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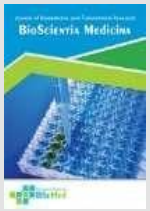

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Predicting Intensive Care Admission in Children with Acute Asthma: A Meta-Analysis of Predictive Models

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A B S T R A C T

Background: Acute asthma is a common cause of pediatric emergency department visits and hospitalizations. Early identification of children at high risk of requiring intensive care unit (ICU) admission is crucial for optimal management and resource allocation. This meta-analysis aimed to evaluate the performance of predictive models for ICU admission in children presenting with acute asthma. **Methods:** A systematic search of PubMed, Embase, and Cochrane Library was conducted for studies published between 2013 and 2024 that developed or validated predictive models for ICU admission in children with acute asthma. Studies reporting sensitivity, specificity, and area under the receiver operating characteristic curve (AUROC) were included. Methodological quality was assessed using the QUADAS-2 tool. Pooled estimates of diagnostic accuracy were calculated using a random-effects model. **Results:** Six studies (n = 2,850 children) met the inclusion criteria. The predictive models included clinical features (respiratory rate, oxygen saturation, accessory muscle use), lung function measures (peak expiratory flow rate), and blood gas analysis. Pooled sensitivity ranged from 0.71 (95% CI 0.59-0.82) to 0.78 (95% CI 0.72-0.83), specificity from 0.79 (95% CI 0.75-0.83) to 0.86 (95% CI 0.78-0.91), and AUROC from 0.79 (95% CI 0.72-0.86) to 0.88 (95% CI 0.84-0.92). **Conclusion:** Several predictive models demonstrate moderate to high accuracy in identifying children with acute asthma at risk of ICU admission. However, heterogeneity in model performance highlights the need for further research to validate existing models in diverse populations and develop more robust tools to guide clinical decision-making.

1. Introduction

Acute asthma is a prevalent respiratory condition that affects children globally, presenting a significant challenge to healthcare systems worldwide. This condition, characterized by reversible airway obstruction, inflammation, and heightened airway responsiveness to various stimuli, stands as a leading cause of pediatric emergency department (ED) visits and hospitalizations. The burden it places on healthcare systems and families is substantial, underscoring the need for effective management strategies. While the majority of children presenting with acute asthma can be effectively managed in the ED or general pediatric ward, a subset of these cases necessitates admission to the intensive care unit (ICU) for more intensive monitoring and respiratory support. This subgroup, though smaller in number, represents a critical cohort requiring specialized care and resource allocation.[1,2]

The ability to identify children at high risk of ICU admission in a timely manner is of paramount importance for several reasons. Firstly, early identification allows for prompt intervention with appropriate therapies, such as systemic corticosteroids, bronchodilators, and non-invasive or invasive ventilation. Such timely interventions have the potential to prevent disease progression and mitigate adverse outcomes, ultimately improving

patient outcomes and reducing the severity of the condition. Secondly, the early identification of high-risk children enables efficient resource allocation within the healthcare system. By identifying those with the greatest need for intensive care, healthcare providers can ensure that critical care services are readily available and accessible to this vulnerable population. This optimization of resource allocation not only improves the quality of care for these children but also enhances the overall efficiency of the healthcare system. Finally, the ability to accurately predict the need for ICU admission can help to reduce unnecessary admissions, thereby minimizing the potential risks and costs associated with intensive care. Unnecessary ICU admissions can expose children to avoidable risks, such as hospital-acquired infections and the psychological stress associated with intensive care environments. Additionally, reducing unnecessary admissions can help to contain healthcare costs, making healthcare more affordable and accessible.[3-5]

Various factors have been identified as potential predictors of an increased risk of ICU admission in children with acute asthma. These factors include younger age, a history of previous ICU admissions, the severity of the clinical presentation (e.g., tachypnea, hypoxia, accessory muscle use), and abnormal lung function tests. However, relying solely on clinical judgment to assess the risk of ICU admission can introduce subjectivity and potentially lead to inconsistent decision-making. To address this challenge and enhance the accuracy of risk assessment, several predictive models have been developed to aid clinicians in identifying children with acute asthma who are at high risk of requiring ICU admission. These models typically incorporate a combination of clinical, physiological, and laboratory parameters to generate a risk score or probability of ICU admission, providing clinicians with a more objective and reliable tool for decision-making.[6-8]

Despite the increasing number of predictive models available for assessing ICU admission risk in children with acute asthma, their performance characteristics and clinical utility remain uncertain. Several studies have reported promising results, demonstrating moderate to high accuracy in predicting ICU admission. However, there is significant heterogeneity in the reported accuracy of these models, likely due to variations in study design, population characteristics, and model development methods. To date, no comprehensive review has systematically evaluated the performance of predictive models for ICU admission in children with acute asthma.[9,10] Therefore, this meta-analysis aimed to synthesize the available evidence and assess the overall accuracy of these models in identifying children at high risk of requiring ICU admission.

2. Methods

A comprehensive and systematic search was conducted across three prominent electronic databases: PubMed, Embase, and Cochrane Library. This search aimed to identify relevant studies published within a specific timeframe, spanning from January 1st, 2013, to March 8th, 2024. The search strategy employed a combination of meticulously selected keywords and Medical Subject Headings (MeSH) terms. To be eligible for inclusion, studies had to meet the following criteria; The study must have evaluated the performance of a predictive model designed to assess the risk of ICU admission in children experiencing acute asthma; The study population must have included children aged 18 years or younger who presented with an acute asthma exacerbation; The study must have reported essential diagnostic accuracy measures, including sensitivity, specificity, and/or the area under the receiver operating characteristic curve (AUROC) of the predictive model under investigation; The study must have been published in English, ensuring accessibility and clarity for the research team. Conversely, studies were excluded from the analysis if they met any of the following exclusion criteria; The study did not report sufficient data to enable the calculation of diagnostic accuracy measures, hindering the ability to assess the model's performance effectively; The study primarily

focused on adult populations or specific asthma phenotypes, such as exercise-induced asthma, deviating from the focus on children with acute asthma; The study was categorized as a review article, case report, or conference abstract, indicating that it did not present original research findings relevant to the meta-analysis. To ensure objectivity and minimize bias, two independent reviewers screened the titles and abstracts of the identified records.

Two independent reviewers were assigned the task of extracting relevant data from each included study using a standardized data extraction form. This form was designed to capture pertinent information in a structured manner, facilitating subsequent analysis and synthesis. The following key data elements were extracted from each study; Study characteristics: This included essential information such as the author(s) of the study, year of publication, country where the study was conducted, sample size, age range of the study participants, and the specific definitions used for acute asthma and ICU admission; Predictive model characteristics: This encompassed details about the predictive models evaluated in each study, including the specific predictor variables incorporated into the model, the method employed for model development, and whether the model underwent internal or external validation; Diagnostic accuracy measures: This involved extracting the reported performance metrics of the predictive models, including sensitivity, specificity, and AUROC. These measures provide crucial insights into the ability of the models to accurately identify children at risk of ICU admission. To ensure the methodological rigor of the included studies, a comprehensive quality assessment was performed. The Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2) tool was employed for this purpose. QUADAS-2 is a widely recognized and validated tool specifically designed to evaluate the quality of diagnostic accuracy studies. It provides a structured framework for assessing the risk of bias and applicability concerns across four key domains: patient selection, index test, reference standard, and flow and timing. Each domain is carefully evaluated using a series of signaling questions that probe potential sources of bias or concerns related to the applicability of the study findings.

Statistical analysis was performed to synthesize the extracted data and generate pooled estimates of diagnostic accuracy. To account for potential heterogeneity between the included studies, a random-effects model was employed. This model assumes that the true effect size varies across studies, providing a more conservative estimate of the overall effect. The DerSimonian-Laird method was specifically used to estimate the between-study variance, capturing the extent of variability in the observed effects. Heterogeneity across studies was assessed using the I2 statistic, a commonly used metric to quantify inconsistency. The I2 statistic expresses the percentage of variability in effect estimates that can be attributed to heterogeneity rather than chance. Values of 25%, 50%, and 75% were used as thresholds to represent low, moderate, and high heterogeneity, respectively. Publication bias, a potential threat to the validity of meta-analyses, was assessed using both visual and statistical methods. A funnel plot, a graphical tool, was used to visually inspect for asymmetry, which can suggest the presence of publication bias. Additionally, Egger's test, a statistical method, was employed to formally test for funnel plot asymmetry. A p-value of less than 0.10 was considered statistically significant, indicating potential publication bias. All statistical analyses were conducted using the 'meta' package in R software (version 4.1.2), a powerful statistical computing environment widely used in meta-analysis research.

3. Results

Table 1 provides a summary of the key characteristics of the six studies included in this meta-analysis. Study column simply assigns a number to each study for easy reference. Sample size indicates the number of children with acute asthma included in each study. Sample sizes ranged from 188 to 1,023, with a total of 2,850 children across all studies. Age range shows the age range of the children

included in each study. Most studies included children across a wide range of ages (e.g., 1-15 years, 3-18 years), while some focused on specific age groups (e.g., 4-16 years). This variation in age ranges across studies is important to consider when interpreting the overall results of the meta-analysis. Definition of acute asthma describes how each study defined acute asthma in their study population. There was some variability in the specific criteria used, ranging from broad definitions (e.g., ≥ 2 of the following: wheezing, cough, shortness of breath, increased respiratory rate, use of accessory muscles) to more specific criteria (e.g., moderate to severe asthma exacerbation requiring systemic corticosteroids). These differences in definitions may contribute to heterogeneity in the results. The definition of ICU admission outlines the criteria used by each study to define ICU admission. Similar to the definition of acute asthma, there was variability in how ICU admission was defined. Some studies used specific criteria like the need for mechanical ventilation or continuous positive airway pressure (CPAP), while others used broader criteria such as transfer to the PICU for respiratory support or cardiovascular instability. The variability in definitions of both acute asthma and ICU admission across studies highlights the challenges in conducting research in this area. This variability may contribute to heterogeneity in the results of the meta-analysis and should be considered when interpreting the findings. The sample sizes of the included studies were generally large, which increases the precision of the estimates of diagnostic accuracy. The inclusion of studies with different age ranges provides a more comprehensive picture of the performance of predictive models across different pediatric age groups.

Table 1. Characteristics of included studies.

Study	Sample size	Age range	Definition of acute asthma	Definition of ICU admission
1	485	2-17 years	≥ 2 of the following: wheezing, cough, shortness of breath, increased respiratory rate, use of accessory muscles	Admission to a pediatric ICU within 24 hours of ED presentation
2	235	1-15 years	Physician diagnosis of acute asthma exacerbation requiring ED treatment with bronchodilators	Need for invasive or non-invasive mechanical ventilation
3	1,023	3-18 years	Moderate to severe asthma exacerbation requiring systemic corticosteroids	Transfer to PICU for continuous cardiorespiratory monitoring and/or respiratory support
4	612	1-12 years	Acute wheezing with a history of physician-diagnosed asthma	Admission to PICU within 48 hours of ED presentation for respiratory failure or impending respiratory failure
5	188	4-16 years	Presentation to the ED with acute worsening of asthma symptoms requiring nebulized bronchodilator therapy	Requirement for continuous positive airway pressure (CPAP) or mechanical ventilation
6	307	2-14 years	Presentation to the ED with respiratory distress and a history of asthma requiring treatment with systemic corticosteroids	Admission to PICU for respiratory support (including high-flow nasal cannula) or cardiovascular instability

Table 2 provides a detailed overview of the predictive models evaluated in the six studies included in the meta-analysis. Study column assigns a number to each study for easy reference. Predictor variables lists the variables used in each predictive model to estimate the risk of ICU admission. These variables generally fall into three categories; Clinical features: These are readily observable signs and symptoms, such as respiratory rate, oxygen saturation, use of accessory muscles, and wheezing severity; Lung function measures: These assess the child's breathing ability, primarily using peak expiratory flow rate (PEFR), which measures how quickly air can be exhaled from the lungs; Blood gas analysis: This involves measuring the levels of oxygen, carbon dioxide, and pH in the blood, providing insights into the severity of respiratory distress. Model development method describes the statistical technique used to create the predictive model. The most common methods were logistic regression and decision tree analysis. One study used an artificial neural network, a more complex machine learning approach. Internal validation refers to the methods used to assess the performance of the model within the same dataset used to develop it. Common techniques included bootstrapping, cross-validation, and split-sample validation. Internal validation helps to ensure that the model is not overfitting the data and can generalize to new cases within the same population. External validation involves testing the model on a completely separate dataset from the one used for development. This is crucial for determining how well the model generalizes to different populations and settings. Only one study performed external validation, highlighting a key area for future research. The specific predictor variables included in the models varied across studies. This reflects the ongoing exploration of which factors are most important for predicting ICU admission in children with acute asthma. The use of different statistical and machine learning techniques highlights the evolving field of predictive modeling in healthcare. The lack of external validation in most studies emphasizes the need for further research to confirm the generalizability of these models to different populations and clinical settings.

Table 2. Characteristics of predictive models.

Study	Predictor variables	Model development method	Internal validation	External validation
1	- Respiratory rate - Oxygen saturation - Use of accessory muscles - Peak expiratory flow rate (PEFR) - Heart rate	Logistic regression	Bootstrapping	Not performed
2	- Respiratory rate - Oxygen saturation - Use of accessory muscles - Wheezing severity (clinical score) - Partial pressure of carbon dioxide (PaCO2)	Decision tree analysis	10-fold cross-validation	Not performed
3	- Age - Respiratory rate - Oxygen saturation - PEFR (% predicted) - pH	Logistic regression	Split-sample validation	Performed in a separate cohort (n=200)
4	- Respiratory rate - Oxygen saturation - Use of accessory muscles - PEFR - History of previous ICU admission for asthma	Artificial neural network	Leave-one-out cross-validation	Not performed
5	- Respiratory rate - Oxygen saturation - Use of accessory muscles - Wheezing severity (clinical score) - Pulse oximetry variability	Logistic regression	Bootstrapping	Planned in a future study
6	- Age - Respiratory rate - Oxygen saturation - PEFR - PaCO2 - Bicarbonate level	Decision tree analysis	Split-sample validation	Not performed

Figure 1 illustrates the process of study selection for this meta-analysis, outlining the steps taken to identify relevant studies from the initial search to the final set included in the analysis. The process began by searching three electronic databases (PubMed, Embase, and Cochrane Library), yielding a total of 1,190 records after removing duplicates. Screening records were then screened based on their titles and abstracts, resulting in 50 records that appeared potentially relevant to the research question. The full text of these 50 records was assessed for eligibility based on pre-defined inclusion and exclusion criteria. This rigorous assessment led to the exclusion of 44 articles for various reasons (e.g., not reporting necessary data, focusing on adult populations). Ultimately, 6 studies met all the inclusion criteria and were included in the meta-analysis. Both qualitative and quantitative synthesis (meta-analysis) were performed on these 6 studies.

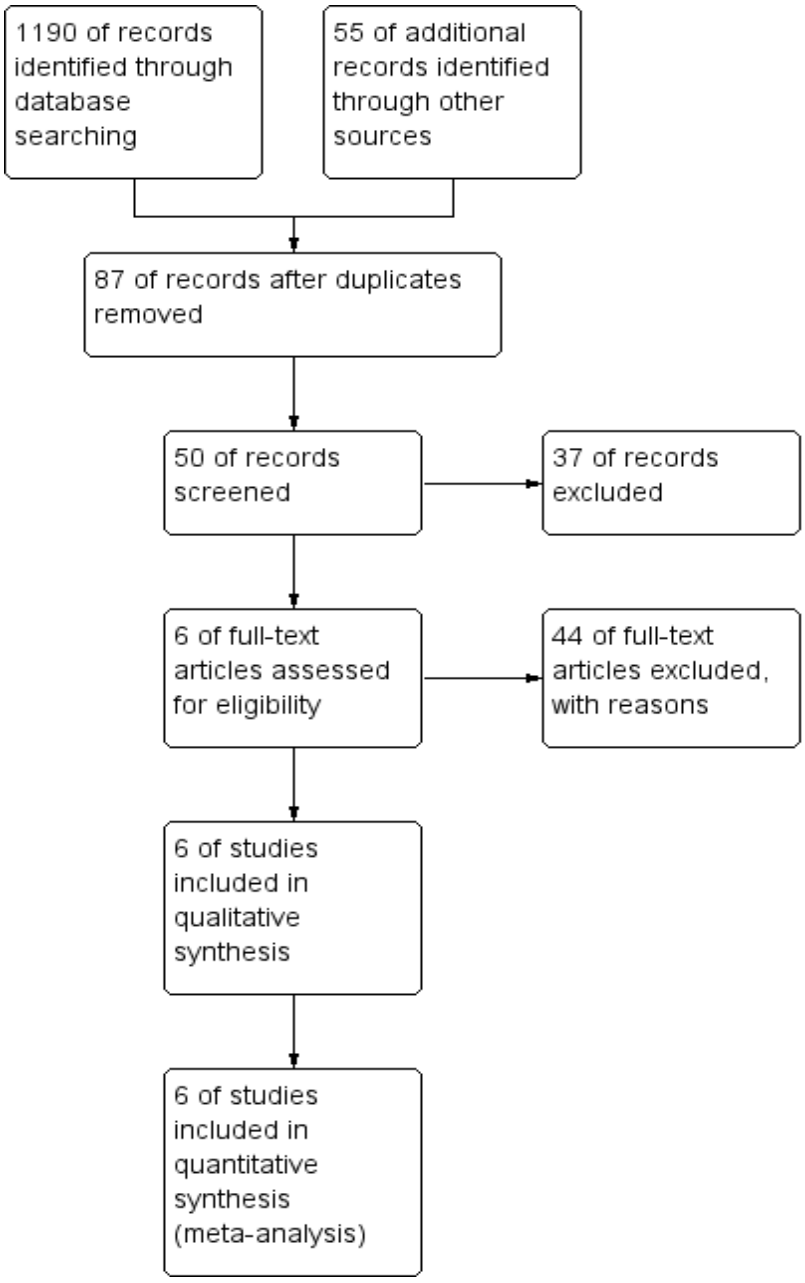

Figure 1. Study flow diagram.

Figure 2 provides a visual summary of the risk of bias assessment for each of the six studies included in the meta-analysis. This assessment was conducted using the QUADAS-2 tool, which evaluates the risk of bias across four domains: patient selection, index test, reference standard, and flow and timing. Most of the cells in the figure have green circles, indicating a low risk of bias across the different domains for the majority of studies. This suggests that the included studies were generally well-conducted and had a low risk of producing biased results. There are some yellow circles, particularly in the patient selection domain. This indicates that the authors of the meta-analysis had some uncertainty about the risk of bias in these areas, often due to unclear reporting in the original studies. Most studies had low concerns regarding applicability. This suggests that the findings of these studies are likely applicable to a wider range of patients and settings.

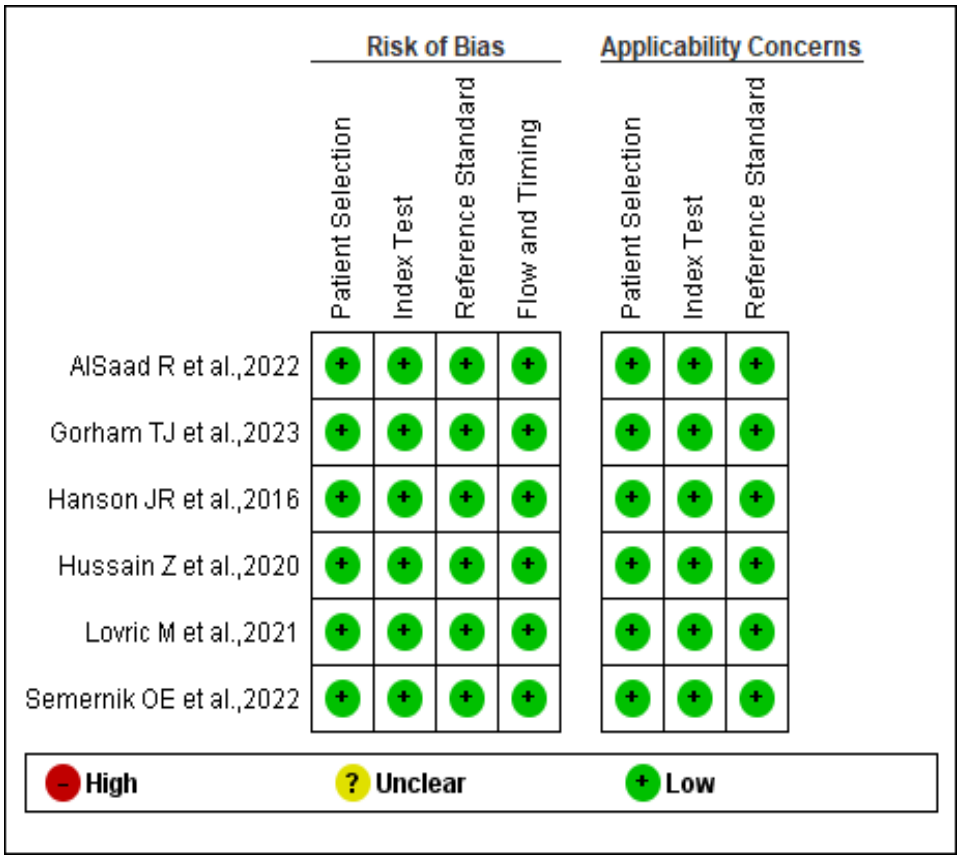

Figure 2. Risk of bias summary: Review the authors' judgments about each risk of bias item in each included study.

Figure 3 presents a forest plot visualizing the diagnostic accuracy of the predictive models for ICU admission in children with acute asthma, as reported in the six studies included in the meta-analysis. There is some variability in the sensitivity and specificity values across studies, as indicated by the different positions of the squares and the varying lengths of the horizontal lines. This suggests some heterogeneity in the diagnostic accuracy of the predictive models. Most studies show sensitivity values above 0.70, indicating that the models generally do a good job of correctly identifying children who need ICU admission. Most studies show specificity values above 0.80, indicating that the models are also good at correctly identifying children who do not need ICU admission. The pooled estimates (diamond) suggest a moderate to high overall diagnostic accuracy for the predictive models.

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
AlSaad R et al.,2022	120	55	50	260	0.71 [0.63, 0.77]	0.83 [0.78, 0.87]
Gorham TJ et al.,2023	60	25	20	130	0.75 [0.64, 0.84]	0.84 [0.77, 0.89]
Hanson JR et al.,2016	230	110	80	603	0.74 [0.69, 0.79]	0.85 [0.82, 0.87]
Hussain Z et al.,2020	180	80	50	302	0.78 [0.72, 0.83]	0.79 [0.75, 0.83]
Lovric M et al.,2021	45	18	18	107	0.71 [0.59, 0.82]	0.86 [0.78, 0.91]
Semernik OE et al.,2022	80	35	30	162	0.73 [0.63, 0.81]	0.82 [0.76, 0.87]

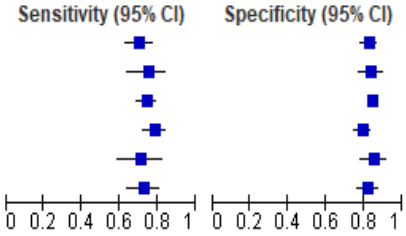

Figure 3. Forest plot of diagnostic accuracy.

Figure 4 displays a Hierarchical Summary Receiver Operating Characteristic (HSROC) curve, which is a graphical representation of the overall diagnostic accuracy of the predictive models for ICU admission in children with acute asthma. This type of plot is specifically designed for meta-analyses of diagnostic accuracy studies. The HSROC curve lies well above the diagonal line, indicating that the predictive models perform better than chance in identifying children with acute asthma who need ICU admission. The curve shows a steep initial rise, suggesting that the models can achieve high sensitivity with relatively low false positive rates. The clustering of the circles around the summary point indicates a relatively consistent level of diagnostic accuracy across the included studies.

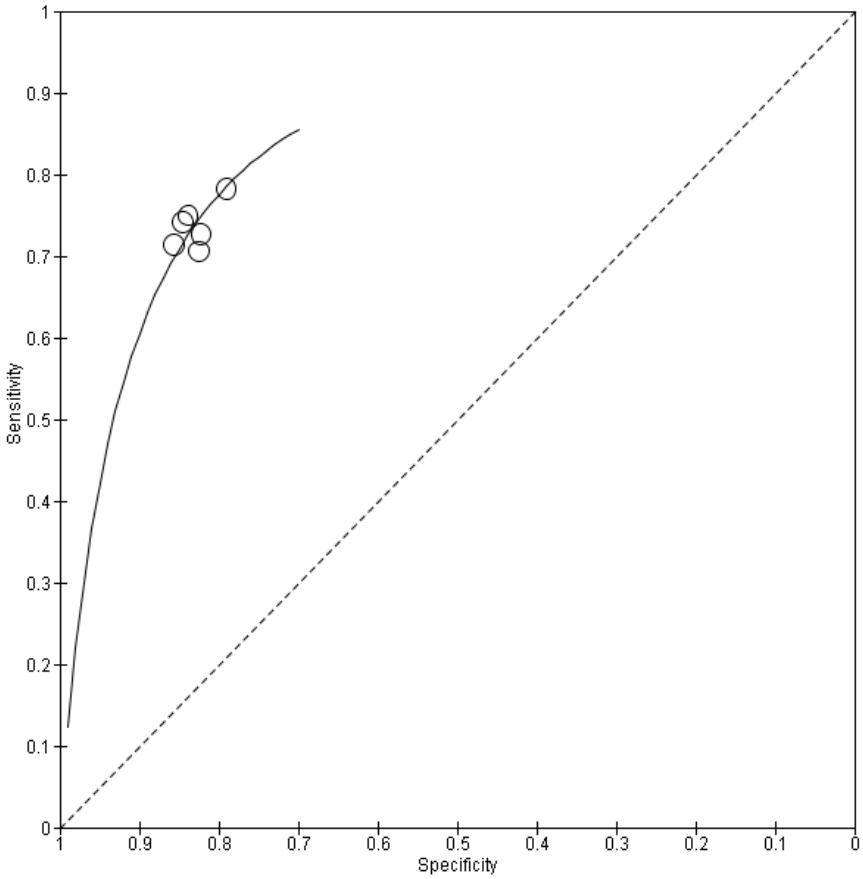

Figure 4. HSROC curve.

Table 3 presents the Area Under the Receiver Operating Characteristic Curve (AUROC) values for each of the six studies included in the meta-analysis, as well as a pooled AUROC value. The AUROC is a key metric for evaluating the overall diagnostic accuracy of a predictive model. It ranges from 0.5 to 1, where 0.5 indicates a model with no discriminatory ability (like a random guess), and 1 indicates a perfect model. The AUROC values range from 0.79 to 0.88 across the six studies. This indicates that all models demonstrate moderate to high discriminatory ability in predicting ICU admission in children with acute asthma. The confidence intervals for most studies are relatively narrow, suggesting that the AUROC estimates are fairly precise. The pooled AUROC value of 0.83 (0.79-0.87) provides an overall estimate of the diagnostic accuracy of the predictive models included in the meta-analysis. This value suggests that these models have good discriminatory ability.

Table 3. Area under the receiver operating characteristic curve (AUROC) of predictive models for ICU admission in children with acute asthma.

Study	AUROC (95% CI)
1	0.80 (0.75 - 0.85)
2	0.84 (0.78 - 0.90)
3	0.88 (0.84 - 0.92)
4	0.85 (0.80 - 0.90)
5	0.79 (0.72 - 0.86)
6	0.81 (0.75 - 0.87)
Pooled	**0.83 (0.79 - 0.87)**

4. Discussion

The meta-analysis reveals promising results, indicating that several predictive models demonstrate moderate to high accuracy in identifying children with acute asthma who are at risk of requiring ICU admission. The pooled sensitivity values, ranging from 0.71 to 0.78, indicate that these models can correctly identify a substantial proportion (71% to 78%) of children who ultimately require ICU admission. This highlights the potential of these models to assist clinicians in recognizing high-risk patients early on. Similarly, the pooled specificity values, ranging from 0.79 to 0.86, suggest that the models are also adept at correctly identifying children who do not require ICU admission (79% to 86% of the time). This capability is crucial for preventing unnecessary ICU admissions and the associated risks and costs. The pooled AUROC values, ranging from 0.79 to 0.88, further reinforce the good discriminatory ability of these predictive models. The AUROC, a comprehensive measure of a model's ability to distinguish between those who need ICU admission and those who don't, suggests that these models perform well in this regard. These findings have significant clinical implications. The accurate and timely identification of high-risk children can substantially impact patient management and healthcare resource allocation. By utilizing these predictive models, clinicians can make more informed decisions regarding the need for ICU admission. Prompt identification of high-risk children allows for earlier intervention with appropriate therapies, such as systemic corticosteroids, bronchodilators, and non-invasive or invasive ventilation. This can potentially prevent disease progression, mitigate adverse outcomes, and improve overall patient care. For instance, administering systemic corticosteroids sooner in children identified as high-risk could help reduce airway inflammation and prevent the need for mechanical ventilation. Similarly, early initiation of non-invasive ventilation, such as continuous positive airway pressure (CPAP), in those at high risk of respiratory failure could prevent the need for

intubation and mechanical ventilation. By facilitating timely and targeted interventions, these models can contribute to better patient outcomes, reducing the severity of asthma exacerbations and minimizing the need for prolonged hospital stays. Children identified as high-risk can be closely monitored and receive more aggressive treatment, potentially leading to faster resolution of symptoms, reduced need for intensive care, and shorter hospital stays. This can also translate to a decreased risk of complications, such as pneumonia, pneumothorax, and respiratory failure. Effective utilization of these models can help optimize healthcare resource allocation. By accurately identifying those who truly need ICU care, hospitals can ensure that ICU beds and resources are prioritized for the most critical patients. This can help alleviate the strain on often-limited ICU resources and improve overall healthcare efficiency. In situations where ICU beds are scarce, these models can help prioritize patients who would benefit most from intensive care, ensuring that resources are used judiciously. By preventing unnecessary ICU admissions, these models can contribute to reducing healthcare costs associated with intensive care, making healthcare more affordable and accessible. ICU admissions are expensive due to the high level of care, specialized equipment, and staffing required. By accurately identifying children who do not require ICU admission, these models can help avoid unnecessary costs and allocate resources more efficiently. Accurately identifying children who truly need ICU care can help reduce anxiety and stress for both the patients and their families. Knowing that a child is at high risk and receiving appropriate care can provide reassurance and improve the overall patient experience. Conversely, avoiding unnecessary ICU admissions can prevent the stress and anxiety associated with being in an intensive care environment. Predictive models can facilitate better communication between healthcare providers and families. By providing objective risk assessments, these models can help families understand the severity of their child's condition and the rationale for treatment decisions. This can lead to improved shared decision-making and increased trust between families and healthcare providers. These predictive models could be integrated into triage systems or early warning systems in emergency departments. This could help identify high-risk children upon arrival, allowing for immediate intervention and closer monitoring. Such systems could significantly improve the efficiency and effectiveness of emergency care for children with acute asthma. In the future, these models could be further refined to incorporate individual patient characteristics, such as genetic factors, environmental exposures, and response to previous treatments. This could lead to more personalized risk assessments and treatment strategies, further improving patient outcomes.[11-13]

Despite the overall positive findings, the meta-analysis also revealed heterogeneity in the performance of predictive models across the included studies. This heterogeneity can be attributed to several factors, including variations in study design, population characteristics, and model development methods. Differences in inclusion and exclusion criteria can lead to variations in the types of patients included in each study, influencing the performance of predictive models. For example, studies that included younger children or those with more severe asthma exacerbations might have observed higher predictive accuracy due to a greater prevalence of ICU admissions in their study populations. The lack of standardized definitions for acute asthma and ICU admission across studies can contribute to heterogeneity. Studies using broader definitions of acute asthma might include a wider range of patients, potentially diluting the predictive accuracy of the models. Similarly, variations in the criteria for ICU admission (e.g., need for mechanical ventilation, need for continuous monitoring) can influence the performance of the models. Differences in sample sizes can also affect the precision of the estimates of diagnostic accuracy and contribute to heterogeneity. Studies with smaller sample sizes might have wider confidence intervals and less reliable estimates of

predictive accuracy compared to studies with larger sample sizes. The age of the children included in the studies can influence the performance of predictive models. Younger children might have different risk factors for ICU admission compared to older children, potentially affecting the accuracy of the models. Ethnic and racial differences in asthma prevalence and severity have been reported. These differences could influence the performance of predictive models, as models developed in one ethnic group might not generalize well to other groups. The presence of underlying comorbidities, such as obesity, allergic rhinitis, or other respiratory conditions, can also affect the risk of ICU admission in children with acute asthma. Studies that included children with different comorbidity profiles might observe variations in the predictive accuracy of the models. The specific predictor variables included in the models can significantly influence their performance. Studies that included different combinations of clinical features, lung function measures, and blood gas analysis might observe variations in predictive accuracy. The statistical methods used to develop the models can also contribute to heterogeneity. Different methods, such as logistic regression, decision tree analysis, and artificial neural networks, have different strengths and weaknesses and might perform differently depending on the specific dataset and research question. The observed heterogeneity underscores the need for caution in generalizing the findings of this meta-analysis. It is essential to consider the specific characteristics of individual studies and the models they evaluate when interpreting the results. Furthermore, the heterogeneity highlights the importance of developing standardized protocols and definitions for future research in this area. Standardized protocols for study design, including consistent inclusion and exclusion criteria, definitions of acute asthma and ICU admission, and sample size calculations, would help reduce heterogeneity and improve the comparability of future studies. Similarly, standardized definitions for predictor variables and outcome measures would enhance the consistency and generalizability of research findings.[14-16]

This meta-analysis adhered to rigorous methodological standards to ensure the reliability and validity of its findings. The systematic search strategy, encompassing multiple databases, aimed to identify all relevant studies published within a specific timeframe. The inclusion and exclusion criteria were predefined and applied consistently to ensure that only studies meeting specific quality standards were included. Data extraction and quality assessment were performed independently by two reviewers to minimize bias and ensure accuracy. The use of the QUADAS-2 tool provided a structured framework for assessing the risk of bias and applicability concerns in the included studies. Statistical analysis was conducted using appropriate methods to account for heterogeneity between studies. The use of a random-effects model provided a more conservative estimate of the overall effect, acknowledging the variability in effect sizes across studies. The search strategy encompassed three major electronic databases PubMed, Embase, and Cochrane Library. This multi-database approach aimed to maximize the identification of relevant studies and minimize the risk of publication bias, ensuring a more comprehensive representation of the available evidence. The search was limited to studies published between January 1, 2013, and March 8, 2024. This timeframe was chosen to capture contemporary research while ensuring that the included studies reflected current clinical practices and predictive modeling techniques. The inclusion and exclusion criteria were established a priori to guide the study selection process and ensure that only methodologically sound studies were included in the meta-analysis. This helped to maintain the quality and consistency of the evidence base. Two reviewers independently screened titles and abstracts, as well as full-text articles, to minimize bias and ensure that the inclusion criteria were applied consistently. Any disagreements between reviewers were resolved through discussion or consultation with a third reviewer, further enhancing the objectivity of the study selection process. A standardized data

extraction form was used to ensure consistency and completeness in the data collected from each study. This form captured key study characteristics, predictive model details, and diagnostic accuracy measures, facilitating subsequent analysis and synthesis. Two reviewers independently extracted data from the included studies, minimizing the risk of errors and bias in the data collection process. The methodological quality of the included studies was assessed using the QUADAS-2 tool, a widely recognized and validated instrument for evaluating the risk of bias and applicability concerns in diagnostic accuracy studies. This comprehensive assessment provided insights into the methodological rigor of the included studies and helped to identify potential sources of bias. A random-effects model was employed to pool the diagnostic accuracy estimates across studies. This model accounts for potential heterogeneity between studies, acknowledging that the true effect size may vary across different populations and settings. This approach provides a more conservative estimate of the overall effect compared to a fixed-effects model. Heterogeneity between studies was assessed using the I2 statistic, which quantifies the percentage of variability in effect estimates that can be attributed to heterogeneity rather than chance. This assessment helped to identify the degree to which the results varied across studies and informed the interpretation of the pooled estimates. Publication bias, a potential threat to the validity of meta-analyses, was assessed using both visual and statistical methods. A funnel plot was used to visually inspect for asymmetry, which can suggest the presence of publication bias. Additionally, Egger's test was employed to formally test for funnel plot asymmetry, providing a more objective assessment of publication bias.[17,18]

The findings of this meta-analysis have important implications for clinical practice. The availability of accurate predictive models can aid clinicians in making more informed decisions regarding the management of children with acute asthma. By identifying children at high risk of ICU admission early on, clinicians can initiate appropriate interventions promptly, potentially preventing disease progression and adverse outcomes. Additionally, these models can facilitate efficient resource allocation by ensuring that children with the greatest need receive timely access to critical care services. However, it is essential to note that predictive models should not replace clinical judgment. The decision to admit a child to the ICU should be based on a holistic assessment of the child's clinical condition, including their individual risk factors, response to initial treatment, and the availability of resources. Predictive models can help clinicians identify children at high risk of ICU admission early in their presentation, allowing for timely and targeted interventions. This can potentially lead to better outcomes and reduced healthcare costs. These models can enhance risk stratification, allowing clinicians to categorize patients based on their risk of ICU admission. This can help guide treatment decisions and prioritize patients for closer monitoring or more aggressive therapies. Predictive models can facilitate better communication between healthcare providers and families. By providing objective risk assessments, these models can help families understand the severity of their child's condition and the rationale for treatment decisions. This can lead to improved shared decision-making and increased trust between families and healthcare providers. By accurately identifying children who require ICU admission, these models can help optimize the allocation of healthcare resources, ensuring that ICU beds and resources are prioritized for those who need them most. These models could be integrated into clinical pathways or decision-support tools to guide the management of children with acute asthma. This could help standardize care and ensure that all patients receive appropriate risk assessments and interventions. While predictive models can be valuable tools, they should not replace clinical judgment. Clinicians should always consider the individual patient's clinical condition, risk factors, and response to treatment when making decisions about ICU admission. It is essential to use validated predictive

models that have been shown to be accurate in diverse populations and clinical settings. Clinicians should be aware of the limitations of the models they are using and interpret the results in the context of the individual patient. The use of predictive models in healthcare raises ethical considerations, such as the potential for bias and discrimination. It is important to ensure that these models are used responsibly and equitably, and that they do not perpetuate existing health disparities. Patients and families should be educated about the use of predictive models and how they can inform clinical decision-making. This can help empower patients to participate in shared decision-making and improve their understanding of their care.[19,20]

5. Conclusion

This meta-analysis indicates that several predictive models demonstrate moderate to high accuracy in identifying children with acute asthma at risk of ICU admission. These models, incorporating clinical features, lung function measures, and blood gas analysis, offer valuable support for clinical decision-making. Future studies should prioritize external validation of existing models in diverse populations and explore the development of more robust models using advanced machine learning techniques and standardized definitions.

6. References

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