

Cost-effectiveness of Lung Cancer Screening Combining with CVD and COPD Screening: A Microsimulation Study

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Abstract Objective

This study aims to estimate the cost-effectiveness of lung cancer (LC), cardiovascular disease (CVD), and chronic obstructive pulmonary disease (COPD), the so-called "big-3 diseases", combining screening and identify the optimal target screening population in China.

Methods

A stage shift microsimulation model constructed and different screening strategies were set. Cost, quality-adjusted life years (QALYs), incremental cost-effectiveness ratios (ICER) and net health benefits (NHB) under different screening strategies were calculated. Strategies with a mean ICER less than \$38,223 (3 times as much as China's GDP per capita in 2022) were deemed to be cost-effective, and the optimal one in this case is the strategy with the largest NHB obtained at the same willingness to pay (WTP). One-way and probabilistic sensitivity analysis was conducted to estimate results' stability.

Results

ICERs in all strategies ranged from \$2,186.5 to 11,227.6 per QALY, which was less than China's GDP per capita in 2022. This value was basically lower in combined screening for "big-3 diseases" than in screening for LC alone. The largest NHB and probability of cost-effectiveness were both obtained in the strategy with "big-3 diseases" screening for people over 45 years old with a smoking history of 20 pack-year at least.

Conclusion

The optimal target screening population should be current smokers or smoking quitters in the past 15 years, aged over 45 years old, with a smoking history of 20 pack-year at least. These findings may provide data support for the revision of lung cancer screening guidelines.

Introduction

Lung cancer (LC), cardiovascular disease (CVD), and chronic obstructive pulmonary disease (COPD), the so-called "big-3 diseases", are expected to shift from current leading causes of death worldwide to causes of the majority of death by 2050 for their rocketing incidence.¹ With China's rapid and massive urbanization, "big-3 diseases" bring enormous health problem in China as well as globally.²

In order to alleviate such burden, China has promulgated "Healthy China 2030 Plan", putting forward cancer survival rate improvement through screening as a part of the work in strengthening public health

services covering entire population. CVD and COPD are listed as key diseases for prevention in this plan. In 2015, the United Nations General Assembly identified CVD as a target in achieving the goal of reducing premature deaths from non-communicable diseases by one-third by 2030.³

"Big-3 diseases" have many things in common: all of them can be detected early, and their progression can be slowed or even stopped when treated in time. The National Lung Screening Trial (NLST) has demonstrated that low-dose computed tomography (LDCT) can be used for early screening of LC and can reduce its mortality by 20%⁴. In addition, these diseases share same risk factors (e.g., smoking, unhealthy diet, inactivity as well as air pollution, etc.), for which their target population is relatively similar. In fact, patients died of CVD were slightly more than that of LC in NLST. LDCT can simultaneously detect CVD risk based on coronary artery calcification (CAC) and earlier-stage COPD through emphysema or air trapping evaluation.⁵ Our previous studies,^{6, 7} as well as many others,^{8–11} have shown that LDCT screening of LC is cost-effective. However, it is still unclear of the effectiveness of screening for all three diseases at the same time. This study aims to estimate the cost-effectiveness of "big-3 diseases" screening with LDCT and identify the optimal target screening population in China based on a microsimulation model.

Methods

Study Population

In this study, we used publicly available data from China Health and Retirement Longitudinal Survey (CHARLS), a project designed to collect a set of high-quality micro-data representing Chinese households and participants aged 45 years and older¹². Data are available via the website http://charls.pku.edu.cn/pages/data/2011-charls-wave1/en.html. CHARLS baseline data were collected in 2011–2012 from a total of 17,708 samples. In this study, a total of 6,408 samples were selected from 45–74 years old patients with complete information of demographic data, smoking history, blood biomarkers, and physical examination data. Those who had been previously informed of malignant tumor, CVD, and COPD were excluded. Participants in CHALS program were followed every two years, and our study used the third and fourth waves of data collected in 2015 and 2018 to establish a predictive model of changes in relevant parameters.

Measures

Model structure and screening strategies In this study, different screening strategies were formed by different screening inclusion criteria and screening diseases (LC only or LC, CVD, and COPD screening simultaneously). The screening inclusion criteria were set based on diverse screening starting ages (45, 50, 55, 60, 65, and 70 years), smoking duration (20, 25, 30 pack-years) and years since quit smoking. The threshold of years since quit smoking was set to be 15 years in this study since15 years and shorter was recommended by most guidelines in China and other countries.^{5, 13–15} For brevity, we denoted a screening strategy as "disease screened"-"age starting screening"-"smoking pack-year"-"years since quit". For

example, the screening strategy which screened "big-3 diseases" simultaneously and included adults aged 45 years and above, with a smoking history of at least 25 pack-year, current smoker or smoking quitter for less than 15 years was denoted as 3D-45-25-15.

Microsimulation model was used to simulate clinical outcomes, cost, and effectiveness of adults over 45 years under different screening strategies. In this study, the state transition models of LC, CVD and COPD were constructed respectively, and the LC model was detailed in our previous study⁷. The CVD model was modified according to the research of Huang et al¹⁶, which included four states: healthy, non-fatal CVD event, post CVD event, and fatal CVD event. The model assumed that after LDCT examination and scoring of coronary artery calcification (CAC), population with a positive result would be treated with statins, reducing the probability of developing atherosclerotic cardiovascular diseases (ASCVD)¹⁷. The COPD model was established according to Behr et al., whose model included 6 states: healthy, GOLD stages (I, II, III, and IV), and death.¹ The model hypothesized that COPD stage distribution would change in the presence of screening,¹ and treatment of stage I COPD detected by screening with inhaled medication, rather than chronic bronchitis treatment, would slow the rate of disease progression (eFigure 1).¹⁸ At the end of each cycle of the model, participants would move to another state or remain in the original state according to the corresponding probability. All screening strategies were annual screening and the age of termination of screening was set as 74 years.¹⁵ The model consisted of 45 cycles, each lasting for 1 year, and would stop when all participants reach 90 years of age or die.

Parameters Smoking (starting and quitting probability), LC (incidence and death probability), and LDCT (sensitivity, specificity, screening compliance, over-diagnosis rate, excess relative risk of LC per screening) related transition probabilities are detailed in previous research.⁷

Incidence probability of ASCVD. The validated China-PAR model was adopted in this study to predict ASCVD risk in China.¹⁹ Independent variables in this model included gender, age, untreated and treated systolic blood pressure (SBP), total cholesterol, high-density lipoprotein cholesterol (HDL-C), waist circumference, smoking status, diabetes, geographic region, and family history of ASCVD. This model was able to predict 10-year ASCVD Risk for a participant, which would be converted into annual incidence probability. The baseline data of 2011 and the third wave data of 2015 were used to establish the prediction model of each independent variable (except age and gender), so as to update the values according to each participant's characteristics in each cycle. In addition, the first year and long-term recurrent probability during and after non-fatal CVD event were obtained from Li et al.²⁰

Incidence probability of fatal CVD event. For healthy (asymptomatic) population, the probability of fatal CVD events related to age, gender, and smoking exposure were calculated respectively based on all-cause and CVD mortality of Chinese population in 2011 obtained from *China Health statistics Yearbook 2012*,²¹ and the hazard ratio (HR) values in Asian populations from literature.²² Calculation method adopted was the calculation process of non-LC death probability in previous studies.⁷ For the population with non-fatal CVD events, the probability of fatal-CVD events occurring in the first year was obtained by subtracting the

non-CVD mortality (obtained from *Yearbook 2012*²¹) from the death probability (obtained from Li et al²⁰). The standardized mortality ratio (SMR) on CVD background mortality 1 year after the occurrence of non-fatal CVD events was obtained from Chen et al²³, and then the fatal-CVD probability was calculated.

Transition probability of COPD model. In this study, in order to calculate the probability of developing COPD, data of participants without COPD were obtained from the 2011 baseline data of CHALS and were matched with corresponding data in 2015. Then, logistic regression was used to construct a COPD risk prediction model. The independent variables of the model included age, gender, smoking status, smoking pack-years and duration of smoking cessation, and the 4-year COPD risk of an participant can be calculated, which can later be converted into annual transition probability. The GOLD grade stage distribution of COPD without screening was obtained from the study of Wang et al.²⁴ and the stage distribution under screening was derived from the study of Behr¹ and Mohamed et al²⁵. The average time for COPD progression at different stages was obtained from literature, which assumed 50% participants would progress into the next stage during this average time. Annual COPD progression probability was calculated using this equation: $P = 1 - (P_t)^{\frac{1}{t}}$ (*P* is the annual exacerbation rate, *Pt* refers to the non-exacerbation rate in t years)¹. The mortality of COPD in different stages was obtained from relevant literature²⁶.

Other parameters. The probability of CAC positive results was calculated by the prediction model proposed by Zhang et al.²⁷ The ASCVD occurrence probability for people with CAC would decrease when receiving statin treatment, and relative risk was acquired from literature.²⁸ Similarly, the probability of progressing from given stage to the next stage for COPD patients would decrease with inhaled treatment, and relative risk was calculated by a stage for COPD patients would decrease with inhaled treatment, and relative risk was calculated based on mean changing value through FEV₁ per year.¹⁸

Cost. This study evaluated the cost and effectiveness from the perspective of healthcare system. There are four parts of the cost: screening-related, and LC, CVD, and COPD treatment-related cost. The screening and LC treatment related cost have been detailed in previous research.⁷

According to relevant guidelines,¹⁷ moderate-intensity statins, as the initial treatment for lipid reduction, can achieve good clinical outcomes under long-term treatment²⁹. The cost of statins in this study was calculated based on atorvastatin treatment for one year (10mg/d), and the drug price was taken as the average of published bidding prices of 31 provinces in China in 2022. Non-fatal and fatal CVD treatment costs were obtained from *2022 China Health Statistical Yearbook*,³⁰ and treatment costs for patients in post-CVD status were obtained from literature.²³ COPD treatment costs included inhalation therapy (mono bronchodilator) and maintenance therapy (e.g. oxygen inhalation, expectorant, etc.), which took reference from Qu et al.¹⁸ Patients of stage I COPD, when not detected, are normally treated as having chronic bronchitis. Treatment costs of COPD acute exacerbations included outpatient fees and stage-specific hospitalization fees.¹⁸ All costs were discounted in the year of 2022 and then converted into US dollars according to the average exchange rate (CNY 6.7261 to USD 1)³¹in 2022 (Table 1).

Table 1 Model Parameters

| Parameters | Base case(range) | Distribution | Source |
|---|-------------------------|------------------------------|--------------------|
| Discount rate | 0.03(0, 0.08) | triangle(0, 0.03, 0.0.08) | 42 |
| Overdiagnosis rate when screening | 0.11 | beta(120,969) | 43 |
| RR of incident ASCVD after statin treatment | 0.79(0.77, 0.81) | beta(1257.9, 334.4) | 28 |
| RR of exacerbation after treatment | 0.88(0.85, 0.93) | beta(222.24, 30.1) | 18 |
| Specificity of LDCT | 0.765(0.70, 0.93) | beta(56936, 17497) | 4 |
| Sensitivity of LDCT | 0.937(0.89, 1) | beta(649, 44) | |
| Screening compliance | 0.3532(0.305, 1) | beta(197251,558480) | 44 |
| LC stage-specific annual probabili | Estimated ⁴⁵ | | |
| Stage I | 0.047(±50%) | beta(414.708, 8380.292) | - |
| Stage II | 0.109(±50%) | beta(200.565, 1631.435) | |
| Stage III | 0.22(±50%) | beta(1310.297, 4657.703) | |
| Stage IV | 0.43(±50%) | beta(379.543, 502.457) | |
| Stage distribution with screening | | | Estimated 4, 46-52 |
| LC Stage I | 0.623(0.563, 0.717) | beta(804, 487) | |
| LC Stage II | 0.091(0.067, 0.13) | beta(118, 1173) | - |
| LC Stage III | 0.170(0.168, 0.177) | beta(220, 1071) | |
| LC Stage IV | 0.115(0.048, 0.130) | beta(149, 1142) | |
| COPD Stage I | 0.636(0.61, 0.662) | beta(807, 463) | 1,25 |
| COPD Stage II | 0.315(0.289, 0.341) | beta(400, 870) | - |
| COPD Stage III | 0.046(0.034, 0.058) | beta(59, 1211) | |

| COPD Stage IV | 0.003(0, 0.006) | beta(4, 1266) | | | |
|--|--------------------------|--------------------------------|-------|--|--|
| Stage distribution without screenir | 53 | | | | |
| LC Stage I | 0.19(0.152, 0.228) | beta(1331, 5682) | | | |
| LC Stage II | 0.164(0.131, 0.197) | beta(1161, 5852) | _ | | |
| LC Stage III | 0.347(0.278, 0.416) | beta(2432, 4581) | | | |
| LC Stage IV | 0.299(0.239, 0.359) | beta(2089, 4924) | _ | | |
| COPD Stage I | 0.537(0.523, 0.551) | beta(2719, 2189) | 24 | | |
| COPD Stage II | 0.38(0.366, 0.394) | beta(1798, 3110) | | | |
| COPD Stage III | 0.074(0.067, 0.081) | beta(349, 4559) | | | |
| COPD Stage IV | 0.009(0.006, 0.012) | beta(42, 4866) | _ | | |
| Excess relative risk of LC per screening | 0.001(0.0003, 0.0019) | beta(6,5995) | 8, 54 | | |
| Health utility value of different stages of LC | | | | | |
| LC Stage I | 0.85(0.78, 0.89) | beta(136.78,24.14) | 32-34 | | |
| LC Stage II | 0.75(0.68, 0.8) | beta(149.31,49.77) | | | |
| LC Stage III | 0.69(0.56, 0.79) | beta(42.18,18.95) | _ | | |
| LC Stage IV | 0.69(0.38, 0.7) | beta(21.46,9.64) | | | |
| Non-fatal CVD event | 0.76(0.54, 0.96) | beta(2.1, 0.67) | 1 | | |
| Post CVD event | 0.773(0.6, 0.9) | beta(15.31, 4.5) | 28 | | |
| COPD Stage I | 0.897(0.65, 0.97) | triangle(0.65, 0.897, 0.97) | 1,18 | | |
| COPD Stage II | 0.755(0.58, 0.86) | triangle 0.58, 0.76, 0.86) | | | |
| COPD Stage III | 0.748(0.54, 0.80) | triangle(0.54, 0.748, 0.8) | | | |
| COPD Stage IV | 0.549(0.54, 0.80) | triangle(0.54, 549, 0.7) | | | |

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| Cost (\$) | | | |
|--------------------------------------|------------------------|--------------------|-----------------------------|
| Screening related | | | |
| Cost of LDCT test | 53.49(44.62, 73.94) | gamma(4,13.3725) | 55 |
| Cost of publicity in screening | 1.54(±50%) | gamma(4,0.385) | 56 |
| Cost of management in screening | 1.85(±50%) | gamma(4,0.4625) | |
| Cost of human resources in screening | 3.08(±50%) | gamma(4,0.77) | 57 |
| Cost of diagnostic test | 291.34(±50%) | gamma(4,72.835) | 55 |
| LC treatment related | | | |
| Treatment for LC stage I | 8704.68(±50%) | gamma(4,2176.17) | 55 |
| Treatment for LC stage II | 13603.55(±50%) | gamma(4,3400.8875) | |
| Treatment for LC stage III | 14791.04(±50%) | gamma(4,3697.76) | |
| Treatment for LC stage IV | 19005.64(±50%) | gamma(4,4751.41) | |
| CVD treatment related | | | |
| Annual cost of statin | 13.95(±50%) | gamma(4,3.4875) | Public bidding announcement |
| Treatment for non-fatal CVD event | 2211.79(±50%) | gamma(4,552.9475) | 30 |
| Treatment for fatal CVD event | 2915.08(±50%) | gamma(4,728.77) | 30 |
| Treatment for post CVD event | 957.18(±50%) | gamma(4,239.295) | 23 |
| COPD treatment related | | | |
| Treatment for COPD stage I | 269.52(±50%) | gamma(4,67.38) | 18 |
| Treatment for COPD stage II | 796.37(±50%) | gamma(4,199.09) | |
| Treatment for COPD stage III | 1016.51(±50%) | gamma(4,254.13) | |
| Treatment for COPD stage IV | 1016.51(±50%) | gamma(4,254.13) | |
| Cost of exacerbation stage II | 1383.42(±50%) | gamma(4,345.85) | |
| Cost of exacerbation stage III | 2706.2(±50%) | gamma(4,676.55) | |
| Cost of exacerbation stage IV | 4028.98(±50%) | gamma(4,1007.24) | - |
| Cost of chronic bronchitis treatment | 529.23(±50%) | gamma(4,132.31) | |

LDCT, Low-dose computed tomography; LC, lung cancer; ASCVD, atherosclerotic cardiovascular diseases; CVD, cardiovascular diseases; COPD, chronic obstructive pulmonary disease; RR, relative risk.

Health utility value and discount rate. The health utility value of different status of models in this study was obtained from published studies.^{1, 18, 28, 32–34} If a participant had multiple diseases (LC, CVD, and COPD) at the same time, the health utility would be set as the one with the lowest utility value among coexisting diseases. An annual discount rate of 3% was adopted to discount the cost and utility value into 2022 equivalents.

Statistical Analysis

This study bootstrapped 100,000 real participants from included cases to maintain the correlations between the attributes of participants (e.g., age, sex, blood biomarkers). R (Version 4.1.2) was used to construct the model. Under different screening strategies, the cumulative person-years of different states over the entire model cycle were calculated. Healthcare costs and quality-adjusted life-years (QALYs) for all participants in different scenarios were calculated, and then the average cost and effectiveness of each strategy can be obtained. China's GDP per capita in 2022 was 12,741 US dollars ³¹. The program would be regarded cost-effective, as recommended by WHO, if the incremental cost-effectiveness ratio (ICER) is less than three times as much as China's GDP per capita (\$38,223 in this study). The ICER was calculated as incremental cost divided by incremental effectiveness compared with the baseline strategy. In addition, net health benefit (NHB), calculated based on different willingness to pay (WTP), was adopted to compare different strategies and to help select the optimal one. One-way sensitivity analysis was conducted after changing each parameter over a plausible range to examine the effect of the uncertainty of each model parameter. In addition, probabilistic sensitivity analyses were conducted by running the model for 1,000 times, with each run sampled from the prespecified distributions of each parameter (Table 1).

The model was verified in the following aspects. First, the lung cancer incidence rate of each age group over 45 years old simulated by the model was compared with data in *Yearbook 2012*³⁵. Second, the non-LC, CVD, and COPD mortality rate of each age group over 45 years simulated by the model was compared with data in *Yearbook 2012*.³⁶

Results

The study simulated the effects of LC screening alone and combined screening for LC, CVD, and COPD in 100,000 participants aged 45–74 years in China. Results showed that compared with the baseline strategy, every other strategy had an increased average cost and effectiveness (eTable 1, eTable 2), and ICER in all scenarios, ranging from \$2186.5 to 11227.6 per QALY, were lower than 1 time of China's GDP per capita. In addition, the lower the screening entry criteria were, the higher the cost and effectiveness were. The ICERs of strategies screening for "big-3 diseases" simultaneously were lower than that of strategies screening for LC only (eFigure 2).

Among strategies screening for LC alone, the program with the lowest ICER was LC-60-30-15. Taking this strategy as a standard comparator, we calculated the incremental cost and effect for combined screening for "big-3 diseases", and drew the ICER plane (Fig. 1). In this plane, the ICER scatter points of combined screening strategies are distributed in the first, third, and fourth quadrants. A strategy would be regarded as "dominant" when its ICER is in the fourth quadrant, which means it is less costly and more effective compared with the standard comparator. When the ICER of one strategy is in the first quadrant, it is more costly but also more effective compared with the standard scheme and ICER in the third quadrant refers to completely opposite situation, i.e. less costly but also less effective. Both latter two cases require further assessment.

Analysis showed that some combined screening strategies would result in lower per capita cost than for LC alone and the number of person-years accumulated under different scenarios varies across the model cycle (eTable 3). With the same screening inclusion criteria, compared with single-LC screening strategy, the three-disease screening strategy reduced the incidence of ASCVD events; the proportion of stage I increased while the proportion of stage II, III and IV decreased in COPD distribution, and the cumulative person-years of the state of death were also reduced. The difference was more obvious when the screening inclusion criteria was lower. In addition, in scenarios of combined screening, the overall mortality rate was reduced, the cumulative person-years of various stages of lung cancer increased (eFigure 3).

To identify the optimal screening program, we calculated the NHB for each screening strategy with different willingness to pay (Fig. 2). Results showed that NHB increased with WTP's gradual rising. Within 3 times GDP per capita, 3D-45-20-15 and 3D-45-25-15 strategy had similar NHB, which were the largest among all strategies, with the former one slightly higher than the latter.

In previous base-case analysis, it was found that the 3D-45-20-15 strategy provided best health results. In our study, one-way sensitivity analysis on this strategy was carried out by altering the value of each parameter to analyze corresponding change of ICER. Results showed that the maximum ICER was 8247.33 per QALY, which is less than one time of GDP per capita(eTable 4). eFigure 4 presents a scatter plot of 1000 ICER values for 5 strategies screening "the big-3 diseases" simultaneously which showed good health outcomes at base-case analysis compared to strategy LC_60_30_15. The result is similar to the base-case analysis, with scatter points falling in the first and third quadrants, and the points in the first quadrant are both less than 1 times GDP per capita. The probability sensitivity analysis indicated that when WTP was above \$2,500 per QALY, the 3D-45-20-15 strategy had the highest probability of being cost-effective, making it the dominant scheme (Fig. 3).

The age-specific LC incidence rate and non-LC, CVD, and COPD mortality rate generated by the model were basically close to the corresponding values and trends in *Yearbook 2012* (eFigure 5).

Discussion

Based on a nationally representative CHARLS database, this study used a microsimulation model to simulate the cost and effectiveness of LDCT screening of LC combined with CVD and COPD with different inclusion criteria. It was found that screening both for LC alone and "big-3 diseases" simultaneously were cost-effective, and the latter one was more economically attractive and could produce more health benefits than the former. The optimal target screening population, in the case of screening for three diseases at the same time, should be current smokers or smoking quitters in the past 15 years who are over 45 years old with a smoking history of 20 pack-year at least.

Results of this study are similar to those of Behr et al, whose research assessed the maximum acceptable cost (MAC) per screened participant for LDCT LC screening, and investigated the effect of additional screening for COPD, CVD, or both on the MAC.¹ Their study showed that screening for all "big-3 diseases" simultaneously had the largest MAC, which was substantially larger than screening for LC only. In addition, these researchers explored the impact of screening populations on cost-effectiveness and found that, similar to our findings, cost-effectiveness varied with screening populations. There are also some differences between Behr's study and ours. The former one carried out cost-effectiveness analysis based on a macro model. In comparison, our research is a microsimulation model based on real participants, which can reflect real scenarios. Furthermore, important parameters such as screening compliance, sensitivity, specificity, and cancer risk caused by increased screening radiation exposure were considered in model operation. In the analysis of different screening populations, Behr's study simulated current smokers and people over the age of 60, which separated two variables of smoking history and age. Our study combined smoking history and age together to develop different screening inclusion criteria since these two factors are strongly correlated, making it more effective in the identification of high-risk groups and leading to a more realistic result.

"Big-3 diseases" share many similar characteristics, such as similar disease risk factors, greater disease burden to health, and treatment at the early stage can effectively delay the development of the disease. LDCT examination can be used to evaluate pulmonary nodules, emphysema/air trapping, and CAC, which can contribute to Big-3's early diagnosis.³⁷ In the context of China's urbanization, the impact of "big-3 diseases" on health is increasing day by day, and it has become the main cause of life years lost. Therefore, simultaneous screening of the "big-3 diseases" can produce greater health benefits at a lower cost. The results of this study showed that when the three diseases were screened at the same time, compared with LC screening alone, the cumulative person years of model states decreased in ASCVD events, COPD stage II, III, IV, and death, and increased in COPD stage I.³⁸

In this study, 3D-45-20-15 was identified as the optimal screening strategy. Although its ICER scatter point was located in the first quadrant compared with strategy LC-60-30-15, it could generate the maximum NHB within 3 times as much as GDP per capita. This is different to previous findings, which suggested that screening for lung cancer should begin at age 50 or older.^{6, 39} This may be due to the epidemic characteristics of "big-3 diseases" in China. The age-specific incidence and mortality of LC increased significantly after 45 years of age¹⁵. The highest incidence of CVD was in the age group of 50–70 years

old, accounting for about half in all.⁴⁰ In addition, although the prevalence of COPD in China is lower than in western countries, its mortality rate is significantly higher.⁴¹ Early screening for "big-3 diseases" can slow down disease progression and reduce their mortality.

This study identified that the strategy LC-60-30-15 was the most cost-effective option for LC screening alone, which is different from our previous studies^{6, 7} that had lower screening inclusion criteria. This may be due to the fact that this study model took both the disease burden of CVD and COPD into account, masking the health effects of lung cancer screening to some extent.

Limitations

There are certainly some limitations to this study. First, the CHARLS database only provides micro-data of participants over 45 years old, thus the situation of participants under 45 years old could not be simulated in this study. Second, in order to facilitate modeling and calculation, the CVD model did not set according to specific type of disease (such as myocardial infarction, stroke, etc.) that CVD represents, which may be somewhat deviated from reality. Third, the incidence of LC in non-smoking population (especially women) has received more and more attention in recent years. Due to the lack of relevant prediction models, this study cannot simulate the effect of LC screening in this population. Finally, "big-3 diseases" are closely related to smoking, and if smoking cessation intervention is given at the same time as screening, greater health effects may be achieved, which will be a new direction for future research.

Conclusions

Screening for LC, CVD and COPD with LDCT simultaneously was recommended because it offers more health benefits than screening for LC only. The optimal target screening population should be current smokers or smoking quitters in the past 15 years who are over 45 years with a smoking history of 20 pack-year at least.

Declarations

Competing interests

The authors declare that they have no competing interests.

Ethics approval and consent to participate.

Ethical approval for all the CHARLS waves was granted from the Institutional Review Board at Peking University. The IRB approval number for the main household survey is IRB00001052-11015. CHARLS stated that informed consent had been obtained from all respondents.

Consent for publication

Not applicable.

Availability of data and materials

Data is publicly available. See: http://charls.pku.edu.cn/

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None

Authors' contributions

Study conception: JY; Data analysis: JY, FX; Writing: JY, FX, XR. Checking: YS, MF; Supervision: MC, HR. All authors have read and approved the final manuscript.

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Figures



Figure 1

Cost-effectiveness plane for all strategies which screen "big-3 diseases" simultaneously and the strategy of "LC-60-30-15". QALY, quality-adjusted life-year.



Figure 2

NHB values of different screening strategies at different WTP. WTP, willingness to pay. NHB, net health benefit.



Figure 3

Probability of cost-effectiveness of baseline and five optimal strategies for each type of intervention (screening lung cancer along and "big-3 diseases" simultaneously). WTP, willingness to pay.

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