic guidelines for economic evaluations and health technology assessment [21,22]. The base case analysis was conducted from the healthcare payer perspective with a lifetime horizon. Quality-adjusted life years (QALYs) and life years (LYs) gained were designated as the principal health outcome measures to illustrate the changes in health-related quality of life and life expectancy attributed to the implementation of LCS. In addition, the incremental cost-effectiveness ratio (ICER) was reported to represent the economic value of LCS with LDCT compared with no screening. The willingness to pay (WTP) per QALY gained for medical procedures in Lithuania ranges from one to three-times the gross domestic product (GDP) per capita, translating to a threshold between €23,806–71,417, as the GDP per capita was €23,806 in Lithuania in the year 2022 [3,23]. A 3.5% discount rate was applied to both health and costs outcomes, thereby following the Lithuanian national health technology assessment guidelines [22].

Model inputs

The model inputs included screening outcomes, eligible population, lung cancer epidemiology, survival data, utilities and costs. The paragraphs below describe the data input used for the analysis. Lithuanian-specific data were used when available. International sources were used to compensate for data scarcity in Lithuania. The screening outcomes were based on the NELSON study and therefore did not diverge from the core model described previously [17]. The main model inputs are presented in Table 1.

Epidemiological data & eligible population

The eligible population was calculated based on the age inclusion criteria outlined by the NELSON study (50–74 years), and the smoking behaviors. The Lithuanian population aged 50–74 years was 916,668, and the local

Table 1. Base case analysis parameters.

Parameter	Base-case value	PSA distribution	Ref.
Discount rate for costs	3.5 %	Fixed	[22]
Discount rate for health outcomes	3.5 %	Fixed	[22]
Time horizon	Lifetime (42 years)	Fixed	
Screening uptake rate	46.5 %	Beta	[24–26]
Stage distribution			
Stage I	9.1%	Dirichlet	[27]
Stage II	13.1%	Dirichlet	[27]
Stage III	32.3%	Dirichlet	[27]
Stage IV	45.5%	Dirichlet	[27]
Total population	2,830,097	Gamma	[3]
Population aged 50–74 years	32.39%	Beta	[28]
Male	46.60 %	Beta	[3]
Female	53.40 %	Beta	[3]
Smoking rate	18.6 %	Beta	[3]
Lung cancer incidence aged 50–74 years	1100	Gamma	local experts [‡]
Costs			
Recruitment costs			
Information package	€2.51	Gamma	[29]
Screening costs			
CT scan	€42.48	Gamma	[29]
Diagnostic costs per person			
Screening round 1	€2536	Gamma	[29], local experts [‡]
Screening round 2 onwards	€2478	Gamma	[29], local experts [‡]
No screening	€2920	Gamma	[29], local experts [‡]
Treatment costs per cycle			
Stage I			
Pre-progression state			
First half-year (per cycle)	€1426	Gamma	[30], local experts [‡]
Follow-up costs year 1–2 (per cycle)	€33	Gamma	[29,31]
Follow-up costs year 3–5 (per cycle)	€16	Gamma	[29,31]
Post-progression state (one-time cost)	€16,696	Gamma	[30,32–37], local experts [‡]
Follow-up costs (per cycle)	€22	Gamma	[30]
Stage II			
Pre-progression state			
First half-year (per cycle)	€1755	Gamma	[30], local experts
Follow-up costs year 1–2 (per cycle)	€33	Gamma	[29,31]
Follow-up costs year 3–5 (per cycle)	€16	Gamma	[29,31]
Post-progression state (one-time cost)	€16,696	Gamma	[30,32–37], local experts [‡]
Follow-up costs (per cycle)	€22	Gamma	[30]
Stage III			
Pre-progression state			
First year (per cycle)	€10,374	Gamma	[30,32–37], local experts [‡]
Second year (per cycle)	€1159	Gamma	[30,32–37], local experts [‡]
Follow-up (per cycle)	€22	Gamma	[30]
Post-progression state (one-time cost)	€618	Gamma	[30]
Follow-up (per cycle)	€22	Gamma	[30]

[†] Lung cancer-free participants refer to people who either do not have lung cancer or have not been identified with lung cancer.
[‡] An overview of the local experts can be found in S6 Table.
 CT: Computed tomography; D/PFS: Disease/progression-free survival; NA: Not applicable; OS: Overall survival; PSA: Probabilistic sensitivity analysis.

Table 1. Base case analysis parameters (cont.).

Treatment costs per cycle			
Stage IV			
Pre-progression state			
First year (per cycle)	€14,640	Gamma	[30,32–37], local experts [‡]
Second year (per cycle)	€1728	Gamma	[30,32–37], local experts [‡]
Follow-up (per cycle)	€22	Gamma	[30]
Post-progression state (one-time cost)			
Follow-up (per cycle)	€22	Gamma	[30]
End of life	€2393	Gamma	[38]
Utilities			
Pre-progression state			
Stage I	0.71	Beta	[39]
Stage II	0.68	Beta	[39]
Stage III	0.67	Beta	[39]
Stage IV	0.66	Beta	[39]
Post-progression state			
Stage I	0.67	Beta	[39]
Stage II	0.67	Beta	[39]
Stage III	0.66	Beta	[39]
Stage IV	0.66	Beta	[39]
Lung cancer-free participants [†]			
Age-dependent utility values			
45–54	0.94	Beta	[40]
55–64	0.90	Beta	[40]
65–74	0.86	Beta	[40]
≥75	0.76	Beta	[40]
Survival			
OS (5-year survival rate)			
Stage I	54.8%	NA	[41]
Stage II	28.6%	NA	[41]
Stage III	10.6%	NA	[41]
Stage IV	2.2%	NA	[41]
D/PFS (1-year D/PFS rate)			
Stage I	50%	NA	[42]
Stage II	50%	NA	[43]
Stage III	10.5%	NA	[44]
Stage IV	1.4%	NA	[32,45,46]
Background mortality			
Life expectancy by age	General population	Beta	[47]

[†] Lung cancer-free participants refer to people who either do not have lung cancer or have not been identified with lung cancer.

[‡] An overview of the local experts can be found in S6 Table.

CT: Computed tomography; D/PFS: Disease/progression-free survival; NA: Not applicable; OS: Overall survival; PSA: Probabilistic sensitivity analysis.

smoking rate was 18.6%, regardless of the pack years, for both sexes in the year 2022 [3,28]. Consequently, the total population eligible for screening amounted to 170,808 in Lithuania. The screening participants were estimated to be 79,426 based on an uptake rate of 46.5%, which was determined by the uptake rates observed in the current national screening programs for breast, colorectal and prostate cancer in Lithuania [24–26]. Real-world evidence from the NHS England LCS Programme demonstrated a comparable uptake rate of 49%, supporting the feasibility of achieving participation rates within this range in routine LCS practice [48]. The adherence rate was assumed to be 100%, based on a study evaluating the cost-effectiveness of LCS with LDCT [49]. The number of lung cancers

detected in the no screening arm was calculated by the lung cancer incidence rate in the age category 50–74 and the current stage distribution at the time of diagnosis [27].

Survival

OS data was obtained from the Lithuanian Cancer Registry database and used to calculate the transition probability of patients transiting from the post-progression to death health state [41]. This registry covered the entire territory of Lithuania and contained comprehensive data concerning patient demographics and tumor characteristics, tracking all cancer patients until their death. The survival analysis included patients with primary invasive lung cancer (International Classification of Diseases, Tenth Revision [ICD-10] C34) diagnosed between 2013 and 2017, the most recent period with complete data. Patients were followed up until 31 October 2022. Among the extracted survival data, patients diagnosed before the age of 75 were categorized by the stage at diagnosis. Patients who died due to other causes than lung cancer were included in the analysis. Missed individuals were assumed to follow the OS rates of patients with lung cancer stage II.

Disease-free survival (DFS) and progression-free survival (PFS) were used to inform the transition probabilities of patients transiting from the pre- to post-progression health state in the Markov trace. DFS data for stage I patients were derived from a retrospective study conducted in the UK [42]. For stage II patients DFS rates were obtained from a clinical trial for early-stage lung cancer patients receiving surgery and chemotherapy [43]. PFS data for stage III and IV patients were synthesized from various clinical trials, representing the different lung cancer types and treatment options [32,44–46,50,51].

To reflect a lifetime horizon, survival extrapolation was performed using the statistical method supported by the NICE Technical Support Document and Guyot *et al.* using R Studio (2022.12.0 + 353) [52,53]. Details about distribution functions fitted per extrapolated survival curve are presented in [Supplementary Table 1](#). Background mortality was used to account for all-cause mortality in the model and was based on life tables for Lithuania for the year 2020 and applied to both the screening and no screening arm [47].

Utilities

Lung cancer stage-specific utility values were obtained from a study using the British matrix, as suggested by the experts in the absence of the local data recommended by national guidelines [22,39]. For individuals in the preprogression state, the utility estimates were 0.71, 0.68, 0.67 and 0.66 for stages I, II, III and IV, respectively. The utility value of stage III lung cancer was applied (0.67) to progressive stage I and II patients in postprogression state, whereas the utility value of stage IV lung cancer (0.66) was used for progressive stage III and IV patients in the postprogression state, reflecting the disease deterioration [39]. Age-dependent utility norms for the general population were applied to those without a lung cancer diagnosis. In the absence of Lithuanian-specific life tables, EQ-5D index values from Poland were used as proxies because the two countries exhibit comparable population health characteristics, including life expectancy, population ageing and healthcare expenditure, as well as analogous cultural and healthcare systems, as suggested by the experts [40,54].

Costs

Direct costs, which encompassed recruitment, screening, diagnostic workup and treatment costs, were included to evaluate the cost-effectiveness of LCS from a healthcare perspective. Costs derived from international sources in the absence of Lithuania-specific data were adjusted to the Lithuanian context using purchasing power parities (PPP) and inflated to 2022 values in accordance with the Lithuanian health technology assessment guidelines [22,55,56]. Specifically, all costs were first inflated to 2022 price levels. Costs reported in Polish currency were then converted into US dollars by dividing the Polish costs by Poland's PPP, after which the resulting US dollar values were converted into Lithuanian costs by multiplying them by Lithuania's PPP.

Recruitment costs, consisting of an information package, were retrieved from the pricelist published by the Lithuanian NHIF and applied to the eligible screening population [29]. Screening costs were calculated based on the unit costs for an LDCT scan, which were obtained from the NHIF pricelist [29].

Diagnostic procedures for lung cancer patients consist of imaging studies with chest CT or FDG-PET, percutaneous cytologic analysis or biopsy, bronchoscopy, surgical procedures, among which endobronchial ultrasound is the most operated one, as well as the pulmonologist consultation and lung cancer tissue genetic testing. The unit costs per diagnostic procedure were derived from the NHIF pricelist and clinical experts [29]. Additionally, clinical experts were consulted to provide the utilization values per diagnostic procedure, reflecting the situation in the

Vilnius (Lithuanian capital) area. The weighted diagnostic costs per person were calculated based on these costs and utilization per procedure ([Supplementary Table 2](#)) and were applied to screening participants who received a positive or a false-positive CT scan result in the screening arm and to those individuals who experienced lung cancer-related symptoms in the no screening arm. Additional costs of a pulmonologist consultation were applied to patients in the no screening arm, as they were diagnosed through clinical presentations.

The lung cancer pathway and utilization values were obtained from Lithuanian clinical experts. For stage I and II lung cancer patients in the pre-progression state, the first-line treatment options consisted of surgery with or without (neo) adjuvant chemotherapy and radiotherapy. For stage III and IV lung cancer patients, besides the conventional therapies, novel treatments (immunotherapy and targeted therapy) were also included in the treatment pathway. Respiratory surgery costs were provided by the Lithuanian clinical experts. Due to the lack of Lithuanian-specific costing data, radiotherapy and chemotherapy for lung cancer were retrieved from a Polish costing study as Poland is economically similar to Lithuania [30]. Novel treatment costs per patient were calculated based on costs retrieved from Lithuania's NHIF [33], and median or mean treatment durations published by international clinical trials [32,34–37]. One-time the cycle cost of first-line stage III patients was applied to stage I and II patients entering the post-progression state in the Markov trace, mimicking the treatments that stage I and II patients receive as their cancer progress or recurs. Radiotherapy and chemotherapy costs were applied to stage III and IV patients entering the post-progression state [30]. More information regarding the treatment costs and utilization values is reported in [Supplementary Table 3](#). For all patients follow-up costs after first- and second-line treatment were taken into account. Follow-up costs for stage I and II patients after first-line treatment included pulmonologist consultation and CT scan costs in the first 5 years after the initial treatment, which corresponds to the guideline of the European Society of Medical Oncology (ESMO) ([Supplementary Table 4](#)) [31]. For post-progression stage I and II patients and all stage III and IV patients, the follow-up costs were obtained from a Polish costing study [30]. End-of-life costs were obtained from a British study and applied to all patients who died from lung cancer, as this was the best available source [38].

Sensitivity analyses

One-way (univariate) sensitivity analysis (OSA) was performed using a variance of 20% on deterministic parameters to identify the principal determinates influencing the ICER, and the results are presented in a tornado diagram. Probabilistic sensitivity analysis (PSA) was conducted by 1000 iterations to evaluate model uncertainty, and the results are presented in an incremental cost-effectiveness scatterplot.

Scenario analysis

Several scenario analyses were conducted to explore the cost-effectiveness of LCS under different costs, clinical estimates, and different assumptions in the model structure. The cost-effectiveness was tested under various CT scan costs and immunotherapy costs. Additionally, the cost-effectiveness of LCS was investigated by applying lower diagnostic costs for false-positive screened individuals while the diagnostic remained unchanged for the true-positive cases, given the uncertainty regarding variations in the diagnostic follow-up pathway for false-positive screened individuals. Another scenario focused on the cost-effectiveness by increasing the background mortality rate, as the general health of smoking individuals is overall reduced, leading to a higher background mortality rate [57]. Additionally, a scenario was included that investigated screening-associated disutility [58]. Lastly, variations in the lung cancer incidence in the screening and no screening arm were analyzed as the Lithuanian lung cancer incidence is not in line with the incidence in the Dutch NELSON study population which affected the screening performance data in our study [59,60]. All the parameters used in scenario analyses are summarized in [Supplementary Table 5](#) and all scenario analyses are listed in [Table 3](#).

Results

Base-case results

Annual LCS with volumetric-enabled LDCT resulted in an increment of 6117 early-stage (I and II) lung cancers and a reduction of 1874 late-stage (III-IV) lung cancers for one screening cohort over a lifetime horizon in Lithuania. Consequently, early detection of lung cancer led to 2606 premature lung cancer deaths averted, resulting in 21,639 LYs gained, 15,391 QALYs gained and 0.96 QALY gained per lung cancer patient.

The recruitment costs and screening costs for an LCS program were approximately €0.4 million and €38.1 million, respectively. Over a lifetime horizon, LCS led to a reduction in treatment costs amounting to €37.8 million,

primarily attributed to a decrease of €64.0 million in the treatment costs associated with late-stage (III and IV) lung cancer. The total incremental costs were approximately €21.1 million. This resulted in an ICER of €1372 per QALY gained for annual screening in Lithuania from a healthcare payer perspective (Table 2).

Sensitivity analyses

OSA showed that the most influential parameter was the costs provided in the first 6 months to individuals in stage IV pre-progression state, varying the ICER from €748 to €1996 per QALY. Other key drivers were the screening costs, diagnostic costs provided to the false-positive individuals, stage I treatment costs, utility value for stage I pre-progression patients, smoking rate and diagnostic costs for the screening and no screening arm. All ICER variations of the OSA were under the WTP threshold of €23,806 per QALY, equal to one-time the GDP per capita in Lithuania (Figure 1). PSA resulted in a probabilistic ICER of €1303 per QALY with a cost-effectiveness probability of 100%. Figure 2 shows the outcomes of the probabilistic simulations and the cost-effectiveness acceptability curve in which all outcomes were under the WTP threshold.

Scenario analysis

All scenario outcomes fell below the WTP threshold (one-time the GDP of €23,806), as presented in Table 3. The major impact of CT scan costs on the ICER is shown by the fact that an increase in CT scan costs by 50% resulted in an increased ICER of €2610 per QALY. Meanwhile, lowering the diagnostic costs for false-positive cases by 50% resulted in a decreased ICER of €651 per QALY. The scenario focusing on the lung cancer incidence in Lithuania showed that increasing the lung cancer incidence rate in the Lithuanian population, resulted in total cost savings (€89.8 million) and more incremental QALYs gained (18,618).

Discussion

This study provided evidence on the cost-effectiveness of LCS with volumetric-enabled LDCT screening for high-risk individuals, compared with no screening in Lithuania. The base case analysis revealed an ICER of €1372 per QALY, with incremental costs of €21.1 million and incremental QALYs of 15,391. In addition, LCS resulted in 6117 more lung cancers detected at an early stage, and 2606 premature lung cancer cases averted. Sensitivity analysis indicates that results are robust, showing an average probabilistic ICER of €1303 per QALY. The PSA demonstrated a broad range of incremental costs. Although all PSA simulations remained below the willingness-to-pay threshold, the variation in incremental cost (–€56.5 million to +195 million) indicates uncertainty regarding the potential budget impact of nationwide implementation, likely driven by variability in model assumptions and key input parameters.

This is to our knowledge the first analysis evaluating the cost-effectiveness of LCS in Lithuania. Our findings are consistent with the existing literature. A systematic review showed that most of the studies reported that LCS would be cost-effective [49]. Cost-effectiveness studies from Poland and Hungary showed an ICER of €1354 per life year and €6968 per QALY [30,61]. Compared with a German study (ICER: €30,291 per QALY) our cost-effectiveness ICER appears relatively low. This may be explained by our inclusion of costly late-stage immunotherapy, the relatively lower CT scan costs in Lithuania compared with Germany, and our use of a lifetime time horizon versus the 15-year horizon in the German study [62].

The sensitivity analysis indicated that lung cancer stage IV treatment costs had the biggest impact on the ICER, primarily explained by the elevated expense related to immunotherapy. Reducing the immunotherapy costs by 50% resulted in an ICER of €2741 per QALY, surpassing the base case ICER and aligning more closely with the studies that did not incorporate late-stage immunotherapy costs [49,61].

Secondly, the CT scan costs (€42) were an influential parameter affecting the ICER. However, these costs might increase over time, as with each repetition of LDCT, the assessment duration is prolonged due to the necessity for radiologists to compare with prior scans. Nevertheless, scenario analyses revealed that increasing the CT scan costs by 10% and doubling the CT scan costs increased the ICER to €1620 and €3849 per QALY, respectively, indicating that this rise in CT scan costs resulted in marginal changes in the ICER. Conversely, LDCT LCS could potentially be more cost-effective with the usage of artificial intelligence (AI) guided imaging reading. Introducing the use of AI guided imaging reading in a volume-based LDCT screening program reduces radiologists' workload by shortening the time of lung nodule detection and assessment of its size dynamics and improves the screening performance [63].

Table 2. Base case cost-effectiveness analysis results: clinical outcomes, health outcomes, direct costs and health economic outcomes.

Clinical and health outcomes	Screening	No screening	Incremental
Lung cancer diagnoses			
Total	16,083 (100%)	11,840 (100%)	4243
Stage I	7169 (45%)	1080 (9.1%)	6089
Stage II	1606 (10%)	1578 (13.3%)	28
Stage III	3621 (23%)	3809 (32.2%)	-188
Stage IV	3687 (23%)	5373 (45.4%)	-1686
Missed individuals	NA	4,243	NA
Stage III and IV averted	1874		
Lung cancer deaths			
Total	11,393	13,999	-2606
Stage I	3321	500	2820
Stage II	1097	1077	20
Stage III	3393	3567	-175
Stage IV	3583	5220	-1638
Missed individuals	NA	3634	NA
Life Years			
Total	2195,320	2173,681	21,639
Stage I	39,309	5896	33,414
Stage II	5512	5370	141
Stage III	5018	5254	-236
Stage IV	2497	3636	-1138
Missed individuals	NA	10,541	NA
Lung cancer-free individuals [†]	2142,985	2142,985	0
QALYs			
Total	1882,749	1867,358	15,391
Stage I	29,741	4459	25,282
Stage II	4075	3967	108
Stage III	3357	3515	-158
Stage IV	1648	2399	-751
Missed individuals	NA	9089	NA
Lung cancer-free individuals [†]	1,843,928	1,843,928	0
Cost outcomes (€)			
Total	€386,774,935	€365,658,478	€21,116,457
Recruitment costs	€428,729	–	€428,729
Screening costs	€38,120,648	–	€38,120,648
Diagnostic costs	€71,046,593	€50,706,113	€20,340,481
Treatment costs	€277,178,965	€314,952,365	€-37,773,400
Stage I	€30,649,255	€4604,976	€26,044,278
Stage II	€7268,733	€7103,921	€164,812
Stage III	€110,515,073	€115,783,743	€-5268,670
Stage IV	€128,745,904	€187,459,724	€-58,713,821
Health economic outcomes			
ICER per QALY	€1372		
NMB [‡]	€345,286,878		

[†] Lung cancer-free individuals refer to the screening participants who do not have lung cancer.

[‡] Calculated based on one-time the GDP (€23,806).

ICER: Incremental cost-effectiveness ratio; NA: Not applicable; NMB: Net monetary benefit; QALYs: Quality-adjusted life year.

Table 3. Results of scenario analyses: costs, quality-adjusted life years and incremental cost-effectiveness ratios.

Scenario name	Screening		No screening		Incremental total costs	Incremental QALYs	ICER
	Total costs	Total QALYs	Total costs	Total QALYs			
Base case	€386,774,935	1882,749	€365,658,478	1867,358	€21,116,457	15,391	€1372
Time horizon - 5 year	€161,360,805	675,831	€151,055,279	675,070	€10,305,526	762	€13,525
Time horizon - 10 year	€279,182,129	1158,514	€263,621,538	1154,953	€15,560,591	3561	€4369
Time horizon - 15 year	€360,828,338	1485,292	€341,589,894	1477,813	€19,238,444	7479	€2572
Decrease discount rate (costs: 0%, health outcomes: 0%)	€488,971,210	2649,956	€462,723,124	2622,861	€26,248,085	27,095	€969
Increase discount rate (costs: 6%, health outcomes: 6%)	€333,965,873	1547,052	€315,415,215	1536,248	€18,550,659	10,804	€1717
Screening uptake rate of 25%	€379,298,025	1885,862	€367,746,862	1877,587	€11,551,163	8275	€1396
Screening uptake rate of 75%	€396,686,187	1878,623	€362,890,155	1853,799	€33,796,033	24,825	€1361
Adherence rate of 90%	€381,674,936	1884,817	€367,034,411	1875,300	€14,640,525	9,517	€1538
Adherence rate of 70%	€378,390,537	1886,440	€368,273,875	1881,420	€10,116,663	5,019	€2016
Adherence rate of 50%	€377,395,553	1887,053	€368,788,281	1883,693	€8,607,272	3,360	€2562
OS for missed individuals equals stage I patients	€386,774,935	1882,749	€365,658,478	1871,891	€21,116,457	10,859	€1945
OS for missed individuals equals stage III patients	€386,774,935	1882,749	€365,658,478	1863,438	€21,116,457	19,312	€1093
OS for missed individuals equals stage IV patients	€386,774,935	1882,749	€365,658,478	1860,817	€21,116,457	21,932	€963
Reduction of LC incidence in screening population according to LC incidence ratio between Lithuania and The Netherlands	€342,228,966	1896,167	€369,270,500	1885,113	-€27,041,535	11,054	-€2446
Adjust the lung cancer incidence in the non-screened population to match the incidence rate observed in The Netherlands (0.86%)	€510,715,976	1857,844	€600,512,022	1839,226	-€89,796,046	18,618	-€4823
Increase background mortality by 100%	€334,024,144	1454,154	€315,220,705	1444,736	€18,803,439	9419	€1996
Include increase OS for stage III and IV patients by an HR of 0.9	€390,521,046	1882,838	€371,091,914	1867,470	€19,429,131	15,368	€1264
Include increase OS for stage III and IV patients by an HR of 0.8	€394,265,368	1882,927	€376,522,917	1867,583	€17,742,451	15,345	€1156
Include screening-associated disutility	€386,774,935	1881,265	€365,658,478	1867,358	€21,116,457	13,907	€1518
Decrease CT scan costs by 50% (€21)	€367,714,611	1882,749	€365,658,478	1867,358	€2,056,133	15,391	€134
Increase CT scan costs by 10% (€47)	€390,587,000	1882,749	€365,658,478	1867,358	€24,928,522	15,391	€1620
Increase CT scan costs by 50% (€64)	€405,835,259	1882,749	€365,658,478	1867,358	€40,176,781	15,391	€2610
Double CT scan costs (€84.96)	€424,895,583	1882,749	€365,658,478	1867,358	€59,237,105	15,391	€3849
Double recruitment costs (€5.02)	€387,203,664	1882,749	€365,658,478	1867,358	€21,545,186	15,391	€1400
Decrease immunotherapy unit costs by 50%	€299,851,737	1882,749	€257,671,611	1867,358	€42,180,125	15,391	€2741
Decrease diagnostic costs for false positive individuals by 50% (€1213)	€375,682,991	1882,749	€365,658,478	1867,358	€10,024,513	15,391	€651

†The positive screening outcomes were decreased using a ratio based on the difference between the lung cancer incidence in Lithuania and The Netherlands.
CT: Computed tomography; HR: Hazard ratio; LC: Lung cancer; OS: Overall survival.

It was observed that the increased incidence rate due to screening was 35.8%. This over-exceeding screen-detected lung cancer is also seen in other countries, such as The Netherlands where the NELSON was performed [7]. This may be attributed to asymptomatic patients in the no screening scenario, in whom the underlying disease remained undetected. Therefore, to provide a conservative estimate of the benefits provided by LCS, we also included this asymptomatic cohort in the no-screening arm and called them “missed individuals”. However, the proportion of the missed individuals in Lithuania amounted to 24.6%. This might be partially explained by the mismatch of the high smoking rate in Lithuania decades ago (41.2% in the year 2000), and the lung cancer incidence nowadays (0.52%), as the counterparts in The Netherlands were 32% smoking rate in the year 2000 and 0.87%

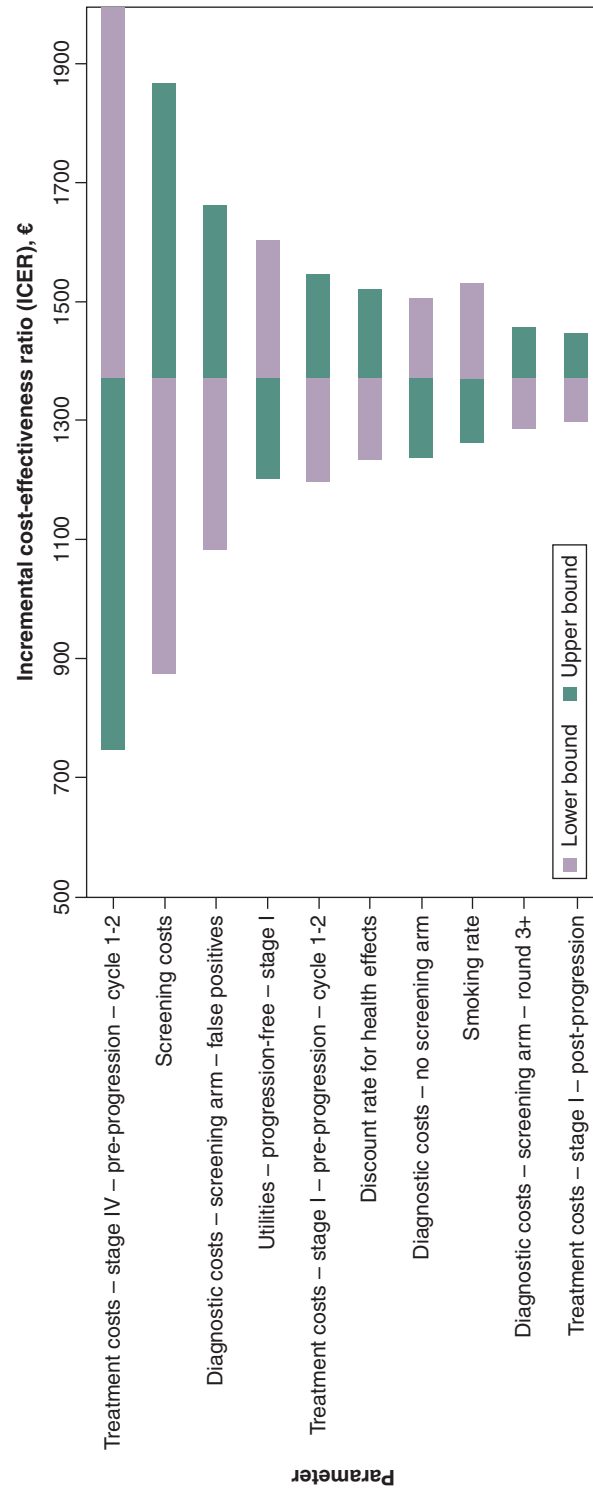


Figure 1. One-way sensitivity analysis tornado diagram. The lower bound value corresponds to a 20% decrease while the upper bound corresponds to a 20% increase in the base case parameter value.

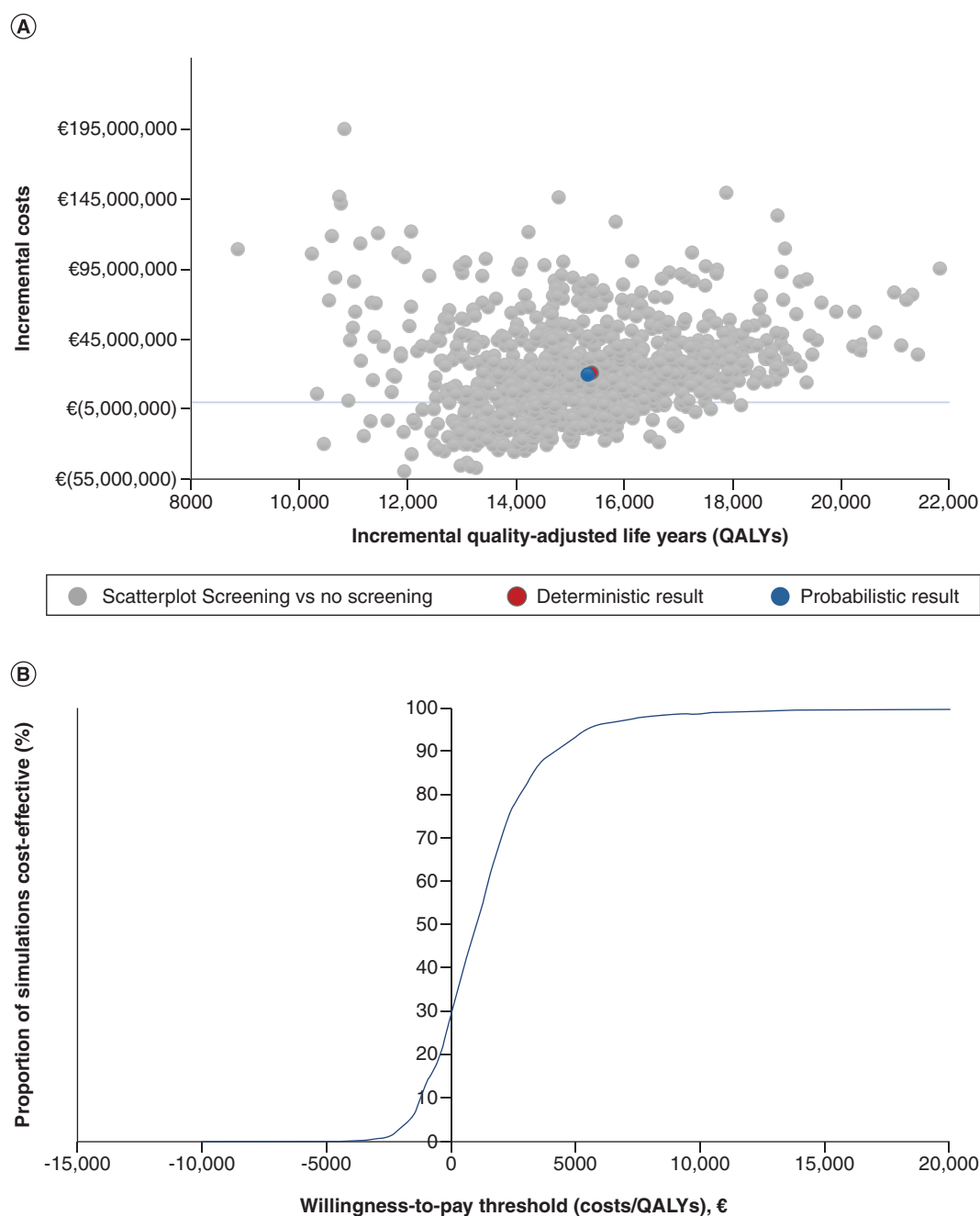


Figure 2. Results obtained from 1000 Monte Carlo simulations for the probabilistic sensitivity analysis. (A) Incremental cost-effectiveness scatterplot. (B) Cost-effectiveness acceptability curve.
QALY: Quality-adjusted life year.

incidence nowadays [64]. The trend in incidence correlates with the high tobacco consumption decades ago [65]. The discrepancy between lung cancer incidence and smoking rate could be due to other competing mortality outcomes such as ischemic heart disease [66]. Therefore, we have employed scenario analysis to explore a higher lung cancer incidence in the no-screening arm, and results showed more health gain and cost-saving compared with the base case.

The low participation rate (5.8%) and adherence rate of the implemented LCS screening program in the United States are causing some concerns [67,68]. However, in Europe, the participation rate seemed more favorable with

53.0% and 51.1% for the UK LCS pilot and the NELSON study, respectively [69,70]. Various uptake rates and adherence rates were tested in our analysis, revealing that high uptake rates would yield more health advantages and efficient utilization of resources allocated to screening. An uptake rate of 25% resulted in 0.58 QALY gained per lung cancer patient compared with 1.34 QALY gained per lung cancer patient at an uptake rate of 75%. To achieve high uptake rates personalized recruitment strategies have been proven to increase the coverage of screening programs [71]. Therefore, a centrally organized information system, covering the recruitment of participants, is recommended when implementing LCS in Lithuania, as the current running nationwide screening programs in Lithuania have limited coverage and participation [72,73]. Evidence from LCS pilot studies suggests that the implementation of such systems may involve substantial infrastructural requirements, including a robust data management system and the allocation of additional administrative resources for program coordination. These resources are needed to support key functions such as patient navigation, reminder systems, provider education, targeted awareness initiatives, appointment scheduling, and systematic recall [74,75].

Most limitations of this model mirror those observed in the original UK model [17]. Additionally, although a literature search was performed for the best Lithuania-specific available data, studies on quality of life and costing data were lacking. Therefore, data sources from the UK and Poland were used as an alternative for missing data. These limitations were mitigated by OSA and PSA. One of the strengths of the model was the Lithuanian OS data used to reflect the local context. This data included patients diagnosed between 2013 to 2017 and were followed up till 2022. For the costing part, we did include novel therapies for stage III and IV patients while the increased use of novel therapies for lung cancer treatment started after 2017, indicating that the local OS data partly reflects the introduction of novel therapies. Moreover, to enhance treatment accessibility and improve life expectancy of cancer patients, changes to pharmaceutical policies have been introduced by the Lithuanian government since 2017 [72]. This change aimed to benefit all individuals who face out-of-pocket pharmaceutical expenses. Therefore, the analysis potentially underestimates the health outcomes for stage III and IV patients, as improvements in OS data are expected since 2017, indicating a potential overestimation of the ICER.

Currently, the chest LDCT is underutilized in an LCS program. Extending screening to lung cancer, chronic obstructive pulmonary disease, and cardiovascular disease is likely to improve the cost-effectiveness and health benefits [76–78]. Furthermore, screening in the high-risk population defined solely by age and smoking behaviors may not be socially fair, as lung cancer also occurs among ever- and never-smokers and an increasing trend of lung cancer among never-smokers has been observed [79,80]. In addition, due to the strict eligibility criteria, LCS misses out on more than 50% of lung cancers [81,82]. This was supported by a prospective cohort study which showed a higher cumulative lung cancer diagnosis hazard in the screening group who were selected irrespective of their smoking history [83]. Therefore, further implementation studies could focus on expanding the target group for screening, as well as the detection of other comorbidities alongside lung cancer concurrently through the LDCT, as envisioned by the Lithuanian lung cancer experts and representatives. Thereafter, further investigations into the cost-effectiveness of LCS under the new findings and insights could be carried out to pave the way for evidence-based decision-making.

Conclusion

This study provides evidence that annual LCS with volume-based LDCT compared with no screening for a high-risk population could be cost-effective in Lithuania. Premature lung cancer deaths were averted, resulting in QALYs and LYs gained. The screening and diagnostic costs were the main drivers for the incremental costs. Although we aimed to include only Lithuanian-specific data, some inputs were derived from other countries due to unavailable local data. Future screening studies should focus on the optimization of the program and further investigations into the cost-effectiveness of such optimized LCS program. This could include investigating a central information and recruitment system to increase the screening uptake rate, monitoring the potential over-exceeding screen-detected lung cancers and the possibility of extending screening to other diseases such as chronic obstructive pulmonary disease, and cardiovascular disease.

Supplementary data

To view the supplementary data that accompany this paper please visit the journal website at <https://becarispublishing.com/doi/epdf/10.57264/cer-2026-0034>

Author contributions

HT Berge, G Piazza and X Pan contributed to the conception and design of study. HT Berge, G Piazza and T Bukšnys conducted the data acquisition. HT Berge, G Piazza and D Ramaker were responsible for the data analysis. All authors reviewed and participated in the interpretation of the data. E Danila provided critical feedback and supervision throughout the research process. HT Berge and G Piazza drafted the manuscript. All authors participated in the data validation, data interpretation and critical revision of the paper. Final approval of the manuscript was given by all authors.

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Competing interests disclosure

H ten Berge, G Piazza, D Ramaker and X Pan are employed by iDNA. T Bukšnys is employed by AstraZeneca. The authors have no other competing interests or relevant affiliations with any organization or entity with the subject matter or materials discussed in the manuscript apart from those disclosed.

Writing disclosure

No funded writing assistance was utilized in the production of this manuscript.

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Summary points

- Cancer mortality in Lithuania is above the European average. Lung cancer stands as the leading cause of cancer-related mortality in Lithuania, with low overall survival. Screening with low-dose computed tomography for high-risk individuals can facilitate the detection of lung cancer at earlier stages, subsequently reducing lung cancer-specific mortality.
- This study evaluated the long-term clinical and economic outcomes of an annual lung cancer screening (LCS) program compared with no screening, adopting a lifetime horizon and the Lithuanian healthcare system perspective.
- A validated cost-effectiveness model originally developed for the UK was adapted to the Lithuanian context and informed by data from the Dutch–Belgian NELSON trial. The model comprised a decision tree with an integrated Markov structure reflecting lung cancer progression across stages I–IV, including transitions to post-progression and death.
- Overall survival data was obtained from real-world data registered by National Cancer Institute of Lithuania.
- The total incremental cost of the LCS program was €21.1 million. The primary contributors that affect the ICER the most were treatment costs for stage IV patients and CT scan costs for the screening. Also, the CT scan costs for screening were the primary contributor to the overall program costs.
- Annual LCS using increased the detection of 6117 early-stage (I and II) lung cancers while reducing the number of 1874 late-stage (III and IV) cases over a lifetime horizon in Lithuania. This shift toward earlier detection consequently averted 2606 premature lung cancer deaths in the screened cohort.
- The screening program yielded 15,391 incremental QALYs and 21,639 additional life-years. On a per-patient basis, this equates to 0.96 QALY gained for each individual diagnosed with lung cancer, demonstrating the health benefits of screening.
- The results demonstrate that annual LCS represents a potentially cost-effective strategy in Lithuania, yielding an ICER of €1372 per QALY gained in comparison to no screening.

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