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Pulmonary nodule malignancy probability: a meta-analysis of the Brock model

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AIM: This study aims to quantify the performance of the Brock model through a systematic review and meta-analysis and to clarify its overall accuracy in predicting malignant pulmonary nodules.

MATERIALS AND METHODS: A systematic search was conducted in databases including the Cochrane Library, Excerpta Medica database (EMBASE), MEDLINE, Web of Science, Chinese Biological Medicine Database (CBM), China National Knowledge Infrastructure (CNKI), VIP, and Wanfang from their inception until May 1, 2024, to collect observational cohort studies involving the Brock model. The primary outcome was the pooled area under the receiver operating characteristic curve (ROC) the area under curve (AUC) for the Brock model. Secondary outcomes included sensitivity and specificity. The metaprotocol was registered in the International Prospective Register of Systematic Reviews (CRD42024538163).

RESULTS: A total of 52 studies involving 85,558 patients were included. The pooled AUC was 0.796 (95% confidence interval [CI]: 0.771-0.820), with a pooled sensitivity of 0.82 (95% CI: 0.76-0.87) and specificity of 0.80 (95% CI: 0.72-0.86). Subgroup analysis showed that the performance of the full model was significantly better than that of the simplified model (0.822, 95% CI: 0.794-0.849 versus 0.687, 95% CI: 0.611-0.763). The model performed excellently for pulmonary nodules with diameters of 1- to 8 mm (AUC: 0.927, 95% CI: 0.900-0.954). However, its performance was lower in Asian populations (AUC = 0.741, 95% CI: 0.703-0.780), solitary pulmonary nodules (AUC = 0.767, 95% CI: 0.693-0.842), and subsolid pulmonary nodules (AUC = 0.747, 95% CI: 0.661-0.832).

CONCLUSION: This meta-analysis confirms the Brock model's overall strong performance. However, the results indicate certain application limitations of the Brock model, with reduced accuracy for larger nodules (>15 mm), solitary pulmonary nodules, subsolid nodules, and in Asian populations.

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Introduction

Pulmonary nodule is one of the common radiological manifestations, which is defined as round shadows with a diameter of less than 30 mm in chest computed tomography (CT) images.[1,2] The global detection rate of pulmonary nodules has been steadily increasing annually. A study conducted in Western Europe indicated that the detection rate of pulmonary nodules in the general population is 41.8%, and even among never-smokers, it is as high as 38.8%.[3] In China, the detection rate of pulmonary nodules is lower but still reaches 20.1%.[4] Among the detected pulmonary nodules, those with a size of 4- to 10 mm account for more than 80% of the total, and the probability of malignancy for these nodules is less than 2%.[5] However, due to the large population base in the world, lung cancer remains the second most commonly diagnosed cancer and the leading cause of cancer-related deaths worldwide.[6] Worse in China, lung cancer ranks first in both incidence and mortality.[7]

Due to the slow growth behaviour of pulmonary nodules, the current management strategy for pulmonary nodules primarily involves observation and follow-up, especially when the diameter of the nodule is less than eight millimetres. The observation and follow-up period can even extend up to five years.[8] During the follow-up waiting period, patients with pulmonary nodules often experience significant psychological distress, with 24% to 57% of patients developing negative emotions.[9] This period is described by patients as a 'near-cancer' experience.[10] With the widespread adoption of lung cancer screening, pulmonary nodules have become 'easy to detect but difficult to treat', making the early and accurate differentiation of benign and malignant nodules critically important.

The malignancy prediction models for pulmonary nodules provide a basis for the diagnosis and treatment of pulmonary nodules and effectively guide clinical decision-making. Currently, there are several relatively well-recognised prediction models, among which the Brock model is the most highly regarded. It is recommended by the British Thoracic Society guidelines[11] and acknowledged by the Fleischner Society.[12] The Brock model, also known as the Pan-Canadian Early Detection of Lung Cancer Study (PanCan) model or Vancouver model, was developed by McWilliams *et al.*, in 2013 using patient data from the multicenter PanCan.[13] The model is divided into parsimonious and full models, each with versions that include or exclude spiculation, resulting in a total of four formulae for Brock. The full model includes nine predictors: age, sex, family history of lung cancer, emphysema, nodule diameter, nodule density, nodule location, the number of nodules, and spiculation. The specific details of the Brock model formula can be found in the supplementary file titled 'Brock Model Formula'.

Although the Brock model is the most highly regarded, its performance in external validation has been inconsistent.[14,15] Moreover, due to the inclusion of four formulae in the Brock model, its application has been somewhat confusing. Therefore, the aim of this study is to quantify the overall performance of the Brock model by conducting a systematic review and meta-analysis to validate the accuracy of the model in predicting malignant lung nodules, as well as to assess its effectiveness across different types, sizes, numbers of lung nodules, formulae, and populations.

Materials and methods

This systematic review and meta-analysis was reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for diagnostic test accuracy (DTA) studies.[16] We had registered the protocol for this review on the International Prospective Register of Systematic Reviews website (CRD42024538163), and it is available online.

Eligibility criteria

Observational cohort studies that reported on the diagnostic accuracy of the Brock model in predicting the probability of malignancy of pulmonary nodules were considered. Peer-reviewed papers and grey literature were included, whereas reports on predicting models that did not include the Brock model were excluded. Furthermore, reviews, systematic reviews, meta-analyses, case reports, comments, guidelines, the literature with only abstracts and articles written in languages other than English or Chinese were excluded. The literature that does not provide data on true positives (TPs), false positives (FPs), false negatives (FNs), true negatives (TNs), or the number of individuals applying the Brock model, as well as at least three of the following metrics: sensitivity (Sens), specificity (Spec), accuracy (Acc), positive predictive value (PPV), and negative predictive value (NPV), will also be excluded. For the diagnosis of malignant nature of pulmonary nodules, pathological confirmation is required. For benign pulmonary nodules, if diagnosed through follow-up, the follow-up period should be no less than one year. Those who do not meet the aforementioned criteria will be excluded.

Search strategy

We searched eight databases, including the Cochrane Library, Excerpta Medica database (EMBASE), MEDLINE, Web of Science, the Chinese Biological Medicine Database (CBM), the China National Knowledge Infrastructure (CNKI), VIP Database for Chinese Technical Periodicals (VIP), and Wanfang Data (Wanfang). All relevant literature in English or Chinese was retrieved from inception until 1 May 2024.

The key phrase used was ('pulmonary nodule*' OR 'lung nodule*') AND (probability OR malignancy OR diagnosis OR differential OR predictive) AND (Brock OR Vancouver OR PanCan). Reference lists of all included studies were examined to identify further potentially relevant studies. Two authors conducted the literature search independently and uploaded their findings into NoteExpress for double-check.

Data extraction and quality assessment

Two authors (Shun C and Weilan L) independently extracted data and cross-checked its accuracy post extraction. We used a standardised data acquisition form (Supplementary files) for data collection, which specifically includes the authors, publication year, region, number of patients, gender, age (mean ± standard deviation [SD]), range of included nodule diameters, nodule diameter (mean ± SD), number of nodules (solitary or multiple), nodule density, area under the receiver operating characteristic curve (AUC), 95% confidence intervals (CIs) of AUC, TP, FP, FN, TN, Sens, Spec, Acc, PPV, and NPV. For literature lacking the aforementioned data, reasonable data conversion were used for supplementation, with calculations verified using MedCalc 20.022.

The quality of the included literature was assessed using the Quality Assessment of Diagnostic Accuracy Studies version 2 (QUADAS-2) tool,[17] with evaluations performed using the 'Risk of bias' module in Diagnosis test accuracy review by RevMan 5.4 software. Similarly, two individuals (Shun C and Weilan L) independently conducted the evaluations and cross-checked the results. Inconsistent items were resolved through consultation, and if consensus could not be reached, a third author (Weiting L) was consulted for discussion and the final decision. The final tabular and graphical presentations of the QUADAS-2 results are shown in electronic supplementary material Figure S 1 and Figure S 2.

Outcome of the meta-analysis

The primary outcome measure was the diagnostic accuracy of the Brock model, presented as the AUC along with the 95% CI. Secondary outcome measures included sensitivity and specificity. Additionally, a preplanned subgroup analysis was conducted to explore the optimal conditions for the model's applicability, with comparisons based on model formulae, region, diameter, and the number and density of pulmonary nodules.

Statistical analysis

The meta-analysis of AUC was performed using a random-effect model in MedCalc (version 20.022). Heterogeneity was assessed using the I^2 statistic and the P value of the Q statistic; if the I^2 statistic were greater than 50% and the P value was less than 0.05, high heterogeneity was assumed, and a sensitivity analysis was subsequently performed. Since the software requires the values of AUC and Standard Error (SE) for computation, SE values can be converted from 95% CI. Therefore, studies that did not provide AUC and SE or 95% CI were excluded from the analysis.

To avoid the shortcomings of traditional Summary the receiver operating characteristic curve (SROC) meta-analysis, the meta-analysis of sensitivity and specificity was conducted using a bivariate model, specifically implemented through the 'midas' command in STATA 17.0 and Meta-DiSc 2.0 (https://ciberisciii.shinyapps.io/MetaDiSc2/).[18] Since the use of STATA software requires the provision of TP, FP, FN, and TN values for calculations, any literature that does not provide the aforementioned data or provides data that cannot be converted to calculate the aforementioned values will be excluded from the analysis.

Result

Based on the search strategy, we retrieved a total of 834 articles from eight databases. According to the eligibility criteria, we excluded some articles and ultimately retained 52 articles for further analysis, as shown in Fig 1. The included articles cover the Americas (12),[19–30] Asia (29),[31–59] Europe (10),[27,60–68] and Oceania (1).[69] Due to incomplete general information provided in some articles, we only collected data for 85,558 patients, including 41,558 males and 34,445 females. The average age range of the patients was 50.8- to 69 years, and the average diameter of lung nodules ranged from 3.98 to 22 mm. Detailed information can be found in the electronic supplementary material, Table S1. Two independent researchers evaluated the quality of the included studies using pre-established assessment criteria and the QUADAS-2 tool. They reached complete agreement throughout the evaluation process, with no discrepancies observed. The results showed a higher risk of bias in the domain of index test (approximately 75%) and flow and timing (approximately 50%). The higher risk of bias in the domain of the index test was due to the lack of preset thresholds and the retrospective nature of most studies, whereas the higher risk in the domain of flow and timing was because some benign lung nodules were ultimately determined by follow-up with no change or disappearance, rather than being confirmed by pathological results. Detailed information can be found in Figures S1 and S2.

AUC

Due to some studies providing model validation results for more than one population, a total of 52 papers yielded 86 sets of AUC data. These included 41 for the full model,[20,22,24,25,27–29,31–33,39,43,44,46,51,53,54,56,60–67] 15 not specified,[23,42,45,47,48,50,55,57–59,68,70] 14 for the parsimonious model,[28,30,34,36–38,40,41,49,52,56] 5 for the full model without spiculation,[21,22,65] and 11 for the improved or modified model[19,26,35,39,65] (Table S2). The aggregated AUC from these 86 sets, calculated using a random-effect model, was 0.796 (95% CI: 0.771-0.820, $P<0.001$, Fig 2). However, the results exhibited high heterogeneity (Q-test significance level $P<0.0001$, $I^2 = 98.94\%$). Consequently, five sets of data with AUC or AUC 95% CI less than 0.5 (Wu-2021, Huang-2024,

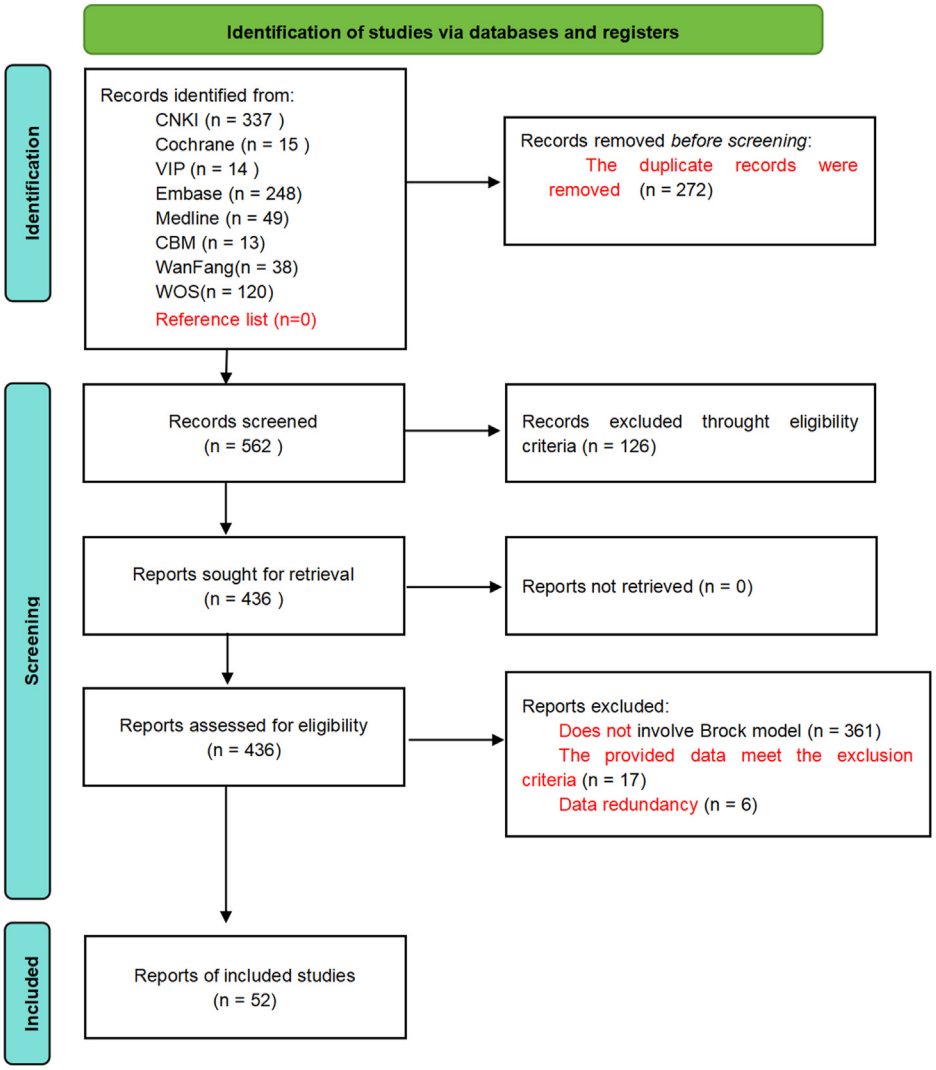

Figure 1 Study flow diagram.
CBM, Chinese Biological Medicine Database; CNKI, China National Knowledge Infrastructure. VIP, VIP Database for Chinese Technical Periodicals; WOS, Web of Science.

Yang-2018-1, Wen-2023, and Liu Q-2023) were excluded, yielding a pooled AUC of 0.813 (95% CI: 0.791-0.834, $P<0.001$, Fig S 3). High heterogeneity persisted (Q-test significance level $P<0.0001$, $I^2 = 98.96\%$). The high heterogeneity might be related to the use of different classification models or specific applicability conditions; thus, subgroup analyses were performed based on predefined classification criteria.

Subgroup analysis by model formulae showed the following results: not-specified group[23,42,45,47,48,50,55,57–59,68,70]: a pooled AUC of 0.728 (95% CI: 0.683-0.774, $P<0.001$, Q-test significance level $P<0.0001$, $I^2 = 84.98\%$). Full model group[20,22,24,25,27–29,31–33,39,43,44,46,51,53,54,56,60–67]: a pooled AUC of 0.822 (95% CI: 0.794-0.849, $P<0.001$, Q-test significance level $P<0.0001$, $I^2 = 99.34\%$). Full model without spiculation group[21,22,65]: a pooled AUC of 0.922 (95% CI: 0.898-0.946, $P<0.001$, Q-test significance level $P=0.0002$, $I^2 = 81.86\%$). Parsimonious model group[28,30,34,36–38,40,41,49,52,56]: a pooled AUC of 0.687 (95% CI: 0.611-0.763, $P<0.001$, Q-test significance level $P<0.0001$, $I^2 = 96.03\%$). Improved or modified model group[19,26,35,39,65]: a pooled AUC of 0.877 (95% CI: 0.845-0.910, $P<0.001$, Q-test significance level $P < 0.0001$, $I^2 = 77.80\%$). Details are provided in Fig S 4.

Subgroup analysis by region revealed the following results: North America (USA) group[19–30]: a pooled AUC of 0.831 (95% CI: 0.790-0.872, $P<0.001$, Q-test significance level $P<0.0001$, $I^2 = 98.70\%$). Asia group[31–59]: a pooled AUC of 0.741 (95% CI: 0.703-0.780, $P<0.001$, Q-test significance level $P<0.0001$, $I^2 = 99.37\%$). Europe group[27,60–69]: a pooled AUC of 0.857 (95% CI: 0.831-0.884, $P<0.001$, Q-test significance level $P<0.0001$, $I^2 = 89.39\%$). Due to only one study from Oceania (Australia), and considering that 99.2% of patients in that study were of Caucasian ethnicity,[69] it was included in the European analysis. Details are provided in Fig S 5.

Subgroup analysis by lung nodule diameter included only 38 sets of data due to the lack of average diameter information in some studies. The Fleischner Society recommends giving greater attention to pulmonary nodules larger than 8 mm,[71] whereas the American College of Radiology classifies solid pulmonary nodules larger than 15

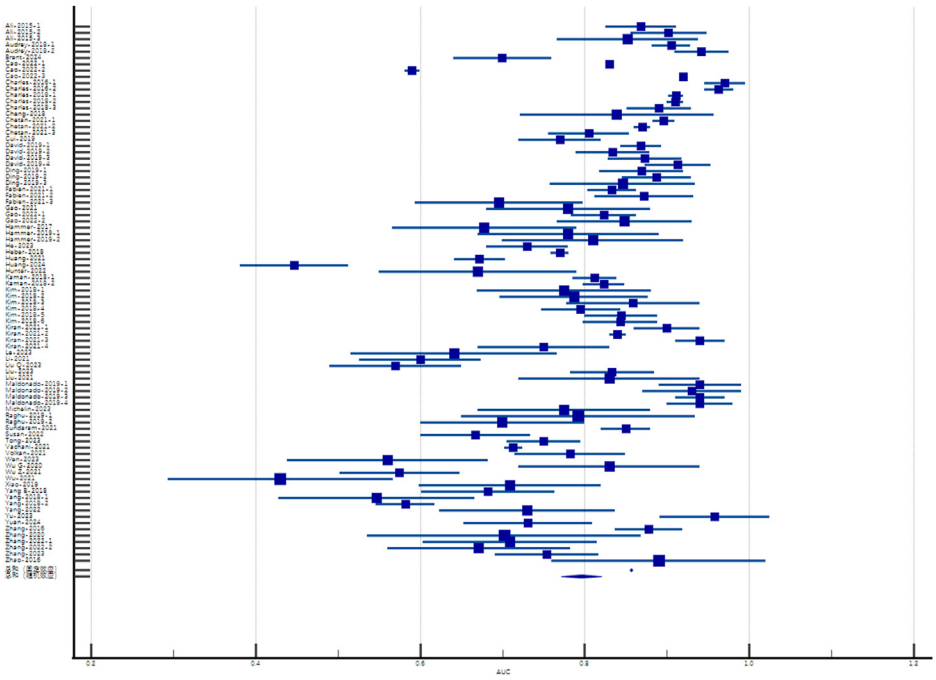

Figure 2 Summary results of 86 AUC data. AUC, Area Under the Curve.

mm as 'very suspicious'.[72] Therefore, we categorised the pulmonary nodules into three groups: 1-8 mm, 8.01-15 mm, and ≥15.01 mm; 1- to 8-mm group[19,22,50,62,64,65]: a pooled AUC of 0.927 (95% CI: 0.900-0.954, $P<0.001$, Q-test significance level $P<0.0001$, $I^2 = 88.81\%$); 8.01- to 15-mm group[23,28,31,35,36,43,44,54,55,58,63,64,66]: a pooled AUC of 0.824 (95% CI: 0.796-0.853, $P<0.001$, Q-test significance level $P<0.0001$, $I^2 = 83.79\%$); ≥15.01-mm group[20,25,30,33,39,50,51,58,67,68]: a pooled AUC of 0.740 (95% CI: 0.710-0.770, $P<0.001$, Q-test significance level $P=0.0002$, $I^2 = 68.00\%$). Details are provided in Fig S 6.

Subgroup analysis by the number of lung nodules included 42 sets of data as only one study separately validated results for multiple lung nodules. Data from studies that did not distinguish between solitary and multiple nodules were combined. Mixed group[19–22,30–33,37,39,47,54,58–67,70]: a pooled AUC of 0.836 (95% CI: 0.804-0.867, $P<0.001$, Q-test significance level $P<0.0001$, $I^2 = 98.17\%$). Solitary group[34,43,48,52,56–58,68]: a pooled AUC of 0.767 (95% CI: 0.693-0.842, $P<0.001$, Q-test significance level $P<0.0001$, $I^2 = 90.53\%$). Details are provided in Fig S 7.

Subgroup analysis by lung nodule density, following the latest European guidelines, categorised nodules into solid and subsolid types.[73] Mixed group[19–22,30,33,35–39,43,55,60,61,63–66,68]: a pooled AUC of 0.818 (95% CI: 0.776-0.859, $P<0.001$, Q-test significance level $P<0.0001$, $I^2 = 98.13\%$). Solid group[21,25,29,58,61,67,70]: a pooled AUC of 0.765 (95% CI: 0.694-0.837, $P<0.001$, Q-test significance level $P<0.0001$, $I^2 = 94.55\%$). Subsolid group[21,26,31,44,47,49,52,61,69]: a pooled AUC of 0.747 (95% CI: 0.661-0.832, $P<0.001$, Q-test significance level $P<0.0001$, $I^2 = 99.81\%$). Details are provided in Fig S 8.

Sensitivity and specificity

Due to the inability to collect TP, FP, TN, and FN data from many literature sources, only 31 sets of relevant data (including multiple sets of data from single studies) were extracted from 22 papers.[19,21–23,25,35,37–40,43,44,47,49,53,55,62,63,65–67,70] Using the 'midas' command in STATA 17.0 software, it was determined that this set of data did not exhibit heterogeneity caused by threshold effect (proportion of heterogeneity likely due to threshold effect = 0.13 > 0.05). However, it still showed high heterogeneity (significance level of Q-test: $P=0.000$, $I^2 = 100\%$, Fig S 9). Therefore, directly combining sensitivity and specificity indicators may underestimate the accuracy of diagnosis but still has reference value. The forest plot generated by Meta-DiSc 2.0 displaying sensitivity and specificity is shown in Fig 3, with the combined sensitivity being 0.82 (95% CI: 0.76-0.87) and specificity being 0.80 (95% CI: 0.72-0.86); the Youden index calculated using this method was 0.62.

The 'midas' command in STATA 17.0 was used to calculate and subsequently analyse the bivariate model, and the SROC curve was plotted, as shown in Fig 4, with a combined AUC of 0.88 (95% CI: 0.85-0.91). The publication bias detection result was $P=0.349 > 0.10$, indicating no obvious asymmetry in the funnel plot (Fig S 10), suggesting a low possibility of publication bias. Finally, by setting the pretest probability at 0.5 to display the relationship between pretest probability, likelihood ratio, and post-test probability, the Fagan plot indicated that a pretest probability of 50% connected to the middle column with a positive likelihood ratio results in a post-test probability of 81% (Fig 5).

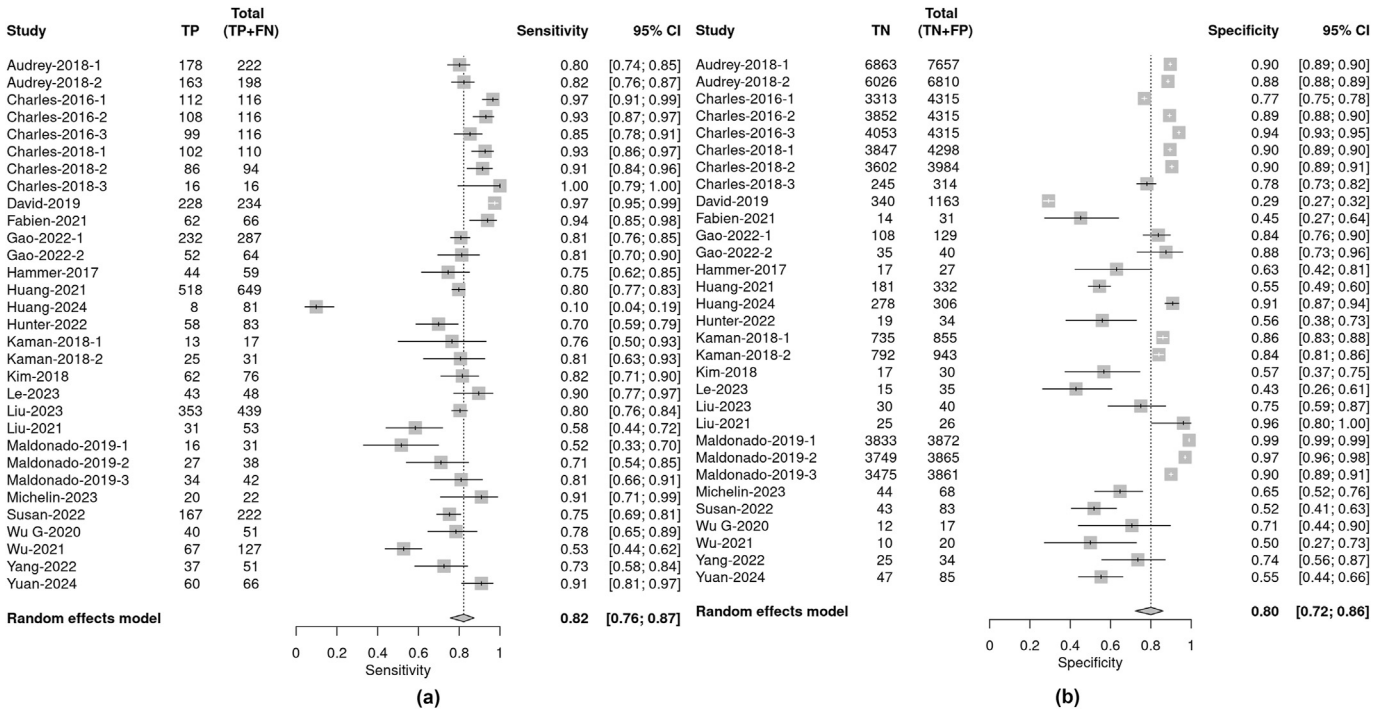

Figure 3 The sensitivity and specificity Forest plot.
CI, confidence interval; FN, false negative; TP, true positive.

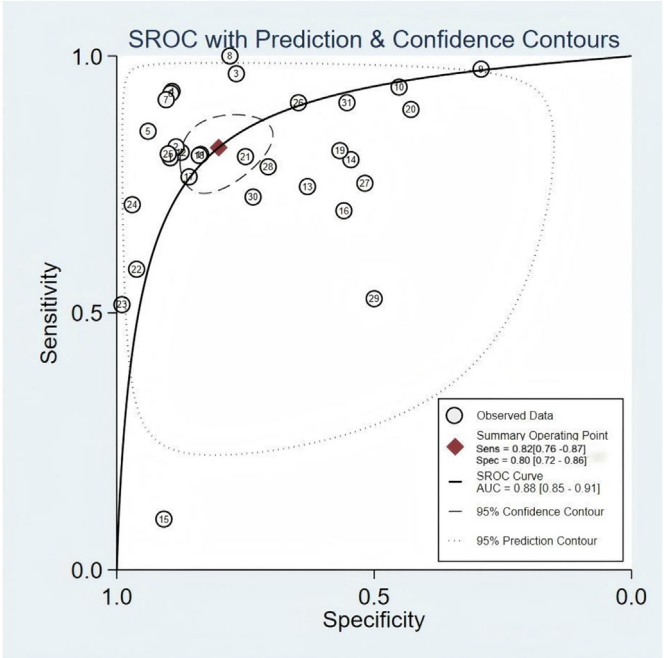

Figure 4 SROC for the Brock model (bivariate approach).

Discussion

Although the Brock model was developed over a decade ago, this is the first meta-analysis of the Brock model to our knowledge. Quantifying the model's performance, we found a pooled AUC of 0.796 (95% CI: 0.771-0.820, 52 studies), with sensitivity at 0.82 (95% CI: 0.76-0.87, 22 studies) and specificity at 0.80 (95% CI: 0.72-0.86, 22 studies). This analysis, including data from over 85,000 individuals from multiple continents (excluding Africa and South America), demonstrates the Brock model's good and stable performance. However, significant heterogeneity across studies suggests complex, confounding factors that affect model validation. Subgroup analyses indicated the greatest heterogeneity reduction in groups by pulmonary nodule diameter, followed by model formulae, implying that the model's performance varies significantly with different nodule sizes and model formulae.

Model formulae

There is a significant performance difference between the full and parsimonious models, with the full model (AUC: 0.822) outperforming the parsimonious model (AUC: 0.687), suggesting that using the full model improves prediction accuracy. Notably, the full model without spiculation performed even better (AUC: 0.922), possibly because spiculation data were not collected in the British Columbia Cancer Agency (BCCA) cohort used for model development,[13] reducing its predictive strength relative to other factors. However, this finding is based on only three studies and requires further validation. Additionally, some studies proposed modifications to the full model, such as using nodule volume,[65] the mean of the largest and perpendicular diameters, removing predictors,[19,26] or adjusting coefficients,[39] which improved performance (AUC: 0.822). However, these modifications lack external validation, leaving their robustness across populations

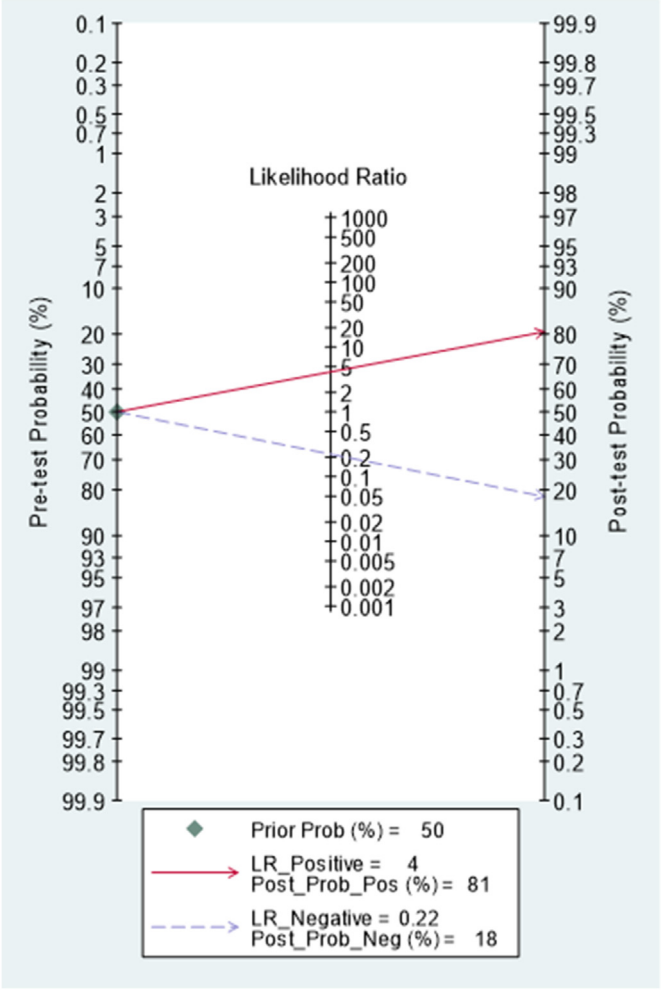

Figure 5 Fagan graph. LR, Likelihood Ratio.

uncertain. Future research should consider validating these modified models, and if they consistently outperform the original, revising the Brock model may enhance its predictive accuracy. AUC, Area Under the Curve; LR, Likelihood Ratio.

Regions

The Brock model performed poorest in Asia (AUC: 0.741), with very high heterogeneity (I^2 = 99.37%), suggesting lower and less stable performance in Asian populations.[74] A similar model, the Mayo model, encountered comparable validation challenges in Asia. This may be due to both models' inclusion of 'upper lobe location' as a predictor of malignancy, whereas tuberculosis, which commonly affects the upper lobes, is highly prevalent in Asia,[75] potentially increasing FPs. However, a Chinese study noted that despite high tuberculosis rates, upper lobe nodules still present a higher malignancy risk (OR: 1.750, P=0.005).[76] Therefore, accounting for the impact of tuberculosis and excluding it when feasible may improve the accuracy of predicting malignant nodules in Asian populations.

Diameters

The model's predictive performance decreases as nodule size increases. For nodules with an average diameter of ≥15.01 mm, the AUC dropped to 0.740 (95% CI: 0.710-0.770) with high homogeneity, indicating that the Brock model's performance is significantly impacted by nodule size. Data from the Brock model development cohort indicate that the model was trained on relatively small nodules,[13] which may explain its reduced performance for larger nodules during external validation. For nodules larger than 15 mm, supplementing the Brock model with additional predictive models or methods is recommended to improve diagnostic accuracy.

Count and density

The Brock model's performance declined, particularly for solitary and subsolid pulmonary nodules. In the development cohort, solitary nodules accounted for only 4.75% (571/12010) and subsolid nodules 15.99% (1920/12010) cases,[13] both representing relatively small proportions, which may have reduced the accuracy of the derived coefficients. Additionally, since the model used solid nodules as the reference without calculating specific coefficients for these types, interference between nodules of different densities may have occurred. Future models should calculate separate coefficients for different nodule types using logistic regression to improve performance for specific nodule types.

Due to the lack of original data from many studies, the meta-analysis of sensitivity and specificity is less comprehensive than that of AUC. However, since original data were used, this meta-analysis avoided systematic errors from differing software calculations, retaining substantial reference value. By integrating data from multiple studies using STATA software, the Brock model's AUC, sensitivity, and specificity were found to be 0.88, 0.82, and 0.80, respectively, indicating strong performance. Bayesian analysis showed that with a prior probability of 50%, the model could improve accuracy by 31%, which has significant clinical implications. This suggests that clinicians can use the model to aid decision-making on pulmonary nodule interventions, potentially speeding malignant nodule diagnosis and reducing benign nodule overdiagnosis.

Limitations

First, due to limited data, the findings are not applicable to Africa or South America. Second, only English- and Chinese-language studies were included, leading to an over-representation of studies from the United States, the United Kingdom, and China, whereas studies in other languages were under-represented. Third, substantial heterogeneity was observed in data integration. Despite extensive subgroup analyses, heterogeneity remained high, likely due to the complex factors involved in model validation.

Additionally, variations in data types required certain conversions during extraction, causing a minor loss of precision, which does not significantly impact the overall findings.

Conclusion

In conclusion, this meta-analysis confirms the Brock model's overall strong performance. However, the results indicate certain application limitations of the Brock model, with reduced accuracy for larger nodules (>15 mm), solitary pulmonary nodules, subsolid nodules, and in Asian populations. Furthermore, the full model consistently outperforms the parsimonious model, suggesting clinicians should prioritise its use when possible and consider supplementary diagnostic methods for these specific populations to enhance predictive accuracy.

To improve the predictive accuracy of the Brock model, it is possible to consider making appropriate modifications to the existing model. Based on the findings of this study, the following suggestions are proposed: 1. adjusting the model parameters according to the characteristics of different populations in various regions; 2. modifying the parameters based on the number and density of pulmonary nodules; and 3. incorporating new predictive factors such as serum biomarkers, genomic data, other auxiliary diagnostic tools, or artificial intelligence, in addition to the existing model.

Ethics

The research in this article neither involves experiments on humans or animals nor does it involve the collection of any sensitive personal information. The data used in the article cannot be traced back to specific individuals, so ethical review is not required.

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Author contribution

1. Guarantor of integrity of the entire study: Shun Chen, and Feng Lu.
2. Study concepts and design: Shun Chen, Weilan Lin, and Lianyu Zou.
3. Literature research; Manuscript preparation: Shun Chen, Weilan Lin, and Weiting Liu.
4. Experimental studies/data analysis: Shun Chen and Yu Chen.
5. Statistical analysis: Shun Chen.
6. Manuscript editing: Shun Chen, Weilan Lin, Weiting Liu, Lianyu, Zou, Yu Chen, and Feng Lu.

Conflict of interest

The authors declare no conflict of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.crad.2024.106788.

References

1. Wu Z, Tang J, Zhuang R, *et al*. The microbiome of lower respiratory tract and tumor tissue in lung cancer manifested as radiological ground-glass opacity. *Front Bioeng Biotechnol* 2022;**10**:892613.
2. MacMahon H, Naidich DP, Goo JM, *et al*. Guidelines for management of incidental pulmonary nodules detected on CT images: from the Fleischner Society 2017. *Radiology* 2017;**284**:228–43.
3. Cai J, Vonder M, Du Y, *et al*. Who is at risk of lung nodules on low-dose CT in a Western country? A population-based approach. *Eur Respir J* 2024;**63**.
4. Wu J, Li R, Zhang H, *et al*. Screening for lung cancer using thin-slice low-dose computed tomography in southwestern China: a population-based real-world study. *Thorac Cancer* 2024;**15**:1522–32.
5. Mazzone PJ, Lam L. Evaluating the patient with a pulmonary nodule: a review. *JAMA* 2022;**327**:264–73.
6. Sung H, Ferlay J, Siegel RL, *et al*. Global Cancer Statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 Countries. *CA Cancer J Clin* 2021;**71**:209–49.
7. Zheng RS, Chen R, Han BF, *et al*. [Cancer incidence and mortality in China, 2022]. *Zhonghua Zhong Liu Za Zhi*. 2024;**46**:221–31.
8. Glandorf J, Vogel-Claussen J. Incidental pulmonary nodules - current guidelines and management. *Rofo* 2024;**196**:582–90.
9. Hillyer GC, Milano N, Bulman WA. Pulmonary nodules and the psychological harm they can cause: a scoping review. *Respir Med Res* 2024;**86**:101121.
10. Slatore CG, Wiener RS. Pulmonary nodules: a small problem for many, severe distress for some, and how to communicate about it. *Chest* 2018;**153**:1004–15.
11. Baldwin DR, Callister ME. The British Thoracic Society guidelines on the investigation and management of pulmonary nodules. *Thorax* 2015;**70**:794–8.
12. MacMahon H, Naidich DP, Goo JM, *et al*. Guidelines for management of incidental pulmonary nodules detected on CT images: from the Fleischner Society 2017. *Radiology* 2017;**284**:228–43.
13. McWilliams A, Tammemagi MC, Mayo JR, *et al*. Probability of cancer in pulmonary nodules detected on first screening CT. *N Engl J Med* 2013;**369**:910–9.
14. Nomenoglu H, Findik G, Cetin M, *et al*. Efficiency of pulmonary nodule risk scoring systems in Turkish population. *Updates Surg* 2024;**76**:2903–15.
15. Susam S, Cinkooglu A, Ceylan KC, *et al*. Comparison of Brock University, Mayo Clinic and Herder models for pretest probability of cancer in solid pulmonary nodules. *Clin Respir J* 2022;**16**:740–9.
16. McInnes M, Moher D, Thombs BD, *et al*. Preferred reporting items for a systematic review and meta-analysis of diagnostic test accuracy studies: the PRISMA-DTA statement. *JAMA* 2018;**319**:388–96.
17. Whiting PF, Rutjes AW, Westwood ME, *et al*. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. *Ann Intern Med* 2011;**155**:529–36.
18. Plana MN, Arevalo-Rodriguez I, Fernandez-Garcia S, *et al*. Meta-DiSc 2.0: a web application for meta-analysis of diagnostic test accuracy data. *BMC Med Res Methodol* 2022;**22**:306.
19. Winter A, Aberle DR, Hsu W. External validation and recalibration of the Brock model to predict probability of cancer in pulmonary nodules using NLST data. *Thorax* 2019;**74**:551–63.
20. Heideman BE, Kammer MN, Paez R, *et al*. The lung cancer prediction model "stress test": assessment of models' performance in a high-risk prospective pulmonary nodule cohort. *CHEST Pulm* 2024;**2**:100033.

21. White CS, Dharaiya E, Dalal S, *et al*. Vancouver risk calculator compared with ACR lung-RADS in predicting malignancy: analysis of the National lung screening trial. *Radiology* 2019;**291**:205–11.
22. White CS, Dharaiya E, Campbell E, *et al*. The vancouver lung cancer risk prediction model: assessment by using a subset of the National lung screening trial cohort. *Radiology* 2017;**283**:264–72.
23. Maldonado F, Varghese C, Rajagopalan S, *et al*. Validation of the BRODERS classifier (Benign versus aggRessive nODule Evaluation using Radiomic Stratification), a novel HRCT-based radiomic classifier for indeterminate pulmonary nodules. *Eur Respir J* 2021;**57**.
24. Gao R, Tang Y, Khan MS, *et al*. Cancer risk estimation combining lung screening CT with clinical data elements. *Radiol Artif Intelligence* 2021;**3**.
25. Hammer MM, Nachiappan AC, Barbosa EJM. Limited utility of pulmonary nodule risk calculators for managing large nodules. *Curr Probl Diagn Radiol* 2018;**47**:23–7.
26. Hammer MM, Palazzo LL, Kong CY, *et al*. Cancer risk in subsolid nodules in the National lung screening Trial. *Radiology* 2019;**293**:441–8.
27. MacMahon H, Li F, Jiang Y, *et al*. Accuracy of the vancouver lung cancer risk prediction model compared with that of radiologists. *Chest* 2019;**156**:112–9.
28. Raghu VK, Zhao W, Pu J, *et al*. Feasibility of lung cancer prediction from low-dose CT scan and smoking factors using causal models. *Thorax* 2019;**74**:643–9.
29. Vandana S, Gm K. S. NV. A comparison of the PanCan model and Lung-RADS to assess cancer probability among persons with screening-detected, solid lung nodules. *Chest* 2020;**159**:1273–82.
30. Anil V, Chengyi Z, InLu AL, *et al*. The probability of lung cancer in patients with incidentally detected pulmonary nodules: clinical characteristics and accuracy of prediction models. *Chest* 2021;**161**:562–71.
31. Wei-yun C, Hai-fen L, Jun T, *et al*. Comparison of the Brock model and LU-RADS in differentiating malignant subsolid pulmonary nodules from benign nodules. *Milit Med J Southeast China* 2022;**24**:573–7.
32. Yuan C. *A prediction model for probability of malignancy in solitary pulmonarynodules detected on 18F-FDG PET/CT: establishment and validation*. 2018. p. 52. Master.
33. Xiaonan C, A HM, Daiwei H, *et al*. Comparison of Veterans Affairs, Mayo, Brock classification models and radiologist diagnosis for classifying the malignancy of pulmonary nodules in Chinese clinical population. *Transl Lung Cancer Res* 2019;**8**:605–13.
34. Hui D, Chuanxian H, Us H, *et al*. Study on the predictive model of lymph node metastasis in thyroid cancer based on CT and ^18F-FDG PET/CT. *Int J Radiat Med Nucl Med* 2019;**43**:17–21.
35. Zhen G. *Development and validation of a diagnostic nomograph forpathology invasiveness of early lung adenocarcinoma by tumor autoantibodies detection combined with radiomies features*. Master. 2022.
36. Hua H, Delun Y, Shuo S, *et al*. Application value of radiomics-based machine learning model in identifying the degree of pulmonary ground-glass nodule infiltration. *Chin J Clin Thorac Cardiovasc Surger* 2023;**30**:522–31.
37. Ziyang H. *The application of dynamic Bayesian Network in differential diagnosis of benign and malignant pulmonary noduled*. 2021 [Master].
38. Yu-yan H, Tai-bing D, Min P, *et al*. Establishment and validation of probability prediction model for benign and malignant pulmonary nodules. *J Hebei Med Univ* 2024;**45**:278–83.
39. Kim H, Goo JM, Park CM. A simple prediction model using size measures for discrimination of invasive adenocarcinomas among incidental pulmonary subsolid nodules considered for resection. *Eur Radiol* 2019;**29**:1674–83.
40. Development Jian L. Validation and comparison of predictive models for the probability of malignancy in incidental small pulmonary nodules. *Master* 2023:47.
41. You L. *Evaluation of models for predicting the probability of malignancy in patients with pulmonary nodules*. 2021 [Master].
42. Liu Q, Lv X, Zhou D, *et al*. Establishment and validation of multi-classification prediction models for pulmonary nodules based on machine learning. *Clin Respir J* 2024;**18**:e13769-e13769.
43. Xuejiao L, Bin LI, Yan LI, *et al*. Evaluation of four predictive models for identifying malignancy of solitary pulmonary nodules in Health check-up population. *Cancer Res Prev Treat* 2023;**50**:477–82.
44. Haolei L, Ge Y, Yi X, *et al*. Predictive modeling of different malignancy risk assessment in patients with cardiac structure lesions. *J Mod Med Health* 2021;**37**:4246–8.
45. Tong L, Sun J, Zhang X, *et al*. Development of an autoantibody panel for early detection of lung cancer in the Chinese population. *Front Med (Lausanne)* 2023;**10**:1209747.
46. Xiaoxia W. *Molecular diagnosis of lung adenocarcinoma based on hsa-miR-199b-3p expression in tumour -educated platelet*. 2023 [Master].
47. Wu G, Woodruff HC, Shen J, *et al*. Diagnosis of invasive lung adenocarcinoma based on chest CT radiomic features of part-solid pulmonary nodules: a multicenter study. *Radiology* 2020;**297**:451–8.
48. Wu Z, Huang T, Zhang S, *et al*. A prediction model to evaluate the pretest risk of malignancy in solitary pulmonary nodules: evidence from a large Chinese southwestern population. *J Cancer Res Clin Oncol* 2021;**147**:275–85.
49. Bin WU, Jun MA, Hongcan S. Establishment and verification of a mathematical prediction model for benignancy and malignancy in subsolid pulmonary nodules. *Chin J Clin Thorac Cardiovasc Surg* 2021;**28**:311–8.
50. Xiao F, Yu Q, Zhang Z, *et al*. Establishment and verification of A novel predictive model of malignancy for non-solid pulmonary nodules. *Chin J Lung Cancer* 2019;**22**:26–33.
51. Bumhee Y, Woo JB, Hye SS, *et al*. Comparison of four models predicting the malignancy of pulmonary nodules: a single-center study of Korean adults. *PLoS One* 2018;**13**:e0201242.
52. Jiawen Y. *Low-dose computer tomography screening for lung cancer and differentiating HRCTfeatures of benign and malignant solitary subsolid nodules*. 2018 [Doctor].
53. Yanbing Y, Ziting YU, Fang W, *et al*. Value of VRC and Lung-RADS in the diagnosis of pulmonary nodules by baseline CT screening. *J Pract Radiol* 2022;**38**:26–9.
54. Lu Y. Value of the Brock model and the Lung Reporting and Data System in the differential diagnosis of benign and malignant pulmonary nodules. *Chin J Prim Med Pharm* 2023;**30**:1838–42.
55. Rui Y, Taoli W, Wenhui YU, *et al*. Construction and validation of A prediction model for pulmonary nodule nature based on clinicopathological Features,Imaging and serum biomarkers. *J Mod Lab Med* 2024;**39**:146–51. 157.
56. Man Z. *Establishment of a mathematic model for predicting malignancy in solitary pulmonary nodules*. 2016 [Doctor].
57. Xue Z. *A prediction model on 18F-FDG PET/CT for probability of malignancyin solitary pulmonary nodules of smokers with pulmonary fibrosis*, vol. 38; 2020. Master.
58. Kai Z, Zihan W, Xin W, *et al*. The diagnostic value of machine-learning-based model for predicting the malignancy of solid nodules in multiple pulmonary nodules. *Chin J Surg* 2022;**60**:573–9.
59. Bo-wen Z, Pei L, Jian-qian C, *et al*. Differential diagnosis model for pulmonary nodules based on hybrid Bayesian network. *Chin J Prev Control Chronic Dis* 2023;**31**:81–5. 89.
60. Al-Ameri A, Malhotra P, Thygesen H, *et al*. Authors' response—risk of malignancy in pulmonary nodules: a validation study of four prediction models. *Lung Cancer (Amsterdam, Netherlands)* 2015;**90**:119–20.
61. Chetan MR, Dowson N, Price NW, *et al*. Developing an understanding of artificial intelligence lung nodule risk prediction using insights from the Brock model. *Eur Radiol* 2022;**32**:5330–8.
62. Nuhc Respiratory Medicine, Chou Radiology, Ou Optellum Ltd, *et al*. External validation of a convolutional neural network artificial intelligence tool to predict malignancy in pulmonary nodules. *Thorax* 2020;**75**:306–12.
63. Chung K, Mets OM, Gerke PK, *et al*. Brock malignancy risk calculator for pulmonary nodules: validation outside a lung cancer screening population. *Thorax* 2018;**73**:857–63.
64. Venkadesh KV, Setio AAA, Schreuder A, *et al*. Deep learning for malignancy risk estimation of pulmonary nodules detected at low-dose screening CT. *Radiology* 2021;**300**:438–47.
65. Gonzalez MS, Delorme S, Husing A, *et al*. Evaluation of prediction models for identifying malignancy in pulmonary nodules detected via low-dose computed tomography. *JAMA Netw Open* 2020;**3**:e1921221.
66. Michelin B, Labani A, Bilbault P, *et al*. Potential added value of an AI software with prediction of malignancy for the management of incidental lung nodules. *Res Diagn Interv Imaging* 2023;**8**:100031.
67. Seher S, Akın Ç, Can CK, *et al*. Comparison of Brock University, Mayo Clinic and Herder models for pretest probability of cancer in solid pulmonary nodules. *Clin Respir J* 2022;**16**:740–9.

68. Volkan E, Necati Ç, Aynur Y, *et al*. Is the Yedikule-solitary pulmonary nodule malignancy risk score sufficient to predict malignancy? An internal validation study. *Interact Cardiovasc Thorac Surg* 2021;**33**:258–65.
69. Henry Z, M MH, Yi A, *et al*. Screen-detected subsolid pulmonary nodules: long-term follow-up and application of the PanCan lung cancer risk prediction model. *Br J Radiol* 2016;**89**:20160016.
70. Hunter B, Chen M, Ratnakumar P, *et al*. A radiomics-based decision support tool improves lung cancer diagnosis in combination with the Herder score in large lung nodules. *EBioMedicine* 2022;**86**:104344.
71. Farjah F, Monsell SE, Smith-Bindman R, *et al*. Fleischner Society guideline Recommendations for incidentally detected pulmonary nodules and the probability of lung cancer. *J Am Coll Radiol* 2022;**19**:1226–35.
72. Christensen J, Prosper AE, Wu CC, *et al*. ACR lung-RADS v2022: assessment categories and management recommendations. *Chest* 2024;**165**:738–53.
73. Cardillo G, Petersen RH, Ricciardi S, *et al*. European guidelines for the surgical management of pure ground-glass opacities and part-solid nodules: task Force of the European Association of Cardio-Thoracic Surgery and the European Society of Thoracic Surgeons. *Eur J Cardiothorac Surg* 2023;**64**.
74. Papalampidou A, Papoutsi E, Katsaounou PA. Pulmonary nodule malignancy probability: a diagnostic accuracy meta-analysis of the Mayo model. *Clin Radiol* 2022;**77**:443–50.
75. Paton NI, Borand L, Benedicto J, *et al*. Diagnosis and management of latent tuberculosis infection in Asia: review of current status and challenges. *Int J Infect Dis* 2019;**87**:21–9.
76. Ye M, Tong L, Zheng X, *et al*. A classifier for improving early lung cancer diagnosis incorporating artificial intelligence and liquid biopsy. *Front Oncol* 2022;**12**:853801.