

Uptake of lung cancer screening with low-dose computed tomography in China: A multi-centre population-based study

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Summary

Background Optimal uptake rates of low-dose computed tomography (LDCT) scans are essential for lung cancer screening (LCS) to confer mortality benefits. We aimed to outline the process model of the LCS programme in China, identify the high-risk individuals with low uptake based on a prospective multi-centre population-based cohort, and further explore associated structural characteristics.

Methods A total of 221,955 individuals at high-risk for lung cancer from the National Lung Cancer Screening cohort were included. The logistic regression model was performed to identify the individual characteristics associated with the uptake of LCS, defined as whether the high-risk individual undertook LDCT scans in designated hospitals within six months following the initial risk assessment. The linear regression model was adopted to explore the structural characteristics associated with the uptake rates in 186 communities.

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Findings The overall uptake rate was 33.0%. The uptake rate was negatively correlated with the incidence of advanced-stage lung cancer (Pearson's coefficient -0.88 , p -value 0.0007). Multivariable regression models found that lower uptake rates were associated with males (OR 0.88 , 95%CI $0.85-0.91$), current smokers (OR 0.93 , 95%CI $0.90-0.96$), individuals with depressive symptoms (OR 0.92 , 95%CI $0.90-0.94$), and the structural characteristics, including longer structural delays in initiating LDCT scans (30–90 days vs. ≤ 14 days: $\beta -7.17$, 95%CI $-12.76 \sim -1.57$; >90 days vs. ≤ 14 days: $\beta -13.69$, 95%CI $-24.61 \sim -2.76$), no media-assisted publicity ($\beta -6.43$, 95%CI $-11.26 \sim -1.60$), and no navigation assistance ($\beta -5.48$, 95%CI $-10.52 \sim -0.44$).

Interpretation Multifaceted interventions are recommended, which focus on poor-uptake individuals and integrate the 'assessment-to-timely-screening' approach to minimise structural delays, media publicity, and a navigation assistance along the centralised screening pathway.

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Keywords: Lung cancer; Screening; Uptake; Population-based study; China

Research in context

Evidence before this study

We searched PubMed without language or date restrictions for the uptake of LDCT screening before January 10, 2022. We required the following search terms in either the title or the abstract: ((uptake) OR (compliance) OR (participation) OR (attendance)) AND ((lung cancer) OR (lung tumor)) AND (screening). A total of 38 studies (published between 2011 and 2022) reported the uptake rates of LCS or its influencing factors. We identified that 63% (24/38) were cross-sectional surveys reporting uptake rates ranging from 8% to 89%, and 24% (9/38) were prospective studies with limited sample sizes, of which six were based on randomised controlled trials and seven reported factors associated with the uptake from the perspectives of individuals, providers, and psychological factors. Evidence is scarce regarding the uptake rates of large-scale LCS programmes and potential differences in the uptake associated with the programme infrastructure.

Added value of this study

This is the largest study to date to evaluate the uptake rates of a centralised LCS programme in developing countries based on a multi-centre population-based cohort. The overall uptake rate of LCS was 33%. Our study highlights that lower uptake rates were associated with males, current smokers, and other subgroups at high risk for lung cancer. Also, lower uptake rates were highly correlated with higher incidences of advanced-stage lung cancer. Significantly decreased uptake rates in screening settings with structural delays >30 days (time intervals between the risk assessment and the LDCT scans) were found. Involving media publicity and a navigation assistance encouraged the uptake. Our findings provide new insights into the LCS

process model and the feasibility of the real-world multifaceted intervention.

Implications of all the available evidence

Our study provides timely evidence and experience for implementing the centralised LCS programme in real practice. Individuals with a high risk for lung cancer but relatively poor uptake should receive greater attention and intense intervention. This is essential for LCS to confer mortality benefits. Our study suggests that the 'assessment-to-timely-screening' approach to reducing structural screening delays, point-of-care LDCT scans, and packages of interventions to target multiple points in the process of the centralised LCS programme are effective strategies for optimal LCS uptake. Better integration and allocation of medical services are needed for existing LCS programmes to establish a simplified, streamlined, and standardised time frame for advocacy, recruitment, risk assessment, smoking cessation and screening counselling, referral, expanded access to LDCT, and full life cycle management.

Introduction

Lung cancer is the leading cause of cancer-related death both worldwide and in China.^{1,2} In 2020, nearly 40% of the total lung cancer deaths occurred in China.² Results from rigorous randomised controlled trials (RCTs) demonstrated the effectiveness of lung cancer screening (LCS) with the use of low-dose computed tomography (LDCT) on mortality reduction.^{3,4} Evidence from National Lung Cancer Screening (NLCS) cohort in China also filled the knowledge gap that one-off LDCT screening significantly decreased lung cancer mortality and all-cause mortality by 31% and 32%, respectively.⁵ These findings supported the

mortality benefit of LCS and screening asymptomatic adults at high risk for lung cancer has been implemented in several countries such as the United States, Canada, South Korea, and China, and is currently being considered in the United Kingdom and elsewhere.⁶

As screening programmes are implemented more widely, what types of screening programmes to deliver screening effectively have received increasing attention. A centralised LCS means individuals were referred via a screening programme or a clinic for the baseline LDCT scan.⁷ It requires successful completion of multiple steps, including maintaining high uptake rates, to achieve similar long-term effectiveness.^{8,9} Differed from the uptake rates in RCTs that were more than 90%, the uptake of LCS is dramatically lower in real-world cohorts, resulting in diminished screening benefits.¹⁰ Monitoring uptake rates for LCS outside clinical trials is important in understanding how LCS is being implemented.

At present, data on uptake rates remain limited, especially in centralised LCS programmes, yet they are fundamental in guiding interventions and policy decisions to optimise LCS effectiveness. In practice, reported uptake rates varied, ranging from 8% to 89%.^{11–16} Such variation can be explained by the regional differences where the screening was conducted, screening programmes types, and structural characteristics which refer to a series of operating procedures and methods implemented by the communities and hospitals when conducting cancer screening. Barriers to LDCT uptake occur across individual and healthcare-system levels, leading to inequities in disseminating and implementing LCS.¹⁷ Outreaching LCS to underserved populations to ensure that eligible individuals receive LDCT screening will be of critical importance in reducing disparities. Multi-visit, stepwise LCS procedures may result in lost opportunities to provide timely LDCT scans and lead to incomplete engagement along the screening pathway. There has been a body of literatures and guidelines calling for research addressing how to best stimulate the uptake rate in LCS and investigating the association between the uptake rates and structural characteristics, as these issues have not been well examined previously.^{10,12,18}

To address these knowledge gaps, in this study, we aimed to: 1) report uptake rates across the diverse populations in centralised LCS using data from the NLCS programme, 2) identify high-risk individuals with low uptake of LCS and examine the correlation between the uptake probability and the incidence of advanced-stage lung cancer, and 3) explore structural characteristics that may be associated with the uptake rates.

Methods

Data source

To describe the uptake rates and identify the factors associated with undertaking LDCT scans, a multi-centre

population-based prospective study embedded in the NLCS programme was conducted. Briefly, the NLCS is a non-profit programme funded by the Ministry of Finance and the National Health Commission of China starting from 2012, aiming to improve the coverage of LCS and reduce the disease burden of lung cancer. Under the framework of the NLCS programme, study sites were selected based on the coverage of cancer registration and vital statistics, and the migration rate was lower than 5%, representing a relatively stable population.¹⁹ A national representative observational study was conducted with the best consideration of economic and geographical variations of the selected sites. A total of 12 cities in 8 provinces were included in the current analyses, among which 458 communities were involved. A flow chart illustrating the study design is shown in [Figure 1](#). All the participants provided written informed consent.

To identify the structural characteristics that may influence the screening uptake from the perspective of the programme organisers, a cross-sectional study was conducted where we randomly selected 186 communities out of the abovementioned 458 communities of the NLCS programme. Each community was required to complete an epidemiological questionnaire to collect information on infrastructure. The study obtained approval from the ethics committees of China National Cancer Center/Cancer Hospital, Chinese Academy of Medical Sciences, and Peking Union Medical College (approval number 15-070/997).

NLCS programme procedure and study population

In the involved communities, the programme was advocated, and the participants were recruited following a standard procedure. Television, websites, and brochures were used to publicize our LCS programme. All interested individuals were directed to the nearest accredited community health service centre or hospital for further information about the programme. Individuals were eligible for the NLCS programme if they were 40–74 years old, asymptomatic of lung cancer (without self-reported hemoptysis and unexplained weight loss) and had not been diagnosed with lung cancer at the cohort entry. After informed consent, the participants were interviewed by well-trained operators for lung cancer risk assessment and their eligibility for LCS. All participants were required to complete an epidemiological survey, including contact information, sociodemographic information, baseline comorbidities, lifestyle factors, and history of diseases.

Participants were included in the current study if they were labelled as being at high risk of lung cancer based on a sex-specific scoring system derived from the Harvard Cancer Risk Index.⁵ Approximately one-third of lung cancer cases in China occur in females, amongst whom a large majority are non-smokers. To include females, especially non-smoking females, who are

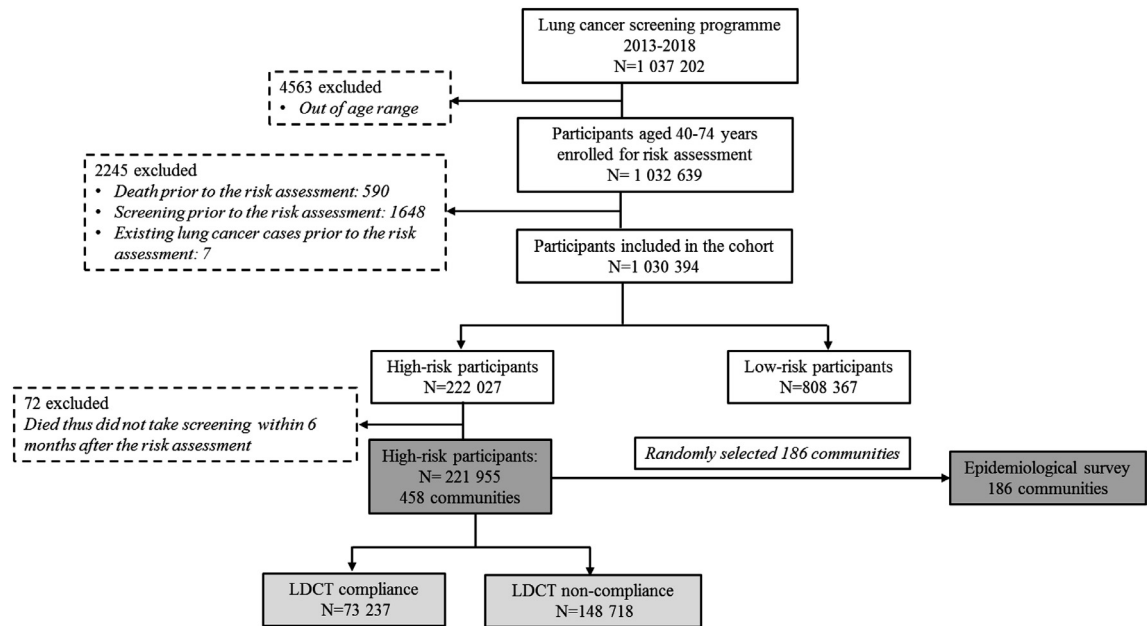


Figure 1. Study flow chart.

potentially at high risk of lung cancer into the LCS programme, the risk score was calculated using seven covariates for males and females, respectively (Supplementary Context). Individuals categorised as being at high risk of lung cancer would be informed of smoking harm, potential benefits and risks associated with LDCT scans and then make a collaborative decision on undertaking LDCT scans with healthcare providers. The high-risks were subsequently referred to one-off LDCT scans at no cost in designated hospital settings. Different strategies were used to motivate the high-risk participants to take LDCT scans in each community, including the media-assisted advertisement, navigation assistance, express service, arranged transportation, timely LDCT scans, etc. The flow chart of the entire screening process was conceptualised in Supplementary Figure 1.

Variable definitions

To identify the individual factors associated with the screening uptake, the following variables were considered: demographic variables (age at recruitment, sex, education level [low: primary school or below, medium: secondary school to high school, high: college or above], and body mass index), lifestyle factors (smoking status [non-smoker, former smoker, and current smokers], passive smoking, occupational exposure to hazardous substances [including asbestos, rubber, dust, pesticide, radiation, beryllium, uranium, and radon for at least one year], frequent exercise [\geq three times/week, with each lasting over 30 min], frequent alcohol drinking, and frequent tea drinking), a

history of respiratory diseases [including pulmonary tuberculosis, chronic bronchitis, emphysema, asthma, bronchiectasis, and silicosis or pneumoconiosis], number of baseline comorbidities, psychological dysfunction (depressive symptoms for more than six months such as a persistent feeling of sadness and loss of interest), and a family history of lung cancer. Former smokers were defined as those who had previously smoked tobacco over once per day for at least six months but had quit smoking at the time of the interview. Baseline comorbidities included digestive diseases, hepatobiliary diseases, hypertension, diabetes, and hyperlipidemia, which were the most common chronic diseases influencing health conditions of the Chinese population and shared common lifestyle risk factors with cancer.

To identify the structural characteristics associated with uptake rates, the following variables were considered: structural delays (time intervals from the risk assessment to the LDCT scan), distance (from the community to the screening hospital), media (if media was used to deliver information on lung cancer screening to the high-risk population and motivate them to undergo LDCT scans), arranged transportation (whether the community centrally organize residents to go to the screening hospital), navigation assistance (if a navigation service was used to provide autonomous booking and hospital navigation services), express services (if there were express services of diagnosis and treatment for screening-positive participants in the screening hospital), and work incentives (including pay incentives or rewards).

Outcome definitions

From the individual level, the primary outcome was whether the high-risk individuals undertook LDCT scans within six months following the initial baseline risk assessment (yes or no question). From the structural level, the primary outcome was the uptake rate of the high-risk participants in the selected communities (continuous variable). The secondary outcome was the incidence of advanced-stage lung cancer (Stage II–IV, continuous variable). International Classification of Diseases (the 10th revision) was used to identify lung cancer cases (C34). The ascertainment of lung cancer was retrieved via national linkages to the cancer registry system every six months.

Statistical analyses

Continuous variables were presented using mean \pm standard deviation (SD) and categorical variables were presented by frequency (n) and proportion (%). Given that p-values are sensitive to the sample size,²⁰ we reported standardized differences which referred as the difference in the means or proportions divided by a pooled estimate of the SD.^{21,22} Standardized differences greater than 0.1 were considered meaningful.²¹

To describe the uptake rates of the NLCS programme, we reported the crude rates by year of programme (2013–2018), age group (40–49, 50–59, 60–69, and 70–74 years), sex, smoking status (non-smokers, current smokers, and former smokers), education level (low, medium, and high) and economic status (developed and developing areas). Economic status was determined based on each province's gross domestic product (GDP) in 2018 and classified as developed areas (Beijing, Zhejiang, and Jiangsu Provinces) or developing areas (Anhui, Hunan, Liaoning, Guangxi, and Henan Provinces). Uptake rates standardized by these variables were also reported with the entire study population as the standard group. Taking sex as an example, the expected cases for males and females were estimated if they had the same composition of other variables (age group, education level, smoking status, and economic status) as in the standard population. Standardized rates were then calculated by dividing the total of expected cases by the standard population.

The abovementioned variables with standardized differences greater than 0.1 were entered into a multivariable logistic regression model to identify individual factors associated with LDCT uptake. For these analyses, we excluded the participants who died thus did not take LDCT scans within six months from the baseline risk assessment. Multiple imputation for the missing information on the candidate risk factors was performed through the method of chained equations using the R package MICE. A linear regression model was used for continuous variables and logistic regression for binary/categorical data. To explore the associations between the uptake probabilities and the incidence of

lung cancer at advanced stages, we calculated propensity scores to estimate the uptake probabilities of LCS among the high-risks, considering the abovementioned individual factors. Pearson's correlation and non-linear cubic regression splines were adopted to characterize this association. The multivariable linear regression model was performed to explore the association between the structural characteristics as the independent variables and uptake rates in 186 communities as the continuous dependent variable. Linear assumptions were checked graphically.

There was a possibility for the non-compliant individuals to take LDCT scans in medical facilities other than the designated hospitals, however, this information was not recorded. As such, we conducted sensitivity analyses excluding participants who did not take the LDCT scans in our programme but were diagnosed with lung cancer within six months after the initial risk assessment. Considering the clustering effect that individuals in the same community may share common characteristics, sensitivity analyses were conducted using the mixed-effects regression model to account for this issue. The statistical analyses were performed using R version 3.6.1 (The R Foundation). All tests were two-sided, and p-values of 0.05 or less were considered statistically significant.

Role of the funding source

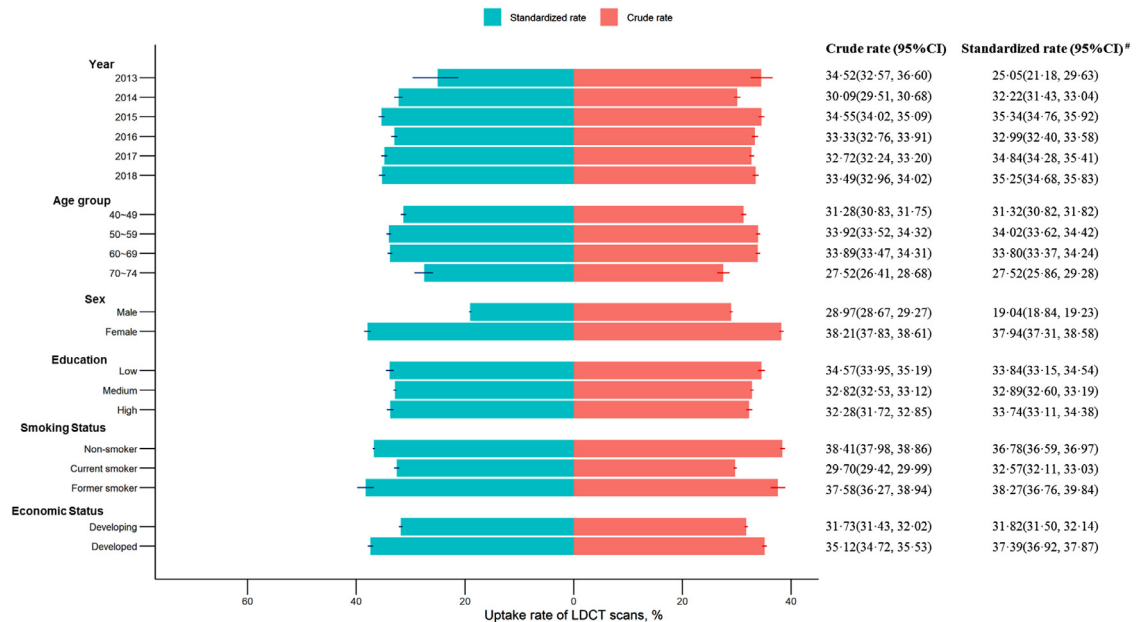
The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding authors had full access to the dataset and had final responsibility for the decision to submit for publication.

Results

Overview of the uptake rates

Amongst the 1,032,639 participants enrolled in 2013–2018 in the NLCS programme, 1,030,394 individuals took the risk assessment procedure, and 222,027 were labelled as the high-risks. Excluding the 72 individuals who died within six months after risk assessment and before the screening, a total of 221,955 individuals in 458 communities were included in our study (Figure 1).

The overall uptake rate of LDCT scan was 33.0% (73,237/221,955) amongst all high-risks for lung cancer. The uptake rates did not increase significantly from 2013 to 2018 (Figure 2). Significant higher uptake rates were found amongst females (38.2%), those aged between 50 and 69 (33.9%), non-smokers (38.4%) or former smokers (37.6%), or individuals residing in developed areas (35.1%). After standardization, a borderline significant trend was found across different years ($P=0.0705$). The standardized uptake rate (SUR) of females (37.9%) was almost twice of that amongst



#: Standardized by year of program, age group, sex, education level, smoking status, and economic status. A borderline significant trend was found from 2013 to 2018 (P=0.0705).

Figure 2. Crude and standardized uptake rates of lung cancer screening by subgroups.

males (19.0%). Low-educated individuals had similar SUR as the high-educated ones (33.8% vs. 33.7%). The SUR was the highest amongst the former smokers (38.3%), followed by the non-smokers (36.8%) and the current smokers (32.6%). Participants in the developed areas had higher SUR (37.4%) than those in the developing areas (31.8%).

Individual-level factors associated with the LDCT uptake

The characteristics of the study population are presented in Table 1. Of all participants, the mean (SD) age was 55.9 (8.3) years, 56.4% were male, 61.8% were current smokers and 34.5% were non-smokers, 68.0% had chronic respiratory diseases, and 41.9% had a family history of lung cancer. The univariate analysis revealed that sex, smoking status, passive smoking, occupational exposure to hazardous substances, chronic respiratory diseases, a family history of lung cancer, number of baseline comorbidity, and psychological dysfunction were significantly associated with the LDCT uptake with the standardised difference >0.1.

As presented in Table 2, after controlling for other covariates, females were more likely to take the LCS than males (OR 1.14, 95% CI 1.10–1.17). Relative to the non-smokers, the probability of screening uptake in the former smokers was 18% higher (OR 1.18, 95% CI 1.12–1.24), whereas the probability was 7% lower in the current smokers (OR 0.93, 95% CI 0.90–0.96). Longer duration of passive smoking was associated with higher uptake rates (compared with no passive

smoking, 0–19 years: OR 1.06, 95% CI 1.02–1.09; 20–39 years: OR 1.09, 95% CI 1.06–1.12; and ≥40 years: OR 1.16, 95%CI 1.13–1.20). Individuals with a family history of lung cancer, chronic respiratory diseases, and occupational exposure were 85%, 17% and 26% more likely to undergo LDCT scans (OR 1.85, 95% CI 1.81–1.89; OR 1.17, 95% CI 1.14–1.20; and OR 1.26, 95% CI 1.24–1.29). The participants who had more baseline comorbidities had higher uptake rates (OR 1.39, 95% CI 1.35–1.43; OR 1.32, 95% CI 1.28–1.35; and OR 1.31, 95% CI 1.28–1.35, in comparison of those with ≥3, 2, 1 and those without comorbidities). The participants who had psychological dysfunction were less likely to undergo LDCT scans (OR 0.92, 95% CI 0.90–0.94).

A total of 1266 lung cancer cases occurred during a median follow-up of 3.2 years (interquartile range [IQR]: 2.1–4.8 years), of which 893 (70.5%) had known disease stages and 437 were at Stage II–IV. The propensity scores of the uptake were negatively associated with the incidence of advanced-stage lung cancer (Pearson’s correlation coefficient: –0.88 [95% CI –0.97~ –0.57], p: 0.0007, Supplementary Figure 2). The sensitivity analysis included 221,857 individuals, amongst whom 73,237 (33.0%) took the LDCT scans (Supplementary Table 1). Similar associated factors and their correlations with the screening uptake were identified as the main findings (Supplementary Table 2). The mixed-effects model accounting for the clustering effect showed similar results to the main analysis (Supplementary Table 3).

	Total (N = 221,955)	No (N = 148,718)	Yes (N = 73,237)	Standardized difference
Demographics				
Age				
mean (SD)	55.90 (8.3)	55.85 (8.3)	56.01 (8.0)	0.019
40–49	57,028 (25.7)	39,187 (26.3)	17,841 (24.4)	0.071
50–59	82,695 (37.3)	54,647 (36.7)	28,048 (38.3)	
60–69	74,056 (33.4)	48,958 (32.9)	25,098 (34.3)	
70–74	8176 (3.7)	5926 (4.0)	2250 (3.1)	
Sex				
Male	125,228 (56.4)	88,954 (59.8)	36,274 (49.5)	0.208
Female	96,727 (43.6)	59,764 (40.2)	36,963 (50.5)	
Education level				
Low	34,356 (15.5)	22,480 (15.1)	11,876 (16.2)	0.032
Medium	148,192 (66.8)	99,552 (66.9)	48,640 (66.4)	
High	39,407 (17.8)	26,686 (17.9)	12,721 (17.4)	
Body mass index				
<18.5	4250 (1.9)	2864 (1.9)	1386 (1.9)	0.049
<24	108,899 (49.1)	74,074 (49.8)	34,825 (47.6)	
<28	87,103 (39.2)	57,602 (38.7)	29,501 (40.3)	
≥28	21,420 (9.7)	13,967 (9.4)	7453 (10.2)	
Missing	283 (0.1)	211 (0.1)	72 (0.1)	
Lifestyle factors				
Smoking status				
Non-smoker	76,615 (34.5)	47,184 (31.7)	29,431 (40.2)	0.189
Current smoker	137,253 (61.8)	96,486 (64.9)	40,767 (55.7)	
Former smoker	8087 (3.6)	5048 (3.4)	3039 (4.1)	
Passive smoking				
No	42,701 (19.2)	31,031 (20.9)	11,670 (15.9)	0.134
0–19 years	28,142 (12.7)	19,116 (12.9)	9026 (12.3)	
20–39 years	114,491 (51.6)	75,264 (50.6)	39,227 (53.6)	
≥40 years	35,781 (16.1)	22,789 (15.3)	12,992 (17.7)	
Missing	840 (0.4)	518 (0.3)	322 (0.4)	
Occupational exposure to hazardous substances				
No	140,069 (63.1)	98,895 (66.5)	41,174 (56.2)	0.212
Yes	81,886 (36.9)	49,823 (33.5)	32,063 (43.8)	
Frequent exercise				
No	158,150 (71.3)	104,878 (70.5)	53,272 (72.7)	0.049
Yes	63,805 (28.7)	43,840 (29.5)	19,965 (27.3)	
Frequent alcohol drinking				
Never	103,748 (46.7)	69,259 (46.6)	34,489 (47.1)	0.016
Yes, and is currently drinking	107,959 (48.6)	72,692 (48.9)	35,267 (48.2)	
Previously yes, but not now	10,248 (4.6)	6767 (4.6)	3481 (4.8)	
Frequent tea drinking				
Never	103,292 (46.5)	69,645 (46.8)	33,647 (45.9)	0.036
Yes, and is currently drinking	104,988 (47.3)	70,327 (47.3)	34,661 (47.3)	
Previously yes, but not now	13,675 (6.2)	8746 (5.9)	4929 (6.7)	
Disease history				
Chronic respiratory diseases				
No	71,053 (32.0)	53,645 (36.1)	17,408 (23.8)	0.271
Yes	150,901 (68.0)	95,072 (63.9)	55,829 (76.2)	
Missing	1 (0.0)	1 (0.0)	0 (0.0)	

Table 1 (Continued)

	Total (N = 221,955)	No (N = 148,718)	Yes (N = 73,237)	Standardized difference
Number of baseline comorbidity				
0	52,680 (23.7)	39,728 (26.7)	12,952 (17.7)	0.231
1	55,157 (24.9)	36,285 (24.4)	18,872 (25.8)	
2	48,171 (21.7)	30,711 (20.7)	17,460 (23.8)	
≥3	49,815 (22.4)	30,964 (20.8)	18,851 (25.7)	
Missing	16,132 (7.3)	11,030 (7.4)	5102 (7.0)	
Psychological dysfunction				
Depressive symptoms for more than 6 months				
No	146,249 (65.9)	100,546 (67.6)	45,703 (62.4)	0.109
Yes	75,706 (34.1)	48,172 (32.4)	27,534 (37.6)	
Family history of lung cancer				
No	118,849 (53.5)	87,987 (59.2)	30,862 (42.1)	0.392
Yes	92,909 (41.9)	52,887 (35.6)	40,022 (54.6)	
Missing	10,197 (4.6)	7844 (5.3)	2353 (3.2)	

Table 1: Baseline characteristics of the participants by LDCT uptake groups.

Presented are n (%) unless otherwise specified.

% may not sum up to 100% due to rounding.

LDCT: Low Dose Computed Tomography.

SD: Standard deviation.

Structural characteristics associated with the uptake rates

The characteristics of the participants from the 186 surveyed communities were similar to those from the unsurveyed communities (Supplementary Table 4). The median uptake rate of the surveyed communities was 35.7% (IQR: 26.4–44.8%) (Table 3, Supplementary Figure 3). As shown in Table 3, of the 186 communities, 61.3% provided timely LDCT scans for the high-risk participants within 30 days after risk assessment, whereas 34.4% had structural delays to LDCT screening with a median time interval of 30–90 days and 4.3% had delays of more than 90 days; 74.7% were located within 10 km to the screening hospital; 54.3% were provided with transportation to the screening hospitals for the participants; 73.1% used a navigation assistance to provide booking and navigation services; 92.5% established express services for diagnosis and treatment for those with positive screening results; 73.1% adopted social media to publicise the screening programme; and 67.2% incorporated work incentives. The uptake rates of the communities with arranged transportation, a navigation assistance, express service, media-assisted publicity, and incentives were higher than those of their counterparts.

When dividing the uptake rates of the communities into quartiles, the distribution of distances (in kilometres) between the community and the screening hospital were similar across categories, with medians (IQRs) of 5 (3–15), 5 (3–10), 5 (3–8), and 5 (2–13) in the first, second, third, and fourth quartiles, respectively (Supplementary Figure 4a). The structural delays (in days) were significantly shorter in the quartiles of higher

uptake rates, with medians (IQRs) of 48 (24–74), 40 (17–59), 45 (18–68), and 18 (11–28) days, respectively (Supplementary Figure 4b). According to the qualitative ratings of the reasons for non-participation, 84.4%, 62.4%, and 47.3% of the 186 communities agreed that the most common reasons were ‘participants were asymptomatic and did not think they would get lung cancer’, ‘they preferred not to know their lung cancer status’, and ‘lung cancer screening was time-consuming’, respectively (Supplementary Figure 5).

The multivariable linear regression analysis revealed that compared with the uptake rates of the settings with shorter structural delays (median time interval ≤14 days), those in the setting with the structural delays of 14–30, 30–90, and >90 days were 4.3%, 7.2%, and 13.7% lower, respectively (β -4.34, 95% CI -9.72–1.05; β -7.17, 95% CI -12.76–-1.57; β -13.69, 95% CI -24.61–-2.76). Involving media-assisted publicity (β 6.43, 95% CI 1.60–11.26) and a navigation assistance (β 5.48, 95% CI 0.44–10.52) remained to be significantly associated with higher uptake rates (Table 2). The assumptions made by the linear regression model were well met (Supplementary Figure 6).

Given that males and current smokers were less likely to undergo the LDCT scans, we conducted subgroup analyses to describe how the stratified uptake rates varied in the settings with changing significant structural characteristics. The males who received media-assisted publicity and had a structural delay ≤14 days showed an uptake rate of 46.6%, which was more than twice that of the males who received no media campaign and had a structural delay >90 days (19.9%). The males in the setting with a screening navigation assistance and a structural

Factors from two dimensions	Measures of association
Individual level^a	OR (95%CI)
Sex	
Female vs. Male	1.14 (1.10, 1.17)
Smoking status	
Current smoker vs. non-smoker	0.93 (0.90, 0.96)
Former smoker vs. non-smoker	1.18 (1.12, 1.24)
Passive smoking	
0–19 years vs. No	1.06 (1.02, 1.09)
20–39 years vs. No	1.09 (1.06, 1.12)
≥ 40 years vs. No	1.16 (1.13, 1.20)
Occupational exposure to hazardous substances	
Yes vs. No	1.26 (1.24, 1.29)
Chronic respiratory diseases	
Yes vs. No	1.17 (1.14, 1.20)
Number of baseline comorbidity	
1 vs. none	1.31 (1.28, 1.35)
2 vs. none	1.32 (1.28, 1.35)
≥3 vs. none	1.39 (1.35, 1.43)
Depressive symptoms for more than 6 months	
Yes vs. No	0.92 (0.90, 0.94)
Family history of lung cancer	
Yes vs. No	1.85 (1.81, 1.89)
Structural level^b	β (95%CI)
Structural delay (day)	
14–30 vs. ≤14	–4.34 (–9.72, 1.05)
30–90 vs. ≤14	–7.17 (–12.76, –1.57)
>90 vs. ≤14	–13.69 (–24.61, –2.76)
Media	
Yes vs. No	6.43 (1.60, 11.26)
Navigation assistance	
Yes vs. No	5.48 (0.44, 10.52)

Table 2: Multivariable regression models on individual and structural characteristics.

^a Logistic regression model on individual characteristics.
^b Linear regression model on structural characteristics.

delay ≤14 days had an uptake rate three times of those without the assistance and had a structural delay >90 days (39.4% vs. 13.7%, Supplementary Figure 7). The uptake rate was 44.2% of the current smokers with media campaign and a structural delay ≤14 days, compared to the uptake rate of 23.5% amongst those without media campaign and a structural delay >90 days. The uptake rate was 39.7% amongst the current smokers in the setting with a navigation assistance and a structural delay ≤14 days, which nearly tripled that amongst the current smokers without these infrastructures (14.0%, Supplementary Figure 8).

Discussion

To the best of our knowledge, this is the largest and most comprehensive population-based study evaluating

	Community Number (%)	Uptake rate Median (interquartile range)
Total	186 (100.0)	35.7% (18.4%)
Distance (kilometre)		
≤5	77 (41.4)	33.8% (17.8%)
5~10	62 (33.3)	34.9% (18.2%)
>10	47 (25.3)	37.9% (18.3%)
Arranged transportation		
Yes	101 (54.3)	36.9% (17.6%)
No	85 (45.7)	33.2% (18.2%)
Navigation assistance		
Yes	136 (73.1)	37.8% (20.2%)
No	50 (26.9)	30.3% (17.8%)
Express service		
Yes	172 (92.5)	35.9% (18.6%)
No	14 (7.6)	33.5% (16.8%)
Media		
Yes	136 (73.1)	38.3% (18.8%)
No	50 (26.9)	33.5% (18.7%)
Incentives		
Yes	125 (67.2)	36.9% (18.0%)
No	61 (32.8)	32.9% (21.4%)
Structural delay (day)		
≤14	47 (25.3)	40.0% (25.0%)
14–30	67 (36.0)	35.4% (18.2%)
30–90	64 (34.4)	35.9% (17.5%)
>90	8 (4.3)	29.6% (3.6%)

Table 3: Uptake rates of 186 communities by structural characteristics.

LCS uptake in developing countries, including more than 220 thousand eligible participants recruited from multiple centres. We found that the overall uptake rate of LDCT screening was as low as 33.0%. Males, current smokers and individuals with psychological dysfunction were less likely to undertake LCS, indicating the necessity of tailored interventions for these subgroups to address potential LCS disparities. Accelerating referral to LDCT scans was independently associated with higher uptake rates, as was the utilisation of social media and the navigation assistance.

The study depicted a process model of the LCS in China. In western countries, potential participants in centralised LCS programmes are referred for screening mostly by primary care providers, and lung cancer specialists at the screening settings perform several services, including eligibility determination, shared decision-making, LDCT scans, and result management.²³ However, the process model in China varies slightly. Interrelated steps that include LCS advocacy, risk assessment, screening counselling, and referral are delivered by healthcare providers in a community-based setting, typically community healthcare centres (CHCs).

Since the 1990s, China has devoted tremendous efforts to reforming and expanding promising CHCs to strengthen primary care networks to deliver not only disease prevention and medical treatment for common diseases, but also healthcare surveys, health education and promotion.²⁴ Under the three-tiered healthcare system in China, nearly 35,000 similar CHCs served as the first line of defence in protecting the health of more than 700 million residents in 2018.²⁵ The Chinese CHCs in programme areas shoulder the responsibility of the dissemination and the first half of the LCS implementation. Our process model will guide the endeavours of centralised LCS to better identify potential targets for interventions from the perspectives of service providers and demanders to improve the quality and equity of the LCS continuum in China, as well as other developing countries with similar lung cancer epidemics or social-economic situation, such as areas with limited medical resources, or settings where non-smoking women account for a large proportion of lung cancer cases. Additionally, under the framework of centralised cancer screening, this population-based study may provide experience for policymakers to make evidence-based decisions on constructing successful LCS strategies.

An optimal uptake is essential for LCS to confer mortality benefits. Modelling studies have demonstrated that LDCT screening for lung cancer may avert lung cancer deaths and gain life-years compared with no screening, assuming a 100% uptake rate of LDCT scans.²⁶ Our study confirms that greater uptake rates of LCS are highly correlated with a lower incidence of advanced-stage lung cancer. Therefore, successful implementation of LCS programmes to identify early-stage lung cancer requires optimising uptake rates, which would result in further reduction of lung cancer mortality. However, in this study, the overall uptake was suboptimal, which appears to be a common problem in a real-world LCS programme involving large high-risk populations.¹² The uptake rate in the current study was higher than those reported using national data in the U. S., which increased from 3.8% to 16% between 2010 and 2017,^{27,28} but substantially lower than those reported in RCTs (90%). After the risk assessment, only 33% of high-risk individuals showed up for the LDCT screening. Our study found that most participants believed they would not get lung cancer due to no presence of symptoms or preferred not to know. This highlights the importance of raising people's awareness of cancer prevention, which is in line with the Healthy China Initiative,²⁹ published by the National Health Commission. Also, some high-risk participants considered multiple visits to LCS as time-consuming. Our study calls on multifaceted interventions to simplify the screening procedure and provide structural benefits to improve the uptake rate of LDCT scans in real-world LCS programmes.

Our findings provide new insights into the structural intervention targeting multiple points in the programme to encourage uptake. For the first time, we observed that the screening settings where individuals received timely LDCT scans (within two weeks) experienced dramatically higher uptake rates than those with longer waiting times. This study provides pragmatic suggestions for simplifying the pathway from assessment to screening while implementing centralised LCS programmes. A simplified structural intervention would incorporate a streamlined and standardised time frame for risk assessment, counselling, referral, expanded access to LDCT scans, and full life cycle management, with an emphasis on the integration of and linkage to the screening pathway. The organisational structure would designate activities to take place in a predetermined schedule.³⁰ For example, following a positive result of a cancer risk assessment, the candidate would receive pre-screening counselling (e.g. dissemination of basic knowledge about lung cancer, benefits and harms of screening, and shared decision-making) on the same day in the same setting. At this time, the candidate would be scheduled for a screening appointment at qualified medical institutions within the following one to two weeks. This 'assessment-to-timely-screening' approach needs to be implemented in the centralised LCS programme. Our findings add important dimensions to the need to accelerate the time from risk assessment to LDCT screening with a patient-centred approach. Further studies are needed to evaluate the effectiveness of a simplified structural intervention in reducing delays in LDCT uptake and decreasing mortality.

In accordance with previous studies,^{11,18,31} our study adds evidence for using social media and a navigation assistance to motivate LDCT uptake rather than the traditional publicity approaches, such as distributing pamphlets and displaying roll-up banners. Using social-media campaigns to promote awareness of LCS can help the target populations and the service providers to obtain a deeper understanding of scheduled LDCT scans. The American Thoracic Society also recommends the utilisation of mass communication and social media, with the integration of patient navigators, to reach the targeted populations and thus increase the screening uptake.¹⁸ A previous study demonstrated that digital systems are valuable tools to enhance engagement with LCS effectively, for example, weekly visits to the screening web pages and scheduled LDCT exams.³¹ A mobile application integrating risk assessments, screening appointments, and health education on cancer prevention has been developed in China to make the streamlined screening services more accessible for the general population aged over 18. Mobile phone users can complete the epidemiological questionnaire and the risk assessment for lung cancer online. Furthermore, media campaigns deployed in China should incorporate

smoking cessation and online interventions with different frequencies and intensities for subpopulations with varying uptake rates.

Disparities in the uptake of LCS were observed across diverse subgroups in our study. We found socioeconomic inequality in LCS uptake and the lower SUR in the developing areas (31.8% vs. 37.4%). Previous research has shown that the lung cancer mortality reduction due to one-off LDCT screening was statistically significant in developed areas compared to developing areas in China.⁵ Our findings revealed that lower uptake of LCS, and a correspondingly higher incidence of advanced-stage lung cancer, may partially compromise the effectiveness of one-off LCS in developing areas. This study shows that LCS programmes should consider area-adapted screening strategies.

As expected, higher uptake rates were found amongst individuals with a family history of lung cancer, a history of respiratory diseases, occupational exposures, passive smoking, and other baseline comorbidities, which are common risk factors for lung cancer. Moreover, we noted that current smokers were less likely to take the LDCT scans, which is in line with previous findings,^{11,32} where most current smokers were unaware that they were at risk for lung cancer or preferred not to learn their lung cancer status. China is the largest tobacco consumer worldwide with more than 300 million smokers, accounting for nearly one-third of the world's total, and over half of adult men in China are current smokers.³³ These findings call for a multipronged approach to enhance engagement and extensively scale up LCS amongst current smokers in China. A positive finding from this study pertains to former smokers: their attitudes towards screening appeared to be no worse than those of non-smokers. This further highlights the importance of integrating smoking cessation and tobacco abstinence into the centralised LCS programme. Unlike previous studies that found females were less likely to take the LDCT scans,^{18,34} females in this study were more likely to participate. This may be attributable to females being primarily non-smokers in China. In our cohort, 79% of the females did not smoke. Tailored interventions targeting these underserved subgroups may increase the overall uptake rates of LCS.

Notably, the structural characteristics may be more relevant to the uptake of LDCT scans than individual factors. Our post-hoc analyses demonstrated that the participation rates of males and current smokers increased substantially with the involvement of important structural interventions, indicating that the evidence-based structural strategies played an essential role in the screening uptake of the high-risk population of lung cancer. Our findings provide insights for policymakers to consider implementing structural interventions first, which might be more effective than conducting individual-targeted intervention first, especially in scenarios where individual-targeted intervention is unavailable. Individualised interventions such as smoking cessation programmes or education to increase individuals'

awareness of LCS can be considered as an add-on to facilitate the successful implementation of the LCS programme.

A few limitations should be acknowledged. First, the epidemiological information collected in the current study was self-reported, leading to potential information bias. For example, participants who attend screening may be more likely to report occupational exposures. However, we conducted strict quality control training for investigators each programme year to ensure that participants clearly understood all the questions. Despite this, further studies are required to measure these exposures quantitatively. The use of a single item to measure depressive symptoms for more than six months has not been validated. Second, the interaction between sex and smoking status may be associated with the uptake rates. However, we were not able to check this interaction because, in the current study, males without a smoking history were excluded from the high-risk group as a premise. Further studies are required to evaluate the potential interactive effect. Third, we used aggregate-level data collected from a cross-sectional survey in 2018 as a proxy for structural characteristics. Some attributes may vary slightly across the study period. However, a significant policy change (the 'Healthy China Initiative') to expand screening and early treatment was implemented in China after 2019. This study is considered to have a high data validity, as the LCS consistently used the same inclusion criteria for participants, risk assessment questionnaire, and structural policy during the study period. Fourth, the influence of individual emotional barriers, such as fear, anxiety, and avoidance of cancer information about lung cancer, on LDCT uptake was not quantitatively assessed in this study. Additionally, observational studies of associated risk factors are potentially biased by unmeasured confounding.

In conclusion, our findings provide timely scientific values and experience for successfully constructing centralised LCS programs transitioning from an academic experiment into the standard-of-care in healthcare settings. Maintaining an optimal uptake of LCS among the high-risk populations in the centralised screening program remains challenging. Multifaceted interventions to increase uptake are recommended, which focus on the individuals with poor compliance and integrate the 'assessment-to-timely-screening' approach to minimise structural delays, media publicity, and a navigation assistance at the structural level.

Contributors

Jie He conceived the national lung cancer screening project and took responsibility for its all aspects. Ni Li and Wei Cao designed the study and conceived this article, with further contributions from Fengwei Tan, Kuangyu Liu, Zheng Wu, and Fei Wang. Ni Li, Wanqing Chen, and Fengwei Tan led the data collection supported by Lingbin Du, Ning Wang, Shipeng Yan, Shaokai Zhang, Ji Cao, Dong Dong, Donghua Wei,

Lianzheng Yu, Yunyong Liu, Jufang Shi, Jiansong Ren, and Liang Zhao. Fengwei Tan, Wei Tang, Kai Su, and Fang Li led the quality control by medical records reviews. Ni Li, Wei Cao, Kuangyu Liu, Fei Wang, and Yiwen Yu wrote the manuscript, with further contributions from Yan Wen, Yongjie Xu, Chao Qin, Jiang Li, Xuesi Dong, Zhuoyu Yang, and Yadi Zheng. Ni Li, Wei Cao, Fei Wang, and Zheng Wu verified the underlying data, and completed all the statistical analysis. All authors interpreted data, contributed to critical revisions, and approved the final version of the article.

Data sharing statement

The analysed datasets in the study cannot be shared with the third parties due to the relevant regulations of the Ministry of Industry and Information Technology of China. Data sharing can only be possible after reaching a consensus agreement with the Ministry.

Declaration of interests

All authors declare no conflict of interest.

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Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.eclinm.2022.101594.

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