



ARTIFICIAL INTELLIGENCE FOR RESPIRATORY DISEASE DIAGNOSIS: A PRISMA 2020 SYSTEMATIC REVIEW OF CURRENT CLINICAL APPLICATIONS AND FUTURE DIRECTIONS

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ABSTRACT

Respiratory diseases remain among the leading causes of morbidity and mortality worldwide, imposing a substantial clinical and economic burden. Early and accurate diagnosis is essential for improving patient outcomes, yet conventional diagnostic approaches often depend on expert interpretation, are resource intensive, and may be limited by interobserver variability. Reviews in pulmonary medicine also emphasize that successful implementation requires rigorous validation, regulatory oversight, and clinically meaningful evaluation beyond algorithmic accuracy. To systematically evaluate current evidence regarding the diagnostic applications, clinical performance, advantages, limitations, and future directions of artificial intelligence technologies in respiratory disease diagnosis. This systematic review will be conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) guidelines. Eligible studies will be identified through comprehensive searches of PubMed/MEDLINE, Embase, Scopus, Web of Science, IEEE Xplore, and the Cochrane Library. Studies evaluating AI-based diagnostic models for respiratory diseases in human populations will be considered. Two reviewers will independently perform study selection, data extraction, and quality assessment. This review aims to provide clinicians, researchers, and policymakers with a comprehensive synthesis of current evidence regarding AI-assisted respiratory disease diagnosis and to identify priorities for future research and clinical translation.

KEYWORDS: Artificial intelligence; Machine learning; Deep learning; respiratory diseases; Pulmonary medicine; Diagnosis; Medical imaging; PRISMA; Systematic review.

INTRODUCTION

Respiratory diseases account for a substantial proportion of global mortality and disability, encompassing a broad spectrum of acute and chronic disorders including asthma, COPD, pneumonia, tuberculosis, lung cancer, interstitial lung disease, pulmonary fibrosis, and emerging viral infections. Accurate diagnosis is fundamental to effective treatment and prognosis but is frequently challenged by heterogeneous clinical presentations, dependence on specialist expertise, and variability in interpretation of imaging and physiological investigations.

The digital transformation of healthcare has created unprecedented opportunities for computational approaches capable of extracting clinically meaningful information from complex datasets. Artificial intelligence (AI), particularly machine learning (ML) and deep learning (DL), has emerged as one of the most promising technologies for supporting respiratory disease diagnosis. AI systems can integrate information from chest radiographs, computed tomography (CT), lung ultrasound, pulmonary function testing, electronic health records, respiratory sounds, and wearable devices to assist clinicians in diagnosis, risk stratification, and decision support.^[1]

Convolutional neural networks have achieved high performance in automated detection of pulmonary nodules, pneumonia, tuberculosis, COVID-19 pneumonia, emphysema, and diffuse interstitial lung disease using thoracic imaging. Similarly, machine learning algorithms have demonstrated utility in spirometry interpretation, asthma phenotyping, COPD classification, and prediction of disease exacerbations. AI has also shown potential in analyzing respiratory acoustics, enabling automated recognition of wheeze, crackles, and cough patterns for early disease detection. Studies in asthma and other chronic respiratory diseases indicate growing adoption of AI across screening, diagnosis, phenotyping, and management, although methodological quality and external validation remain variable.^[2]

Although the literature has expanded rapidly over the past decade, important challenges remain before AI can be routinely integrated into respiratory clinical practice. Many published models rely on retrospective single-centre datasets, exhibit limited external validation, and may be susceptible to spectrum bias, data leakage, and inadequate reporting. Furthermore, concerns regarding explainability, fairness, reproducibility, regulatory approval, cybersecurity, and ethical governance continue to influence clinical acceptance. Broader evaluations of AI in healthcare have highlighted that studies frequently overstate clinical readiness relative to the strength of their underlying evidence.^[3]

Given the accelerating pace of AI development and the increasing diversity of respiratory applications, an updated systematic synthesis of current evidence is warranted. This review aims to evaluate the diagnostic performance, methodological characteristics, strengths, limitations, and future opportunities of AI technologies across respiratory diseases.^[4]

OBJECTIVES

- The primary objective of this systematic review is to synthesize evidence regarding the use of artificial intelligence for respiratory disease diagnosis.
- To identify current AI methodologies applied in respiratory diagnostics.
- To evaluate diagnostic accuracy and clinical performance across different respiratory diseases.
- To compare AI applications across imaging, physiological testing, respiratory sounds, and multimodal clinical data.
- To identify methodological limitations and potential sources of bias.
- To summarize barriers to clinical implementation.
- To highlight emerging research directions and future opportunities.

Methods

Study Design: This systematic review has been designed in accordance with the **PRISMA 2020 Statement**. Where diagnostic test accuracy studies predominate,

reporting will also align with the PRISMA-DTA extension to ensure complete and transparent reporting of diagnostic evidence.

Eligibility Criteria

Inclusion Criteria

- Original peer-reviewed studies
- Human participants
- AI, machine learning, or deep learning used for respiratory disease diagnosis
- Diagnostic performance reported
- English-language publications
 - Studies involving diseases such as Lung cancer, COPD, Asthma, Tuberculosis, Pneumonia, COVID-19, Interstitial lung disease, Pulmonary fibrosis, Sleep apnoea, Other respiratory disorders

Exclusion Criteria

- Editorials
- Commentaries
- Conference abstracts without full text
- Animal studies
- Non-English publications
- Narrative reviews
- Case reports
- Studies without diagnostic outcomes

Information Sources: The following electronic databases will be searched from database inception to the final search date PubMed/MEDLINE, Embase, Scopus, Web of Science Core Collection, IEEE Xplore, Cochrane Library

Search Strategy: A comprehensive search strategy will combine controlled vocabulary and free-text terms. An example PubMed search is ("Artificial Intelligence" OR "Artificial Intelligence" OR "Machine Learning" OR "Deep Learning" OR "Neural Network" OR "Computer Vision") AND "Respiratory Tract Diseases", OR "Pulmonary Disease", OR "Lung Disease", OR COPD, OR Asthma, OR Pneumonia, OR Tuberculosis, OR COVID-19, OR Lung Cancer, OR Interstitial Lung Disease.^[5]

Study Selection: All retrieved records will be imported into a reference management system, and duplicate citations will be removed. Two independent reviewers will screen titles and abstracts, followed by full-text assessment of potentially eligible studies. Disagreements will be resolved through discussion or consultation with a third reviewer. Reasons for exclusion at the full-text stage will be documented to facilitate preparation of the PRISMA 2020 flow diagram.

Data Extraction

Following full-text screening, data from eligible studies will be extracted independently by two reviewers using a standardized data extraction form developed specifically for this review. A pilot extraction will be performed on a

subset of studies to ensure consistency between reviewers. Disagreements will be resolved through discussion, and where necessary, consultation with a third reviewer.^[6]

The following information will be extracted Bibliographic information (author, year, country), Study design, Clinical setting, Respiratory disease investigated, Sample size and participant characteristics, Data source (chest radiograph, CT, lung ultrasound, spirometry, respiratory sounds, electronic health records, wearable devices, or multimodal data), AI methodology (machine learning, deep learning, convolutional neural networks, transformers, ensemble learning, hybrid approaches), Reference standard used for diagnosis, External or internal validation strategy, Diagnostic performance metrics including Sensitivity, Specificity, Accuracy, Area under the receiver operating characteristic curve (AUC), Positive predictive value, Negative predictive value, F1-score where reported, Explainability techniques (e.g., Grad-CAM, SHAP, LIME), Major findings, Study limitations, Funding source and potential conflicts of interest. When multiple AI models are reported within the same study, data will be extracted separately for each model to facilitate comparative synthesis.^[7]

Risk of Bias Assessment

The methodological quality of included studies will be evaluated independently by two reviewers. For diagnostic accuracy studies, risk of bias and concerns regarding applicability will be assessed using the **Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2)** instrument. The four domains include Patient selection, Index test, Reference standard, Flow and timing. Each domain will be judged as having low, high, or unclear risk of bias. Studies primarily developing or validating diagnostic prediction models will additionally be assessed using the **Prediction model Risk of Bias Assessment Tool (PROBAST)** where appropriate. No numerical quality score will be calculated, consistent with current methodological recommendations.^[8]

Outcomes

The primary outcome will be the diagnostic performance of AI-based systems for respiratory disease diagnosis, measured by reported sensitivity, specificity, and AUC.

Characteristics of Included Studies

Table 1: Characteristics of Included Studies (template).

Author	Year	Country	Disease	Dataset	AI Model	Imaging/Data Type	Sample Size	Validation	Main Performance
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Table 2: Respiratory Diseases Included in AI Diagnostic Studies

Disease	Number of Studies	Primary Data Type	Most Common AI Model	Typical Outcome Measures
Lung Cancer		CT	CNN	AUC, Sensitivity
COPD		Spirometry/CT	Random Forest/CNN	Accuracy
Asthma		Clinical + Spirometry	ML	Accuracy

Secondary outcomes will include Diagnostic accuracy by respiratory disease, Performance by imaging modality, Performance by AI architecture, Internal versus external validation, Explainability methods like Clinical implementation readiness, Regulatory status where reported, Generalizability across healthcare settings.^[9]

Data Synthesis

A narrative synthesis will summarize the characteristics and findings of all included studies.

Where sufficient methodological homogeneity exists regarding disease category, index test, and reference standard, quantitative synthesis (meta-analysis) may be performed using hierarchical summary receiver operating characteristic (HSROC) or bivariate random-effects models, as recommended for diagnostic test accuracy reviews. Statistical heterogeneity will be explored through subgroup and sensitivity analyses where feasible.

Subgroup Analyses

Where data permit, subgroup analyses will be conducted according to Respiratory disease like Lung cancer, Pneumonia, COVID-19, Tuberculosis, COPD, Asthma, Interstitial lung disease, Sleep apnea. AI methodology like Machine learning, Deep learning, Convolutional neural networks, Transformer-based models, Hybrid algorithms, Diagnostic modality, Chest radiography, Computed tomography, Lung ultrasound, Spirometry, Respiratory sound analysis, Electronic health records, Multimodal systems, Geographic region, Prospective versus retrospective studies, Single-center versus multicenter datasets, Internal versus external validation.

Publication Bias

If an adequate number of comparable studies are available for quantitative synthesis, potential publication bias will be explored using methods appropriate for diagnostic accuracy reviews (e.g., Deeks' funnel plot asymmetry test), recognizing the limitations of publication-bias assessment in this context.^[10]

RESULTS

Study Selection: The database search, duplicate removal, title and abstract screening, full-text eligibility assessment, and final inclusion of studies will be reported using a PRISMA 2020 flow diagram.

Tuberculosis		Chest X-ray	CNN	Sensitivity
Pneumonia		Chest X-ray	CNN	AUC
COVID-19		CT/CXR	CNN	Sensitivity
ILD		HRCT	Deep Learning	Classification Accuracy
Sleep Apnea		PSG/Wearables	ML	AUC

Table 3: AI Algorithms Used Across Included Studies.

Algorithm	Primary Application	Advantages	Reported Limitations
Convolutional Neural Networks	Medical imaging	High image classification performance	Requires large datasets
Random Forest	Clinical prediction	Interpretable	Limited image capability
Support Vector Machine	Classification	Effective with small datasets	Feature engineering required
Gradient Boosting	Risk prediction	High predictive power	Computational complexity
Vision Transformer	Advanced imaging	Long-range feature extraction	Large training datasets
Ensemble Learning	Multimodal prediction	Improved robustness	Increased complexity

Table 4: Diagnostic Modalities Used by AI.

Diagnostic Modality	Respiratory Diseases	Typical AI Approach
Chest Radiography	TB, Pneumonia, COVID-19	CNN
CT Imaging	Lung Cancer, ILD	Deep Learning
Lung Ultrasound	Pneumonia	CNN
Spirometry	COPD, Asthma	Machine Learning
Respiratory Sounds	Asthma, COPD	Deep Learning
Wearable Devices	Sleep Apnea	Machine Learning
Electronic Health Records	Multiple Diseases	Ensemble Models

Table 5: Common Challenges Reported in AI Studies.

Challenge	Potential Impact	Possible Mitigation
Small datasets	Overfitting	Multicenter datasets
Lack of external validation	Poor generalizability	Independent validation cohorts
Class imbalance	Reduced performance	Data augmentation
Poor explainability	Low clinician trust	Explainable AI methods
Dataset bias	Reduced fairness	Diverse populations
Variable image quality	Reduced robustness	Standardized acquisition

Table 6: Future Research Priorities.

Priority Area	Expected Clinical Benefit
Multicenter prospective validation	Improved generalizability
Federated learning	Privacy-preserving collaboration
Explainable AI	Greater clinician confidence
Multimodal AI	Improved diagnostic accuracy
Integration with EHR	Clinical decision support
Cost-effectiveness evaluation	Health system adoption
Regulatory evaluation	Safer implementation

Risk of Bias

- The results of the QUADAS-2/PROBAST assessments will be summarized and evidence will be synthesized by major respiratory disease categories.

Lung Cancer: Studies evaluating AI for pulmonary nodule detection, malignancy prediction, radiomics, and CT-based computer-aided diagnosis will be summarized.

Pneumonia: Evidence regarding AI-assisted diagnosis from chest radiography, CT imaging, and lung ultrasound will be reviewed.

COVID-19: Studies investigating deep learning approaches for COVID-19 detection and severity assessment will be summarized with attention to methodological quality and external validation.

Tuberculosis: Applications of AI for automated tuberculosis detection using chest radiographs and digital screening programs will be evaluated.

Chronic Obstructive Pulmonary Disease: Evidence related to spirometry interpretation, CT phenotyping, exacerbation prediction, and disease classification will be synthesized.

Asthma: Studies using AI for diagnosis, phenotyping, biomarker integration, and respiratory sound analysis will be reviewed.

Interstitial Lung Disease: Evidence concerning automated CT pattern recognition, fibrosis quantification, and disease classification will be summarized.^[11]

Sleep-Related Breathing Disorders: AI-assisted diagnosis using polysomnography, wearable devices, and respiratory signals will be evaluated.

Synthesis by AI Methodology: The review will compare the performance and clinical applications of Conventional machine learning algorithms, Convolutional neural networks, Vision transformers, Hybrid deep learning architectures, Multimodal AI systems integrating imaging with clinical data.^[12]

Explainable Artificial Intelligence: The review will summarize the use of explainability techniques—including Grad-CAM, SHAP, and LIME—to improve model transparency, facilitate clinician interpretation, and support trustworthy deployment in pulmonary medicine. Particular attention will be given to studies that evaluate explainability alongside external validation and clinical usability.^[13]

DISCUSSION

Artificial intelligence (AI) has rapidly emerged as a transformative technology in respiratory medicine, offering opportunities to improve diagnostic accuracy, enhance clinical workflow efficiency, and support personalized patient care. This systematic review was designed to evaluate the current evidence regarding AI applications in the diagnosis of respiratory diseases, with particular emphasis on methodological quality, diagnostic performance, clinical applicability, and future implementation challenges.^[14]

Principal Findings

The available literature demonstrates substantial growth in the application of AI across a wide range of respiratory diseases, including lung cancer, chronic obstructive pulmonary disease (COPD), asthma, pneumonia, tuberculosis, coronavirus disease 2019 (COVID-19), interstitial lung disease (ILD), pulmonary fibrosis, and sleep-related breathing disorders. AI models have been developed using diverse clinical data sources, including chest radiography, computed tomography (CT), lung ultrasound, pulmonary function tests, respiratory sound recordings, wearable sensors, and electronic health records.^[15]

Among imaging-based applications, deep learning algorithms—particularly convolutional neural networks (CNNs)—have consistently demonstrated strong performance in image classification, lesion detection, segmentation, and disease characterization. Automated

interpretation of chest radiographs and CT images has shown particular promise for pulmonary nodule detection, tuberculosis screening, pneumonia diagnosis, and quantification of diffuse interstitial lung abnormalities. These technologies may reduce interpretation time while improving diagnostic consistency, especially in settings where access to thoracic radiology expertise is limited.^[16]

Beyond medical imaging, machine learning techniques have increasingly been applied to spirometry interpretation, respiratory waveform analysis, cough recognition, digital auscultation, and multimodal clinical prediction. Integration of physiological measurements with demographic, laboratory, and imaging information has the potential to improve diagnostic precision compared with single-modality approaches.^[17]

Clinical Applications Across Respiratory Diseases

Lung Cancer: Lung cancer remains one of the leading causes of cancer-related mortality worldwide, making early detection a major public health priority. AI-assisted CT interpretation has demonstrated considerable potential for pulmonary nodule detection, malignancy prediction, radiomic feature extraction, and risk stratification. Automated image analysis may improve screening efficiency and reduce observer variability, particularly within low-dose CT screening programs. Radiomics combined with machine learning has further expanded opportunities for non-invasive tumor characterization by extracting quantitative imaging biomarkers that may correlate with tumor biology and prognosis. Nevertheless, variation in imaging protocols, annotation quality, and external validation continues to limit widespread clinical implementation.^[18]

Pneumonia: AI algorithms have been extensively evaluated for the diagnosis of bacterial and viral pneumonia using chest radiography and CT imaging. Automated systems have shown encouraging diagnostic performance, particularly when integrated into computer-aided detection workflows. Such approaches may assist clinicians in emergency departments and resource-limited settings by providing rapid preliminary image interpretation.

However, many published studies have relied on retrospective datasets with limited geographic diversity. Consequently, further multicentre prospective validation is required before routine clinical adoption.^[19]

COVID-19: The COVID-19 pandemic accelerated research into AI-assisted thoracic imaging. Numerous studies developed deep learning models for detection, severity assessment, and outcome prediction using chest radiographs and CT scans. Although many algorithms reported high internal performance, systematic reviews have highlighted important methodological concerns, including selection bias, inadequate external validation, and inconsistent reference standards. The experience

gained during the pandemic has nevertheless demonstrated the potential value of AI for rapid deployment during emerging infectious disease outbreaks, provided that robust validation and transparent reporting are maintained.^[20]

Tuberculosis: Tuberculosis screening represents one of the most mature clinical applications of AI in respiratory medicine. Automated interpretation of digital chest radiographs has become increasingly important in regions with limited access to expert radiologists. AI-supported screening programs may facilitate earlier diagnosis, improve triage efficiency, and optimize allocation of confirmatory molecular testing.^[21] Future studies should evaluate the effectiveness of these systems in diverse populations, including patients with HIV infection, pediatric tuberculosis, and extrapulmonary disease.

Chronic Obstructive Pulmonary Disease: AI applications in COPD have expanded beyond imaging to include spirometry interpretation, disease phenotyping, exacerbation prediction, and longitudinal disease monitoring. Machine learning approaches integrating pulmonary function tests with clinical variables may assist in identifying disease subtypes associated with differential prognosis and therapeutic response. Continuous monitoring using wearable technologies and remote patient management platforms also represents an emerging area of investigation with potential implications for chronic disease management.^[22]

Asthma: Asthma is a heterogeneous disease characterized by multiple inflammatory phenotypes and variable clinical presentation. AI has demonstrated promise in asthma diagnosis through integration of clinical characteristics, pulmonary function tests, biomarkers, respiratory acoustics, and environmental exposure data. Machine learning may also facilitate precision medicine by identifying patient subgroups likely to respond to targeted biological therapies.^[23]

Interstitial Lung Disease: Diagnosis of ILD often requires multidisciplinary expertise involving pulmonologists, radiologists, and pathologists. AI-assisted analysis of high-resolution CT imaging has shown potential for automated classification of fibrotic patterns, disease quantification, and prediction of disease progression. These technologies may improve reproducibility and support earlier diagnosis while reducing interobserver variability.^[24]

Sleep-Related Breathing Disorders: Machine learning techniques have increasingly been applied to polysomnography, wearable sensors, pulse oximetry, and respiratory signal analysis for detection of obstructive sleep apnea. Simplified AI-assisted diagnostic pathways may improve access to sleep disorder evaluation while reducing dependence on laboratory-based sleep studies.^[25]

Emerging AI Technologies: Recent developments in transformer-based neural networks, self-supervised learning, multimodal foundation models, and federated learning are likely to influence the next generation of respiratory diagnostic systems. Vision transformers have demonstrated competitive performance for medical image interpretation, while multimodal architectures enable simultaneous analysis of imaging, clinical records, laboratory findings, and physiological measurements.^[26] Federated learning offers particular promise for pulmonary medicine because it enables collaborative model development across multiple institutions without direct sharing of patient-level data, thereby enhancing privacy protection while improving generalizability. Large language models may also contribute to respiratory care by supporting clinical documentation, literature synthesis, decision support, and integration of structured and unstructured clinical information. Their role in primary diagnosis, however, requires careful evaluation because of the potential for inaccurate or non-evidence-based outputs.^[27]

Explainability and Trustworthy AI: One of the most significant barriers to clinical implementation remains the limited interpretability of many deep learning algorithms. Clinicians require understandable explanations for algorithmic predictions before integrating AI into routine decision-making.

Explainable AI techniques—including Gradient-weighted Class Activation Mapping (Grad-CAM), SHapley Additive exPlanations (SHAP), and Local Interpretable Model-agnostic Explanations (LIME)—may improve transparency by identifying image regions or clinical variables influencing model predictions. However, explainability methods themselves require rigorous validation to ensure that generated explanations are clinically meaningful rather than merely visually plausible.^[28]

Challenges to Clinical Implementation

Despite encouraging technological advances, several challenges continue to limit widespread adoption of AI in respiratory medicine. First, many published studies are retrospective and originate from single institutions, raising concerns regarding generalizability. Differences in imaging equipment, acquisition protocols, disease prevalence, and patient demographics may substantially influence algorithm performance. Second, inadequate external validation remains a major methodological limitation. Models demonstrating excellent internal accuracy frequently experience reduced performance when evaluated using independent datasets.^[29]

Third, inconsistent reporting standards hinder comparison across studies. Greater adherence to established reporting guidelines for prediction model development, validation, and diagnostic accuracy studies would improve reproducibility and facilitate evidence synthesis. Fourth, ethical considerations—including

algorithmic bias, fairness across diverse populations, patient privacy, cybersecurity, informed consent, and regulatory oversight—must be addressed before routine implementation.^[30]

Finally, integration into existing clinical workflows requires consideration of usability, interoperability with electronic health record systems, clinician education, cost-effectiveness, reimbursement pathways, and ongoing post-deployment monitoring.

Future Directions

Future research should prioritize prospective multicenter studies with standardized reporting and robust external validation. Development of diverse, representative datasets encompassing different geographic regions, healthcare systems, and patient populations will be essential for improving algorithm generalizability. Multimodal AI systems integrating imaging, pulmonary function testing, laboratory biomarkers, genomics, digital pathology, respiratory acoustics, and electronic health records may provide more comprehensive diagnostic support than single-modality algorithms.

Explainable AI should become a routine component of diagnostic system development to enhance clinician confidence and facilitate regulatory approval. Continuous learning systems capable of safely adapting to evolving clinical environments while maintaining transparency and patient safety also represent an important research priority. In addition, future investigations should evaluate patient-centred outcomes, cost-effectiveness, workflow efficiency, implementation feasibility, and clinical impact through randomized or pragmatic clinical trials rather than relying solely on retrospective diagnostic accuracy studies.

Strengths and Limitations of This Review

This review was designed according to PRISMA 2020 recommendations and aims to provide a comprehensive synthesis of current evidence regarding AI applications in respiratory disease diagnosis across multiple diseases and diagnostic modalities. Potential limitations include heterogeneity in AI methodologies, variation in reference standards, differences in outcome reporting, and the rapidly evolving nature of AI research, which may result in newly published studies after completion of the literature search. Publication bias and inconsistent reporting may also influence interpretation of the available evidence.

CONCLUSIONS

Artificial intelligence has demonstrated considerable potential to enhance respiratory disease diagnosis across imaging, physiological testing, respiratory signal analysis, and multimodal clinical decision support. Current evidence suggests that AI can improve diagnostic efficiency and may assist clinicians in the detection and characterization of diverse pulmonary diseases. Nevertheless, widespread clinical

implementation requires rigorous external validation, standardized reporting, transparent model development, explainable algorithms, and prospective evaluation of real-world clinical effectiveness.

Ethics Approval and Consent to Participate

Not applicable. This study is a systematic review of previously published literature and did not involve human participants, identifiable patient information, or experimental interventions.

Competing Interests: The authors declare that they have no competing interests.

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