



*Strengthening the screening of Lung Cancer in Europe*

## MS5. Cost-effectiveness

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<b>Lead beneficiary</b>	UHAM
<b>Author(s)</b>	Prof. Dr. Tom Stargardt, Carsten Wältner
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## Abbreviations

LC	Lung cancer	RCT	Randomized control trial
PLCO	Prostate, Lung, Colorectal and Ovarian	EU	European Union
QALY	Quality adjusted life year	QoL	Quality of life
LDCT	Low-dose computed tomography	ICER	Incremental cost-effectiveness ratio

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## Executive summary

LC is the leading source of cancer-related mortality worldwide, largely due to late-stage diagnosis. Around 60% to 75% of cases are detected at advanced stages, where five-year survival rates range from 7% to 31%. LDCT screening enables earlier detection and substantially improves survival outcomes. While LDCT screening has been shown to be cost-effective in several regions. However, evidence from Central, Eastern and Southern Europe remains scarce. In addition, studies incorporating modern targeted therapies and immunotherapies and productivity gains are missing.

We evaluated the cost-effectiveness of (national) LDCT screening programs for Croatia, Estonia and Poland. We developed a decision-analytic model (e.g., Markov model) to simulate the effect of the different screening algorithms compared to no screening for a cohort of eligible individuals on quality adjusted life years (QALYs) and costs. The model consists of three parts, (1) a Markov model which captures disease progression (undetected LC cases), (2) a decision tree modeling the screening algorithm for each country and (3) a Markov model simulating treatment and aftercare. Country specific data and data from the literature were used for parametrization.

Results show ICERs ranging from €9,414 per QALY gained for Croatia to €22,201 per QALY gained for Estonia. Moving from no screening to screening in Poland was estimated to cost €20,600 per QALY gained. Cost differences per patient between the two cohorts ranged from €498 in Croatia to €1,654 in Estonia. QALYs gained per patient ranged from 0.0529 in Croatia to 0.0749 in Estonia. Budget impact was estimated to be between 0.1% to 0.3% of a countries' total health care spending.

LDCT screening is cost-effective taking WHO-recommended thresholds for health care interventions into account. LDCT costs per scan, incidence of LC and LDCT sensitivity are factors which mostly influence the outcome (ICER). Biennial screening algorithms lower costs compared to annual screening intervals with the Croatian algorithm representing a compromise of the two different approaches.

If cost-effectiveness and/or budget impact are of primary concern, LC screening programs should carefully define eligibility criteria as this determines incidence and thus the number of screens needed to detect a case of LC. Most LC cases are found in higher age groups and incidence increases with the intensity of smoking history. Use of targeted therapies and/or immunotherapies only mildly effect the cost-effectiveness of LC screening programs.

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## 1. Introduction

Lung cancer (LC) has become by 2022 the most diagnosed cancer worldwide while also leading to the most cancer related deaths (Bray et al. 2024). LC survival is fairly low as most cases are found in later stages where 5-year survival ranges from 7% to 31%. Randomized clinical trials that were launched in multiple countries have shown stage-shifts to earlier diagnosis where 5-year survival is much higher, i.e. 60%-82% (Rami-Porta et al. 2024; Allemani et al. 2018). Evidence on cost-effectiveness, a prerequisite for the implementation of LC screening in most countries, mainly stems from Western Europe, North America or Asia, while it is scarce for countries in Central, Eastern and Southern Europe.

In general, LC screening tends to be slightly less cost-effective compared to other screening programs such as colon or breast cancer (Poon et al. 2022; Fabbro et al. 2022; Mathew et al. 2025). Results on cost-effectiveness range from €3,297 per QALY gained for Italy to more than €100,000 per QALY gained for Switzerland, while for the US cost per QALY can reach up to \$288,100 due to the higher prices (Adams et al. 2023). Studies also demonstrated differences due to mode of screening and/or screening algorithms. Biennial screening is known to lead to lower costs compared to annual screening, while annual screening leads to more QALYs gained (Toumazis et al. 2021).

However, most of the previous results are based on RCT data rather than on data from real-world implementations of LC screening and are therefore highly regulated in recruitment, the length of follow-up or the approach in general. Also, data collection on the same individuals over several years may lead to higher detection rates. I.e., the sensitivity of performed LDCT for individuals that are screened multiple times over their period of eligibility is higher (Nijs et al. 2025). Furthermore, most existing cost-effectiveness studies do not include the newer targeted therapies and immunotherapies into modeling treatment and disregard productivity gains. Budget impact analyses of LC screening programs are also rare.

First, we contribute to the existing literature by using real-world data coming from three different (pilot) programs, with one being the first nationwide implementation of a LC screening program. Second, we incorporate the newer targeted therapies and immunotherapies into cost-effectiveness analyses of LC screening. Third, our models include indirect costs. Finally, we calculate the long-term budget impact of these programs on national health expenditure. Thereby, we provide the much-needed evidence on cost-effectiveness of LC screening in Central, Eastern and Southern European countries.

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## 2. Choice of countries

Part of our task was to categorize European healthcare systems in different archetypes in order to take different national cost levels as well as modes of screening into account. Then, based on different LC screening implementations through SOLACE (pilot) programs we were to develop a decision-analytic model (e.g., Markov model) and to perform cost-effectiveness analysis and budget-impact analysis for LC screening. Country- and pilot-specific input data were to be provided by public health and health economics experts from SOLACE partners.

Given the lack of evidence on LC screening in Central, Eastern and Southern European countries, we choose to model cost-effectiveness of LC screening for three different countries: Croatia, Estonia and Poland.

Thereby our choice represents different archetypes of health care systems and LC screening methodology with respect to the following criteria:

- (1) The three countries differ in the geographical area within the EU. Estonia as an Eastern European country and has a PPP-adjusted health expenditure per capita of €2,104, while Poland (€ 1,908) and Croatia (€ 1,859) belong to the Central and Southern European countries, respectively.
- (2) Spending on prevention as share of current health expenditure differ. While Croatia (5.3%) and Estonia (5.7%) are about the same in their investment in prevention, Poland (1.9%) invests less much less.
- (3) This is also reflected in the cost per LDCT within LC screening programs which show great variability (e.g., Croatia: €84, Estonia: €169, Poland €101).
- (4) Geographical coverage of LC screening also differed between the three countries. Croatia has the first national LC screening program worldwide. Estonia focused in their pilot program on the more urban capital area of Tartu which consists of approx. 10% of Estonia's total population while Poland specifically focused on screening in rural areas.
- (5) Croatia, Estonia and Poland differ in the organization of LC screening recruitment. Croatia and Estonia focus on a GP based approach with referrals to centralized (Estonia) or regionalized (Croatia) screening centers while Poland works with mobile screening units that bring (Laisaar et al. 2025; Samaržija et al. 2025; Moes-Sosnowska et al. 2025).
- (6) Croatia, Estonia and Poland differ in the mode of screening, i.e., the screening interval. Croatia's initial screening is followed up by a second screening after one year and then transitions into a biennial scheme while Estonia and Poland use an annual screening approach.

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### 3. Methods

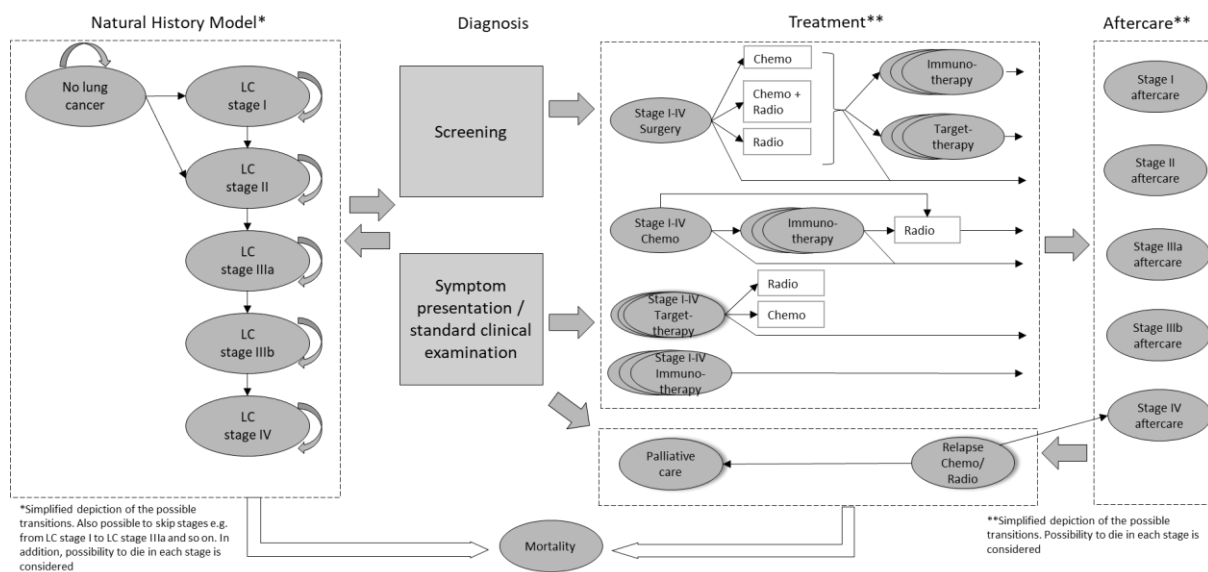
#### 3.1 Model

By following the approach of Hofer et al. 2018 we parametrized a Markov model that consists of three parts. First, we model the natural progression of undetected LC over time for each country in the eligible screening cohort, i.e., the natural history model. Second, we model a decision tree that simulates the screening in accordance with the respective national screening algorithm. Third, we use a second Markov model to simulate stage-specific treatment and aftercare. For each country, the model was customized to reflect variations in treatment but also in data availability, i.e., at different levels of aggregation (Figure 1, Figure 2, Figure 3).

For primary outcomes, we simulated costs per patient, quality adjusted life years (QALYs) gained per patient, the incremental cost-effectiveness ratio (ICER) and budget impact. Model run time was 15 years for Estonia and Poland and 20 years for Croatia due to differences in the underlying cohort that is eligible for the respective national screening program. Discounting according to nationally recommended discount rates was applied.

#### 3.1.1 Model adaptation for Croatia

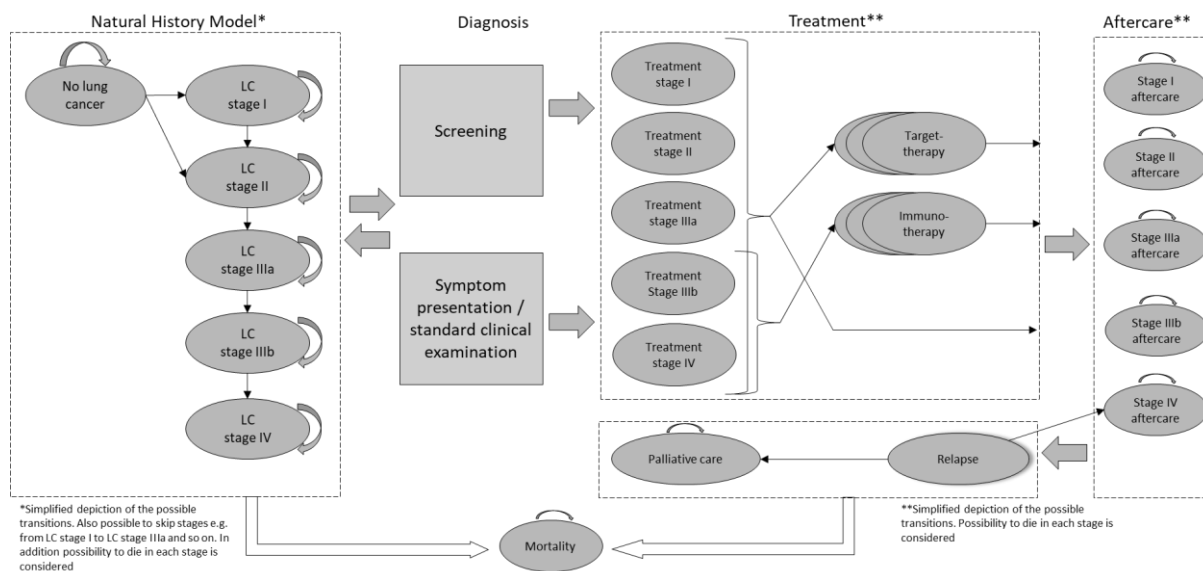
Figure 1: LCS Markov model for Croatia



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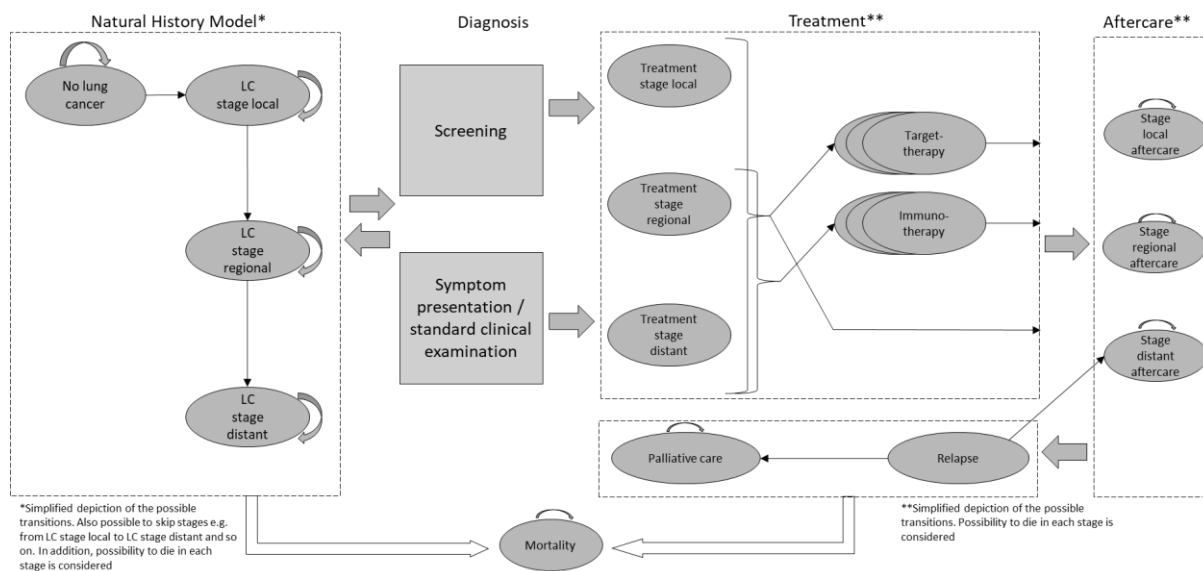
### 3.1.2 Model adaptation for Estonia

Figure 2: LCS Markov model for Estonia



### 3.1.3 Model adaptation for Poland

Figure 3: LCS Markov model for Poland



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## 3.2 Parametrization

### 3.2.1 Adaptation for Croatia

We used epidemiological data from the cancer registry in Croatia on the LC stage distribution before the introduction of LC screening and results from the national screening program to parametrize the natural history model. Cost data comes directly from Croatian reimbursement schemes, both for the screening costs and for treatment costs (bottom-up). Distribution of treatments was obtained from the national screening program. Quality of life (QoL) data was obtained from the literature (Blom et al. 2020). Data on productivity is based on employment in the respective age-groups and on the literature on return to work after treatment for LC (Državni zavod za statistiku 2025; Brink et al. 2024). Data on mortality was derived from the literature and was adjusted for the share of patients that received newer targeted therapies and immunotherapies in the treatment & aftercare model.

### 3.2.2 Adaptation for Estonia

We used epidemiological data from the Estonian cancer registry for LC stage distribution prior to screening and results from the regional screening pilot to parametrize the natural history model. Cost data for treatment stems from the Estonian health insurance fund, aggregated by stage. Prices for pharmaceuticals were obtained from Tartu university hospital. Screening costs were obtained from reimbursement schemes and reflect those used in the pilot. QoL data stems from the literature (Blom et al. 2020). Data on productivity is based on employment rates from official labor statistics (Statistics Estonia 2025; Ministry of Finance of Estonia 2023) and on the literature on return to work after LC treatment (Brink et al. 2024). Data on mortality for the natural history model stems from the literature (Detterbeck and Gibson 2008; David et al. 2017) whereas data on mortality for the treatment & aftercare model was obtained from the Estonian cancer registry (Cancer Registry | National Institute for Health Development (NIHD) 2025) and then adjusted for the share of individuals receiving the newer targeted therapies and immunotherapies.

### 3.2.3 Adaptation for Poland

For the Polish adaptation, we calibrated the natural history model using data from the Polish cancer registry and direct results from the Polish screening pilot. Furthermore, we obtained data on treatment costs per stage from the Polish national health fund (NFZ). Costs of screening were obtained from the mobile screening program. QoL data was obtained from the literature (Blom et al. 2020). Data on productivity and employment were obtained from official labor statistics (Eurostat 2025; Gus 2026) and from the literature on return to work after treatment for LC (Brink et al. 2024). Data on mortality for the natural history model was obtained from the Polish cancer registry and was adjusted for untreated LC (David et al. 2017). For the treatment & aftercare model, we modified mortality rates to reflect the share of individuals that receive the newer targeted therapies and immunotherapies.

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### 3.3 Budget impact analysis

Furthermore, we calculated the budget impact of each of the three programs taking into account the program characteristics, the countries' age distribution and the number of heavy smokers. We first estimated the eligible population size and then the annual inflow and outflow of individuals into eligibility over time. We then simulated the budget impact by running the model for each cohort.

### 3.4 Sensitivity analysis

We conducted both deterministic and probabilistic sensitivity analyses for all three countries. For the deterministic sensitivity analysis, we varied each parameter by 25% while for the probabilistic sensitivity analysis we followed standard procedure according to the literature (Olariu et al. 2017; Briggs et al. 2012).

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## 4. Results

### 4.1 Cost-effectiveness

The base-case results for each of the three countries (Croatia, Estonia and Poland) are displayed in Table 1. Results show an increase in costs per patient for screening while also leading to an increase in QALYs gained per patient compared to no screening. Both, Estonia and Poland, lead to more QALYs gained per patient compared to Croatia, which is due to the fact that both countries rely on an annual screening while Croatia employs a mixture of annual and biennial screening. The ICER per QALY gained ranges from €9,414 for Croatia to €22,021 for Estonia.

Table 1: Base-case results for the three countries included in this analysis

Country	Strategy	Cost per patient	QALYs per patient	ICER (Cost per QALY gained)
Croatia	No screening	€16,881	7.0456	€9,414
	Screening	€17,379	7.0985	
	Δ	€498	0.0529	
Estonia	No screening	€15,709	7.8271	€22,021
	Screening	€17,363	7.9021	
	Δ	€1,654	0.0749	
Poland	No screening	€21,290	7.4964	€20,600
	Screening	€22,663	7.5630	
	Δ	€1,372	0.0666	

### 4.2 Budget-impact analysis

We estimated the budget impact of implementing a nationwide LC screening program for each country, taking into account expected adherence to the program. We found that the impact on additional health care spending differed due to differences in eligibility, mode of screening and adherence. It was estimated to be between 0.1% to 0.3% of a countries' total health care expenditure. For Estonia the budget impact analysis resulted in estimated additional costs of the program of €96,027,451 (discounted) over 15 years. Annual cost in the first year were €9,690,086 which is 0.3% of Estonian total health expenditure. For Croatia the budget impact, is €67,430,628 (discounted) over 20 years. Annual costs for the first- and second-year amount to €8,442,693 and €8,708,948, respectively. From the third-year onwards, costs are much lower due to the change in the screening interval (annual to biennial) which results in less screenings.

### 4.3 Findings across the three countries

Additional costs of a LC screening program compared to no screening came mostly from the screening and the diagnostic follow-up itself. Depending on the country, costs due to screening and diagnostic follow-up amounted to between 51% and 72% of increased costs. Additional treatment costs amounted to between 18% and 27% depending on the country. This is due to the fact of more LC cases

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being detected under screening compared to no screening. Also, with LC screening, more later relapses occur so that more patients are treated for cancer a second time.

Additional aftercare costs & general health expenditure amounted to between 9% and 21% depending on the country. This is due to the costs of treating diseases other than LC during the increased survival time. These additional costs are only partly offset by productivity gains.

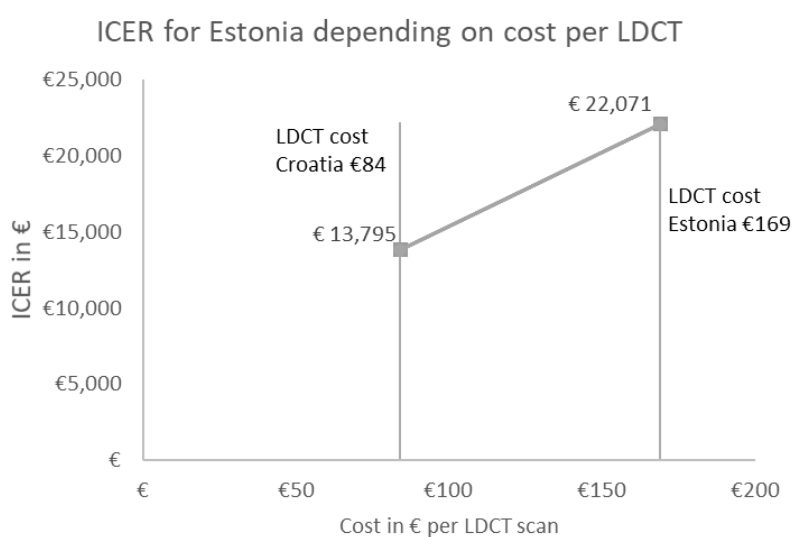
Targeted therapies and immunotherapies were no game changer in cost-effectiveness. Depending on their use, the ICER increased by between 10% and 15%. In addition, the real-world data used for parametrization seems to make a difference as it accounts for actual testing routines rather than relying on assumptions.

#### 4.4 Drivers of cost-effectiveness

Given the results of the sensitivity analyses, we found the following drivers of cost-effectiveness. First, the incidence of lung cancer itself. If the incidence of LC increases (decreases) by 25% the ICER respectively decreases (increases) by around 15-20%. Thus, the choice of cohort to be eligible for such a program is quite important for cost-effectiveness.

Second, if cost per LDCT scan increases (decreases) by 25% we found an impact on the ICER of similar magnitude. This explains to some extent differences in cost between countries. E.g., in Estonia, an LDCT amounts to €169. Compared to other European countries, this is quite high. According to Grover et al. 2022, most LDCT or CT costs in Europe range from €50 to €176. Also, among other Eastern and Southern European countries such as Hungary (€55 according to (Nagy et al. 2023)) and Greece (€91 according to (Pan et al. 2025)), Estonia seems to be an outlier. If we were to use cost per LDCT of €84 of Croatia in the Estonian model, the ICER would decrease by 38% (see figure 4).

Figure 4: Example Estonia - change of LDCT cost per scan and the impact on the ICER



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Finally, the mode of screening, more specifically the interval of screening is another driving factor for cost-effectiveness. Changing an annual screening interval to a biennial approach reduces the ICER in total by approximately 10-15%. This is due to the cost differences decreasing by approximately 43% while the loss in QALYs is more modest.

## 5. Lessons learned for LC screening implementation

Across all three country LC screening is cost-effective given local thresholds or taking WHO-recommended threshold into account (Kouakou and Poder 2022).

If cost-effectiveness and/or budget impact are of primary concern, LC screening programs should carefully define eligibility criteria as this determines incidence and thus the number of screens needed to detect a case of LC. Most LC cases are found in higher age groups and incidence increases with the intensity of smoking history. Cost per LDCT is another very influential parameter though probably less susceptible given that reimbursement is usually driven by historical patterns. Still, future development in AI may present an opportunity to reduce LDCT costs. In addition, the mode of screening (annual, biennial or a combination of the both) influences costs and benefits of LC screening programs. While biennial LC screenings offers better cost-effectiveness and lower budget impact, it also comes with less benefits for participants. Use of targeted therapies and/or immunotherapies while being a cost-driver of its own, only mildly effected the cost-effectiveness of LC screening programs.

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