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Cost-effectiveness of lung cancer screening in Saudi Arabia

Abstract

Objectives: Lung cancer is the deadliest cancer worldwide, with most cases being identified in a late stage where curative treatment is no longer an option. Tobacco use is the primary cause of lung cancer. Screening smokers has been shown to be a cost-effective intervention in multiple countries. This article aims to evaluate the cost-effectiveness of lung cancer screening in the Kingdom of Saudi Arabia.

Methods: A cost-effectiveness model consisting of a decision tree, determining the number of cases and the stage at diagnosis, along with a Markov model that projects the lifetime disease pathway. The model was developed to compare scenarios with and without lung cancer screening. The number of cases was determined using the overdiagnosis rate from the NELSON trial and current incidence rates, adjusted for differences between the trial and Saudi clinical practice. Six scenarios were analyzed, varying by age ranges and geotargeting, and assessed across multiple thresholds.

Results: In each scenario, screening results in additional cases identified, (quality-adjusted) life-years gained, and higher costs. The incremental cost-effectiveness ratios ranged from $31,222 when screening people aged 60–74 in the Eastern region to $110,042 when screening people aged 50–74 nationwide.

Conclusion: Depending on the willingness-to-pay threshold, lung cancer screening could be cost-effective nationwide for individuals aged 55–74, or only in the Eastern region for those aged 60–74, or in neither scenario. Implementing a pilot program in Saudi Arabia would provide additional information to determine the cost-effectiveness of implementing lung cancer screening.

Keywords: lung cancer, screening, LDCT, cost-effectiveness, Saudi Arabia

Volume 16 Issue 6 - 2025

Majid Abdulrahman Almadi,[1,2] Mashael Alrujaib,[3] Albertus Constantijn Sloof,[4,5] Alexander Van Schoonhoven,[4,5] Prof Khaled Alkattan[3]

[1]Gastroenterology Division, Department of Medicine, King Saud University Medical City, King Saud University, Saudi Arabia
[2]Division of Gastroenterology, The McGill University Health Centre, Montreal General Hospital, McGill University, Canada
[3]Alfaisal University, Kingdom of Saudi Arabia
[4]Asc Academics BV, Netherlands
[5]Department of Health Sciences, University Medical Center Groningen, Netherlands

Correspondence: Albertus Constantijn Sloof, Department of Health Sciences, University Medical Center Groningen Asc Academics BV, Netherlands, Tel (+31)6 81192456

Received: December 16, 2025 | **Published:** December 22, 2025

Abbreviations: CT, computed tomography; GDP, gross domestic product; HTA, health technology assessment; ICER, incremental cost-effectiveness ratio; KSA, Kingdom of Saudi Arabia; LCS, lung cancer screening; LDCT, low-dose computer tomography; NLST, national lung screening trial; PSA, probabilistic sensitivity analysis; QALY, quality-adjusted life year; WHO, world health organization; WTP, willingness-to-pay

Introduction

Lung cancer is the second most common cancer, and the primary reason for cancer-related death worldwide, accounting for 18% of all cancer deaths. Annually, 2.2 million people are diagnosed with lung cancer, and 1.8 million people succumb to the disease.[1] In Saudi Arabia, an annual incidence of 458 lung cancer cases was reported, which accounts for 3.3% of all cancer cases in the country.[2] However, an increasing trend in lung cancer cases has been identified in recent years.[3] Most of these cases are identified in the distant stage, where curative treatment is no longer feasible.[2]

The National Lung Screening Trial (NLST), conducted in the United States, reported a 20% reduction in lung cancer mortality in individuals aged 55–74 with a median of 48 pack-years.[4] The Dutch-Belgian lung cancer screenings trial (NELSON) found a reduction of 24% in lung cancer mortality in individuals between the ages of 50 and 74, with a median of 38 pack-years.[5] These trials have led to the recommendation for annual lung cancer screening in the United States and the United Kingdom.[6,7]

The recommendation for the implementation of lung cancer screening (LCS) in the United Kingdom was supported by a cost-effectiveness analysis.[7] This article adapts that analysis to assess the cost-effectiveness of implementing a screening programme in Saudi Arabia. The cost-effectiveness of various scenarios regarding age-related eligibility criteria and geotargeting of the screening program was examined. Furthermore, the specific situation of assessing the cost-effectiveness of health interventions in Saudi Arabia is discussed, and suggestions are made to improve the process in line with international guidelines.

Health technology assessment (HTA) in Saudi Arabia

The Kingdom of Saudi Arabia is planning a transformation of the healthcare system as part of the Vision 2030 project. One objective of the project is to move towards a value-based system where the Centre for National Health Insurance will decide upon a benefits package, taking both clinical and cost-effectiveness evidence into account.[8] For example, the willingness-to-pay (WTP) threshold has not yet been published by the Centre for National Health Insurance; however, a threshold of $13,333 to $20,000 has been suggested.[9,10] This threshold was based on recommendations used in the United Kingdom, adjusted to the Saudi context.

In countries without a formal WTP threshold, it is common to use the World Health Organization (WHO) recommendations, which suggest a range of one to three times the gross domestic product (GDP) per capita. For the Kingdom of Saudi Arabia, this would result in a WTP threshold of $33,040 to $99,120.[11] The cost-effectiveness of lung cancer screening in this study is evaluated using the WTP threshold from the literature and the thresholds based on the WHO recommendations. For both thresholds, the implications and policy recommendations are discussed.

Materials and methods

The cost-effectiveness model follows a two-stage model structure. The first stage is a decision-tree structure designed to use the NELSON trial data to determine the number of lung cancer patients detected per screening round and the stage at diagnosis per patient. The decision tree is repeated multiple times to account for multiple screening rounds for the same patient population. The decision-tree structure is presented in Figure 1.

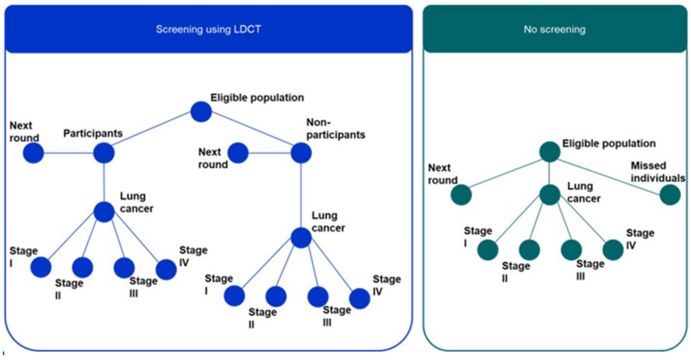

Figure 1 Graphical representation of the decision tree structure.

It was recognized that lung cancer incidence in Saudi Arabia differs substantially from that in the Netherlands and Belgium.[2,12] The number of lung cancer cases in the no-screening arm and the non-participant section of the screening arm are informed by the current Saudi lung cancer incidence. The overdiagnosis rate from the NELSON trial determines the number of cases in the participant section of the screening arm. This method combines the natural incidence of the disease in Saudi Arabia with the improvement in diagnoses resulting from screening. The individuals missed in the no-screening arm represent the difference between the number of cases in the screening arm and the no-screening arm. In estimating the impact of missed individuals, these cases were assigned excess mortality equivalent to that of progression-free stage 2 lung cancer and were assumed not to incur additional costs or quality-of-life decrements. These data are presented in Table 1.

The stage distribution in the no-screening arm and the non-participant section of the screening arm follows the current stage distribution in Saudi Arabia. In the participant section of the screening arm, false-negative and true-positive patients are identified. It is assumed that patients identified as false negatives using conventional methods are assigned the currently observed stage distributions, whereas patients identified through screening are assigned stage distributions observed in the NELSON trial.

The second stage of the model structure follows a Markov state transition design, where patients are assigned transition probabilities for disease progression and mortality based on their stage at diagnosis. The transition probabilities were based on extrapolations of published progression-free survival and overall survival curves. For the overall survival extrapolations, Kaplan-Meier curves were used from an extensive international study that subdivided the lung cancer stages.[13] The extrapolations were performed in the R software.

The progression-free survival extrapolations used Kaplan-Meier curves from published clinical trials for stage I and II,[14] stage III,[15] and stage IV.[16–18] For stage IV, data from three clinical trials were used to account for differences in histological subtypes. A weighted average progression-free survival was used, with the weights being determined by the proportion of these histological subtypes being present in the lung cancer population.[19-21]

The Markov structure tracked patients from diagnosis to death using three-month cycles. Patients progressed within their stage at diagnosis to a progressed state, as progression to the other states would interfere with the time dependencies used for survival and progression. Costs and quality of life were assigned to each cycle depending on the state occupation. These data are presented in Table 1.

Table 1 Parameters used in the cost-effectiveness analysis

Parameter	Base-case value	PSA distribution	Source
Overdiagnosis rate	8.90%	Beta	De Koning et al.[5]
Total population	2,14,30,128	Fixed	Cancer incidence report[2]
Uptake rate	46.50%	Beta	Field et al.[22]
Stage distributions with no screening			
Stage I	16.60%	Dirichlet	Almatroudi et al.[23]
Stage II	4.90%	Dirichlet	Almatroudi et al.[23]
Stage III	9.80%	Dirichlet	Almatroudi et al.[23]
Stage IV	68.60%	Dirichlet	Almatroudi et al.[23]
Screening outcomes round 1			
Scan outcomes			
Negative	79.20%	Dirichlet	Horeweg et al.[24]
Indeterminate	19.20%	Dirichlet	Horeweg et al.[24]
Positive	1.59%	Dirichlet	Horeweg et al.[24]
Indeterminate scan outcomes			
Negative	94.60%	Dirichlet	Horeweg et al.[24]
Positive	5.40%	Dirichlet	Horeweg et al.[24]
True negative	99.90%	Dirichlet	Horeweg et al.[24]
False negative	0.10%	Dirichlet	Horeweg et al.[24]
True positive	38.70%	Dirichlet	Horeweg et al.[24]
False positive	61.30%	Dirichlet	Horeweg et al.[24]
Stage distributions screening			

Table 1 Continued....

Stage I	64.90%	Dirichlet	Youssef-Khan et al.[25]
Stage II	9.50%	Dirichlet	Youssef-Khan et al.[25]
Stage III	18.90%	Dirichlet	Youssef-Khan et al.[25]
Stage IV	6.80%	Dirichlet	Youssef-Khan et al.[25]
Screening outcomes round 2 and beyond			
Scan outcomes			
Negative	92.20%	Dirichlet	Horeweg et al.[24]
Indeterminate	6.60%	Dirichlet	Horeweg et al.[24]
Positive	1.20%	Dirichlet	Horeweg et al.[24]
Indeterminate scan outcomes			
Negative	91.20%	Dirichlet	Horeweg et al.[24]
Positive	8.80%	Dirichlet	Horeweg et al.[24]
True negative	99.90%	Dirichlet	Horeweg et al.[24]
False negative	0.10%	Dirichlet	Horeweg et al.[24]
True positive	44.40%	Dirichlet	Horeweg et al.[24]
False positive	55.60%	Dirichlet	Horeweg et al.[24]
Stage distributions screening later rounds			
Stage I	75.90%	Dirichlet	Youssef-Khan et al.[25]
Stage II	6.90%	Dirichlet	Youssef-Khan et al.[25]
Stage III	13.80%	Dirichlet	Youssef-Khan et al.[25]
Stage IV	3.40%	Dirichlet	Youssef-Khan et al.[25]
Costs			
Recruitment costs			
Pre-invitation notice	$1.00	Gamma	Expert opinion
Invitation letter for participation	$1.00	Gamma	Expert opinion
First reminder	$0.72	Gamma	Expert opinion
Second reminder	$0.55	Gamma	Expert opinion
Telephone triage call	$7.62	Gamma	Expert opinion
Invitation letter for appointment	$0.18	Gamma	Expert opinion
Screening costs			
CT-scan	$146.00	Gamma	Expert opinion
Report reading	$40.00	Gamma	Expert opinion
Number of scans per participant - Round 1	1.188	Gamma	Horeweg et al.[24]
Number of scans per participant - Round 2 and beyond	1.063	Gamma	Horeweg et al.[24]
Diagnostic costs			
Screening	$503.52	Gamma	Horeweg et al.[24]; NHS[26]
No screening	$718.52	Gamma	NHS[26]
Treatment costs			
First 90 days post diagnosis			
Stage I	$1,749.73	Gamma	Snowsill et al.[27]
Stage II	$21,123.98	Gamma	Snowsill et al.[27]
Stage III	$21,123.98	Gamma	Snowsill et al.[27]
Stage IV	$19,809.73	Gamma	Snowsill et al.[27]
Year one			
Stage I	$2,054.41	Gamma	Snowsill et al.[27]
Stage II	$2,244.15	Gamma	Snowsill et al.[27]
Stage III	$1,743.16	Gamma	Snowsill et al.[27]
Stage IV	$998.95	Gamma	Snowsill et al.[27]
Year two onwards			
Stage I	$272.01	Gamma	Snowsill et al.[27]
Stage II	$900.51	Gamma	Snowsill et al.[27]
Stage III	$853.14	Gamma	Snowsill et al.[27]
Stage IV	$741.37	Gamma	Snowsill et al.[27]
End of life costs	$3441.15	Gamma	Round et al.[28]
Survival			
Overall survival (5-year survival rate) by stage at diagnosis			

Table 1 Continued....

Stage I	78.60%	NA
Stage II	54.90%	NA
Stage III	29.20%	NA
Stage IV	5.90%	NA
Disease/progression-free survival after 1 year by stage at diagnosis		
Stage I	87.80%	NA
Stage II	87.80%	NA
Stage III	41.80%	NA
Stage IV	40.10%	NA

Abbreviations: PSA, probabilistic sensitivity analysis; CT, computed tomography

In the model, a payer's perspective is used, focusing on the costs applicable to a national health provider. The cost data available from one public hospital was used and benchmarked to the private sector in Saudi Arabia. Furthermore, for the determination of the health outcomes in the model, life-years and quality-adjusted life-years (QALYs) were used.

The model evaluated six scenarios based on restricting age ranges and geotargeting restrictions. The included age ranges were 50–74, 55–74, and 60–74. For the geotargeting scenarios, the region within Saudi Arabia with the highest lung cancer incidence — the Eastern Region —was selected. Implementing LCS in this region was deemed more efficient.

Two sets of sensitivity analyses were conducted to investigate the uncertainty around the results. A one-way sensitivity analysis was conducted by sequentially varying each parameter value by 20% in both directions. A probabilistic sensitivity analysis was performed by simulating an alternative set of parameter values 1,000 times.

Results

In the nationwide scenario, 476,119 individuals aged 50–74 were eligible for screening. In the Eastern region, among individuals aged 60–74, 32,385 were eligible for screening. The number of additional lung cancer cases identified ranged from 304 to 49. The included populations and lung cases identified per scenario are presented in Table 2.

Table 2 Eligible populations and the number of lung cases identified per screening scenario

Scenario	Eligible population	Participating	Lung cases identified
Entire KSA, aged 50-74	4,76,119	2,21,396	304
Entire KSA, aged 55-74	2,50,096	1,16,295	164
Entire KSA, aged 60-74	1,99,818	92,916	159
Eastern Region, aged 50-74	42,870	19,934	66
Eastern Region, aged 55-74	40,324	18,750	59
Eastern Region, aged 60-74	32,385	15,059	49

Abbreviations: ICER, incremental cost-effectiveness ratio; KSA, Kingdom of Saudi Arabia; QALY, quality-adjusted life year

The cost, health, and cost-effectiveness results per screening scenario are presented in Table 3. The number of life years gained due to the implementation of lung cancer screening ranged from 6,190 to 956. Adjusting for quality of life, between 4,615 and 708 life years were gained.

Table 3 Cost-effectiveness results per screening scenario

Scenario	Costs	LYs	QALYs	ICER (costs/QALY)
Entire KSA, ages 50–74				
Screening	$600,176,625	71,01,532	56,67,200	
No screening	$92,308,833	70,95,342	56,62,585	
Incremental	$507,867,792	6,190	4,615	$110,042
Entire KSA, ages 55–74				
Screening	$267,275,039	33,95,056	26,59,534	
No screening	$51,247,288	33,91,728	26,57,063	
Incremental	$216,477,751	3,328	2,471	$87,595
Entire KSA, ages 60–74				
Screening	$187,776,363	24,85,890	19,23,255	
No screening	$49,724,140	24,82,786	19,20,956	
Incremental	$138,052,233	3,104	2,300	$60,032
Eastern Region, ages 50–74				
Screening	$65,213,605	6,22,804	4,94,796	
No screening	$19,872,892	6,21,486	4,93,815	

Citation: Almadi MA, Alrujaib M, Sloof AC, et al. Cost-effectiveness of lung cancer screening in Saudi Arabia. *J Cancer Prev Curr Res.* 2025;16(6):143–150. DOI: 10.15406/jcpcr.2025.16.00594

Table 3 Continued....

Incremental	$45,340,713	1,318	982	$46,192
Eastern Region, ages 55-74				
Screening	$53,139,827	5,44,323	4,26,551	
No screening	$18,520,856	5,43,129	4,25,664	
Incremental	$34,618,971	1,195	887	$39,044
Eastern Region, ages 60–74				
Screening	$37,296,527	3,90,204	3,00,308	
No screening	$15,186,427	3,89,248	2,99,600	
Incremental	$22,110,100	956	708	$31,222

Abbreviations: ICER, incremental cost-effectiveness ratio; KSA, Kingdom of Saudi Arabia; LY, life year; QALY, quality-adjusted life year

Using the suggested WTP threshold range of $13,333 to $20,000, none of the scenarios result in a currently cost-effective implementation. Using three times GDP per capita ($99,120) results in all but one scenario being cost-effective. Using a threshold of two times GDP per capita ($66,080) results in a cost-effective screening across the entire country for individuals 60–74 years old. Additionally, all geotargeted scenarios, regardless of age restrictions, are cost-effective. When using a value of 1 times GDP per capita ($33,040), the scenario of screening individuals aged 60–74 in the Eastern region is cost-effective.

Sensitivity analyses

The sensitivity analyses were performed on scenarios with age restrictions aligned with the UK national screening recommendation for ages 55–74. The results of the sensitivity analyses are presented with and without geotargeting restrictions.

The results of the one-way sensitivity analyses are presented in Figure 2 and Figure 4 for the entire country and the Eastern region, respectively. The most influential parameters are screening costs, the discount rates for health and cost outcomes, and the utilities for stage I lung cancer patients. The outcomes of the probabilistic sensitivity analyses are reported in Figure 3 and Figure 5 for the entire country and the Eastern region. For the whole country, most simulations are below the three times GDP per capita line, representing that the implementation of lung cancer screening will be cost-effective at a WTP of $99,120. For the Eastern region, almost all simulations fall below the two times GDP per capita line, indicating that the intervention will be cost-effective at a WTP of $66,080.

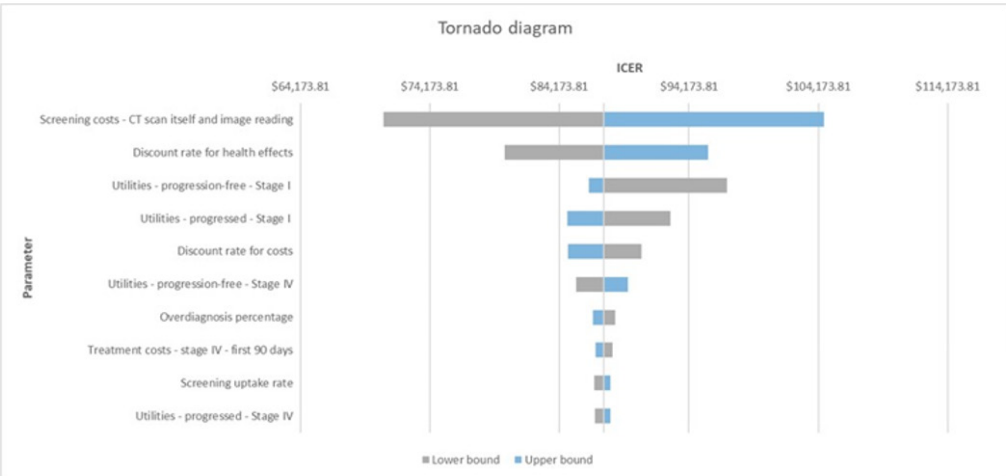

Figure 2 Results of the one-way sensitivity analysis for the scenario where screening is implemented nationwide.

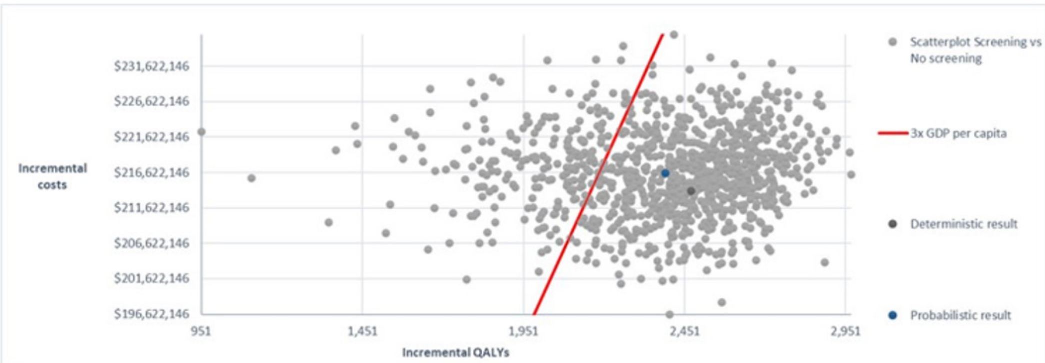

Figure 3 Scatterplot depicting the outcomes of the probabilistic sensitivity analysis for the scenario where screening is implemented nationwide.

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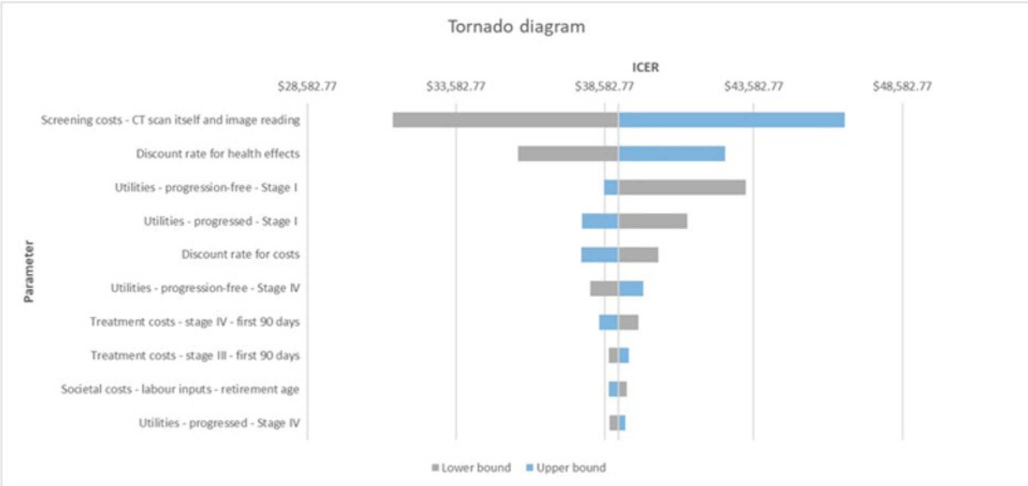

Figure 4 Results of the one-way sensitivity analysis for the scenarios where screening is restricted to the Eastern region.

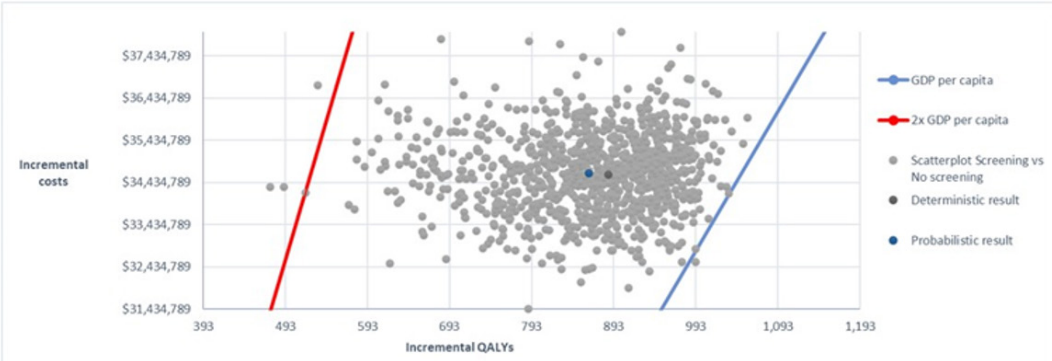

Figure 5 Scatterplot depicting the outcomes of the probabilistic sensitivity analysis for the scenario where screening is restricted to the Eastern region.

Discussion

The current study assessed the cost-effectiveness of implementing lung cancer screening using low-dose computed tomography (LDCT) versus no screening in the Kingdom of Saudi Arabia. The analysis found incremental cost-effectiveness ratios (ICERs) ranging from $31,222 to $110,042, associated with QALY savings of 4,165 and 708.

Previously published cost-effectiveness analyses report ICER estimates ranging from €5,707 ($6,175)[29] to £28,169 ($36,020).[27] Previous publications investigated the cost-effectiveness in Europe, North America, and Australia; this is the first cost-effectiveness analysis of lung cancer screening aimed at a country in the Middle East. In the current study, a previously published model was adapted from the UK to the Saudi Arabian setting. In the UK, an ICER of £5,455 ($6,975) was estimated.[30]

Currently, there is no WTP threshold in Saudi Arabia. A threshold has been suggested, ranging from $13,333 to $20,000. However, following WHO guidelines, thresholds of $33,040, $66,080, and $99,120 should be applied. In previous WTP, thresholds were commonly based on WHO guidelines, in case an official threshold was not available.[31–36] Furthermore, countries with an official WTP threshold tend to have multiple thresholds with higher levels depending on disease severity or unmet need.[37]

In addition, the cost data used are of limited quality, even though they were extracted from Saudi Arabia. The quality of these costs is limited as costing in healthcare in Saudi Arabia remains immature, especially in the public sector. However, there has been a greater focus on costing in healthcare in both the public and private sectors in recent years.

Future developments within the Saudi Arabian demographics could improve the cost-effectiveness of lung cancer screening. Smoking rates determine the probability of developing lung cancer and the eligibility for lung cancer screening. Currently, the population that has been smoking consistently for a long time is small. Higher rates of smoking were found among students, which could be indicative of increasing incidence rates in the future.[38] Furthermore, life expectancy at birth in Saudi Arabia has been increasing consistently and is expected to continue to increase.[39,40] This will likely increase the incidence rates, as lung cancer often develops in older patients.

Conclusion

Using the three times GDP per capita WTP threshold, lung cancer screening in the entire Kingdom of Saudi Arabia for individuals aged 55–74 was considered cost-effective. Using twice GDP per capita, this population should be limited to the Eastern region (ages 50–74), and using one times GDP per capita, this should be further restricted to ages 60–74 in the Eastern Region. In line with internationally applied WTP thresholds, the authors suggest applying a higher threshold due to the increase in lung cancer incidence in Saudi Arabia. Therefore, the authors recommend implementing lung cancer screening in the

Eastern region for individuals aged 55–74. This could allow for efficient use of funds while also laying the groundwork for a broader adoption in Saudi Arabia.

Funding statement

The preparation of this expert opinion manuscript and funding of the journal's article processing charges were supported by AstraZeneca FZ LLC. The funder was not involved in the study design, collection, analysis, interpretation of data, the writing of this article, or the decision to submit it for publication.

Conflict of interest

All authors declare no conflicts of interest.

Acknowledgements

We thank Roma Kwiatkiewicz for her editorial assistance essential to creating this manuscript.

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Citation: Almadi MA, Alrujaib M, Sloof AC, et al. Cost-effectiveness of lung cancer screening in Saudi Arabia. *J Cancer Prev Curr Res.* 2025;16(6):143–150. DOI: 10.15406/jcpcr.2025.16.00594