Original Article

Risk prediction models for lung cancer: Perspectives and dissemination

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Abstract

Objective: The objective was to systematically assess lung cancer risk prediction models by critical evaluation of methodology, transparency and validation in order to provide a direction for future model development.

Methods: Electronic searches (including PubMed, EMbase, the Cochrane Library, Web of Science, the China National Knowledge Infrastructure, Wanfang, the Chinese BioMedical Literature Database, and other official cancer websites) were completed with English and Chinese databases until April 30th, 2018. Main reported sources were input data, assumptions and sensitivity analysis. Model validation was based on statements in the publications regarding internal validation, external validation and/or cross-validation.

Results: Twenty-two studies (containing 11 multiple-use and 11 single-use models) were included. Original models were developed between 2003 and 2016. Most of these were from the United States. Multivariate logistic regression was widely used to identify a model. The minimum area under the curve for each model was 0.57 and the largest was 0.87. The smallest C statistic was 0.59 and the largest 0.85. Six studies were validated by external validation and three were cross-validated. In total, 2 models had a high risk of bias, 6 models reported the most used variables were age and smoking duration, and 5 models included family history of lung cancer.

Conclusions: The prediction accuracy of the models was high overall, indicating that it is feasible to use models for high-risk population prediction. However, the process of model development and reporting is not optimal with a high risk of bias. This risk affects prediction accuracy, influencing the promotion and further development of the model. In view of this, model developers need to be more attentive to bias risk control and validity verification in the development of models.

Keywords: Lung neoplasms; carcinoma; bronchogenic; risk assessment; models; theoretical

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Introduction

Lung cancer is the most common cause of cancer death worldwide. In 2012, there were 1.82 million new cases, accounting for 12.9% of the total number of new cancers and 1.56 million lung cancer deaths, with lung cancer responsible for nearly 1 in 5 cancer deaths (1). In Europe, lung cancer is the most common cause of cancer death in males (267,000, 24.8%) and the second most common cause of cancer death in females (121,000 deaths, 14.2%) (2). The National Lung Screening Trial (NLST) in the United States found a 20% relative reduction in mortality of lung cancer among long-term, high-risk smokers that were screened with low-dose computed tomography (LDCT) (3). That trial suggests that screening may prevent and reduce lung cancer mortality with sensitive risk models. Hence, population screening for the early detection of lung cancer is an important part of current clinical research.

However, LDCT screening has disadvantages including radiation exposure, false positives and over diagnosis. It is therefore essential to identify the most appropriate target population to maximize screening benefits and minimize adverse effects. By preliminary assessment, screening programs for high-risk groups will improve screening efficiency as well as reduce screening costs and resource waste. In fact, the success of any screening program is directly related to high-risk group assessment (4,5) and accomplished with lung cancer prediction models (6,7). To help define the target population for lung cancer screening, some models allow calculation of individual risk for lung cancer based on previously results (8). Model prediction can improve clinical intervention and post-care development, as well as guide the selection of screening populations to promote optimal use of resources. After Bach's study (9), research focus has been on predictive models of lung cancer. Current models have good sensitivity and specificity and were based on traditional variables, biomarkers, LDCT and data mining techniques. The objective of this study was to evaluate prediction models for lung cancer high-risk groups in order to provide a direction for further model development.

Materials and methods

Search strategies and eligibility criteria

A systematic literature search was performed with both English and Chinese databases including EMbase, PubMed, Web of Science, the Cochrane Library, Chinese BioMedical Literature Database (CBM), WanFang Data, and the China National Knowledge Infrastructure (CNKI). The search used a combination of subject mesh terms and free words. Search terms included lung neoplasms, lung cancer, mass screening, early detection of cancer, risk factors, high-risk population, high-risk group, high-risky population, decision support techniques, prediction model and forecast model. A search strategy in PubMed is listed below as an example:

#1 "lung Neoplasms"[MeSH] OR "lung Neoplasms" [Title/Abstract] OR "lung cancer"[Title/Abstract]

#2 "Mass Screening"[MeSH] OR "Early Detection of Cancer"[MeSH] OR "Screening"[Title/Abstract]

#3 "high risk"[Title/Abstract]

#4 "decision support techniques"[MeSH] OR "prediction model" [Title/Abstract] OR "forecast model"[Title/Abstract]

#5 #1 AND #2 AND #3 AND #4

The inclusion criteria were: 1) lung cancer screening; 2) high-risk population prediction model; and 3) report validity and model's statistical method, etc. Literature exclusion criteria were: 1) non-Chinese, non-English, and documents that do not have full text; 2) not related to lung cancer screening or early diagnosis of lung cancer; 3) repeated publications; 4) review and other secondary research literature; 5) conference summary; or 6) patented technology.

Selection of eligible studies and data extraction

Two researchers independently conducted literature screening, data extraction and cross-checking. If disagreements occurred, the two researchers would discuss a solution or submit the disagreement to a third researcher for discussion. If information could not be extracted from an article, the researchers contacted the original author for clarification. When reading the literature, the researchers read the title and abstract first to exclude apparently unrelated literature, and then read the complete text to determine inclusion. Data extraction content mainly included: 1) basic information such as publication year, country or region, research design type, model's statistical method, crowd information, modeling sample, area under the receiver-operating characteristic curve (AUC) and concordance index (C-index); 2) model transparency information, inclusion variables, expressions, limitations, financial support, conflicts of interest and validity evaluation methods; 3) model risk of bias, including blind

method, data bias risk, sensitivity analysis of uncertainty variables, whether the model was calibrated, and external validity; 4) variables included in each model: socio-demographic, exposure history, smoking history, medical history, family history and genetic risk factors; 5) model validity evaluation content including internal validity, cross-validity and external validity; and 6) basic information of single-use models.

Framework for qualitative assessment of multiple-use models

In this study, models were divided into multiple-use and single-use. The model description, transparency and risk of bias assessment were used for multiple-use models. Model descriptions included model publication date, country or region, study type, model's statistical method, population information, modeling samples, model samples and model accuracy (AUC or C-index).

Transparency mainly evaluates the degree of disclosure of specific information by the model. Improving the transparency of the model promotes the use of the model by exposing the model development process, statistical methods, inclusion parameters, model structure and other pertinent information for the user (7). Herein, this study conducted a transparency evaluation of the inclusion variables, expressions, limitations, financial support and conflicts of interest for each model.

Validity directly reflects the accuracy of the model in realistic prediction and is also an important criterion for actual application of the model. This study evaluated the internal validity, intersection angle and external validity of the included models. Internal validity detects the standardization of mathematical methods and models in the process of model construction. Through multiple data training, it avoids unintentional calculation errors and improves the internal accuracy of the model. Cross-validation identifies how different models solve the same problem. External validity aligns the model to actual data and investigates its predictive accuracy. Validity evaluation should be compared and completed (10,11).

Risk of bias assessment was based on the Mcginn checklist (12) and the results of Jamie's study (13). A checklist for model risk of bias assessment was developed and blinded from outcome evaluation by the predictive factor blind method. In this manner, sensitivity analysis of the variables was determined when the model had been calibrated. The five dimensions of external validity were used to evaluate the risk of bias for clinical prediction tools, and the study was rated as high, moderate, or low risk of bias. Studies with a high risk of bias had a fatal flaw that made their results very uncertain. Studies with a low risk of bias met all criteria, making their results more certain. Studies that did not meet all criteria but had no fatal flaw (thus making their results somewhat uncertain) were rated as having a moderate risk of bias (*Table 1*).

Results

Basic information

A total of 11 models that were used multiple times were included in this study (*Figure 1*). Three of those were derived versions. The earliest model was the Bach model published in 2003. The largest number of published models was from the United States, with the remaining from the United Kingdom and Canada. These models were based on case-control studies (six studies) and cohort studies (five studies). Statistically, most of the studies used logistic regression, while three of the models used Cox regression.

Two of the models included racial factors. The other models were mainly limited by age and smoking history. The youngest individual was 20 years old and the oldest 80 years old. Most individuals were 50–75 years old. The definition of smoking history was defined as never smoker, former smoker and current smoker (*Table 2*).

Modeling samples ranged from 594 to 70,962. The accuracy of the model was measured by AUC or C statistic.

Table 1 Framework for quality assessment of multiple-use models

Term	Content
Transparency	1. Variables include (Yes or No)
	2. Model expression (Yes or No)
	3. Limitation
	4. Financial support
	5. Conflict of interest
	6. Validation
Risk of bias	1. Blind evaluation of outcome (Yes or No)
	2. Blind evaluation of predictor (Yes or No)
	3. Sensitivity analysis (Yes or No)
	4. Calibration (Yes or No)
	5. External validation (Yes or No)
Validation methods	1. Internal validation
	2. Cross-validation
	3. External validation

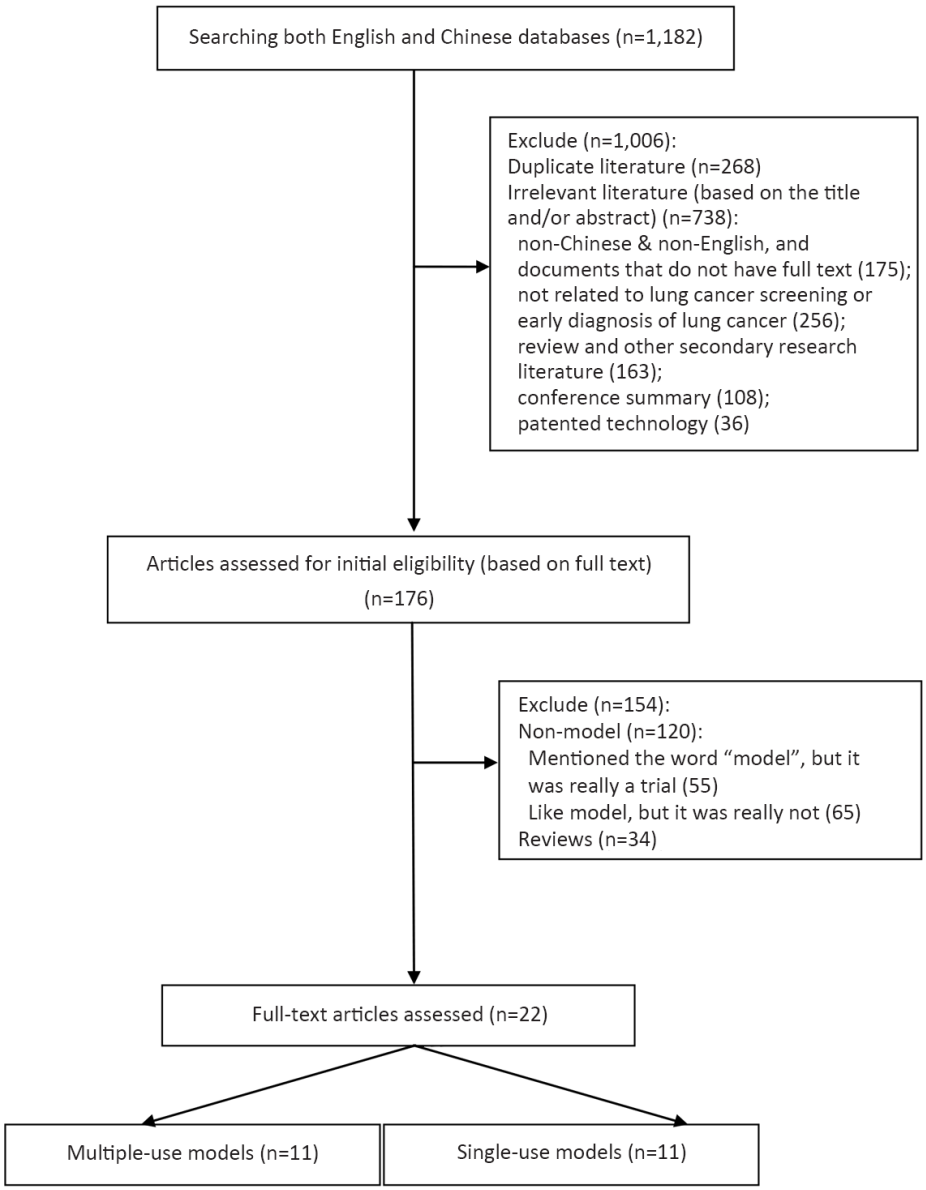

Figure 1 Flowchart of screening result.

According to the summary results, the minimum AUC of each model was 0.57 and the largest was 0.87. The smallest C statistic was 0.59 and the largest was 0.85.

Transparency

The models included in this study listed inclusion variables, but only two models listed the model's expressions. The limitations of each model were primarily uncommon population assessed by the model, the lack of good external validity verification and the inability of the model to assess an individual's lung cancer risk. The model research was supported by national and regional projects, or by public welfare funds such as the Lung Cancer Foundation. Only four studies reported no conflicts of interest with no other studies reporting relevant content. Six studies were validated through external validation and three were cross-validated (*Table 3*).

Risk of bias

Two of the included models had a high risk of bias and the remaining nine were of moderate risk. Sensitivity analysis of uncertain variables was not performed for all models,

Table 2 Characteristics of multiple-use models

Model	Year	Country or region	Research design	Statistical methods	Population	Modeling sample	AUC (95% CI)	C-index (95% CI)
Bach (9)	2003	US	Cohort study	Cox proportional hazards regression	Aged 50–69 years, current and former smokers	18,172		0.72
Spitz (14)	2007	US	Case-control study	Logistic	Never, former and current smokers	Cancer case 1,851/Control 2,001 Never smokers: cancer case 330/Control 379 Former smokers: cancer case 784/Control 884 Current smokers: cancer case 737/Control 738	Never smokers, 0.57 (0.47–0.66); Former smokers, 0.63 (0.58–0.69); Current smokers, 0.58 (0.52–0.64)	Never smokers: 0.59 (0.51–0.67); Former smokers: 0.63 (0.58–0.67); Current smokers: 0.65 (0.60–0.69)
Spitz (15)	2008	US	Case-control study	Logistic	Current and former smokers, White non-Hispanic cases	Current smokers: cancer case 350/Control 244; Former smokers: cancer case 375/Control 371	Former smokers, 0.70 (0.66–0.74); Current smokers, 0.73 (0.69–0.77)	
LLP (16)	2008	United Kingdom	Case-control study	Logistic	Aged 20–80 years	Cancer case 579/ Control 1,157	0.71	
LLPi (17)	2015	United Kingdom	Case-control study	Cox proportional hazards regression	Aged 45–79 years	8,760: cancer case 237, control 8,523		0.852 (0.831–0.873)
PLCO (18)	2009	Canada	Cohort study	Logistic	Aged 55–74 years who were free of the cancers under study	12,314	0.865	
PLCO (19)	2011	Canada	Cohort study	Logistic	Aged 55–74 years, Model 1: the PLCO control arms; Model 2: smokers only	Model 1: 70,962 Model 2: 38,254	Model 1: 0.859 (0.8476–0.8707); Model 2: 0.809 (0.7957–0.8219)	
PLCOM (20)	2012	Canada	Cohort study	Logistic	Aged 55–74 years, former smokers	36,286	0.803 (0.782–0.813)	
Etzel (21)	2008	US	Case-control study	Logistic	African-Americans	Cancer case 491/Control 497	0.75	
Pittsburgh (22)	2016	US	Case-control study	Logistic	Aged 55–74 years, current and former smokers	LDCT 25,929/CXR 25,648	LDCT 0.679/CXR 0.687	
Hoggart (23)	2012	United Kingdom	Cohort study	Survival analysis	Aged 40–65 years, current, former and never smokers	169,035 (90% of the data)	One year-current: 0.82; Former: 0.83; Never: 0.84. 5 year-current: 0.77; Former: 0.72; Never: 0.79	

AUC, area under receiver-operating characteristic curve; 95% CI, 95% confidence interval; C-index, concordance index.

Table 3 Transparency assessment of multiple-use models

Model	Variable included	Model expression	Limitation	Financial support	Conflict of interest	Validation
Bach	Y	N	It does not distinguish among the risks of different histologic types of lung cancer, and it is relevant only to one subset (albeit a large subset) of at-risk individuals — those aged 50 years or older who have a smoking history.	Research institution; National project fund	N	Internal validation/ Cross-validation
Spitz (2007)	Y	N	The models may not be sufficiently discriminatory to allow accurate risk assessment at the individual level. They are needed to be validated in independent populations.	Research institution; National project fund	N	External validation
Spitz (2008)	Y	N	Without an independent validation.	Research institution; National project fund	Y	Cross-validation
LLP	Y	Y	More work is needed to test the applicability of the model in diverse populations, including those from diverse geographic regions.	Research institution; Foundation	N	Cross-validation
LLPi	Y	Y	More work is needed to test the applicability of the model in diverse populations, including those from diverse geographic regions.	Region project fund; Foundation	Y	Internal validation
PLCO (2009)	Y	N	The study model was developed in asymptomatic individuals. It is unclear whether its performance will be substantially different in symptomatic individuals presenting to clinicians.	National project fund	N	Internal validation
PLCO (2011)	Y	N	The models may not be generalizable to other populations. Data on exposure to radon, asbestos, second-hand smoke, occupational carcinogens, and history of adult pneumonia were not available for analysis.	National project fund	N	Internal validation/ External validation
$PLCO_{M2012}$	Y	N	Excluded persons who had never smoked.	Research institution	N	External validation
Etzel	Y	N	The study was hospital-based and the controls were drawn only from the metropolitan area of Houston, Texas; therefore, the results may vary in other geographic locations; the sample size of the study was small.	National project fund	Y	Internal validation/ External validation
Pittsburgh	Y	N	The model is derived in preselected high-risk populations and not necessarily applicable to the general population of smokers, and it was derived and tested in the United States and applicability to other populations will need to be tested.	Research institution; National project fund	N	External validation
Hoggart	Y	N	Measures of carcinogens are limited to occupational exposures.	European Union project fund	Y	External validation

LLP, Liverpool Lung Project; PLCO, the Prostate, Lung, Colorectal and Ovarian; Y, reported; N, no reported.

with only one model blinded by predictive factors and outcome evaluations during development. It is worth noting that six models were calibrated after development, making the risk of bias moderate (*Table 4*).

Validity

Model internal validity design is used to develop data, perform repeated operations and verify consistency of

Table 4 Risk of bias assessment of multiple-use models

Model	Blind evaluation of outcome	Blind evaluation of predictor	Sensitivity analysis	Calibration	External validation	Risk of bias
Bach	N	N	Y	Y	N	M
Spitz (2007)	N	N	N	N	Y	M
Spitz (2008)	Y	Y	N	Y	N	M
LLP	N	N	N	N	N	H
LLPi	N	N	N	Y	N	M
PLCO (2009)	N	N	N	N	N	H
PLCO (2011)	N	N	N	N	Y	M
$PLCO_{M2012}$	N	N	N	Y	Y	M
Etzel	N	N	N	Y	Y	M
Pittsburgh	N	N	N	Y	Y	M
Hoggart	N	N	N	N	Y	M

Y, reported; N, no reported; H, high risk; M, middle risk.

results. Three models were repeated by the bootstrap method, one study was re-verified using a partial sample, and one study used five similar research data sets to perform internal validation of the model. Regarding cross-validity, two articles were verified 10-fold and one article 3-fold. Only six studies were externally validated. Sample size varied with a maximum of 44,233 cases and a minimum of 325 cases (*Table 5*).

Inclusion of variables

According to the statistical results, the variables included in the models were comprised of six aspects: sociodemographic factors, exposure history, smoking history, medical history, family history and genetic risk factors. The most used variables were age and smoking duration by 6 models, and 5 models included family history of lung cancer (*Table 6*).

Single-use models

The single-use models were mostly from China, with two from the United States and one from Germany. The types of studies were either cohort or case-control, with most studies from China case-control. Statistical methods were diverse. In addition to Logistic and Cox regression analysis, data mining techniques such as artificial neural network, artificial neural network, support vector machine, decision tree, support vector machine and Fisher discriminant analysis were employed. In addition to the above variables,

Table 5 Validation and samples of multiple-use models

Model	Internal validation	Cross-validation	External validation
Bach	Operate the model from five related study sites 3 times	10-fold cross-validation	
Spitz (2007)			25% of the data
Spitz (2008)		3-fold cross-validation	
LLP		10-fold cross-validation	
LLPi	Bootstrap 200 times		
PLCO (2009)	Bootstrap 1,000 times		
PLCO (2011)	Bootstrap 200 times		44,233
$PLCO_{M2012}$			37,332
Etzel	156		325
Pittsburgh			3,642
Hoggart			10% of the data

LLP, Liverpool Lung Project; PLCO, the Prostate, Lung, Colorectal and Ovarian.

Table 6 Variables of multiple-use models

Variables	Bach	Spitz (2007)	Spitz (2008)	LLP	LLPi	PLCO (2009)	PLCO (2011)	$PLCO_{M2012}$	Etzel	Pittsburgh	Hoggart
Sociodemographic factors											
Age	Y				Y	Y	Y	Y		Y	
Gender	Y				Y				Y		Y
Race or ethnic group								Y			
Education						Y	Y	Y			Y
BMI						Y	Y	Y			Y
Exposure history											
Dust exposures	Y	Y	Y						Y		
Asbestos exposure	Y	Y		Y					Y		Y
Environmental tobacco											
Smoke exposure		Y									
Smoking history											
Age stopped smoking		Y	Y								
Smoking duration				Y	Y	Y	Y	Y		Y	
Pack-years smoked		Y				Y	Y		Y		
Smoking status							Y	Y		Y	
Smoking intensity								Y		Y	
Smoking quit time							Y	Y			
Cigarettes per day	Y										
Time since smoking cessation	Y										
Medical history											
Emphysema		Y	Y								
Hay fever		Y	Y						Y		Y
Bleomycin sensitivity			Y								
Prior diagnosis of pneumonia				Y							
Prior diagnosis of malignant tumor				Y	Y						
COPD					Y		Y	Y	Y		
Chest X-ray in past 3 years							Y				
Personal history of cancer								Y			
Asthma											Y
Family history											
Family history of cancer		Y	Y								Y
First-degree relatives with cancer			Y								
Family history of lung cancer				Y	Y	Y	Y	Y			
Nodule						Y					
Family history of smoking-related cancer		Y									
Genetic risk factors											
DNA repair capacity			Y								
chr15q25											Y
chr5p15											Y

BMI, body mass index; COPD, chronic obstructive pulmonary disease; LLP, Liverpool Lung Project; PLCO, the Prostate, Lung, Colorectal and Ovarian; Y, the variable was included in the model.

tumor markers, gene loci and psychological factors emerged, providing a valuable reference for model prediction. A large amount of data was extracted from established samples with the smallest sample size a total of 114 cases. Prediction accuracy and validity evaluation were not disclosed by some studies (*Table 7*).

Discussion

This study included 11 multiple-use models and 17 single-use models. Models used multiple times were developed by European and American countries. In essence, a large number of models were based on large-scale national projects, such as the NLST (multicenter randomized controlled trial, 53,456 samples) (41), Liverpool Lung Project (LLP, case-control study: 800 cases and 400 controls, cohort study: 7,500 samples) (42), and the Prostate, Lung, Colorectal and Ovarian (PLCO, multicenter randomized controlled trial, 74,000 samples) (43). These projects provided model development based on a large quantity of detailed data. Most studies were case-control and cohort, which are convenient for model construction.

A model that can be used multiple times is also a model that can be updated. Four studies incorporated a model that was used to derive subsequent models, which were supplements and adjustments to the previous model. These updated models differ from the previous models. The difference between the previous and the updated version was the scope of the population even though the analysis was the same.

Since the development of the Bach model, many studies have focused on the form of predictive models. Predictive models have been highly valued by the academic community in recent years, and gradually, based on the Bach model, risk factor enrichment has increased. Some predictive models included parameters like tumor markers and genes, which have accelerated model development. Variables now include more basic information and family history, which eliminate the need for traditional factors when combined with single-use models. By the use of new medical information technologies, the accuracy of models has improved.

Transparency is of significance to the promotion and application of models. Through dual disclosure of technical documents and non-technical articles, the user can understand the model's developmental process, providing application instruction and guidance (10). The multi-use models included in this study have relatively good transparency, although most cited literature does not report expressions of the model. The expression of the model has significance for model popularization. If the variables included in a model were reported, it would be possible for others to consider and weigh the importance of the variables in model prediction. In addition, some studies did not report relevant conflicts of interest, which does not insure the independence of the model.

The existence of bias makes the accuracy of model prediction difficult to assess and can distort the importance of influence on prediction results. There are many forms of biases in the development of a model including research design, field survey, data entry and data analysis, which in turn affect the predictive accuracy of the model. There are many tools for bias evaluation such as the Cochrane tool for randomized control trial (RCT) (44), QUADAS for diagnostic test studies (45), the Newcastle-Ottawa Scale (NOS) scale for cohort studies and case-control studies (46), and systematic review AMSTAR (47). The bias evaluation tool for model development is still immature. This study has developed a bias evaluation checklist based on related research, and found that the risk of bias in lung cancer prediction models is high. The main problem for sensitivity analysis is the lack of a blinding method and variable uncertainty. The absence of blinding may interfere with subjective thinking of the researcher. Sensitivity analysis of uncertain variables is an important step in the refinement of the variables and the main method to improve the validity of the model. Calibration increases the risk of bias in the model's predictions.

Some models lack verification of external validity. Validation should be ongoing for a model (48). Conducting validation throughout the modeling process is essential in that mistakes can be found and corrected at an early stage of model development. Late validation leaves little time to remedy any issues. The likelihood of finding mistakes increases with the number of validation rounds, minimizing the chance that the model will contain serious errors. For all models, the validation process and its results should be reported. External verification works by comparison of the model's results with data derived from actual events and by comparison of results. External validity is critical to model development in that the ultimate goal of the model is the application to practice to ensure that best choices are made (7). However, only six of the included studies were externally validated. Although the other studies performed validation (internal validation or cross-validation), these are

Table 7 Single-use models for lung cancer prediction

Model	Year	Country or region	Research design	Statistical methods	Variable included	Modeling sample	Validation	AUC (95% CI)	C-index (95% CI)
Wozniak MB (24)	2015	Germany	Case-control study	Logistic	Gender, age and smoking status, 24 microRNAs	100 case; 100 control	Internal validation	0.874	N
Wang X (25)	2015	China	Case-control study	Logistic	Gender, age, education, BMI, family history, medical history, exposure history, lifestyle	705 case; 988 control	Internal validation	0.8851	N
Muller DC (26)	2017	US	Cohort study	Flexible parametric survival	Gender, smoking history, medical history, family history	502,321	Internal validation	N	0.85 (0.82–0.87)
Ma S (27)	2016	China	Cohort study	Logistic	Gender, age, smoke, prolactin, CRP, NY-ESI-1, HGF	543	External validation	0.86 (95% CI: 0.83–0.88	N
Wu X (28)	2016	China	Cohort study	Cox regression analysis	Age, gender, smoking pack-years, BMI, family history, medical history, exposure history, biomarkers	395,875	Internal validation; External validation	0.851, with never smokers 0.806, light smokers 0.847, and heavy smokers 0.732	N
Gu F (29)	2017	US	Cohort study	Cox proportional hazard model	Age, gender, race/ethnicity, education, family history, BMI, smoking status, smoking history	18,729	N	Incidence model: 0.6941; Death model: 0.7376	N
Lin KF (30)	2017	China	Cohort study	Logistic	Age, gender, and BMI, nodule number, family history of lung cancer, family history of other cancer	784	N	N	N
Sha R (31)	2017	China	Case-control study	Logistic	Age, gender, BMI, family history	227 case; 454 control	N	Model 1: 0.827 (0.794–0.861); Model 2: 0.836 (0.804–0.868)	N
Lin H (32)	2011	China	Case-control study	Logistic	Gender, age, smoking status, medical history, exposure history, family history	633 case; 565 control	N	N	0.881
Ni R (33)	2016	China	Case-control study	ANN, SVM, Decision tree	Gender, age, medical history, smoking history, drinking history, family history	214	External validation	N	0.972
Li H (34)	2012	China	Case-control study	Logistic	Gender, age, smoking status, SNPs	N	N	0.637	N
Feng YJ (35)	2013	China	Case-control study	Logistic, Decision tree, ANN, SVM	Gender, age, smoking history, DNMT1, DNMT3a	136 cancer; 140 benign lung disease; 145 control	External validation	Logistic: 0.923; Decision tree: 0.946; ANN: 0.877; SVM: 0.851	N
Wang N (36)	2012	China	Case-control study	Fisher, Decision tree, ANN	Gender, age, smoking status, medical history, genetic factors	251 case 256 control	N	Fisher: 0.722; Decision tree: 0.929; ANN: 0.894	N
Zhang HQ (37)	2012	China	Case-control study	Decision tree, ANN, Logistic, Fisher	Ferritin, AFP, CEA, NSE, CA199, CA242, CA125, CA153, HGH9	150 case 150 control	External validation	Decision tree: 0.923; ANN: 0.86; Logistic: 0.809; Fisher: 0.765	N
Sun RL (38)	2013	China	Case-control study	Logistic	Family history, smoking status, lifestyle, psychology	563 case 563 control	N	N	N
Nie GJ (39)	2009	China	Case-control study	ANN, Logistic	Tumor marker	53 case 61 control	External validation	ANN: 0.88, Logistic: 0.82	N
Chang TT (40)	2011	China	Case-control study	Fisher	Gender, age, smoking status, medical history, exposure history	807 case 807 control	External validation	Non-lung cancer: 0.823; Lung cancer: 0.745	N

AUC, area under receiver-operating characteristic curve; 95% CI, 95% confidence interval; C-index, concordance index; ANN, artificial neural network; SVM, support vector machine; BMI, body mass index; CRP, C-reactive protein; HGF, hepatocyte growth factor; SNP, single nucleotide polymorphism; DNMT, DNA-methyltransferase; AFP, alpha-fetal protein; CEA, carcinoembryonic antigen; NSE, neuron specific enolase; CA, carbohydrate antigen; HGH, human growth hormone.

not adequate for predictive models. A new evaluation model of 2 million high-risk individuals from the Cancer Screening in Urban China Program is being built based on this study. It will integrate analytics including validity, bias and other involved factors that will be applied to this future research project.

Conclusions

This study considers risk prediction models for high-risk lung cancer populations. It rigorously evaluated multiple-use models for transparency, risk of bias and variables. Various models have been developed for different types of populations and were used to predict lung cancer risk based on various conditions (e.g. age and smoking status). The prediction accuracy of the models was high overall, indicating that it is feasible to use models for high-risk population prediction. However, the process of model development and report is not optimal in that the models have a high risk of bias, affecting credibility and predictive accuracy, which influences the promotion and further development of the model. In view of this, model developers need to be more attentive to bias risk control and validity verification in the development of models.

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Footnote

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