

# Cost-effectiveness of Lung Cancer Screening in Urban Chinese Populations

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## Research article

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# Abstract

**Background:** Lung cancer is the leading cause of cancer-related death. Currently, lung cancer screening trials have demonstrated that low-dose computed tomography (LDCT) screening can reduce lung cancer specific and overall mortality. The effectiveness of LDCT has been proven, but its economical efficiency should also be assessed. The purpose of the study is to analyze the cost-effectiveness of annual LDCT screening of high-risk populations in Chinese urban areas.

**Method:** We use Markov model to evaluate LDCT screening from sociological perspective. The sample size is 100,000 smokers who will undergo annual LDCT screening until 76. The study contains 5 screening strategies, the initial screening ages for the five screening strategies and their corresponding unscreened strategies are 40, 45, 50, 55, and 60 years, respectively. Parameters come from the China Lung Cancer Screening Project, cancer registry data, etc. The Incremental Cost-effectiveness Ratio (ICER) between screening and non-screening strategies at the same initial age is evaluated.

**Result:** In base-case scenario, compared with those who are not screened, specific mortality of lung cancer decreased by 18.52%-23.13% of 5 screening strategies. The ICER of LDCT screening is from 13056.82USD to 15736.06USD per quality-adjusted life year (QALY), which is greater than one time and less than three times GDP per capita in China. Initial screening age of 55 is the most cost-effective strategy.

**Conclusion:** Baseline analysis shows that annual LDCT screening in heavy smokers in Chinese urban areas is likely to be cost-effectiveness. Sensitivity analysis shows that sensitivity, specificity and over-diagnosis rate have an impact on cost-effectiveness of LDCT screening, but the results are relatively robust unless the sensitivity, specificity of LDCT screening and over-diagnosis rate take the worst value at the same time. Therefore, the cost-effectiveness of screening strategy depends on the performance of LDCT screening.

## 1. Introduction

According to GLOBOCAN statistics, there were 18.1 million new cancer cases and 9.6 million deaths worldwide in 2018. Among them, lung cancer was the most commonly diagnosed cancer (11.6%) and the leading cause of cancer death (18.4%)<sup>[1]</sup>. Likewise, in 2014, there were 3.804 million new cancer cases and 2.296 million deaths in China. Lung cancer was also the most commonly diagnosed cancer (20%) and the leading cause of cancer death (27.3%)<sup>[2]</sup>.

In the past 30 years, the survival rate of lung cancer has only been moderately improved<sup>[3]</sup>. Even in developed country, the 5-year overall survival rate for lung cancer patients is still about 15%–18%<sup>[4]</sup>. However, for lung cancer patients stage I undergoing surgical resection, the five-year survival rate is much higher than 70%<sup>[5]</sup>. This highlights the importance of early detection and early treatment of lung cancer<sup>[6]</sup>.

Common lung cancer screening methods include Low-dose computed tomography (LDCT) screening and chest X-ray screening. Currently, LDCT screening has been proven effective in reducing lung cancer mortality<sup>[7, 8]</sup>. The National Lung Screening Trial (NLST) in the United States showed that LDCT screening can reduce the specific mortality of lung cancer by 20%<sup>[7]</sup>. Another results of the LDCT screening test in Italy showed that more stage I lung cancer patients (21%) were diagnosed in annual LDCT screening than baseline<sup>[8]</sup>. X-ray screening is not recommended in lung cancer screening guidelines in many countries<sup>[9, 10]</sup>.

Although the effectiveness of LDCT screening has been proven, economic evidence needs been further explored. Scholars in many countries have conducted cost-effectiveness analysis of lung cancer LDCT screening. However, these conclusions were not consistent due to the differences in the cost of diagnosis and treatment and the incidence of lung cancer in various countries. Some studies showed that screening is cost-effective<sup>[11-13]</sup> and the others are different<sup>[14, 15]</sup>. At present, there are few studies on the cost-effectiveness of lung cancer screening in China<sup>[16]</sup>.

In this study, we combine the data from two large lung cancer screening programs in China (National Lung Cancer Screening and Intervention Program—NLCSIP, The Cancer Screening Program in Urban China—CanSPUC) and lung cancer epidemiology data<sup>[17]</sup> in China to conduct a cost-effectiveness analysis of annual LDCT screening based on high-risk populations in Chinese urban areas. we aim to assess the cost-effectiveness of screening versus non screening for lung cancer among high-risk populations in Chinese urban areas—and the most cost-effectiveness initial age to start screening.

## 2. Materials And Methods

### 2.1. Study Design

In this study, we conduct cost-effectiveness analysis from sociological perspective. A state-transition Markov model is developed to simulate the natural history of lung cancer development. In a Markov model, clinical situations are described according to the discrete health states, 'Markov states,' which individuals can be in. All individuals are always in one of these states, and all events of interest are modeled as a transition from one state to another<sup>[18]</sup>. Based on Markov model, we simulate screening and non-screening strategies to obtain the costs and effectiveness. The parameters required for the model simulation include cost-related parameters (screening, diagnosis, treatment), effect-related parameters (quality-adjusted life years), and parameters related to transition probability (morbidity, mortality, clinical-stage distribution of cancers, etc.), which are derived from NLCSIP & CanSPUC, published literatures, and cancer registry data. First, the study conducts a baseline analysis. Second, sensitivity analysis is carried out to assess the robust of the results using reasonable ranges of uncertain parameters.

### 2.2. Study population and screening strategies

Five screening strategies and their corresponding non-screening strategies for lung cancer are compared in cost and effectiveness under a decision analytic model based on a state-transition Markov process, respectively. A hypothetical static cohort of 100,000 high risk smokers ( $\geq 20$  pack years) from Chinese urban areas entered the model and their health histories are simulated by sex until 76 years old. The proportion of males of this research is set according to the 2015 annual report of Chinese people and employment statistics<sup>[19]</sup>. All health states are modelled as Markov states with one-year cycle. The initial screening ages for the five screening strategies and five corresponding unscreened strategies are the age of 40 years, 45 years, 50 years, 55 years, and 60 years. We compare the cost-effectiveness of screening and their corresponding non-screening strategies at the same initial age, respectively.

### 2.3. Markov Model and its Transition Probabilities

**No-screened Cohort.** In the non-screening model, the natural history of lung cancer development is simulated as a transition from health to lung cancer (Based on data from NLCSIP program, we divide the cases of detection into early (stage I) and non-early stage lung cancer), and ultimately to death (death from cancer or death from other causes) (Figure-1a)<sup>[15]</sup>. The probability from health to death comes from China's demographic census<sup>[20]</sup>. The probability of lung cancer-specific death comes from published literature<sup>[21]</sup>. The disease progression parameters from health to lung cancer are calculated on the basis of the lung cancer incidence of smokers in China<sup>[17]</sup>. The incidence of smokers ( $\geq 20$  pack years) is calculated as follows:

First, age and sex specific lung cancer incidences in the common Chinese urban population ( $I_G$ ) are collected from the China Cancer Registry Annual Report 2017 (urban data) at age intervals of 5 years<sup>[17]</sup>. Next, the lung cancer incidences of smokers ( $I_S$ ) in each age and gender group are calculated using the following formula 1<sup>[22]</sup>

$$I_S = OR \times I_G / [1 + (OR - 1) \times R] \quad \text{formula 1}$$

Where OR (2.85 for men and 2.33 for women) is the odds ratio from published literature<sup>[21]</sup>. R is the age- and sex-specific rate of smoking reported in the Global Adult Tobacco Survey (GATS) China 2010 Country Report<sup>[23]</sup>. Further, we calculate the incidence of non-smokers ( $I_N$ ) by the incidence of smokers ( $I_S$ ), the proportion of smokers, and the overall population morbidity ( $I$ ), according to formula 2.

$$I = I_S \times R + I_N \times (1 - R) \quad \text{formula 2}$$

Then, we use the lung cancer relative risk of smokers ( $>20$  pack years) versus non-smokers to calculate the lung cancer incidence  $I_{20}$  of smokers  $>20$  pack years in China using the following formula 3. The relative risk (RR) of lung cancer  $>20$  pack years attributable to smoking is derived from published literature<sup>[24]</sup>.

$$I_{20} = I \times RR \quad \text{formula 3}$$

**Screened Cohort.** Adherent smokers in the screened cohort receive annual LDCT testing. Smokers with positive results in LDCT screen are required to make additional diagnostic biopsy test. The sensitivity and specificity of LDCT for lung cancer are set according to the data from published study <sup>[22]</sup>. In addition, screening is superimposed on the lung cancer natural history module, resulting in early detection as determined by LDCT screening performance characteristics (Figure-1b). The clinical stage distribution of lung cancer patients in the non-screening cohort is from a multicenter retrospective epidemiologic survey from CanSPUC program <sup>[25]</sup>.

The clinical-stage distribution of lung cancer patients in the screened cohort is from opportunistic screening data of multi-center in NLCSIP program. A total of 21,397 asymptomatic individuals were screened by the NLCSIP program, and 199 patients were diagnosed with lung cancer, of which 85.6% were stage I lung cancer patients.

People who are screened may be diagnosed with lung cancer that does not cause clinical disease (over-diagnosis bias), and many of them may not be diagnosed under non-screening conditions. Some studies set the over-diagnosis rate at 0% at baseline <sup>[26, 27]</sup>; Manser et.al set the over-diagnosis rate at 12% to 20% based on early autopsy reports for lung cancer in Australia <sup>[28]</sup>. In this study, the over-diagnosis rate is set as 0% in the baseline, and we set the over-diagnosis rate as 0%-20% in the sensitivity analysis.

Screening can also create lead time bias. Lead time (being interpreted as the extended survival time due to screening) is the difference between the time of screening diagnosis and the time of clinical diagnosis. An average 1-year lead time for screening detected lung cancers is incorporated in the study <sup>[15]</sup>.

## Model Assumptions

(1) People who participate in screening do not increase their cancer risk due to radiation from LDCT. (2) In the screening group, the compliance of the population for screening is 100%, and those people who participate in the screening will continue to participate in the next annual lung cancer screening until the age of 76 years. (3) The clinical-stage distribution of false-negative lung cancer in LDCT screening strategy is the same as that of unscreened individuals.

## 2.4. Costs

The cost includes the screening cost, biopsy diagnosis cost, and lung cancer treatment cost. The LDCT screening cost comes from CanSPUC program, and the cost of biopsy diagnosis comes from the price of medical service in the hospital of CanSPUC program hospital. The lung cancer treatment cost comes from multi-center retrospective survey in the 13 provinces of CanSPUC program, including a total of 15,437 people. The inpatients whose most treatment cost occurred in the investigated hospitals and discharged for the last time between January 1, 2002 and December 31, 2011 were included. All the costs in this study are expressed in USD and are discounted to the price level of 2018 at a discount rate of 3% <sup>[29]</sup> (Table-1).

## 2.5. Quality of life

QALYs take into account both survival and quality of life determined by the progression and severity of lung cancer. We obtain utility scores of quality of life for the health states from a current meta-analysis<sup>[30]</sup>. Utility scores are 0.823 for the early stage lung cancer, 0.573 for the non-early stage lung cancer, and 1 for the health state (Table-1).

Table 1. Parameters used for the modeling of lung cancer screening protocols.		
Variable	Values (range)	Reference
Lung cancer probabilities %	19.00	[25]
Proportion of early-stage cancer among lung cancers detected with no screening		
Proportion of early-stage cancer among lung cancers detected with LDCT	85.60	NLCSIP
RR(>20 pack-years)	3.87	[24]
Sensitivity of LDCT %	87.70 71.80-100	[22]
Specificity of LDCT %	90.60 86.30-91.10	[22]
Mortality %	11.12	[21]
Early-stage lung cancer		
Non-early-stage lung cancer	35.34	
Discount rate	3%	[29]
General population smoking rate (%)	59.30	[23]
Men	63.00	
40-44	40.20	
45-64	1.60	
65-76	3.20	
Women	6.70	
40-44		
45-64		
65-76		
Cost(USD)	68.00	Canspuc
Screening		
Treatment	7984.30	
Early-stage lung cancer		
Non-early-stage lung cancer	8158.39	
Pre-diagnosis cost	91.11	
Diagnostic cost	178.70	

Utility	[30]
Early-stage lung cancer	0.825
Non-early-stage lung cancer	0.573

## 2.6. Effectiveness of Lung cancer screening

The effectiveness of screening is measured by comparing the difference in lung cancer specific deaths and QALYs. The lung cancer specific deaths and QALYs gained under each screening strategy equals to the difference between the screening strategy and its corresponding non-screening strategy.

Primary outcome of the cost-effectiveness analysis is the ICER (Incremental Cost-Effectiveness Ratio) which is calculated by dividing the incremental cost by the incremental QALYs gained for each screening strategy compared to its corresponding non-screening strategy. In this study, the ceiling ratio is defined to the threshold recommend by the World health organization (WHO) <sup>[31]</sup>. When ICER is less than three times the GDP per capita, the strategy is cost-effectiveness. Conversely, the strategy is no cost-effectiveness. China's per capita GDP in 2018 was 9768.78 USD, thus 29306.34 USD (9768.78×3) as the ceiling ratio was given in our study.

## 2.7. Sensitivity analysis

In one way sensitivity analysis, we test the impact of the parameters such as sensitivity, specificity, and over-diagnosis rate on the robustness of the cost-effectiveness. The ranges of parameter variations are set as: 71.8% to 100% for sensitivity, 86.3% to 91.1% for specificity and 0% to 20% for over-diagnosis rate. The worst scenario of LDCT screening is estimated by the combinations of the lowest values of three parameters above.

# 3. Results

## 3.1 Cost analysis

Obviously, every screening strategy is more expensive than its corresponding non-screening strategy for the additional tests in lung cancer screening. For the annual LDCT screening on the same-sized sample, the earlier the age of initial screening people is, the more it would cost regardless of its health outcomes.

The most expensive screening strategy in lung cancer is annual LDCT screening from the initial screening age of 40 years old among the five strategies, costing USD 194.30 million. The screening strategy with lowest cost, as an annual LDCT screening at the age of 60, costs USD 113.88 million.

The younger the initial screening age is in the non-screening strategy, the less it would cost. The lowest cost is USD 2.05 million and the highest cost is USD 5.38 million among the corresponding five non-screening strategies (Table-2).



### 3.2. Effectiveness

The earlier the initial screening age is, the less the number of lung cancer-specific deaths avoided by the screening. When the initial screening age is 40 years old in annual LDCT screening, the number of lung cancer deaths in the LDCT screening strategy is 6924, a reduction of 1574 or 18.52% deaths from lung cancer over its corresponding non-screening strategy (8498 deaths from lung cancer). When the initial screening strategy is at the age 60 in annual LDCT screening, the number of lung cancer deaths in the LDCT screening strategy is 5376, a reduction of 1617 (23.13%) over its corresponding non-screening strategy (6994 lung cancer deaths) (Table-2).

Corresponding to the decline of the number of lung cancer-specific deaths, the younger the initial screening strategy is among the above five age groups, the more QALY is produced. There are 12,217 QALYs saved in the screening strategy in which the initial screening age is the age of 40 in comparison with its corresponding non-screening strategy, and 11907, 11235, 10160 and 8053 QALYs will be saved in the screening strategy of the age of 45, 50, 55 and 60, respectively (Table-2).

### 3.3. ICER

As seen in Table 2, the ICER values for lung cancer screening strategies at the age of 40,45,50,55 and 60 years as the initial age are USD 15736.06, USD 14647.50, USD 13747.41, USD 13056.82 and USD 13473.15, respectively. The most cost-effectiveness lung cancer screening strategy corresponding to the smallest ICER value is the age group of 55. This indicates per QALY saved in lung cancer screening should cost additional USD 13,056.82 for the initial age of 55.

Table-2. Base-Case Results Comparing LDCT Screening with No Screening for different initial ages						
Initial age	Screen	COST million	Lung cancer deaths	Death reduction (%)	QALY thousand	ICER (USD/QALY)
40	Yes	194.30	6924	18.52	3350.51	15736.06
40	no	2.05	8498		3338.29	
45	yes	176.96	6810	18.84	2873.33	14647.50
45	no	2.55	8391		2861.42	
50	yes	157.74	6638	19.33	2404.11	13747.41
50	no	3.30	8228		2392.88	
55	yes	136.93	6167	20.72	1950.27	13056.82
55	no	4.27	7778		1940.11	
60	yes	113.88	5376	23.13	1504.91	13473.15
60	no	5.38	6994		1496.86	

### 3.4 Sensitivity analysis

**3.4.1. Sensitivity.** Sensitivity of LDCT screening is the percentage of people with lung cancer who are correctly judged as lung cancer patients according to the results of LDCT screening. The ICER of screening strategies decrease as the sensitivity of the LDCT screening increases. The maximum and minimum ICERs of the five screening strategies are USD 21783.45 per QALY and USD 10763.54 per QALY when sensitivity ranges from 71.8% to 100%. According to the threshold recommend by the WHO <sup>[31]</sup>, all screening strategies in lung cancer are cost-effectiveness within the range of sensitivity of LDCT screening.(Table-3).

**3.4.2. Specificity.** The value of the specificity in the LDCT screening varies from 86.3% to 91.1%. Similarly, the ICER of screening strategies decrease as the specificity of increases in the LDCT screening. All screening strategies in lung cancer are cost-effectiveness within the range of specificity. The screening strategy starting at the age of 55 ranks the most cost effective in terms of the ICERs (Table-3).

		ICER				
		40 <sup>a</sup>	45 <sup>a</sup>	50 <sup>a</sup>	55 <sup>a</sup>	60 <sup>a</sup>
sensitivity	71.80%	21783.45	20260.50	19015.37	18018.64	18714.41
	100%	12954.08	12062.77	11320.91	10763.54	11074.34
specificity	86.30%	17733.91	16507.20	15492.93	14714.83	15184.35
	91.10%	15503.75	14431.26	13544.44	12864.03	13274.17
<sup>a</sup> Initial age of LDCT screening						

**3.4.3. Over-diagnosis rate.** The invalid diagnostic and treatment costs induced by over-diagnosis in lung screening will result in the increase of the incremental cost. The increase of over-diagnosis rate is also associated with the decrease of incremental QALYs because over-diagnosis reduces the health outcomes in lung screening. When the over-diagnosis rate is 0%, the maximum and minimum ICERs values are from USD 13056.82 per QALY to USD 15736.06 per QALY in the five screening strategies, respectively. And the ICER value are from USD 18499.35 per QALY to USD 23006.90 per QALY in the five screening strategies with the over-diagnosis rate rising to 20%(Figure-2).

Table-4. Multivariate sensitivity analysis Results Comparing LDCT Screening with No Screening for different initial ages						
Initial age	Screen	COST ¥million¥	Lung cancer deaths	Death reduction (%)	QALY ¥thousand¥	ICER (USD/QALY¥)
40	Yes	217.90	7130	16.10	3343.26	43458.23
40	no	2.05	8498		3338.29	
45	yes	198.30	7020	16.34	2866.34	39774.96
45	no	2.55	8391		2861.42	
50	yes	176.65	6851	16.73	2397.58	36895.34
50	no	3.30	8228		2392.88	
55	yes	153.33	6392	17.83	1944.49	34016.88
55	no	4.27	7778		1940.11	
60	yes	127.65	5612	19.75	1500.31	35416.66
60	no	5.38	6994		1496.86	

## 4. Discussion

Our study indicates that annual LDCT screening in lung cancer for high risk smokers in Chinese urban areas can reduce the deaths of lung cancer. An economic evaluation of annual LDCT screening in lung cancer for the Chinese urban high risk smokers is determined by using the cost-effectiveness analysis and increment analysis in this study. In comparison with the corresponding non-screening strategy, this study has shown that the deaths of lung cancer reduces by 18.52%, 18.84%, 19.33%, 20.72% and 23.13% in the screening with an initial age of 40, 45, 50, 55 and 60, respectively. And the result given by sensitivity analysis also illustrates that the LDCT screening in lung cancer can still reduce its deaths by 16.10%-19.75% even under the most unfavorable circumstances.

Due to the fact that younger smokers are less likely to develop lung cancer, screening group with older initial age can reduce more deaths. However, QALYs value obtained from screening strategies is going down with the increase of the initial screening age in this study. The QALYs produced by the screening strategy at the age of 40 years as the initial age groups is the best, followed by the screening strategies at the age of 45, 50, 55, and 60 years as the initial age groups in the five screening strategies (Table 2). Meanwhile, the costs of screening should also decrease dramatically with the increase of the initial screening age.

As far as the cost concerned, all the costs of five screening strategies are greater than their corresponding non-screening strategies. Healthy smokers in screening group are requested to receive annual LDCT

screening in lung cancer. Furtherly, some false-positive healthy smokers diagnosed by LDCT screening have to be performed biopsy diagnosis, both of them constitute the excessive costs of screening strategies.

Although it is a fact that the cost of screening group is much higher than that of its corresponding non-screening group, it is also one of our findings that the health effect of screening group is priority to that of its corresponding non-screening group. Therefore, A prioritized screening strategy could be determined by neither only minimum cost of screening nor only the best health outcome together, but need to be determined by cost of screening and the health outcome. For all this, it is necessary for screening strategies to develop economic evaluation.

Optimal cost-effectiveness can be detected in the screening strategy with its initial age at 55. When taking both cost and effectiveness into consideration, the screening strategy with its initial age at 55 is endowed with the best cost-effectiveness. The ranks of others can be listed from high to low as the screening strategy with its age at 60, 50, 45 and 40. Even in the results of sensitivity analysis, the group with its age at 55 present minimum costs in acquiring a QALY when compared with non-screening groups, which contributes to the above-mentioned conclusion.(Table 2).

It is discovered in this study that the incremental cost and incremental effectiveness between the screening strategies and the non-screening strategies decreased as the initial age of screening group increased, which leads to the result that ICER value of each screening strategy first decreased and then increased as the increase of the initial age of screening groups. The reason is that the trend of incremental cost reduction is greater than that of incremental effect reduction when the initial age of the screening group was no more than 55 years old, and the reverse is true when the initial age is over 55 years old. Therefore, the screening strategy with its initial age at 55 years old is the most cost-effectiveness for Chinese annual LDCT screening on lung cancer among the five screening strategies. the optimal screening strategy on lung cancer presented by our study is consistent with the Screening Guidelines given by U.S. Preventive Services Working Group and Ontario Cancer Care Canada [32, 33].

When compared with other studies, the ICER value of screening strategies in this study is relatively lower. For instance, the ICER value of a study based on SEER National Cancer Database in the United States was presented as 116,300 USD/QALY [15] The Markov model was also applied in that study to simulate the annual LDCT screening on lung cancer received by those severe smokers at age of 60. The ICER value (116,300 USD/QALY) of screening strategies in that study far greater than ours (13,056-15,736 USD/QALY). The gap originates from the discrepancy in the costs of screening and biopsy diagnosis(300 USD for LDCT screening in that study and 68 USD in this one, the cost for biopsy diagnosis also outweigh ours a lot). In addition to the cause of cost, that study assumed that 58% of lung cancer patients in the screening group will be detected in the early stage, while our study has found that 85.6% of lung cancer patients can be confirmed in the early stage, more early-detected patients would make the survival duration and quality of life of screening groups increased, which induce better cost-effectiveness in this study.

It can be concluded from the results of single factor sensitivity analysis that the baseline results are reliable. Though sensitivity and specificity of LDCT screening and over-diagnosis caused by LDCT screening has a certain impact on the research results, the cost-effectiveness of screening has not been eliminated. When adopt worst estimation of sensitivity, specificity and over-diagnosis of LDCT screening in the multiple sensitivity analysis, the ICER value of screening strategies (34016-43458/QALY) outnumbers the value of tripled per capita GDP (USD29306/QALY), and no cost-effectiveness can be found in such a circumstance. However, convincing evidence for the sensitivity, specificity and over-diagnosis has not been provided in China.

Most of present studies tend to explore in a manner confined to screening itself. Actually, the effectiveness of screening can output much more than we can estimate. Following facts are hereby introduced as examples. Firstly, the health education adopted in the screening program would encourage lots of smokers to quit smoking and hereby reduce the risk of lung cancer and other related diseases. Secondly, the patients saved by screening would be able to work and create values, which contributes to the aspects of productivity and tax revenue, etc. Thirdly, despite of its contribution to patients' quality of life, it also has positive impacts on the quality of life of their relatives. The cost-effectiveness of screening can be further improved when taking these neglected factors into consideration.

There are some limitations in this study. Firstly, some assumptions can be modified in further studies. For example, the cost-effectiveness of screening can be reduced because of the increased risk might be brought by the radiation of LDCT screening. In addition, the study assumes that all the people will be voluntarily engaged in the screening, while some people may quit during the process and hereby affects the cost-effectiveness of screening. Consequently, some studies might be carried out concerning the issue of compliance. Secondly, the cost-effectiveness of accidental diagnosis is not included in this study. A previous screening project reported 210 cases of accidental diagnosis found in screening<sup>[34]</sup>, which specifically included 24 cases of kidney stones, 33 cases of uncertain renal masses, 35 cases of adrenal masses and 51 cases of abdominal aortic aneurysm, which should also be regarded as the outcome of screening.

## **5. Conclusion**

In summary, we can draw a conclusion that annual LDCT screening among high-risk smokers (>20 pack years) in urban areas of China is likely to be cost-effectiveness. Which depends on the performance of China's lung cancer screening strategy. Among the five screening strategies, screening from the initiate age of 55 is the most cost-effectiveness.

## **6. Declarations**

### **Ethics Statement**

This study is approved by the Ethics Committee of Cancer Institute and Hospital, Chinese Academy of Medical Sciences. The ethical approval number is 15-070/997

### Conflict of interests

The authors declare that they have no competing interests.

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### Consent for publication

All the authors of this study agreed to be published

### Authors' contributions

Conception and design, acquisition of data, analysis and interpretation of data, drafting of the manuscript, administrative, technical, material support: Chengyao Sun, Xin Zhang and Guoxiang Liu. Analysis and interpretation of data, statistical analysis: Sirou Guo, Yang Liu and Liangru Zhou. Critical revision of the manuscript for important intellectual content, Ju-fang Shi, Ning Wu, and Zhao Zhai. All authors read and approved the final manuscript.

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## Figures



Figure-1a. Markov Model of Annual Screening with LDCT.

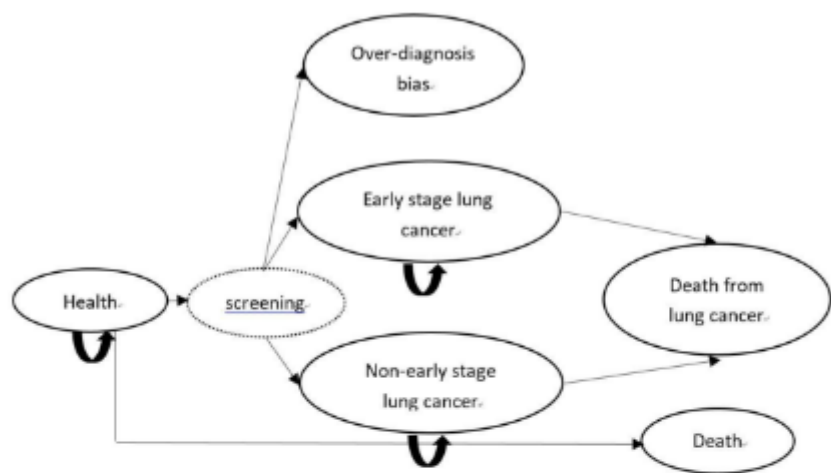


Figure-1b. Markov model of Non-screening group.

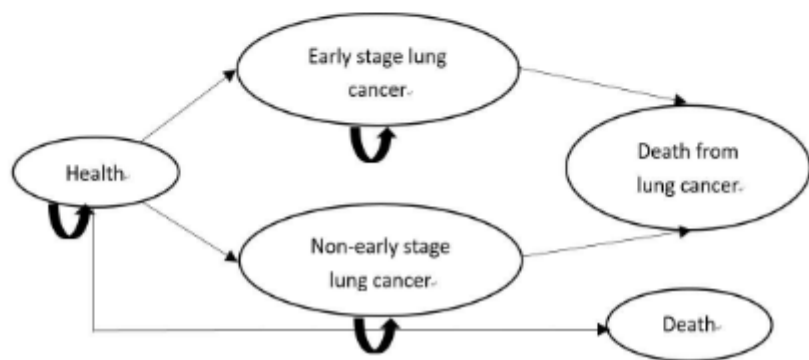
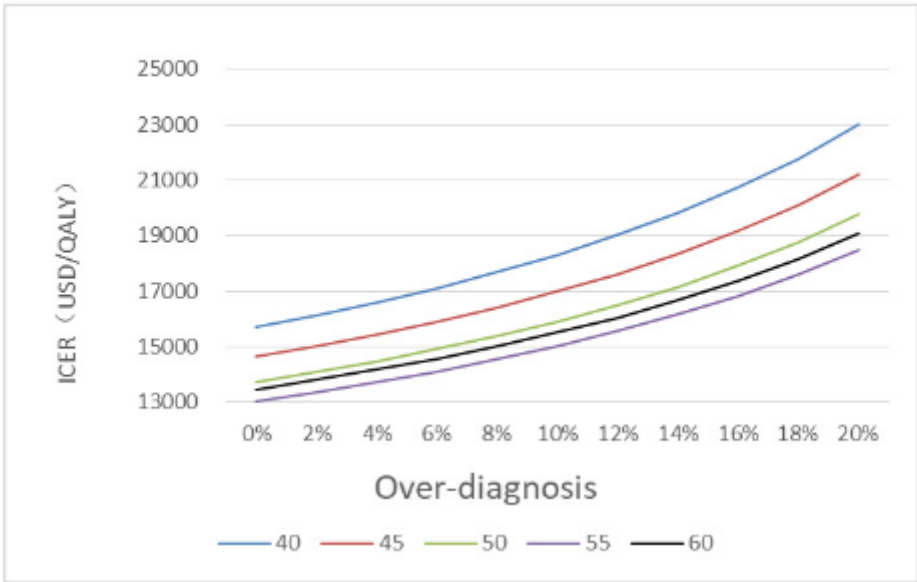


Figure 1

a. Markov Model of Annual Screening with LDCT. b. Markov model of Non-screening group.

Figure-2 Effect of changing over-diagnosis rate on ICER value of each screening strategy.



**Figure 2**

Effect of changing over-diagnosis rate on ICER value of each screening strategy.

