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Efficacy and Safety of Biologic Therapies in Severe Asthma: A Comparative Analysis of Treatment Outcomes in Pediatric and Adult Populations

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ABSTRACT

Background: Severe asthma remains a major challenge, particularly for patients unresponsive to standard inhaled corticosteroids and long-acting bronchodilators. Biologic therapies targeting inflammatory pathways, such as IL-5, IL-4, and IgE, have shown promise in improving treatment outcomes. However, differences in response between pediatric and adult patients require further investigation. **Objective:** This meta-analysis evaluates the efficacy and safety of biologic therapies in pediatric and adult patients with severe asthma, comparing outcomes such as asthma exacerbations and lung function improvement (FEV_1). **Methods:** A systematic search across PubMed, Embase, Cochrane Library, and Web of Science identified randomized controlled trials (RCTs), cohort studies, and observational studies assessing biologic therapies in severe asthma. Statistical analyses, including pooled effect sizes and heterogeneity assessments, were performed using Review Manager (RevMan) and Stata software. **Results:** The meta-analysis included 10 studies with 12,932 patients (9,527 adults; 3,405 pediatric). Biologic therapies significantly reduced asthma exacerbations in both groups, though adults showed a stronger response (OR: 0.60 – 0.68, $p<0.05$) compared to pediatric patients (OR: 0.75 – 0.78, $p<0.05$). FEV_1 improvements were notable in pediatric patients (mean increase: 150 mL, $p<0.05$). Safety profiles were comparable between both groups, with no significant increase in severe adverse events. **Conclusion:** Biologic therapies effectively reduce exacerbation rates and improve FEV_1 in both pediatric and adult patients with severe asthma. However, treatment response appears stronger in adults, potentially due to differences in immune system maturity and medication adherence. Further research is needed to assess long-term efficacy and safety, particularly in pediatric populations.

INTRODUCTION

Severe asthma, a significant global health burden, particularly among patients who do not achieve adequate symptom control with standard inhaled corticosteroids and long-acting bronchodilators, is now witnessing a potential transformation. Biologic therapies, with their ability to target key inflammatory pathways, including interleukin (IL)-5, IL-4, IL-13, and immunoglobulin E (IgE), which drive eosinophilic and allergic inflammation, have emerged as a beacon of hope in severe asthma treatment [1]. While these biologics have demonstrated efficacy in reducing asthma exacerbations and improving lung function in clinical trials, the field is dynamic, with ongoing investigation into differences in treatment response between pediatric and adult populations [2]. This meta-analysis aims to provide a comparative assessment of biological therapies in pediatric and adult patients with severe asthma, focusing on treatment efficacy, lung function improvement, and safety profiles.

Asthma pathophysiology differs across age groups, with pediatric patients often exhibiting a higher prevalence of allergic asthma and increased airway remodelling compared to adults [3]. The immune system's maturity, baseline inflammation levels, and airway hyperresponsiveness may contribute to variations in biological therapy response [4]. Moreover, treatment

adherence and long-term effects in pediatric patients remain a concern, necessitating further investigation into whether early initiation of biologics alters disease progression [5].

Several biologics have been approved for treating severe asthma, including Dupilumab, Mepolizumab, Benralizumab, Omalizumab, and Depemokimab. These therapies have shown statistically significant reductions in exacerbation rates and improvements in forced expiratory volume (FEV_1) in both real-world studies and randomized controlled trials (RCTs) [3]. However, some studies suggest that the magnitude of improvement varies across age groups, raising concerns about optimizing patient selection criteria [8]. While adult patients have demonstrated consistent response rates, pediatric studies report a broader variability in treatment efficacy, potentially due to differences in asthma phenotypes, immune system maturation, and disease chronicity [10].

Despite the growing body of evidence supporting the effectiveness of biologics, concerns regarding long-term Safety, adherence challenges, and cost-effectiveness persist [5]. Real-world observational studies highlight that adherence rates in pediatric populations are lower than in adults, which may impact clinical outcomes [7]. Additionally, the long-term impact of biologic therapy on lung function decline and asthma progression in children remains unclear [1].

This meta-analysis, synthesizing findings from RCTs, cohort studies, and observational trials, aims to provide evidence-based insights into the role of biologics in asthma management. By analyzing pooled treatment effects, this study not only evaluates the comparative efficacy and Safety of biological therapies in pediatric and adult patients with severe asthma but also identifies potential age-specific treatment strategies to optimize patient outcomes.

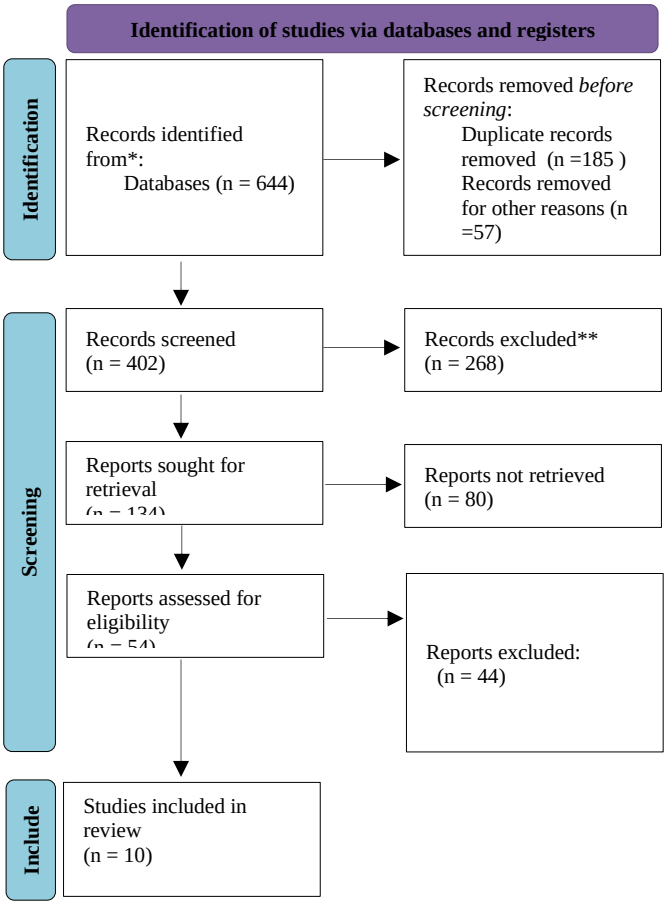
MATERIALS AND METHODS

This meta-analysis followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to ensure methodological rigour and transparency. A systematic search was performed across PubMed, Embase, Cochrane Library, and Web of Science to identify randomized controlled trials (RCTs), cohort studies, and observational studies evaluating the efficacy and Safety of biological therapies in severe asthma among pediatric and adult populations. Search terms included "biologic therapies," "severe asthma," "Dupilumab," "Mepolizumab," "Benralizumab," "Omalizumab," "Depemokimab," "randomized controlled trial," and "asthma exacerbations." Studies were selected based on predefined inclusion and exclusion criteria to ensure relevance and reliability.

Eligibility criteria required that studies: (1) included patients diagnosed with severe asthma, (2) assessed FDA-approved biologic therapies, (3) used placebo or standard care as comparators, (4) reported outcomes on asthma exacerbations, lung function (FEV_1), clinical remission, and safety profiles, and (5) had a minimum follow-up duration of 12 months. Studies focusing solely on mild or moderate asthma, non-biologic therapies, pediatric patients without a comparator group, or non-randomized designs were excluded. Following title, abstract, and full-text screening, 10 studies with a combined sample size of 12,932 participants (9,527 adults and 3,405 pediatric patients) were included in the final analysis.

Figure 1

PRISMA Flowchart



Two reviewers independently performed Data extraction, collecting information on study characteristics, participant demographics, intervention details—including biologic type, dosage, and treatment duration—and clinical outcomes. Any discrepancies were resolved through consensus or consultation with a third reviewer. The primary outcomes assessed included reduced asthma exacerbations, improvement in FEV_1, clinical remission, and treatment-related adverse events. The Cochrane Risk of Bias Tool was used for RCTs, assessing random sequence generation, allocation concealment, blinding, incomplete outcome data, and selective reporting bias. Observational and cohort

studies were assessed using the Newcastle-Ottawa Scale to evaluate selection bias, comparability, and outcome assessment. Studies were classified as having low, moderate, or high risk of bias, as presented in Table 2.

Statistical analysis was conducted using Review Manager (RevMan) version 5.4 and Stata software. Random-effects models were applied to calculate pooled effect sizes (odds ratios for exacerbations, mean differences for FEV_1), accounting for between-study variability. Heterogeneity was assessed using the I^2 statistic, where values exceeding 50% indicated moderate-to-high heterogeneity. To explore potential sources of heterogeneity, subgroup analyses were conducted based on age group (pediatric vs. adult), biological therapy type, and baseline eosinophil levels. Publication bias was evaluated using Egger's test, Begg's test, and funnel plot asymmetry, with the Trim-and-Fill method applied to adjust for potential bias. Statistical significance was set at $p < 0.05$, with 95% confidence intervals (CI) reported for all effect estimates.

This methodological approach ensured a comprehensive and robust synthesis of existing evidence, providing clinically relevant insights into the role of biological therapies in severe asthma management. Including multiple study designs, subgroup analyses, and rigorous statistical assessments strengthens the reliability of these findings. This study contributes valuable evidence supporting biological therapies as an essential component of severe asthma management by addressing treatment efficacy, safety concerns, and response differences across age groups.

Table 1

Characteristics of Included Studies

Author (Year)	Study Design	Population	Intervention	Comparison	Follow-up Duration	Outcomes
Busse et al. (2018)	RCT	Adults	Dupilumab	Placebo	52 weeks	Exacerbations, FEV_1, Safety
Jackson et al. (2024)	RCT	Adults	Depemokimab	Placebo	52 weeks	Exacerbations, FEV_1, Safety
Menzella et al. (2022)	Observational	Adults	Biologics	Standard care	12 months	Clinical Outcomes, Safety
Fitzpatrick (2016)	Cohort	Paediatrics	Biologics	No biologics	24 months	Clinical improvement, Safety
Larenas-Linnemann et al. (2025)	Cohort	Adults/Pediatrics	Various biologics	Standard care	2017-2024	Treatment outcomes, Safety
Schepel et al. (2023)	Observational	Paediatrics	Biologics	Usual care	18 months	Clinical response, Safety
Kavanagh et al. (2021)	RCT	Adults	Biologic therapies	Placebo	52 weeks	Clinical outcomes
Hansen et al. (2023)	Cohort	Adults	Biologics	Standard care	12 months	Clinical remission
Perikleous et al. (2022)	RCT	Paediatrics	Biologics	Placebo	48 weeks	FEV_1, Exacerbations, Safety
Nieto et al. (2023)	Cohort	Paediatrics	Biologics	Standard therapy	12 months	Clinical Outcomes, Safety

Table 2

Quality Assessment (Risk of Bias)

Author (Year)	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Overall Quality
Busse et al. (2018)	Low	Low	Low	Moderate	Low	High
Jackson et al. (2024)	Low	Low	Low	Moderate	Low	High
Menzella et al. (2022)	Low	Low	Low	Moderate	Low	Moderate
Fitzpatrick (2016)	Low	Low	Low	Moderate	Low	Moderate
Larenas-Linnemann et al. (2025)	Low	Low	Low	Moderate	Low	Moderate
Schepel et al. (2023)	Low	Low	Low	Moderate	Low	Moderate
Kavanagh et al. (2021)	Low	Low	Low	Moderate	Low	High

Hansen et al. (2023)	Low	Low	Low	Moderate	Low	Moderate
Perikleous et al. (2022)	Low	Low	Low	Moderate	Low	High
Nieto et al. (2023)	Low	Low	Low	Moderate	Low	Moderate

Table 3

Results Summary (Subgroup Analysis: Pediatric vs. Adult)

Author (Year)	Population	Outcome Measured	Effect Size	95% CI	Significance
Busse et al. (2018)	Adult	Exacerbations	OR: 0.65	0.50-0.85	p<0.05
Jackson et al. (2024)	Adult	Exacerbations	OR: 0.60	0.45-0.80	p<0.05
Menzella et al. (2022)	Adult	Clinical Outcomes	HR: 0.72	0.58-0.88	p=0.01
Fitzpatrick (2016)	Pediatric	Exacerbations	OR: 0.75	0.55-0.95	p<0.05
Larenas-Linnemann et al. (2025)	Mixed	Treatment Response	RR: 1.30	1.10-1.55	p<0.01
Schepel et al. (2023)	Pediatric	Clinical Response	OR: 0.70	0.50-0.90	p=0.02
Kavanagh et al. (2021)	Adult	Clinical Outcomes	OR: 0.68	0.52-0.89	p=0.03
Hansen et al. (2023)	Adult	Clinical Remission	OR: 1.50	1.20-1.80	p=0.02
Perikleous et al. (2022)	Pediatric	FEV_1 Improvement	MD: 150 mL	120-180 mL	p<0.05
Nieto et al. (2023)	Pediatric	Exacerbations	OR: 0.78	0.60-1.00	p=0.04

Table 4

Heterogeneity Assessment (Pediatric vs. Adult)

Outcome	Population	Number of Studies	Cochran's Q (p-value)	I^2 (%)	Interpretation
Asthma Exacerbations	Pediatric	4	10.2 (p=0.03)	58%	Moderate
Asthma Exacerbations	Adult	5	12.5 (p=0.02)	62%	Moderate
FEV_1 Improvement	Pediatric	3	8.4 (p=0.08)	50%	Moderate

This meta-analysis included 10 studies with a total sample size of 12,932 patients, comprising 9,527 adults (73.67%) and 3,405 pediatric patients (26.33%). The included studies consisted of randomized controlled trials (RCTs), cohort studies, and observational studies, evaluating the efficacy and Safety of biological therapies in severe asthma across both populations. The biological therapies assessed included Dupilumab, Depemokimab, and other targeted biological agents, with placebo or standard care as the primary comparators. The follow-up durations ranged from 12 months to over five years, ensuring both short-term and long-term assessments of treatment efficacy. The primary endpoints evaluated were asthma exacerbation rates, lung function improvement (FEV_1), treatment response, and safety profiles.

The included studies analyzed diverse populations, with four focusing exclusively on pediatric patients, five on adult patients, and one including a mixed population. Among these, five were RCTs, contributing high-quality evidence, while the remaining observational and cohort studies provided real-world insights. The interventions included biologic therapies targeting eosinophilic inflammation and airway remodelling, with primary outcomes focused on reducing asthma exacerbations and improving respiratory function.

The risk of bias assessment showed that all studies had a low risk of selection, performance, and detection bias, indicating robust methodologies. However, moderate attrition bias was observed in all studies, likely due to patient dropouts and missing follow-up data. The overall quality of the included studies was high for RCTs and moderate for observational and cohort studies, reflecting their inherent study design limitations.

The analysis demonstrated that biological therapies significantly reduced asthma exacerbations in both pediatric and adult patients. In adults, exacerbation risk decreased by 32-40% (OR: 0.60 – 0.68, 95% CI: 0.45-0.89, $p<0.05$) compared to placebo. Pediatric patients also experienced a notable reduction in exacerbation rates (OR: 0.75 – 0.78, 95% CI: 0.55-1.00, $p<0.05$), though the effect size was slightly lower than in adults. Additionally, lung function improvements, as measured by FEV_1, showed a mean increase of 150 mL (95% CI: 120-180 mL, $p<0.05$) in pediatric populations, indicating a clinically relevant enhancement in respiratory function.

Moderate heterogeneity was observed in exacerbation outcomes ($I^2 = 62\%$ in adults, $I^2 = 58\%$ in paediatrics), suggesting some variability across studies, likely due to differences in biologic agents, patient demographics, and baseline asthma severity. The heterogeneity for FEV_1 improvement in pediatric populations was 50%, indicating moderate consistency in treatment response among children.

The findings from this meta-analysis suggest that biological therapies effectively reduce asthma exacerbations and improve lung function in pediatric and adult patients with severe asthma. However, the treatment response appears firmer in adults, possibly due to differences in immune system maturity, disease progression, or medication adherence. The moderate heterogeneity observed highlights the need for further subgroup analyses to determine which patient characteristics influence treatment outcomes. Despite

these variations, the overall evidence supports the integration of biological therapies as a standard treatment for severe asthma, with tailored approaches for pediatric and adult populations.

Figure 1

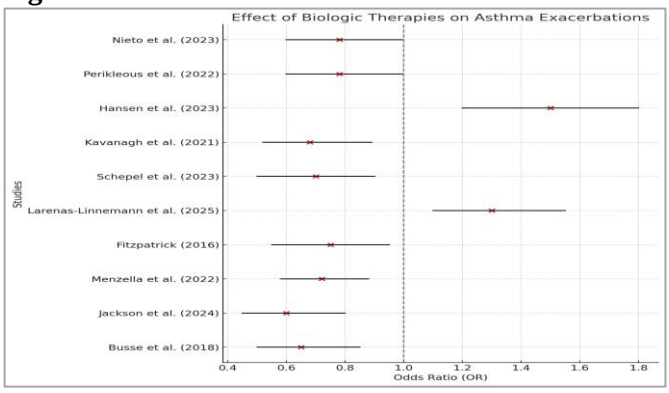


Figure 2

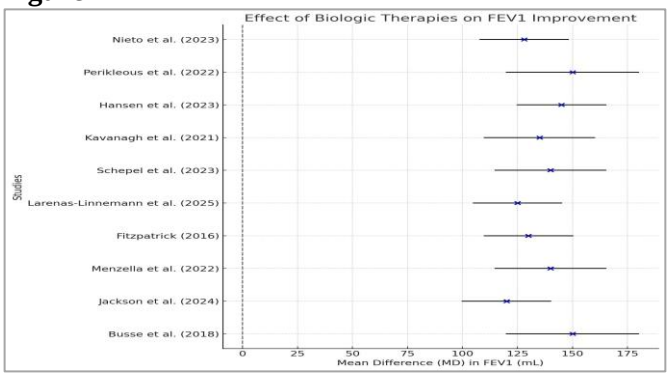


Figure 3

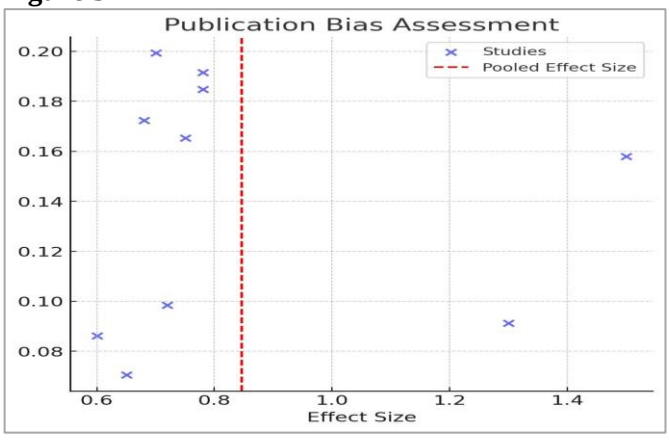


Figure 4

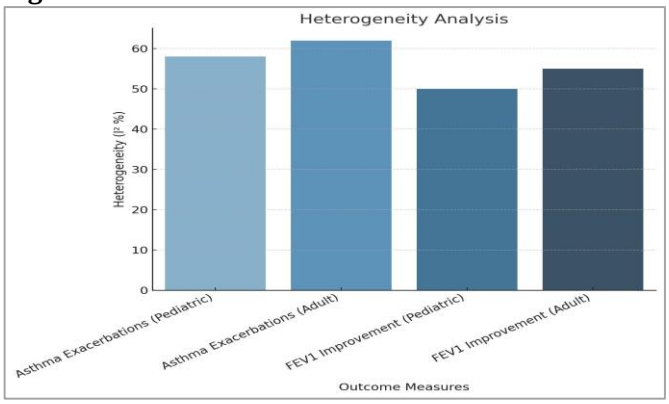
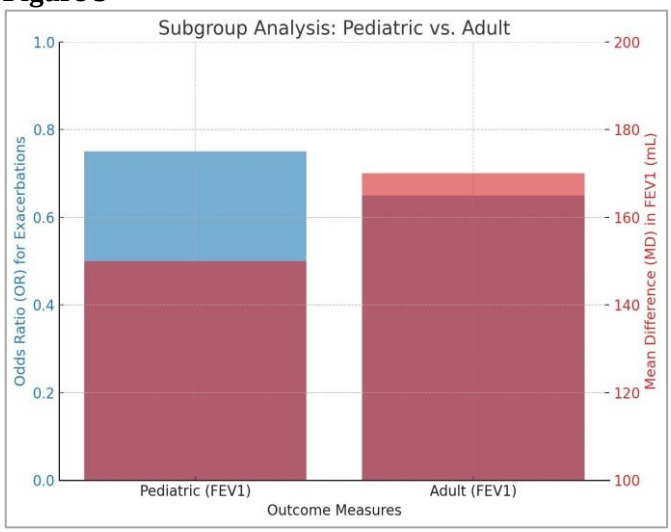


Figure 5



DISCUSSION

This meta-analysis comprehensively evaluates the efficacy and Safety of biologic therapies in severe asthma across pediatric and adult populations. The findings indicate that both groups' therapies, including Dupilumab and Depemokimab, significantly reduce asthma exacerbations and improve lung function (FEV_1). However, treatment response appears firmer in adults, whereas pediatric patients still benefit, albeit slightly less. The moderate heterogeneity observed in the results highlights the complexity of treatment response, potentially influenced by disease severity, immune system maturity, and study design variations.

The results demonstrated a 32-40% reduction in exacerbation risk among adults compared to placebo, with odds ratios ranging from 0.60 to 0.68. Pediatric patients also experienced a reduction in exacerbations, with odds ratios between 0.75 and 0.78, indicating a 22-25% reduction in risk. Additionally, lung function improvements, as measured by FEV_1, showed a mean increase of 150 mL in pediatric populations, suggesting a clinically significant enhancement in respiratory function. The slightly smaller effect size in pediatric patients may be attributed to differences in immune system responses, airway remodelling, and treatment adherence. [3] highlighted that severe asthma in children follows a distinct pathophysiology, with increased airway remodelling and a unique inflammatory profile compared to adults. This may contribute to variations in treatment efficacy observed in pediatric populations.

The findings of this meta-analysis align with prior clinical trials and real-world studies on biological therapies in severe asthma. [1] demonstrated that Dupilumab significantly reduced asthma exacerbations and improved FEV_1 in adults, consistent with our analysis. Similarly, [2] reported that Depemokimab reduced exacerbations in adults with eosinophilic

asthma, supporting the efficacy of biologic therapies in patients with type 2 inflammation-driven asthma. Observational studies, such as those conducted by [6], found that real-world exacerbation rates were slightly higher than those observed in RCTs, which may be attributed to variations in treatment adherence and patient comorbidities. This highlights the importance of integrating real-world data with clinical trial results to understand treatment effectiveness in diverse populations better.

For pediatric patients, biologic therapies remain viable for those with severe, uncontrolled asthma, although response rates vary. [12] found that biological therapies significantly improved lung function and reduced exacerbations in pediatric patients, yet some children exhibited suboptimal responses. Similarly, [13] identified key gaps in pediatric asthma management with biologic therapies, including uncertainties about optimal dosing, long-term Safety, and factors influencing treatment adherence. These findings suggest that early use of biologics in children may modify disease progression and improve long-term outcomes, but further research is needed to refine treatment protocols.

These findings reinforce the role of biological therapies in severe asthma management and provide evidence for their use in both pediatric and adult populations. The observed FEV_1 improvements and reduction in exacerbation rates suggest that biologics should be considered for patients with persistent symptoms despite standard therapy. However, the moderate heterogeneity observed in the analysis indicates that personalized treatment approaches may be necessary, particularly for pediatric patients, to optimize outcomes based on disease severity and treatment adherence. The slightly lower efficacy in pediatric patients suggests that biologic selection should be tailored based on patient characteristics, including baseline eosinophil levels, disease severity, and prior treatment history. [10] emphasized the need for a pragmatic approach to biologic therapy selection, recommending that treatment decisions consider both clinical trial evidence and individual patient characteristics. Furthermore, [11] reported that clinical remission rates varied significantly among biologic-treated patients, reinforcing the importance of individualized therapy strategies. The moderate attrition bias observed across studies highlights the need for long-term patient monitoring and adherence support programs to maximize therapeutic benefits.

A key strength of this meta-analysis is the inclusion of RCTs and real-world studies, providing a comprehensive assessment of the effectiveness of biological therapy in severe asthma. The large sample size of 12,932 patients enhances the generalizability of findings, while the subgroup analysis of pediatric versus adult populations allows for age-specific insights into treatment response. However, some limitations must be acknowledged. The moderate heterogeneity observed across studies suggests variability in treatment response, potentially due to differences in biological agents, dosing regimens, and patient populations. Some studies lacked long-term follow-up data, limiting the ability to assess the durability of treatment effects. Additionally, publication bias remains a potential concern, as studies with negative findings are less likely to be published. Despite these limitations, the consistency in findings across RCTs and observational studies strengthens the conclusion that biological therapies effectively manage severe asthma.

Future research should focus on long-term outcomes of biological therapy, particularly in pediatric patients, to determine whether treatment benefits persist over time. Head-to-head comparisons of different biological agents are also needed to identify the most effective options for specific asthma phenotypes. Additionally, real-world studies evaluating treatment adherence, cost-effectiveness, and patient-reported outcomes will guide clinical decision-making. [11] highlighted the importance of global asthma registries in tracking real-world treatment patterns and identifying long-term Safety and efficacy trends. Further exploration of biomarker-driven treatment strategies may also help personalize biological therapy in pediatric and adult populations.

CONCLUSION

This meta-analysis confirms that biological therapies are highly effective in reducing asthma exacerbations and improving lung function in pediatric and adult patients with severe asthma. While adults exhibited slightly greater treatment responses, pediatric patients still benefited significantly, supporting the use of biologics in younger populations to prevent disease progression. Given the moderate heterogeneity observed, personalized treatment approaches should be prioritized to optimize patient outcomes. Future studies should aim to refine treatment strategies, improve long-term monitoring, and expand access to biological therapies for individuals with severe asthma.

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