Respiratory Research

REVIEW

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Prognostic risk prediction model for patients with acute exacerbation of chronic obstructive pulmonary disease (AECOPD): a systematic review and meta-analysis

Zihan Xu[1], Fan Li[1], You Xin[1], Ye Wang[1*] and Yuping Wang[1*]

Abstract

Background Chronic obstructive pulmonary disease (COPD) is a prevalent respiratory condition and a leading cause of mortality, with acute exacerbations (AECOPD) significantly complicating its management and prognosis. Despite the development of various prognostic prediction models for patients with AECOPD, their performance and clinical applicability remain unclear, necessitating a systematic review to evaluate these models and provide guidance for their future improvement and clinical use.

Method PubMed, Web of Science, CINAHL, Scopus, EMBASE, and Medline were searched for studies published from their inception until February 5, 2024. Data extraction and evaluation were conducted using the Checklist for Critical Appraisal and Data Extraction for Systematic Reviews of Prediction Modelling Studies (CHARMS). The Prediction model Risk Of Bias Assessment Tool (PROBAST) was employed to assess the risk of bias and applicability of the models.

Results After deduplication and screening 5942 retrieved articles, 46 studies comprising 53 models were included. Of these, 17 (37.0%) studies developed from studies conducted in China. All models were based on cohort studies. Mortality was the predicted outcome in 27 (50.9%) models. Logistic regression was used in 41 (77.4%) models, while machine learning methods were employed in 9 (17.0%) models. The median (minimum, maximum) sample size for model development was 672 (106, 150,035). The median (minimum, maximum) number of predictors per model was 5 (2, 42). Frequently used predictors included age (n = 28), dyspnea severity scores (n = 12), and PaCO2 (n = 11). The pooled AUC was 0.80 for mortality prediction models and 0.84 for hospitalization-related outcomes. 52 models have a high overall risk of bias, and all models were judged to have low concern regarding applicability. Major sources of bias included insufficient sample sizes (83.0%), reliance on univariate analysis for predictor selection (73.6%), inappropriate internal and external validation methods (54.7%), inappropriate inclusion and exclusion criteria for study subjects (50.9%) and so on. The only model with low bias was the PEARL score.

Conclusion Current prognostic risk prediction models for patients with AECOPD generally exhibit high bias. Future efforts should standardize model development and validation methods, and develop widely usable clinical models.

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Keywords Chronic obstructive pulmonary disease, Acute exacerbation, Prediction model, Prognostic risk, Systematic review

Introduction

Chronic obstructive pulmonary disease (COPD) is a common respiratory condition defined by chronic cough, difficulty breathing, and airflow limitation [1]. In 2019, the global prevalence of COPD among individuals aged 30 to 79 was 10.3%, accounting for approximately 391 million people [2]. COPD ranks as the third leading cause of mortality among non-communicable diseases (NCDs) both globally and in China [3]. The management of COPD is significantly challenged by acute exacerbations (AECOPD). According to the Global Initiative for Chronic Obstructive Lung Disease (GOLD), AECOPD is characterized by a worsening of respiratory symptoms surpassing usual day-to-day variations and leads to changes in medication [1]. The prognosis of AECOPD can include a decline in health-related quality of life, substantial medical costs, and various complications [4]. Additionally, patients with AECOPD are more likely to die from respiratory diseases compared to those without acute exacerbations [5].

Therefore, it is crucial to identify prognostic risk factors for patients with AECOPD and to develop simple, effective, and clinically valuable prediction models. These models can better estimate the risk of future deterioration in patients with exacerbations, providing reliable references for clinical care, early intervention, and personalized treatment, which are essential for improving patient survival rates and quality of life.

Owing to the heterogeneity of COPD and exacerbations, as well as the poor recognition and self-reporting of these conditions [6], early diagnosis and prognosis of patients with AECOPD have remained challenging in clinical practice and a focal point of research. Although various prognostic models for patients with AECOPD have been developed, which vary widely in type, performance, and applicability, the predictive performance and practical validity of these models remain unclear.

This study systematically reviews prognostic prediction models for patients with AECOPD and evaluates their potential to predict the risk of adverse outcomes. This review discusses the current state of research and explores future directions, providing a reference for the development, validation, and improvement of risk prediction models for patients with AECOPD. Furthermore, this study aims to provide a basis for their application in clinical practice.

Methods

Literature search

This study searched six databases: PubMed, Web of Science, CINAHL, Scopus, EMBASE, and Medline. The search period spanned from the establishment of each database to February 5, 2024. The keywords related to the study population and research methods included: ("acute exacerbation of chronic obstructive pulmonary disease" OR "AECOPD" OR "acute exacerbation of COPD" OR "exacerbation of COPD" OR "COPD exacerbation") AND ("risk assessment" OR "risk prediction" OR "risk index" OR "risk score" OR "predict" OR "prognostic factors" OR "risk calculation" OR "prediction" OR "machine learning" OR "artificial intelligence" OR "algorithm" OR "deep learning" OR "regression"). Based on the filter functions provided by the databases, we selected English literature and journal articles. The search was conducted independently by two researchers. The results from each database were merged and deduplicated using reference management software to obtain the final total number of studies that required further screening.

Screening criteria

The inclusion and exclusion criteria for the target prognostic models in this study were defined based on the Checklist for Critical Appraisal and Data Extraction for Systematic Reviews of Prediction Modelling Studies (CHARMS) [7].

The inclusion criteria were as follows: (1) the primary objective of the study is to develop or improve prognostic models for patients with AECOPD; (2) the prognostic model should assess the prognosis of patients with AECOPD to aid in early identification of adverse outcomes and inform closer monitoring and treatment decisions; (3) the study should involve the development of prognostic models using independent data or the updating of existing models; (4) the target population of the prognostic models should be adult patients diagnosed with AECOPD or those primarily diagnosed with respiratory-related diseases and secondarily with AECOPD; (5) the outcomes of the prognostic models should be any clinical outcomes that may occur in patients with AECOPD; (6) the prognostic timeframe should measure predictors and outcomes at specific points during the clinical course following AECOPD diagnosis; (7) the models should generally be used for

early monitoring of patients with AECOPD; and (8) the models should have the capability to predict individual risks, with at least one metric evaluating the model's performance.

The exclusion criteria were as follows: (1) studies primarily aimed at establishing diagnostic models for AECOPD, predictive models for AECOPD complications, or prognostic models for COPD exacerbations; (2) studies solely conducting external validation or comparison of existing models; (3) cross-sectional studies where predictors and outcomes are measured simultaneously; (4) studies developing models using only one biomarker or one independent prognostic factor; (5) methodological studies and studies purely screening for risk factors; and (6) studies that are non-English, reviews, letters, conference abstracts, duplicate publications, or expert opinions.

Based on the inclusion and exclusion criteria, an initial manual screening of the deduplicated results was conducted by reviewing the titles and abstracts. Articles for which the inclusion could not be determined due to insufficient information were provisionally included. A second screening of the selected articles was conducted through full-text reading. Ultimately, a total of 46 studies were included in the systematic review. The initial screening was performed by a single researcher, while the second screening was independently conducted by two researchers. Any issues or discrepancies encountered during the process were resolved through discussion.

Data collection

The data collection process utilized standardized CHARMS forms for extraction [8]. The information collected included the study title, first author, publication year and journal, country, data source, participants, outcomes to be predicted, predictors, sample size, methods for handling missing data, modeling methods, model performance, model validation, and basic information about the final model. One researcher extracted the data, while another reviewed it. Any discrepancies were resolved through discussion. Items not found in the full text, supplementary materials, or referenced previous studies were marked as "not reported" or "unclear". The extracted data were then summarized and analyzed to provide basic study information and model characteristics.

For statistical analysis, each predictive model developed for different outcomes or characteristics of the AECOPD population was counted separately, excluding those without performance evaluation. For studies using multiple modeling methods for the same population and clinical outcome, only the best method's results were included. If the same model was validated for other outcomes, only initial modeling information was included.

Quality assessment

The Prediction model Risk Of Bias Assessment Tool (PROBAST) is used to evaluate the risk of bias in predictive model studies and the applicability of the model when used in the intended target population and clinical settings [9]. Bias is defined as systematic errors that occur in research, leading to distortion or flaws in results, which hinder the internal validity of the study. Applicability refers to the extent to which the included participants or settings, predictive factors, and outcome definitions align with the specific research question posed in the review. This tool assesses the risk of bias from four aspects: participants, predictors, outcomes, and analysis, while also evaluating the applicability of the first three aspects. The answer for each domain is categorized as low, high, or unclear. If at least one domain is assessed as having a high risk of bias or a high concern for applicability, then the overall assessment is high risk or of high concern regarding applicability. If at least one domain is rated as unclear, and there are no high risk or high applicability concerns, then the overall assessment is unclear. The assessment is conducted independently by two researchers, and any discrepancies are resolved through discussion with a third researcher.

Meta-analysis

To evaluate the performance of prediction models for AECOPD patients, a random-effects meta-analysis was conducted. As this study only included the development of cohort models, a meta-analysis was conducted on prediction models with mortality and hospitalization-related outcomes. The area under the receiver operating characteristic curve (AUC) and its 95% confidence interval were extracted from each study. Studies without reported AUCs were excluded. Heterogeneity was assessed using the I^2 statistic, with high values indicating substantial heterogeneity. Publication bias was assessed using funnel plots and Egger's test.

Results

Literature screening

A total of 5942 articles were retrieved from various databases. After merging, 3802 duplicates were removed, resulting in 2140 unique articles. During the screening process, 2094 articles were excluded, leading to the inclusion of 46 articles in the final review (Fig. 1).

Basic information of the studies

Among the 46 studies, 19 (41.3%) used a prospective study design, while 27 (58.7%) used a retrospective design, with 6 studies using aggregated data. China had the highest number of studies (n = 17; 37.0%), followed by

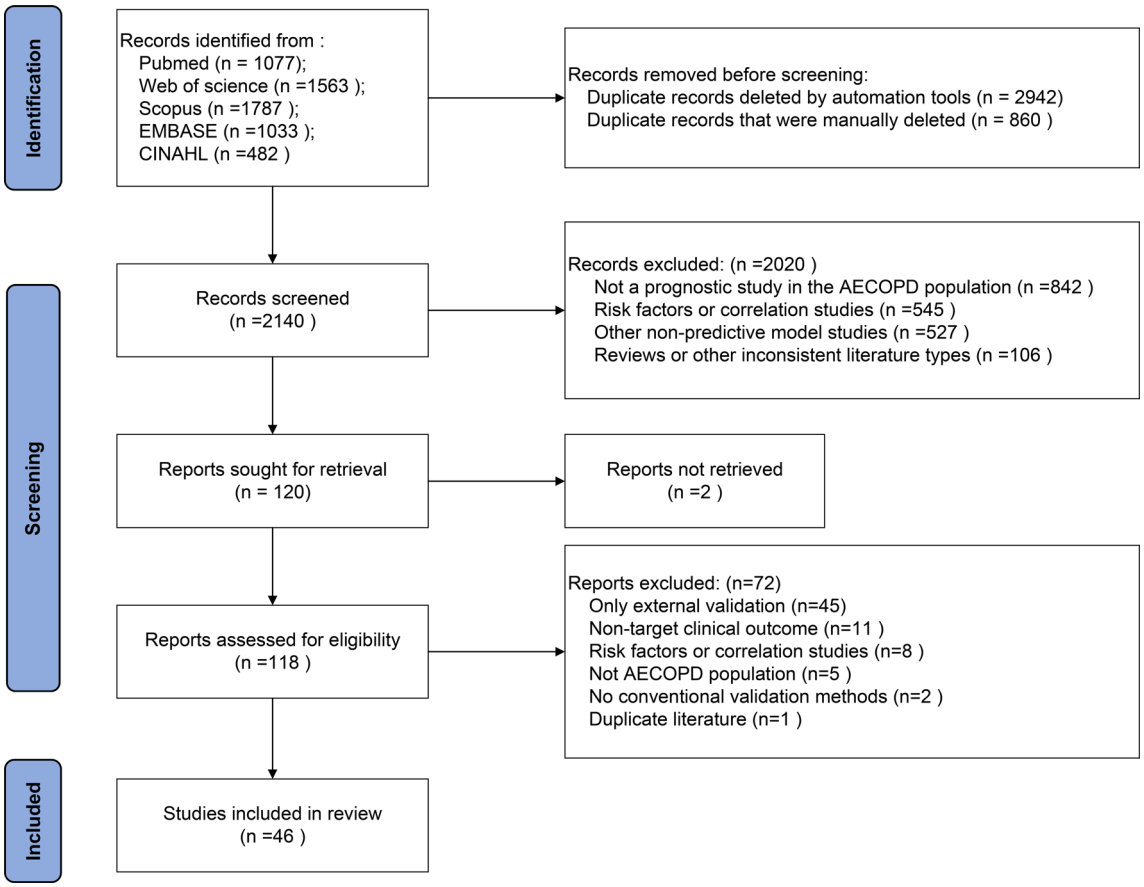

Fig. 1 Literature screening flow diagram

Spain (n = 7; 15.2%), the United States (n = 6; 13.0%), and the United Kingdom (n = 5; 10.9%). Other countries represented include India, France, Canada, Thailand, Israel, Norway, and Greece (Table 1). Regarding the study setting, the majority of studies (n = 28; 60.9%) indicated that screening was conducted in hospitals, while a portion of the studies (n = 19; 41.3%) specified the departments, including 7 in emergency departments (ED), 6 in intensive care units (ICU), 3 in general respiratory wards, and 1 in respiratory and critical care medicine departments, with 3 studies investigating both internal medicine wards and ICU/ED. (See Supplement 1 for details).

Basic information of the models

Among the 46 studies, two studies developed models for two different clinical outcomes each, and one study developed six types of models, resulting in a total of 53 models. Subsequent analyses will use the models, rather than the studies, as the independent units for information summarization and statistical analysis. (See Supplement 2 for details).

Outcomes

Out of the 53 models, 51 were newly developed models, while the remaining 2 models were modified models based on the DECAF score, with outcomes of mortality and ICU admission, respectively. The most common outcome was mortality (n = 29; 54.7%). Hospitalization-related outcomes were the second most common (n = 12; 22.6%), including prolonged hospital stay (n = 5; 9.4%), ICU admission (n = 4; 7.5%), and readmission (n = 3; 5.7%). Other outcomes included composite adverse outcomes, exacerbation, in-hospital acute heart failure, mechanical ventilation, respiratory failure, non-invasive positive pressure ventilation failure, post-discharge survival, and disease severity. While the remaining 2 models were modified models based on the DECAF score, with outcomes of mortality and ICU admission, respectively (Fig. 2).

Modeling methods

The majority of models (n = 38; 71.7%) used univariate analysis to screen predictors before including them in the model, while only a smaller portion (n = 15; 28.3%)

Table 1 Basic information of the studies

Number	Author	Year	Study reigon	Study design	Enrolment period	Study setting	Model name
1	Ying P. Tabak [34]	2009	the United States	Aggregated data	2004.1.1–2006.12.31	Hospitals	BAP65
2	Ying P. Tabak [35]	2013	the United States	Aggregated data	2005.1.1–2007.12.31	Hospitals	–
3	Peter K. Lindenauer [36]	2013	the United States	Aggregated data	2008	Hospitals	–
4	Cassandra M. Batzlaff [37]	2014	the United States	Retrospective cohort	1995.4–2009.11	ICU	–
5	Matthew Bonomo [38]	2022	the United States	Retrospective cohort	2008.11–2018.12	Hospital	–
6	Shi Chen [39]	2023	the United States	Aggregated data	2002–2019	ICU	–
7	M.J. Wildman [40]	2009	the UK	Prospective cohort	2002.3–2003.9	ICU and Respiratory High Dependency Units (RHDU)	–
8	Alex C. Asiimwe [41]	2011	the UK	Retrospective cohort	Unclear	Hospital	–
9	John Stee r[42]	2012	the UK	Prospective cohort	2008.12–2010.6	Hospitals	The DECAF Score
10	C Echevarria [31]	2017	the UK	Prospective cohort	2008.12–2010.6	Hospitals	The PEARL score
11	Tom Hartley [43]	2021	the UK	Retrospective cohort	2008.11–2013.5	Hospitals	The NIVO score
12	Prachya Mekanimitdee [44]	2021	Thailand	Retrospective cohort	2015.10–2017.9	Tertiary care center	The MAGENTA model
13	Susana García-Gutiérrez [45]	2014	Spain	Prospective cohort	2008.6–2010.9	EDs	ABC scores
14	José M Quintana [46]	2014	Spain	Prospective cohort	2008.6–2010.9	EDs	–
15	J. M. Quintana [47]	2014	Spain	Prospective cohort	2008.6–2010.9	ED	–
16	Pedro Almagro [48]	2014	Spain	Prospective cohort	2009.10–2010.10	EDs and internal medicine services	–
17	Cristóbal Esteban [49]	2015	Spain	Prospective cohort	2008.6–2010.9	ED	CART model
18	Juan Luis García-Rivero [50]	2017	Spain	Prospective cohort	2013.1–2013.3	Hospital	–
19	C esar Alameda [51]	2021	Spain	Prospective cohort	2013.12–2014.11	Health centres (HC)	–
20	Ying Wang [52]	2014	Norway	Retrospective cohort	2006.3–2008.12	Hospital	–
21	Yukiyo Sakamoto [53]	2017	Japan	Aggregated data	2010.7.1–2013.3.31	Hospitals	–
22	Akihiro Shiroshita [54]	2022	Japan	Retrospective cohort	2008.4–2020.7	Hospitals	–
23	Jiang-Chen Peng [55]	2022	Israel	Aggregated data	2001–2012	ICU	–
24	A. Mohan [56]	2007	India	Prospective cohort	2004.2–2006.3	Medical wards and ICU	–
25	Karthikeyan Ramaraju [57]	2016	India	Retrospective cohort	2012.8–2013.7	Hospital	–
26	Filia Diamantea [58]	2014	Greece	Prospective cohort	2010.1–2012.6	Respiratory medicine departments	AECOPD-F score
27	N. Roche [56]	2008	France	Prospective cohort	2003.11–2004.2	Emergency departments	–
28	Nicolas Roche [59]	2014	France	Retrospective cohort	2006.10–2007.6	Respiratory medicine department	2008 score-new
29	Liping Fan [60]	2014	China	Prospective cohort	2012.10–2014.5	Respiratory ICU	–
30	Dong Liu [61]	2015	China	Prospective cohort	2013.11–2014.2	Respiratory medical ward or ICU	–
31	Qi-fang Shi [62]	2018	China	Prospective cohort	2016.1–2017.12	ICU	Re-AE INDEX
32	Wei-ping Hu [63]	2019	China	Retrospective cohort	2005–2007	Hospitals	–
33	Mi Zhou [64]	2019	China	Retrospective cohort	2011.2–2018.6	Department of Respiratory and Critical Care Medicine	–
34	Yi Chen [65]	2020	China	Retrospective cohort	2017.1–2018.12	Hospital	–
35	Xing Yu [66]	2020	China	Retrospective cohort	2015.1–2017.12	Hospital	–
36	Junfeng Peng [67]	2020	China	Retrospective cohort	2011–2018	Hospital	–

Table 1 (continued)

Number	Author	Year	Study reigon	Study design	Enrolment period	Study setting	Model name
37	Wei Bi [68]	2020	China	Prospective cohort	2018.1–2018.12	Department of Emergency Internal Medicine	–
38	Fen Dong [69]	2021	China	Retrospective cohort	2015.1.1–2019.12.31	Hospital	–
39	Lan Chen [70]	2021	China	Retrospective cohort	2018.1–2020.9	ED	–
40	Lili Chen and Shiping Chen [71]	2021	China	Prospective cohort	2016.1–2019.12	Hospital	–
41	Lifen Yang [72]	2022	China	Retrospective cohort	No information	Hospital	–
42	Dawei Chen [73]	2023	China	Retrospective cohort	2014.1–2017.1	Hospital	AAAAN Score
43	Lin Yu [74]	2023	China	Retrospective cohort	2012.9–2021.8	Hospital	–
44	Shiyi He [75]	2023	China	Prospective cohort	2020.1–2022.6	Hospital	–
45	Li-Na Yan [76]	2024	China	Retrospective cohort	2020.6–2023.6	Hospital	–
46	Reza Fakhraei [77]	2023	Canada	Retrospective cohort	2012–2018	General Internal Medicine ward	–

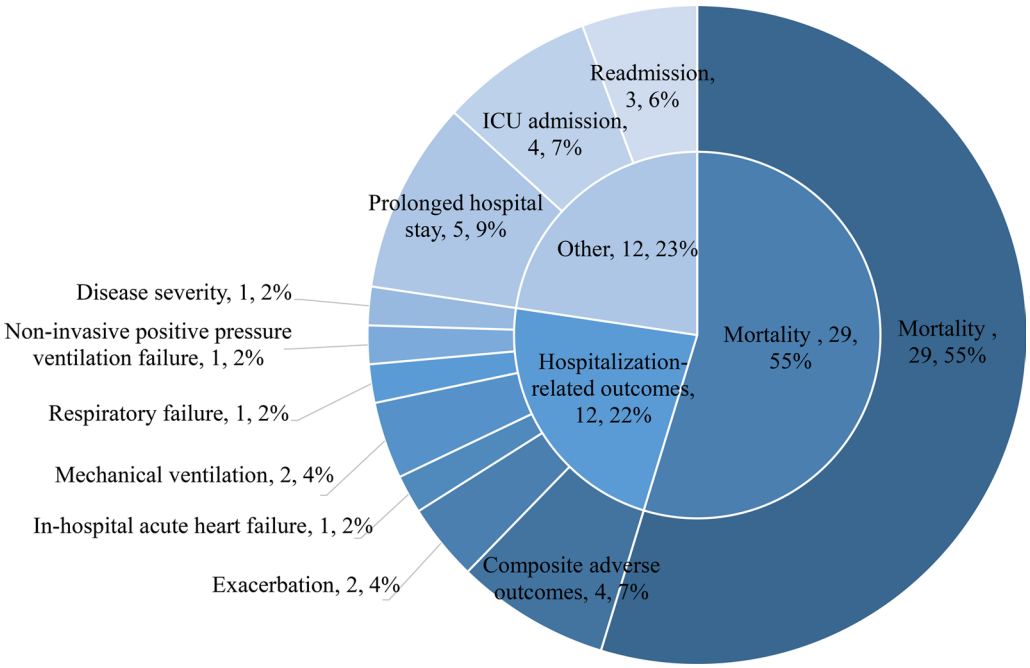

Fig. 2 Frequency Distribution of Different Outcome Types

selected predictors based on prior knowledge. For modeling methods, most models (n = 41; 77.4%) used logistic regression, while fewer (n = 9; 17.0%) applied machine learning methods. Additionally, one study created ROC curves for variables with statistical significance in univariate analysis and developed a scoring system based on variables with high predictive ability. Two modified models were updated directly based on prior knowledge and subsequently validated. In detail, the logistic regression models included 10 with backward regression, 9 with stepwise regression, 2 with LASSO regression, 1 with forward regression, and 19 with no specified method. Machine learning methods included decision tree-based algorithms such as CART (n = 3), Random Forest (n = 2), C5.0 (n = 1), RPART (n = 1), and the gradient boosting algorithm XGBoost (n = 2).

Handling of missing data

A portion of the models (n = 27; 50.9%) did not report any methods for handling missing data. Four models (7.5%) used complete case analysis. Six models (11.3%) used both single imputation and multiple imputation

methods, while seven models (13.2%) used only multiple imputation, and six models (11.3%) used only single imputation. Two models analyzed missing values by placing them in separate columns. One model explicitly stated that it did not handle missing data.

Sample size and predictive factors

The median (minimum, maximum) sample size for model development was 672 (106, 150,035). The median (minimum, maximum) number of candidate predictors was 21 (5, 82). However, only six models had an EPV (events per variable) or EPP (events per predictor) value greater than 10, calculated based on sample size, the number of outcome events, and the number of candidate predictors before selection.

The median (minimum, maximum) number of final predictors in the models was 5 (2, 42) (Fig. 3). Predictive factors used more than ten times included age (n = 28; 52.8%), the MRC (Medical Research Council) scale for assessing dyspnea (n = 12; 22.6%), and $PaCO_2$ (n = 11; 20.8%) (Fig. 4).

Internal and external validation

Three (5.7%) models did not undergo internal or external validation, and another 3 (5.7%) models underwent both internal and external validation (Fig. 5). Among the models that performed internal validation (n = 36; 67.9%), the most commonly used methods were random splitting (n = 18) and the bootstrap resampling method (n = 15). Two models used populations from the same study site but different time periods as their internal validation.

Only 12(22.6%) models conducted external validation, employing different time periods, different study sites, or entirely independent datasets.

Model performance index and presentation

For calibration, the most frequently used assessment methods were the Hosmer–Lemeshow test (n = 20; 37.7%) and calibration plots (n = 12; 22.6%). Other methods included calibration slope (n = 5; 9.4%) and intercept (n = 2; 3.8%). Twenty-five models (47.2%) did not report any calibration assessment.

For discrimination, all models used the C-statistic, with 41 (77.4%) models also employing ROC curves.

Regarding the presentation of the models, excluding the 10 machine learning models, 11 (20.8%) models did not provide a presentation format. 19 (35.8%) models developed scoring systems, 7 (13.2%) models used nomograms, and 6 (11.3%) models constructed regression-based equations. Among these, one model developed an online calculator based on the regression equation.

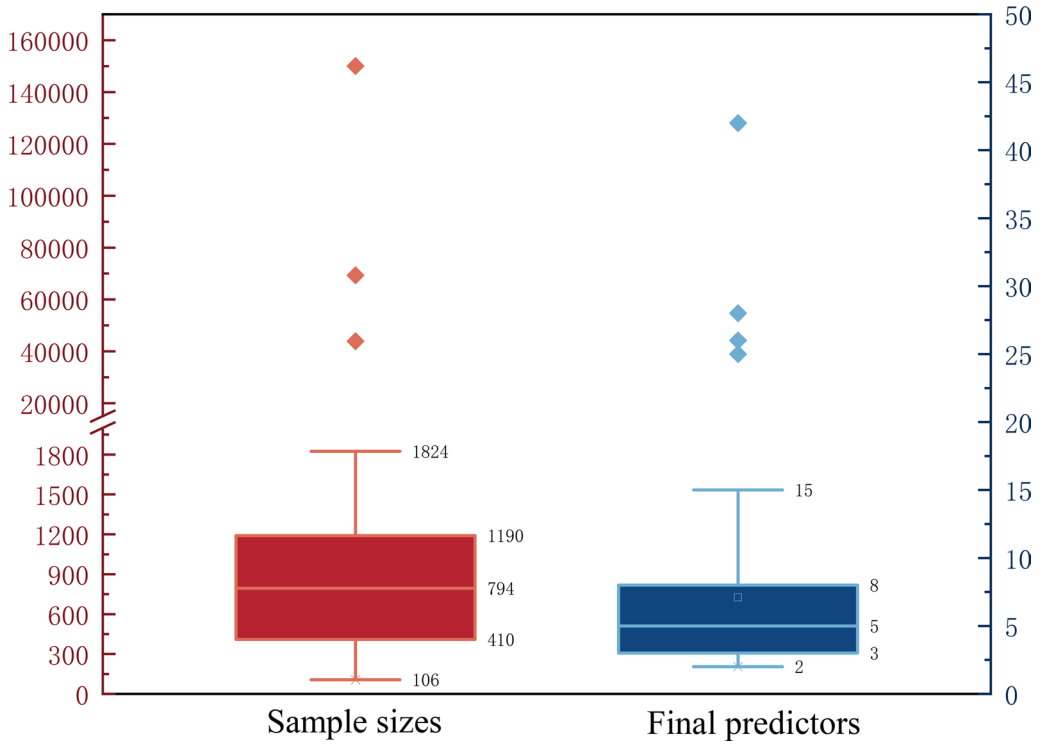

Fig. 3 Sample size and number of predictors

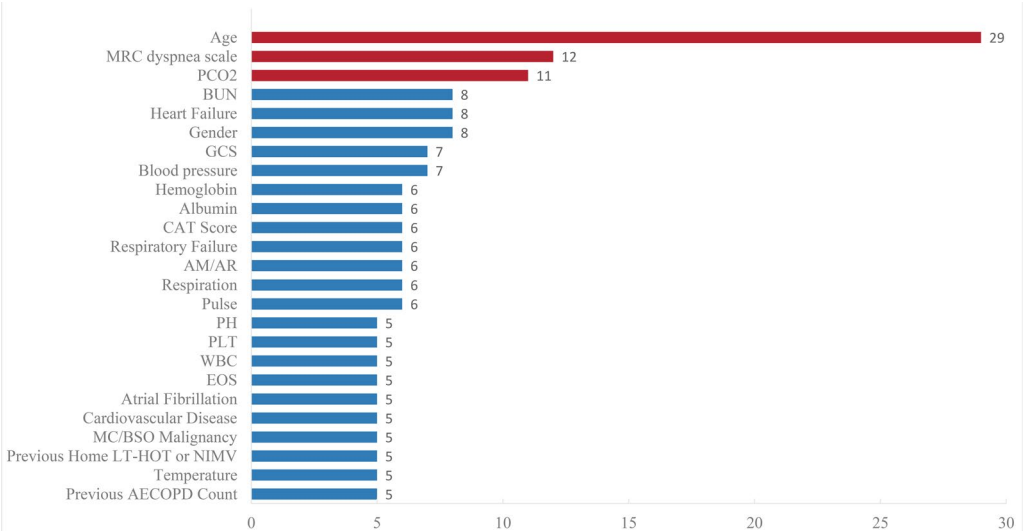

Fig. 4 Predictive factors in 53 models. *MRC* Medical Research Council, *PCO2* Partial Pressure of Carbon Dioxide, *BUN* blood urea nitrogen, *GCS* Glasgow Coma Scale, *CAT Score* COPD Assessment Test Score, *AM/AR* Use inspiratory assistance muscle/accessory breathing, *PH* Potential of hydrogen; *PLT* Platelet count; *WBC* White blood cell, *EOS* Eosinophil count, *MC/BSO* Metastatic cancer/malignant tumors of the blood or solid organs, *LT-HOT* Long-term home oxygen therapy, *NIMV* Non-invasive mechanical ventilation

Risk of bias assessment

Among the 53 models, 52 were judged to have a high risk of bias (ROB) (Fig. 6), all models were judged to have low overall applicability. Specifically, 27 (50.9%) models were rated as high ROB in the domain of participant selection, 22 (41.5%) models in the domain of predictor assessment, 9 (17.0%) models in the domain of outcome assessment, and 50 (94.2%) models in the domain of analysis. The primary sources of bias included insufficient sample sizes (n = 44; 83.0%), the use of univariate analysis to select predictors (n = 39; 73.6%), inappropriate internal and external validation methods (n = 29; 54.7%), inappropriate inclusion and exclusion criteria for study subjects (n = 27; 50.9%), inadequate methods for assessing model performance (n = 22; 41.5%), and inconsistent definitions and measurement methods for predictors across all study subjects (n = 21; 39.6%). The only model evaluated as having a low risk of bias (ROB) was the PEARL score. (See Supplement 3 and Supplement 4 for details).

Meta analysis

For prediction models with mortality as the outcome, the pooled AUC was 0.80 (95% CI: 0.76–0.84). For models with hospitalization-related outcomes, the pooled AUC was 0.84 (95% CI: 0.79–0.88), indicating good predictive accuracy (Fig. 7). However, heterogeneity analysis showed I^2 statistics of 98% and 94%, respectively, indicating high heterogeneity among the studies ($P < 0.0001$). This high heterogeneity could be attributed to differences in study design, patient characteristics, types of prediction models, and follow-up periods. Funnel plots and Egger's test were used to assess publication bias, with results showing no significant publication bias.

Discussion

Based on the results of this review, the research on AECOPD prognostic risk prediction has garnered widespread attention globally, particularly in China. In developed countries, most studies are concentrated in the UK, the US, and Spain, following trends similar to those observed in COPD prognostic risk prediction models[10]. However, in contrast, our study found that China had the highest number of model studies, with 14 (82.4%) published in 2019 or later. In recent years, the prevalence of COPD in China has exceeded the global average and continues to rise[11]. Following the inclusion of COPD action plans in the "Healthy China Initiative (2019–2030)", there has been a surge in scientific research and policy actions, reflecting an emphasis on chronic disease management at both national and societal levels. An example of this is the early screening and comprehensive intervention project for high-risk COPD populations initiated in 2021 [12].

Researchers have explored the prognostic outcomes of patients with AECOPD in various clinical settings. Compared to general wards, the number of patients with AECOPD is higher, and their conditions are more critical in emergency departments and ICUs [13]. Prognostic models are more applicable in these acute care settings. Mortality remains the most scrutinized clinical outcome

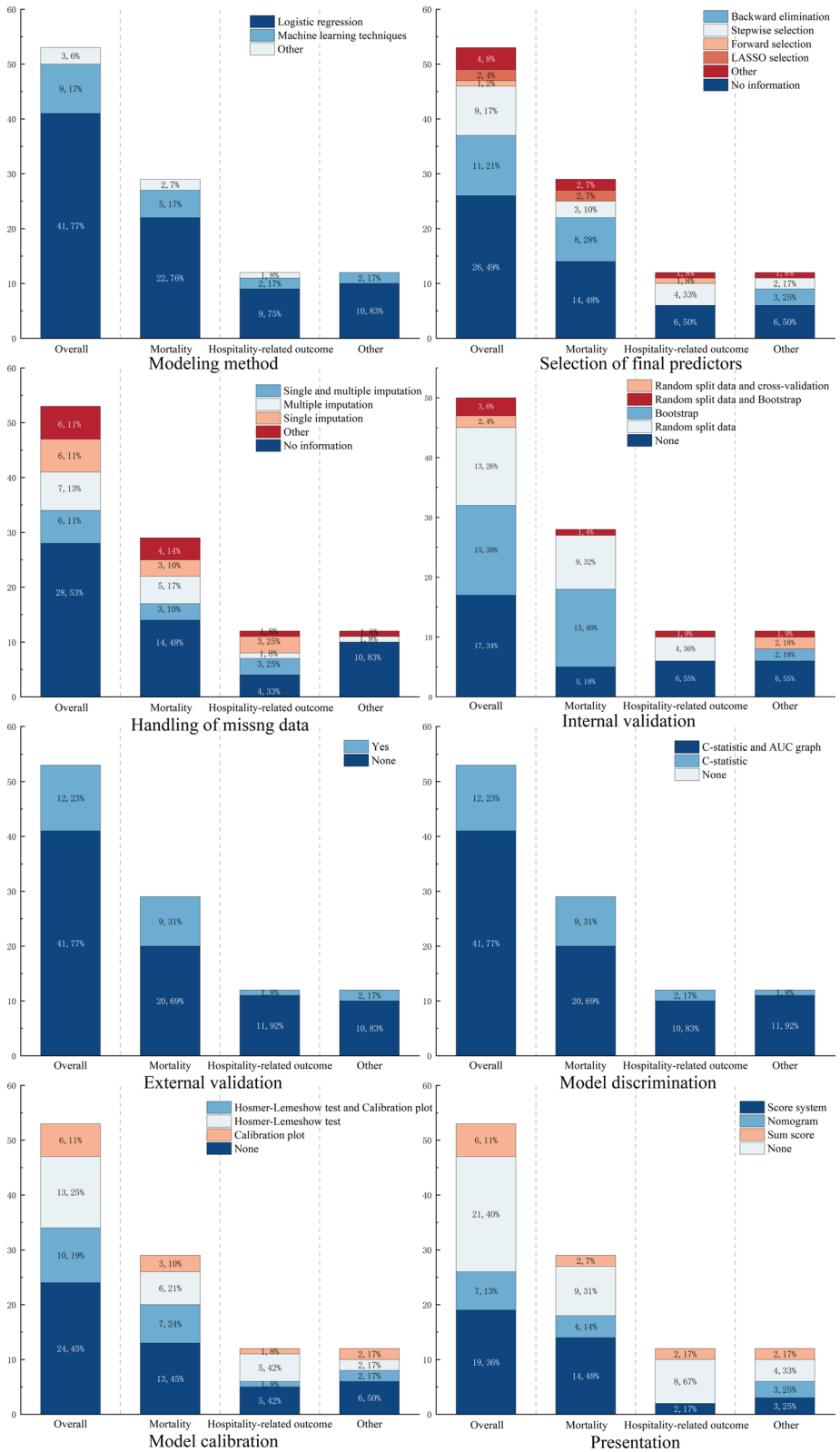

Fig. 5 Basic information of the models

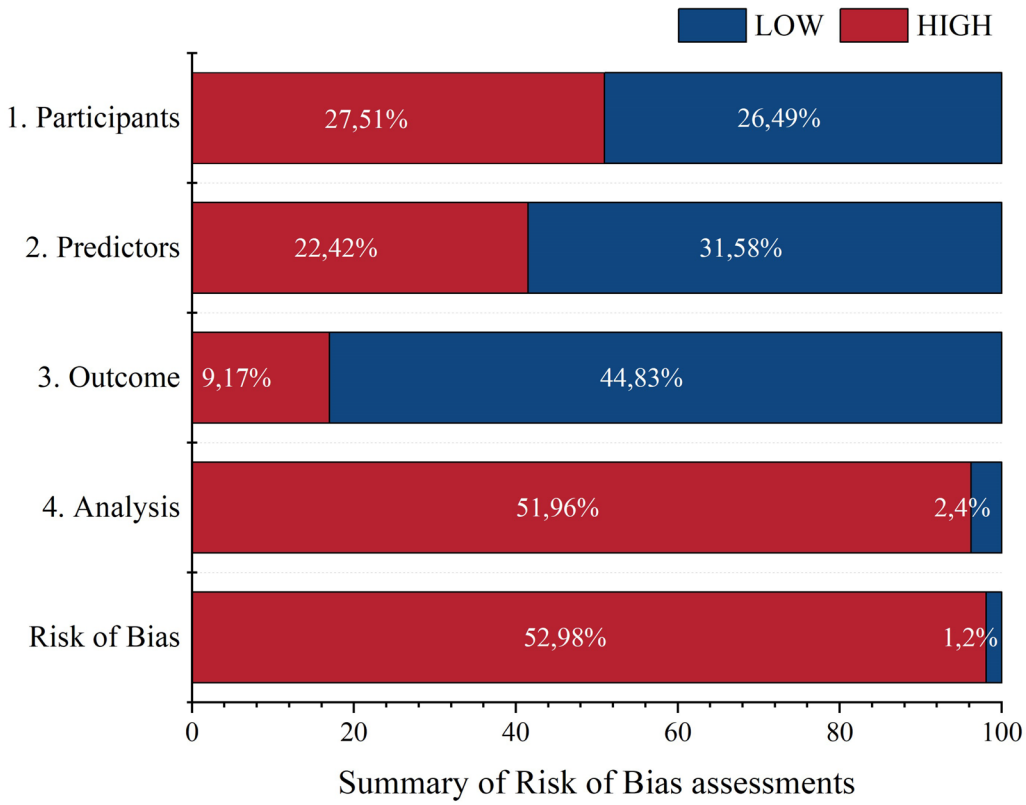

Fig. 6 Distribution of risk of bias assessment based on four domains

due to its strong correlation with the disease burden resulting from exacerbation and death[14]. Hospitalization-related outcomes are also significant, as they not only increase healthcare costs but also elevate the risk of nosocomial infections and other complications[15]. Developing predictive models for hospitalization can optimize resource allocation and improve bed turnover rates, providing more efficient treatment for patients. However, there is limited focus on specific symptomatic prognostic issues, such as the high incidence of cardiovascular events post-discharge[16]. This study synthesizes results from different research to reflect the overall effectiveness of the model regarding the same outcomes in combined AUC. However, high heterogeneity also indicates that the geographical distribution, departmental limitations, and study outcomes of these studies lead to variations in the construction and application of AECOPD prognostic risk prediction models across different countries and healthcare settings, potentially influenced by research design, patient characteristics, types of prediction models, national policies, and healthcare resources.

The generalizability of the model refers to its implementation in different settings. Although there are numerous external validation studies demonstrating the effectiveness of DECAF, BAP65[17], and PEARL[18], the methods and conditions used during model development can impact their performance. Therefore, it is essential to provide detailed and cautious descriptions of the research methods to facilitate better dissemination. By integrating the bias risk factors from modeling studies and considering their generalizability, we have summarized the following issues:

(1) Many studies may exclude patients with comorbidities and complications to emphasize the prognosis of adverse outcomes in AECOPD, which can affect the results to some extent. We believe that comorbidities or complications can serve as predictive factors, or the reasons for exclusion should be clearly stated and explained; otherwise, it may be challenging to generalize under comparable conditions[19].
(2) Numerous multicenter studies do not explicitly detail the measurement, evaluation methods, and standards for predictive factors across different research centers, making it difficult to unify and compare the reliability of results in various environments. It is essential to strictly standardize and clarify the assessment criteria for predictive factors,

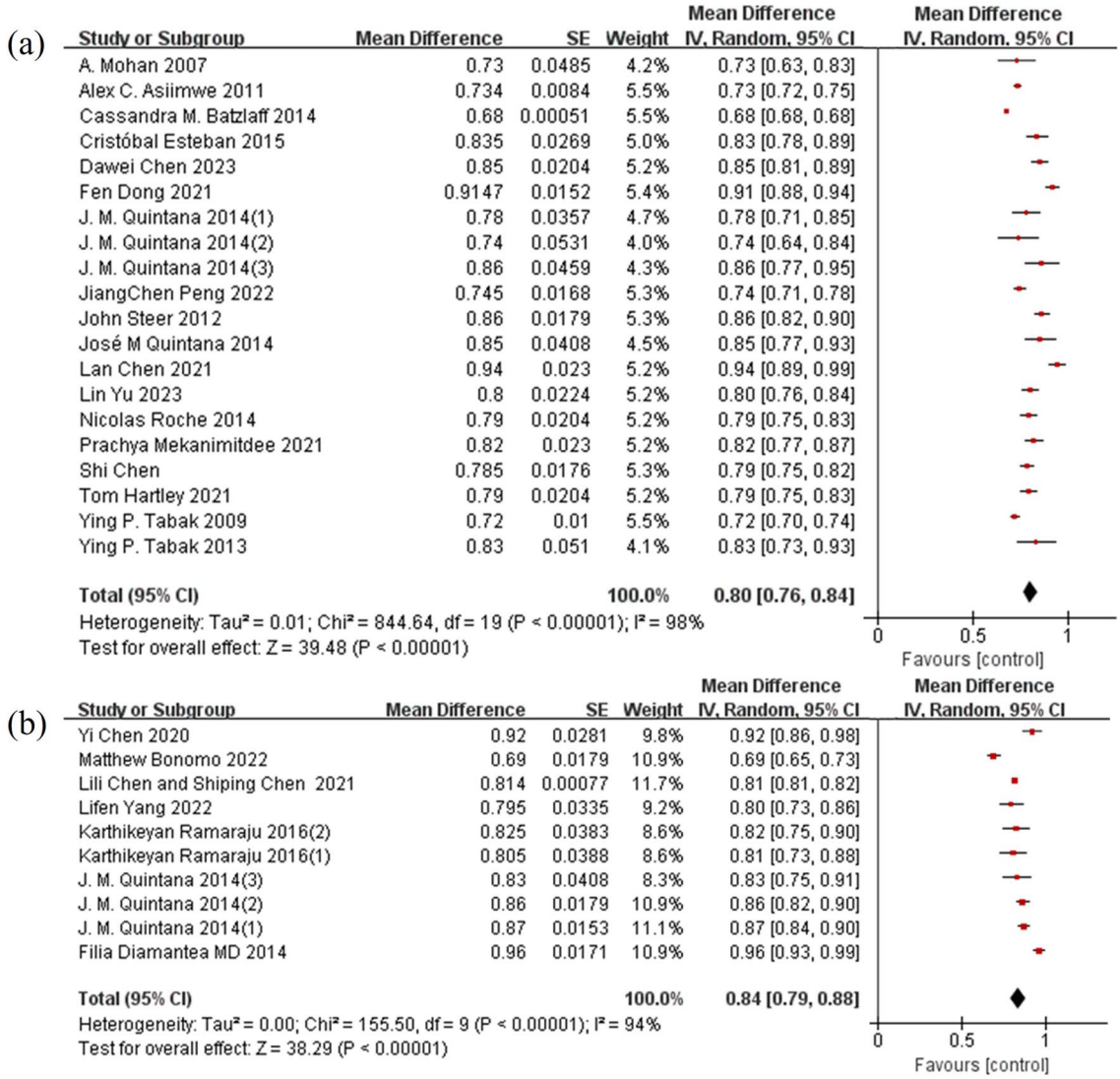

Fig. 7 Meta-analysis of prediction models with mortality or hospitalization as outcomes. **a** Mortality; **b** Hospitalization

ensuring that all study subjects utilize the same definitions and measurement methods. This highlights a limitation of integrated databases; while studies may employ cohort designs[20], prospective methodologies better meet the requirements for this research.

(3) Many studies fail to provide clear definitions for outcome determinations, such as ICU admission or intubation. Objective indicators and thresholds should be emphasized in outcome assessments to avoid subjective physician judgments; otherwise, widespread adoption may be hindered.

In terms of the rigor in statistical methodology and result presentation, we have summarized the following issues:

(1) A larger sample size contributes to a more robust model. When developing predictive models for binary outcomes or event time results, the required sample size should ensure that each candidate variable has at least 10 events. It is important to note that the candidate variables represent the total number of predictive factors considered at any stage of the modeling process, not just those

included in the final model. Many studies overlook this requirement. Future research should place greater emphasis on the importance of sample size in the development of predictive models and select appropriate statistical methods for calculation and analysis, minimizing the loss of modeling sample size as much as possible.

(2) During the model development process, careful evaluation and control of the number and complexity of variable selection are needed. Relying solely on univariate analyses to filter and refine the most predictive variables may overlook contributions from variable combinations[21]. It is advisable to further optimize the variable selection strategy during model development, utilizing prior experience where possible and employing backward elimination of redundant predictors or forward selection of promising predictors[22].

(3) Most models are at risk of overfitting or instability when the sample size is relatively small or when there are numerous and complex candidate predictors[23]. In cases where there may be heightened optimism or overfitting, internal and external validation becomes particularly important. However, studies that simultaneously develop and validate models are limited. Future research should adopt stricter methodologies to validate model stability, and it is recommended to use bootstrap methods rather than random split techniques for this purpose[24].

(4) To be applicable in routine clinical practice, model coefficients are often simplified to numbers that are easy for clinicians to score. The interpretability and visual representation of models are crucial for acceptance by healthcare professionals, especially for machine learning models[25]. However, some models fail to provide detailed presentation formats, which may hinder the understanding and application of model results in actual clinical decision-making.

The predictive factors included in the models of this review include factors such as medical history, clinical manifestation, treatment condition, comorbidities, and laboratory results. Different models focus on various aspects, utilizing a wide range of indicators. Notably, age, dyspnea assessment via the MRC scale, and PaCO2 are frequently emphasized. Age, as the most commonly used factor, reflects the higher social and clinical burden faced by the elderly population [26]. Dyspnea, being one of the primary symptoms during acute exacerbation, is effectively assessed using the MRC dyspnea scale, which is widely used in COPD patients [27]. PaCO2 is a crucial laboratory indicator for evaluating ventilation status. Future research should continue to screen and compare the accuracy of these factors, paying particular attention to the performance and applicability of models across different age groups. Additionally, new clinical findings, such as those related to microbiome ecology [28], novel metabolites [29], and sputum biomarkers [30], should be considered for their potential value in improving or developing new models.

The PEARL score is the only predictive model assessed as having low bias, predicting 90-day readmission or non-readmission mortality [31]. Compared to other models, this study explicitly stated that all sites adhered to data collection guidelines, had a sufficient sample size, and avoided using univariate analysis for predictor selection, ultimately presenting the model results as a score. In previous studies [32], the DECAF score, despite issues of insufficient sample size and the use of univariate analysis for predictor selection, was recommended as a better model for reducing hospital admissions and 90-day mortality due to its simplicity and external validation in multiple countries. From the perspective of predictive factors, both models are simple in structure. The PEARL score emphasizes the patient's medical history and cardiac function, while the DECAF score focuses more on acute physiological changes and lung pathology. Currently, both scores have considerable application ranges [33], but DECAF has been more extensively studied in clinical practice. This also highlights that, although preliminary assessments of modeling studies have been conducted, summarizing and evaluating external validation studies is equally important. Future research should further compare these two scoring models, particularly in different clinical settings and patient populations.

The study did not limit the outcomes of the models, allowing for a broader understanding of the current focus and quality of research on prognostic risk in patients with AECOPD. Using assessment tools, the study provided a comprehensive breakdown and extraction of information on the bias and applicability of the models, offering insights for future research improvements and clinical application testing. Additionally, valuable models were analyzed for their current status and future prospects. However, this study has some limitations. Restricting the literature search to English databases may introduce some limitations regarding population and regional characteristics. Furthermore, as this study only included information from studies that developed models, it did not comprehensively analyze the external validation of these models and conduct a meta-analysis of similar models to calculate summary estimates of model performance and calibration.

Conclusion

This study reviews 53 prognostic risk prediction models for AECOPD, highlighting differences and limitations in their predictive performance. The PEARL score shows a lower degree of bias but requires further validation across diverse populations. Future research should focus on methodological rigor, multi-center validation, and simplifying models for better clinical utility, ultimately advancing AECOPD risk prediction and individualized patient treatment.

Abbreviations

COPD	Chronic obstructive pulmonary disease
AECOPD	Acute exacerbations of chronic obstructive pulmonary disease
CHARMS	Checklist for Critical Appraisal and Data Extraction for Systematic Reviews of Prediction Modelling Studies
PROBAST	Prediction model Risk Of Bias Assessment Tool
MRC	Medical Research Council
eMRC	Extended Medical Research Council
PCO2	Partial Pressure of Carbon Dioxide
BUN	Blood urea nitrogen
GCS	Glasgow Coma Scale
CAT Score	COPD Assessment Test Score
AM/AR	Use inspiratory assistance muscle/accessory breathing
PH	Potential of hydrogen
PLT	Platelet count
WBC	White blood cell
EOS	Eosinophil count
MC/BSO	Metastatic cancer/malignant tumors of the blood or solid organs
LT-HOT	Long-term home oxygen therapy
NIMV	Non-invasive mechanical ventilation

Supplementary Information

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Supplementary Material 1. Study Information: Basic information on all included studies, including authors, year, country, and study design.

Supplementary Material 2. Model Information: Information on all included predictive models, including study outcomes, sample size, and modeling methods.

Supplementary Material 3. ROB and Applicability: Assessment results of bias risk and applicability for all included predictive models.

Supplementary Material 4. Model Evaluation Information: Specific items related to the bias risk and applicability assessment results for all included predictive models.

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Author contributions

XZH conducted the literature search and screening, data extraction and analysis, and drafted the manuscript. WY assisted with the literature search and screening, and provided comprehensive editing. LF contributed to data extraction and analysis, and write sections of the manuscript. XY polished and revised the article. WYP supervised the study, providing guidance and critical revisions to the manuscript.

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Availability of data and materials

All data generated or analysed during this study are included in this published article and its supplementary information files.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

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Competing interests

The authors declare no competing interests.

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