# Prevalence of respiratory viruses in stable and acute asthma: a systematic review and meta-analysis

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Shareable abstract (@ERSpublications)
**This meta-analysis (111 studies) quantifies viral prevalence in acute/stable asthma in children and adults, and highlights links between specific viruses and acute asthma severity. PCR alone may be limited in identifying viral acute asthma triggers.** https://bit.ly/4ts91DT

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## Abstract

***Background*** Respiratory viruses, frequently detected in asthma, are associated with worse outcomes. This meta-analysis systematically quantifies the prevalence of respiratory viruses in stable and acute asthma, across children and adults, and explores factors associated with increased viral burden through meta-regression.

***Methods*** This prospectively registered meta-analysis (PROSPERO-CRD42023375108) included studies employing molecular techniques to assess respiratory virus prevalence in asthma. Three databases were searched in August 2024. Risk of bias and certainty of evidence were assessed. We performed random-effects meta-analysis of proportions.

***Results*** We included 111 eligible studies. Moderate-certainty evidence indicated a pooled prevalence of any respiratory virus of 33.9% (95% confidence interval 24.8–43.7%) in children and 23.0% (12.9–35.0%) in adults with stable asthma. In acute asthma, prevalence increased to 58.8% (52.5–65.0%) in children and 49.9% (41.2–58.5%) in adults (moderate certainty). Rhinovirus was the most frequently identified virus, especially in acute asthma (45.0% in children *versus* 21.2% in adults). Respiratory syncytial virus and bocavirus were more common in younger children, while coronavirus and influenza were more frequently detected in adults; respiratory syncytial virus peaked in older adults too. A higher prevalence of influenza virus B and adenovirus in children, and of influenza virus A and parainfluenza 2 in adults with severe *versus* non-severe acute asthma suggests a potential association with more severe acute attacks.

***Conclusion*** Respiratory viruses are common in both stable and acute asthma. This suggests that the diagnostic value of a positive viral test during acute episodes may be limited and could benefit from complementary biomarkers to improve interpretation.

## Introduction

Asthma remains a major cause of morbidity, mortality and healthcare expenditure worldwide [1, 2] owing to its complex and heterogeneous nature, which necessitates a personalised approach to assessment and management [3]. Viruses, frequently detected in both stable and acute asthma, represent a potentially treatable trait [3]. Indeed, there are indications that viral presence during stable disease may be associated with poorer asthma control, more frequent acute attacks and reduced lung function [4–6]. Although the mere detection of any virus may not be linked to the severity or recovery from acute attacks, the presence of specific viral pathogens, such as rhinovirus, has been associated with adverse outcomes, including prolonged symptom duration and an increased risk of hospitalisation [7].

Despite growing evidence that viruses play a pivotal role in asthma, data on the prevalence and clinical burden of the various respiratory viruses in this patient group remain insufficient [8]. These data are essential to guide the development of targeted preventive and therapeutic strategies, including vaccines and antivirals for the more prevalent and burdensome viruses.

Building on these gaps, previous systematic reviews have addressed the prevalence of viruses in asthma. However, these have focused exclusively on acute attacks and not on stable disease [9–12]. Moreover, some of these reviews are now outdated, and others exhibit methodological shortcomings, such as insufficient literature searches, limited quality appraisal or suboptimal statistical approaches. To address this gap, we performed a systematic review and meta-analysis to quantify the prevalence of respiratory viruses in both acute and stable asthma among children and adults, adhering to rigorous methodological standards. Through meta-regression analyses, we also investigated clinical and methodological factors that may be associated with higher viral prevalence and greater acute asthma severity, aiming to better understand the drivers of viral burden in asthma.

## Methods

This systematic review and meta-analysis was prospectively registered with the International Prospective Register for Systematic Reviews (PROSPERO, ID: CRD42023375108) and its protocol was published [8]. The methodology adhered to the Cochrane Collaboration and Grading of Recommendations Assessment, Development and Evaluation (GRADE) guidelines and was reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) framework [13, 14].

### *Search strategy and selection criteria*

We systematically searched MEDLINE, Embase and the Cochrane Library from inception to 31 August 2024, without language restrictions. We used a structured search strategy which aimed to identify studies focusing on asthma and viruses (supplement 1.1). Additionally, we identified relevant studies by screening the reference lists of all included articles and relevant systematic reviews. Duplicate records were removed using EndNote v20 software (Clarivate, Philadelphia, PA, USA) prior to screening.

We included studies that assessed the prevalence of respiratory viruses in individuals with stable and/or acute asthma. We accepted any recognised definition of asthma, with a clinician's diagnosis deemed sufficient for inclusion. We also accepted any recognised definition of acute (exacerbated) asthma. In the absence of reported acute symptoms, asthma was classified as stable. Only studies using molecular techniques, such as PCR or real-time PCR to detect viruses in respiratory samples (*e.g.* sputum, nasal or pharyngeal swabs, or bronchoalveolar lavage fluid), were considered. We included studies of any design that assessed unselected study participants for the presence of respiratory viruses; we excluded those that selectively tested only individuals with acute asthma based on symptoms suggestive of a viral trigger. We also excluded studies focusing on specific high-risk groups, such as those with known underlying immunodeficiency. To ensure consistency, we excluded studies conducted since the onset of the COVID-19 pandemic owing to potential confounding from altered respiratory virus epidemiology and changes in public health measures and population behaviour [15, 16].

Studies were categorised based on the predominant age of participants: those primarily including participants $\geqslant$16 years were classified as adult studies, while those focusing on participants <16 years were classified as paediatric. This age threshold aligns with the typical transition of asthma patients from paediatric to adult healthcare services.

### *Data extraction and management*

Two authors independently screened titles and abstracts for eligibility, followed by full-text screening of potentially eligible studies. Data extraction was performed using a prospectively designed and pilot-tested spreadsheet. Main study characteristics and baseline data were extracted by one author and verified by a

second author, while data around the prevalence of viruses were extracted by two authors independently. Detailed data extraction parameters are available in supplement 1.2. Discrepancies were resolved through discussion, involving a third senior author if necessary.

### Outcomes

The primary outcome was the prevalence of specific respiratory viruses in stable and acute asthma among paediatric and adult populations. Additionally, we assessed the prevalence of any respiratory virus in studies evaluating at least three viruses, including rhinovirus. As secondary outcomes, we quantified the prevalence of respiratory viruses in severe acute asthma, defined as acute asthma necessitating hospital admission, and in not-necessarily severe acute asthma, defined as asthma attacks that were assessed in the community or the emergency department that may or may not have necessitated a hospital admission. We also examined the proportion of participants testing positive for multiple viruses and compared the viral loads between stable and acute asthma. Planned analyses of seasonal variability in virus prevalence and viral loads were not conducted owing to insufficient comparable data.

### Risk of bias and certainty of evidence assessment

Risk of bias at the study level was appraised using the Hoy *et al.* [17] tool, specifically designed for prevalence studies, therefore rigorously assessing representativeness of the study participants. Risk of bias assessment was performed in duplicate and disagreements were resolved as described previously.

We employed the GRADE methodology to assess the certainty of the evidence on the prevalence of respiratory viruses in stable and acute asthma [14]. Because no official guidance exists for applying GRADE to prevalence studies, and observational designs are optimal for this purpose, we opted to begin our GRADE assessments at a high-certainty assumption.

### Statistical analysis

To accommodate the anticipated significant clinical and methodological heterogeneity, we performed a random-effects meta-analysis of proportions using the inverse variance method and Freeman–Tukey double arcsine transformation [18, 19]. Heterogeneity was assessed using the $I^2$ statistic. Publication bias was assessed using funnel plots, plotting sample size against viral prevalence, which is more accurate for meta-analyses of proportions [20]. Internal validation was performed using a leave-one-out sensitivity analysis. For the stable asthma analyses, we also performed a sensitivity analysis restricted to studies enrolling participants who were free of any acute respiratory infection or exacerbation symptoms for at least 4 weeks.

Meta-regression analyses were performed using random-effect models to evaluate the impact of the following variables on the primary outcomes: participant age, asthma state (stable or acute), acute asthma severity, study publication year, the proportion of samples that were collected during the influenza season, Global Initiative for Asthma (GINA) asthma severity [21], proportion of participants using inhaled corticosteroids (ICS) and the percentage of participants vaccinated for influenza. Meta-regression analyses were conducted using a random-effects model, with inverse-variance weights incorporating between-study variance ($\tau^2$) estimates from the primary meta-analysis. Statistical significance was assessed using the Knapp–Hartung method. Additionally, sensitivity analyses were conducted by restricting to studies with a low risk of bias and by performing meta-analyses using fixed-effects models.

Statistical analysis was performed using R (R Foundation, Vienna, Austria; version 4.4.1). Further details are available in supplement 1.3.

## Results

### Study selection and baseline characteristics

After deduplication, we screened 25 166 abstracts, identifying 399 as potentially eligible. Following full-text assessment, 280 studies were excluded for reasons detailed in figure 1. Ultimately, 110 reports describing 111 studies were included in our meta-analysis (table S1). The included studies were globally representative (figure 2).

Of the included reports, 66 assessed children [7, 22–86] and 46 assessed adults [4–6, 53, 87–127]. In paediatric studies, 28 investigated viruses in stable asthma (overall n=4029 participants; median sample size=137) and 56 in acute asthma (n=9087; median=118). In the adult studies, 20 investigated stable asthma (n=2496; median=93) and 37 investigated acute asthma (n=3988; median=76). Across paediatric and adult populations, 25 studies concurrently evaluated stable and acute asthma within the same cohort.

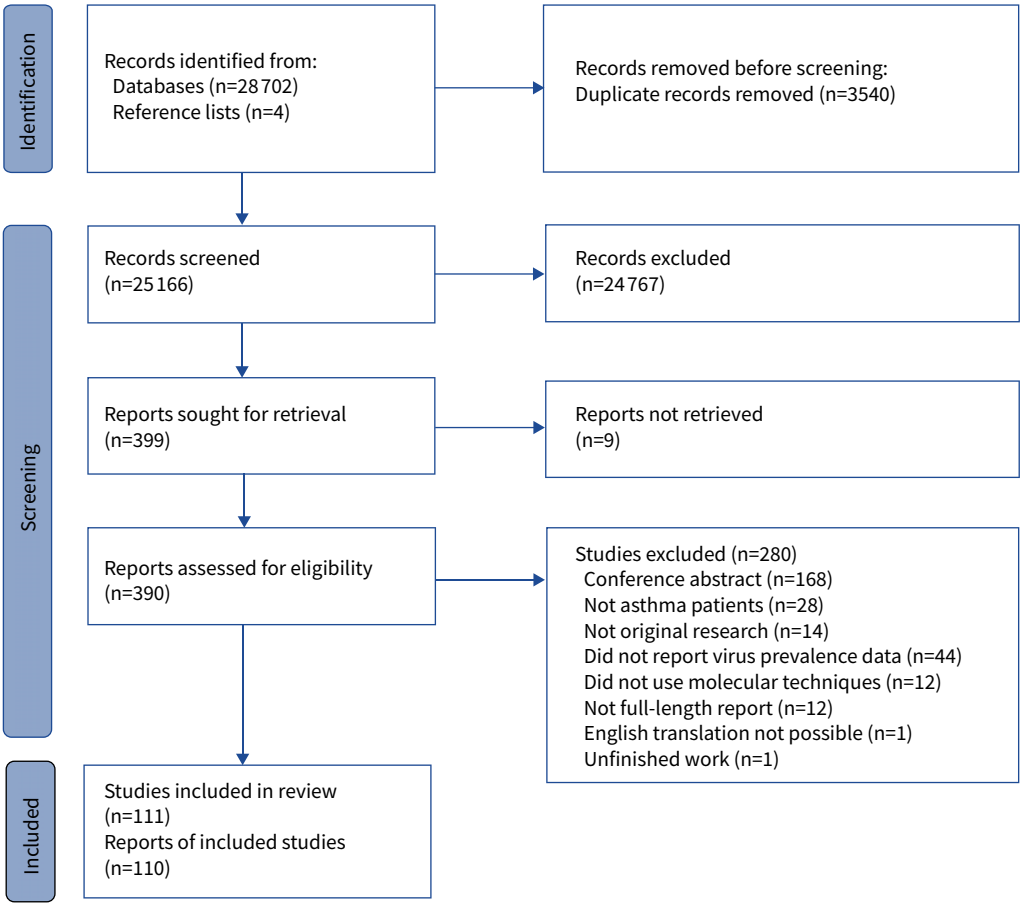


**FIGURE 1** Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) flow diagram.

The main baseline characteristics of study participants are summarised in table S1, although not all variables were consistently reported across the included studies. The definitions of asthma, including stable and acute forms, are summarised in table S2. Based on the available data, among paediatric participants the mean age was 7.5 years and 60.6% were male. The average forced expiratory volume in 1 s ($FEV_1$)/forced vital capacity (FVC) ratio was 0.84 and no participants had a history of smoking. ICS use ranged between 20.0% and 100% across studies (median=68.6%). Adult participants had a mean age of 44.2 years, with 35.2% being male. The average $FEV_1$/FVC ratio was 0.76. ICS use varied between 8.9% and 100% across studies (median=71.7%). Smoking status was infrequently documented across adult studies, with current smokers comprising 0.0–50.0% of participants, ex-smokers 0.0–48.3% and never-smokers 47.6–100%. Influenza vaccination history and number of acute events during the preceding year were reported very rarely across all included studies.

### *Risk of bias assessment*

Overall, 68.5% of studies (76 out of 111) were rated as low risk of bias and 31.5% (35 out of 111) as moderate risk of bias (table S3), with none classified as high risk of bias. However, domain-specific concerns were noted: 96.4% lacked clear random selection of participants, 92.8% had non-response bias risk, 50.5% showed limited sample representativeness and 38.7% had inadequate case definitions.

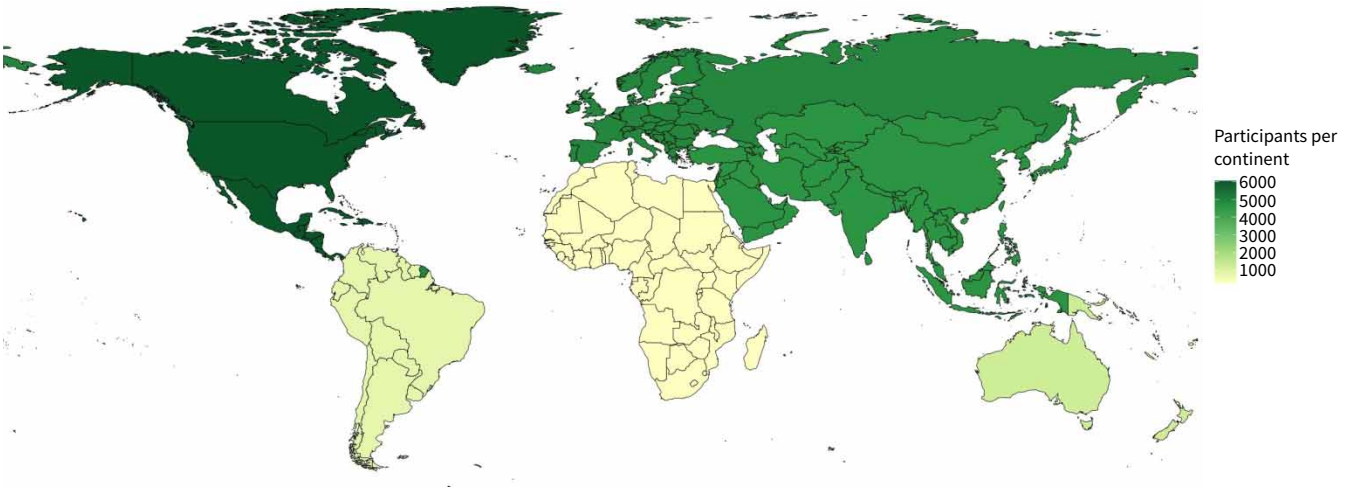


**FIGURE 2** Number of participants included in the meta-analyses, per continent. Darker shades of green indicate a higher number of participants from the respective continent.

### *Prevalence of respiratory viruses*

The main results of our meta-analysis are summarised in figures 3 and 4, with detailed summaries provided in supplement 1 and full analytical outputs in supplements 2 and 3. Among 21 studies comprising 4238 participants, the prevalence of any respiratory virus in children with stable asthma was estimated at 33.9% (95% confidence interval (CI) 24.8–43.7%). In adults with stable asthma, based on 16 studies with 1363 participants, the prevalence was 23.0% (95% CI 12.9–35.0%). There was no significant difference in the overall viral prevalence between children and adults. Rhinovirus, the most frequently detected virus in stable asthma, was identified more often in children (25.1%, 95% CI 18.1–32.7%) than in adults (11.6%, 95% CI 5.7–19.3%; p=0.001). No other significant differences were observed in the prevalence of various respiratory viruses between children and adults with stable asthma. In stable asthma, the average prevalence of other respiratory viruses did not exceed 10.0%.

Among 44 studies comprising 6669 participants, the prevalence of any respiratory virus in children with acute asthma was estimated at 58.8% (95% CI 52.5–65.0%). In adults with acute asthma, based on 29 studies including 2871 participants, the prevalence was 49.9% (95% CI 41.2–58.5%). The overall viral prevalence did not significantly differ between paediatric and adult populations. Rhinovirus was the most frequently detected virus in acute asthma and was significantly more prevalent among children (45.0%, 95% CI 39.0–51.0%) than among adults (21.2%, 95% CI 4.4–28.9%; p<0.001). Respiratory syncytial virus (RSV) was also more common in children (8.7%, 95% CI 6.6–11.2%) than in adults (3.3%, 95% CI 1.8–5.4%; p<0.001). Bocavirus also appeared more prevalent among children (3.4%, 95% CI 1.6–5.8%, *versus* 0.3%, 95% CI 0.0–1.3%), although this difference did not reach statistical significance (p=0.064). By contrast, coronavirus was more frequently detected in adults (5.9%, 95% CI 4.0–8.1%) *versus* children with acute asthma (2.6%, 95% 2.0–3.3%; p<0.001). Influenza also appeared to be more prevalent in adults (8.8%, 95% CI 6.1–11.8%) than in children (5.5%, 95% CI 3.5–7.8%), but the difference did not reach statistical significance (p=0.062). Our meta-analyses revealed similar prevalence between children and adults in metapneumovirus (3.7%, 95% CI 2.6–4.9% and 3.7%, 95% CI 2.4–5.3%), parainfluenza (3.3%, 95% CI 2.3–4.4% and 3.7%, 95% CI 2.1–5.8%) and adenovirus (2.5%, 95% CI 1.4–3.9% and 1.6%, 95% CI 1.0–2.3%).

Our analysis revealed an increased prevalence of viral detection in acute compared with stable asthma, both among children (p<0.001) and adults (p<0.001). Among children with acute *versus* stable asthma, these differences appeared to be driven by an increased prevalence of rhinovirus (p<0.001), RSV (p<0.001) and metapneumovirus (p<0.001). Among adults, only rhinovirus (p=0.044) was observed significantly more frequently during acute asthma.

The prevalence of viruses was similar between cases of acute severe asthma (necessitating hospital admission) and those presenting to primary care or emergency departments (with moderate or severe acute asthma) in both children and adults (figures 5 and 6). Influenza virus B was significantly more prevalent

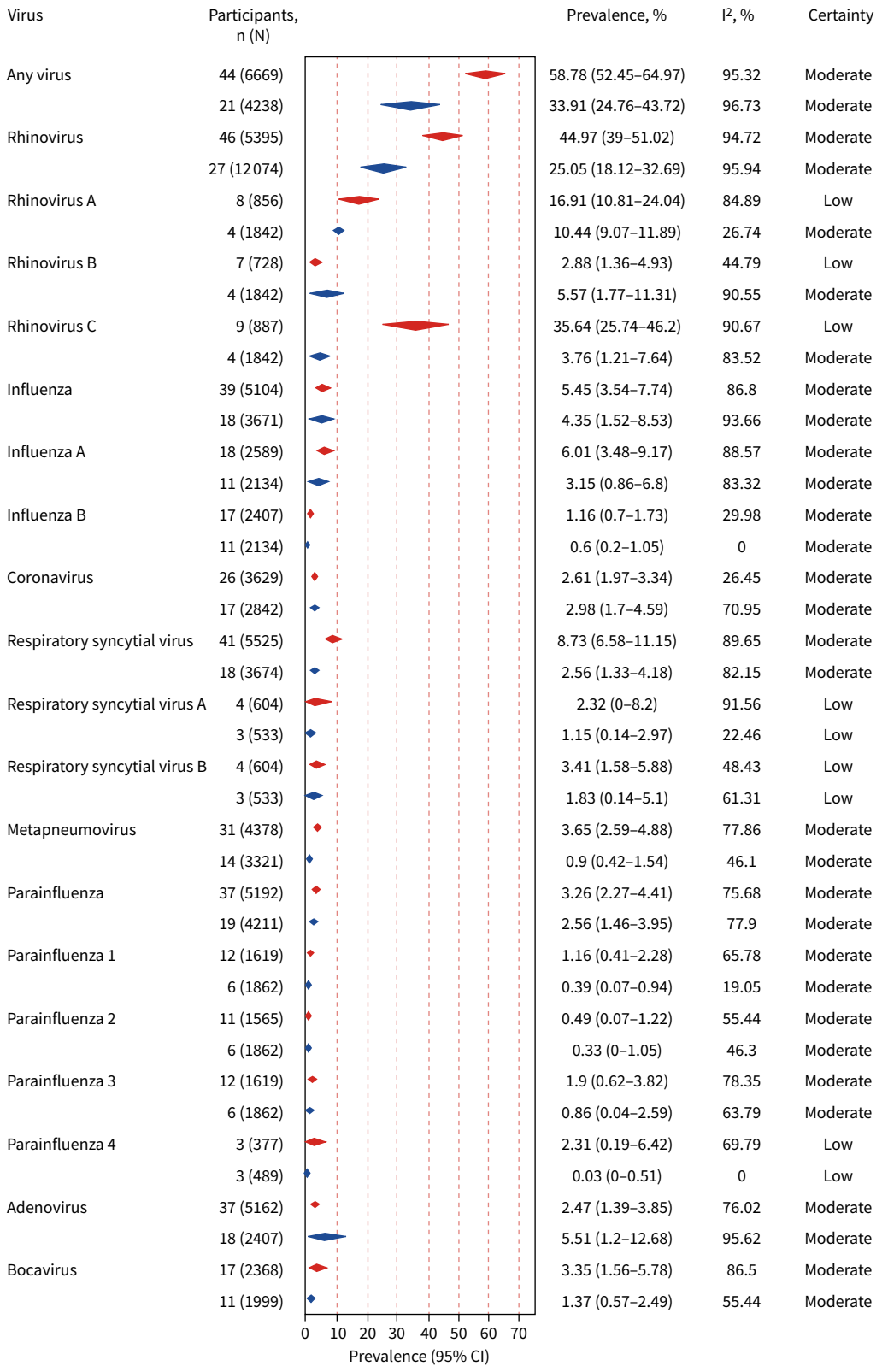


**FIGURE 3** Prevalence of respiratory viruses in paediatric asthma (red diamond: acute asthma; blue diamond: stable asthma). Prevalence reported as the percentage estimate with 95% confidence intervals (CIs). $I^2$ represents the heterogeneity.

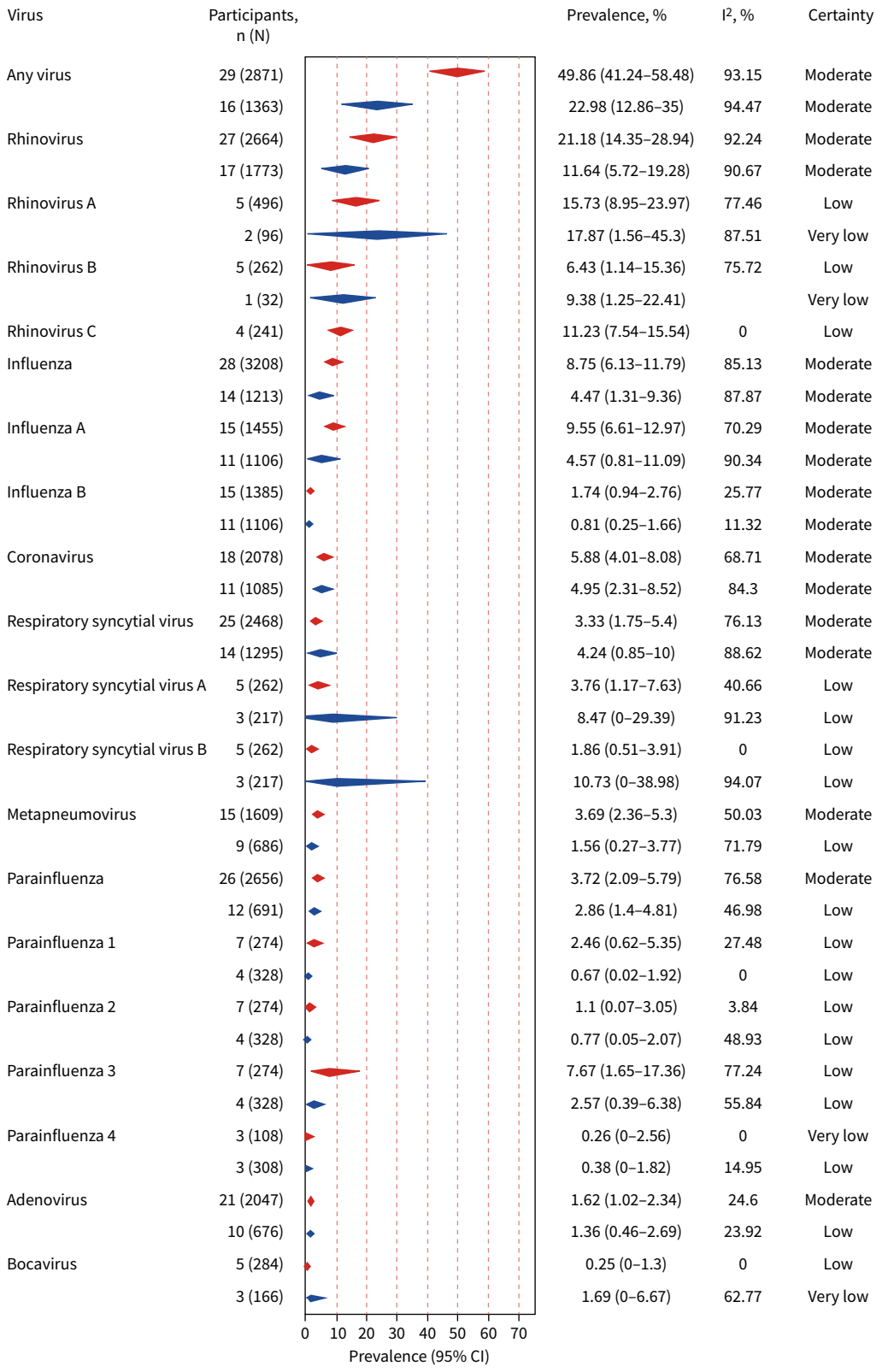


**FIGURE 4** Prevalence of respiratory viruses in adult asthma (red diamond: acute asthma; blue diamond: stable asthma). Prevalence reported as the percentage estimate with 95% confidence intervals (CIs). $I^2$ represents the heterogeneity.

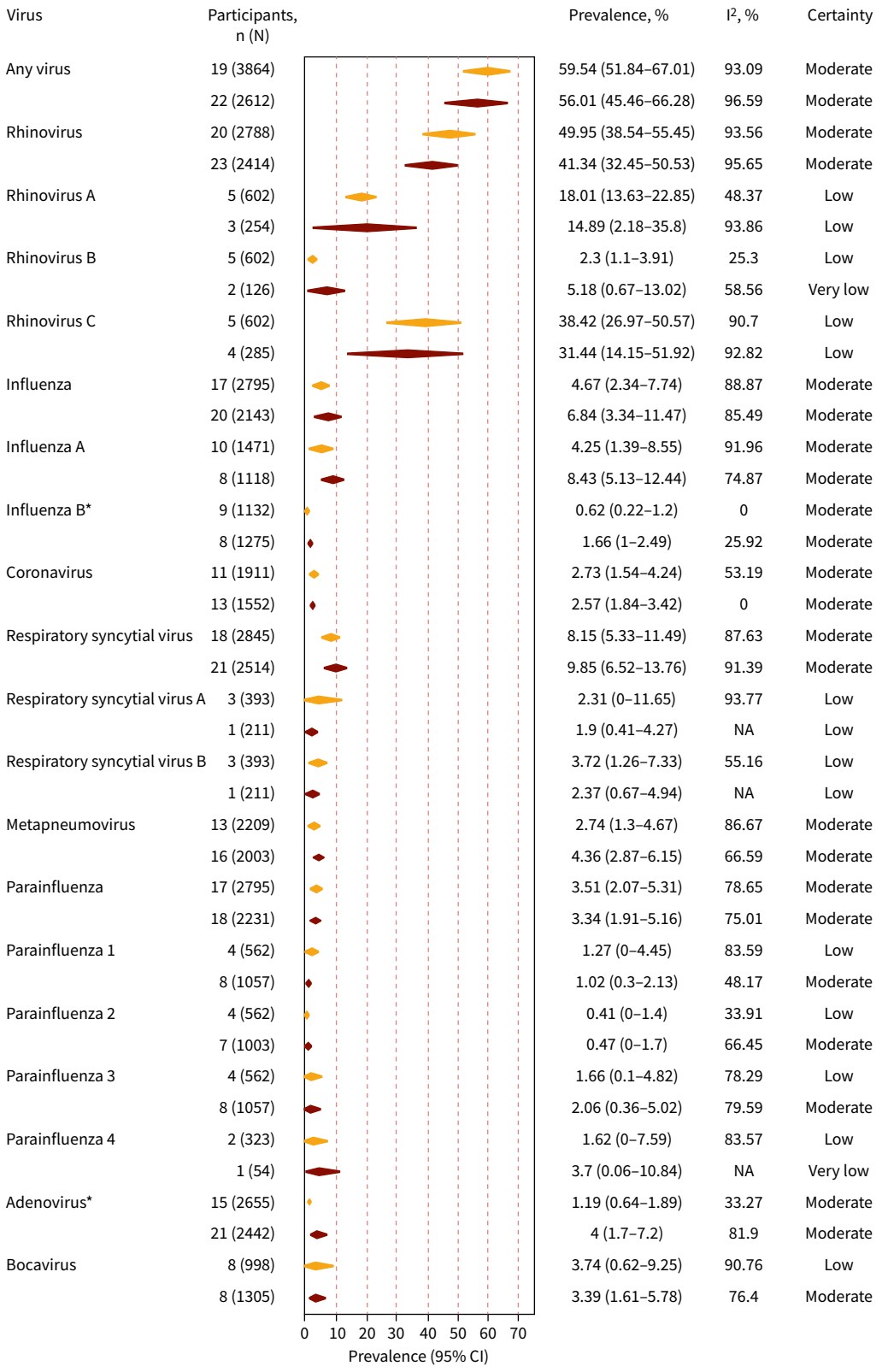


**FIGURE 5** Prevalence of respiratory viruses in severe *versus* non-severe acute attacks in paediatric asthma (dark red diamond: acute severe asthma; orange diamond: acute moderate/severe asthma). Prevalence reported as the percentage estimate with 95% confidence intervals (CIs). $I^2$ represents the heterogeneity. *: statistically significant difference between severe and non-severe acute asthma attacks.

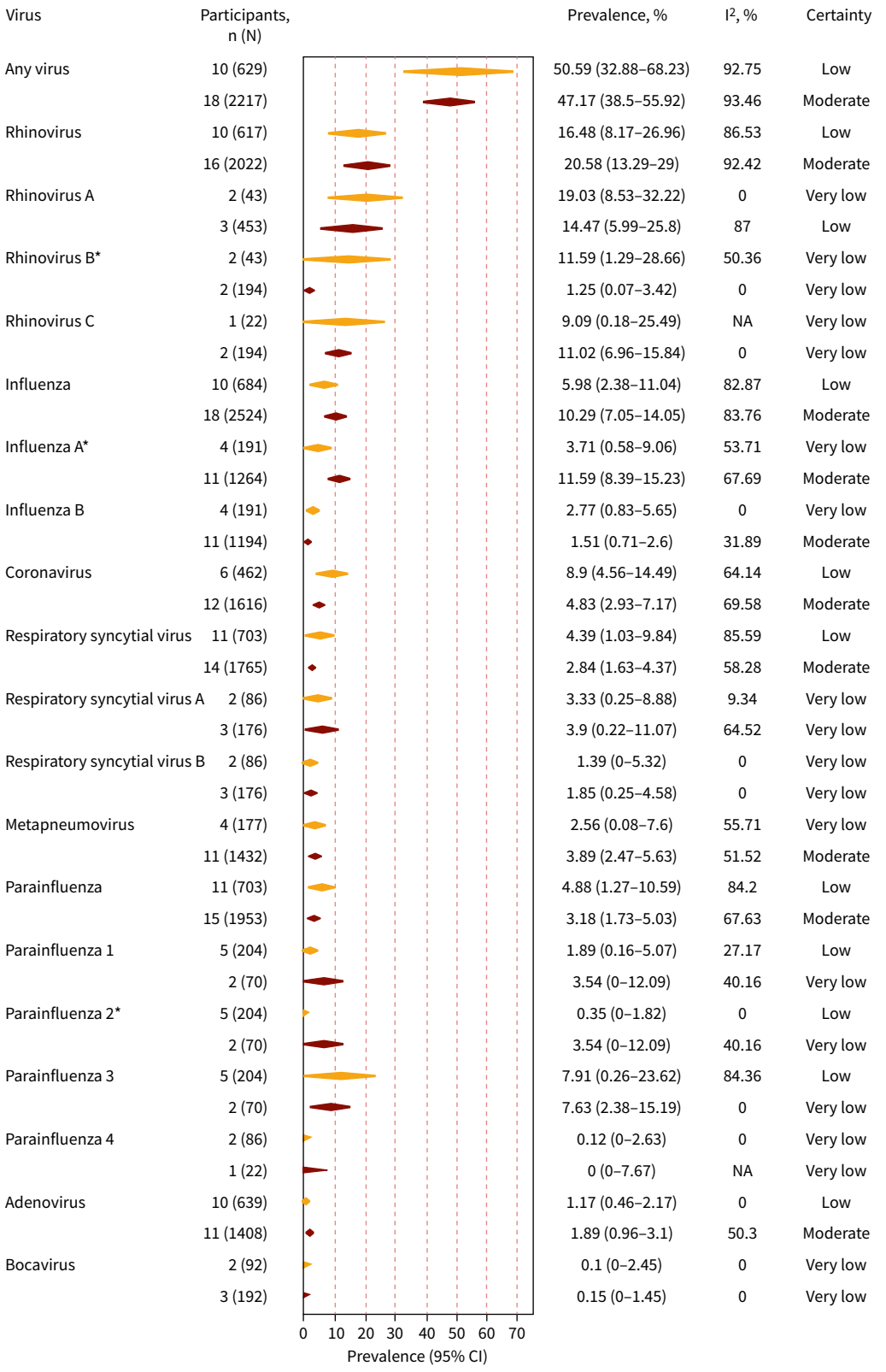


**FIGURE 6** Prevalence of respiratory viruses in severe *versus* non-severe acute attacks in adult asthma (dark red diamond: acute severe asthma; orange diamond: acute moderate/severe asthma). Prevalence reported as the percentage estimate with 95% confidence intervals (CIs). $I^2$ represents the heterogeneity. *: statistically significant difference between severe and non-severe acute asthma attacks.

among children with acute severe asthma compared with moderate/severe acute asthma (1.7%, 95% CI 1.0–2.5%, *versus* 0.6%, 95% CI 0.2–1.2%; p=0.02). A statistically significant difference was also observed for adenovirus (4.0%, 95% CI 1.7–7.2%, *versus* 1.2%, 95% CI 0.6–1.9%; p=0.03). In severe acute asthma in adults, we found increased prevalence compared with moderate/severe asthma of influenza virus A (11.6%, 95% CI 8.4–15.2%, *versus* 3.7%, 95% CI 0.6–9.1%) and parainfluenza 2 (3.5%, 95% CI 0.0–12.1%, *versus* 0.4%, 95% CI 0.0–1.8%). Conversely, the prevalence of rhinovirus B was significantly reduced in severe acute asthma compared with moderate/severe asthma (1.3%, 95% CI 0.1–3.4%, *versus* 11.6%, 95% CI 1.3–28.7%). During stable disease state, co-detection of two or more viruses was infrequent, observed in 2.0% (95% CI 0.0–6.0%) of children and 0.0% (95% CI 0.0–2.0%) of adults. In contrast, during the acute state, co-detection increased significantly, occurring in 9.0% (95% CI 6.0–12.0%) of children (p=0.013) and 3.0% (95% CI 1.0–5.0%) of adults (p=0.023).

Viral load data are summarised in supplement 1.4.

### *Meta-regression and sensitivity analyses*

High $I^2$ estimates and wide prediction intervals across most of the conducted meta-analyses revealed substantial heterogeneity. Meta-regression analyses showed limited effect of accounting for the publication year, baseline ICS use or participant mean age on heterogeneity. Notably, paediatric studies demonstrated a clear association between younger age and a higher prevalence of RSV, metapneumovirus and bocavirus, whereas in adults RSV prevalence was greater in studies involving older populations. Moreover, a higher proportion of participants receiving ICS was strongly associated with a higher prevalence of rhinovirus and parainfluenza in adults with acute asthma (p=0.008 and 0.003, respectively). Limited availability of data on asthma severity, influenza vaccination status and the proportion of samples collected during influenza season across the included studies rendered the respective analyses ineffective.

Our findings remained robust in sensitivity analyses only including studies at a low risk of methodological bias and those performed using fixed-effect models meta-analysis (supplement 3: figures S116 and S117). Sensitivity analyses restricted to studies enrolling participants with stable asthma who were free of acute symptoms for at least 4 weeks were generally consistent with the main analyses, except for some that were based on very small populations (<100 participants), for which estimates were less certain. The only notable difference was a lower rhinovirus prevalence in children with stable asthma (1.1%, 95% CI 0.0–3.8%, compared to 5.5%, 95% CI 1.2–12.7%, in the main analysis), despite this analysis being informed by over 1100 participants.

### *Publication bias, internal validation and certainty of evidence*

Funnel plots showed no evidence of publication bias.

Most analyses were robust to leave-one-out sensitivity analyses. Only certain viral subtypes, such as RSV A/B, parainfluenza 3 and coronaviruses, were sensitive to the omission of specific studies, likely reflecting small study effects or local epidemic dynamics.

The certainty of evidence regarding the prevalence of any virus and regarding most of the specific viral genera assessed was rated as moderate, whereas evidence related to viral species ranged from low to moderate. The primary reason for downgrading the certainty of evidence was inconsistency, attributable to significant variability in viral prevalence estimates across the included studies. Additionally, some meta-analyses of viral species were downgraded due to imprecision, because their estimates were based on very limited study populations.

## Discussion

This meta-analysis quantifies the prevalence of respiratory viruses in children and adults with asthma, extensively updating the evidence base for acute asthma while, for the first time, aggregating data on stable asthma. We demonstrate with moderate certainty that respiratory viruses are present in 33.9% (95% CI 24.8–43.7%) of children and 23.0% (95% CI 12.9–35.0%) of adults with stable asthma, compared to detection rates of 58.8% (95% CI 52.5–65.0%) in children and 49.9% (95% CI 41.2–58.5%) of adults with acute asthma. Rhinovirus, predominantly rhinovirus A, was the most frequently identified virus across all patient groups. Notably, our analyses revealed that children with severe acute asthma requiring hospitalisation had a higher prevalence of influenza virus B and adenovirus compared with those managed as outpatients, suggesting an association with more severe attacks. In adults, influenza virus A and parainfluenza 4 were significantly more prevalent in severe cases, whereas rhinovirus B was less frequently detected. In acute asthma, RSV was more common in preschoolers and older adults, bocavirus was most frequently detected in the youngest children, and metapneumovirus was more prevalent in younger than in

older children. Conversely, coronavirus and, possibly, influenza appeared more frequently in adults with acute asthma than in children, although the latter did not reach statistical significance.

The high prevalence of respiratory viruses in stable asthma suggests that their mere detection in an acute attack does not necessarily imply a viral trigger, because they could also represent an "innocent bystander". Consequently, the diagnostic value of a positive viral sample during an acute event needs to be further evaluated or strengthened by other biomarkers. Additionally, a positive viral PCR in stable asthma may reflect asymptomatic carriage rather than a true trigger, underscoring the need to better understand its clinical relevance.

In parallel, respiratory viruses, particularly rhinoviruses, were more frequently detected in children, likely reflecting both higher exposure (*e.g.* school, daycare) and age-related differences in innate immunity, such as reduced interferon responses in early childhood [128]. Symptomatic infections represent only a fraction of viral exposures, so asymptomatic carriage is also expected to be more common in children.

Interpreting viral prevalence in asthma requires contextualising these findings against baseline rates in the general population. Virus detection rates in acute lower respiratory tract infections do not appear to be lower in the general population than in asthma patients [129, 130]; however, because individuals with asthma experience more frequent acute episodes, their cumulative viral burden is higher [131]. In contrast, during periods without acute illness, respiratory viruses are rarely detected in adults without asthma [132, 133], while detection rates in children remain comparable regardless of asthma status [134, 135]. Notably, the few studies assessing the respiratory virome suggest that eukaryotic viruses may constitute a core component of the virome in both healthy and asthmatic individuals [136, 137]. Thus, it remains unclear whether the presence of viruses in asthma reflects normal viral circulation, an increased susceptibility, delayed viral clearance or an altered immune response, such as an acute or pre-exacerbation state. Notably, there is no evidence supporting persistent airway colonisation by respiratory viruses. These findings underscore the need to interpret viral detection within its clinical context and highlight the importance of developing tailored diagnostic strategies.

Current preventive and therapeutic strategies are limited to addressing acute asthma exacerbations associated with influenza, RSV and COVID-19 [138]. Advancing our understanding of how viruses trigger, or fail to trigger, acute attacks, and developing robust methods to accurately identify these viral triggers, is essential for devising novel, targeted interventions.

This study adds important new insights into the role of respiratory viruses in asthma. By providing the first large-scale quantification of viral detection in stable asthma, our findings establish baseline rates of PCR positivity and place acute exacerbation data into clearer context. The detailed stratified analyses across asthma state, age group and exacerbation severity revealed virus-specific patterns, such as the differing prevalence of rhinovirus B, adenovirus, RSV and influenza subtypes, that individual studies were underpowered to detect. These patterns offer new perspectives on the potential viral drivers of exacerbation severity and highlight the distinct contributions of different viruses across age groups. Together, these findings refine our understanding of viral epidemiology in asthma and generate hypotheses for future mechanistic and longitudinal research, including work needed to clarify the clinical significance of viral detection during periods of stability. They may also help guide public health planning by identifying which respiratory viruses contribute most to the burden of acute asthma, thereby informing prioritisation of preventive strategies such as vaccination or antiviral development.

Previous meta-analyses focused solely on respiratory virus prevalence during acute asthma exacerbations. While their estimates align broadly with ours, they were based on fewer studies and generally had wider confidence intervals [9–12]. Feddema *et al*. [12] found higher prevalence of any virus, rhinovirus and RSV in younger compared to older individuals, and the opposite trend for influenza; consistent with our findings. That study also reported lower virus-related exacerbation rates in the Northern Hemisphere, while two meta-analyses identified regional differences [10, 12]. However, these analyses pooled heterogeneous populations (adults and children, various time periods and exacerbation severities), increasing risk of bias. Given these limitations, we opted not to perform geographic subgroup analyses in our review to reduce potential sources of bias.

This meta-analysis has several limitations. First, significant unexplained heterogeneity in the viral prevalence estimates across the included studies led to downgrading the certainty of evidence of all analyses due to inconsistency. The impact of seasonal fluctuations in viral prevalence (*e.g.* influenza peaks in winter and rhinovirus in spring/autumn), micro-epidemics, variation in treatments (*e.g.* higher ICS doses

are associated with an increased risk of viral infections) and differences in influenza vaccination history on respiratory viral prevalence are well studied [138]. We attempted to explain the observed variability by accounting for these factors in meta-regression analyses, but these were limited by inconsistent reporting of the relevant data across the included studies. Differences in sampling methods, sample handling and the performance characteristics of viral diagnostic techniques across studies are also likely to have contributed to the observed between-study heterogeneity. Second, while all studies were found to be at low or moderate risk of bias, the vast majority were found to be at a potential risk of selection and non-response bias, and this should be considered in the interpretation of the results. Additionally, several studies lacked clear definitions of acute and stable asthma, underreported key participant characteristics, and provided limited information on the timing of sample collection during acute episodes. Third, most studies employed upper respiratory samples, with only a few small studies assessing lower respiratory tract specimens, precluding a meaningful subgroup analysis. This is a notable limitation, because viral detection in the lower airways is likely to be more clinically relevant in acute events, where the transmission of viruses from the upper to the lower respiratory tract may trigger an asthma attack [138]. Fourth, we relied on clinician-diagnosed asthma, which may introduce some degree of misclassification bias; however, this pragmatic approach reflects real-world practice and is commonly adopted in large epidemiological studies to ensure broader generalisability. Moreover, we used hospitalisation as a surrogate for exacerbation severity, recognising that admission decisions may be influenced by contextual factors such as social and frailty drivers. However, given the predominantly young study populations and the widespread use of hospital admission as a severity marker, we believe this remains an appropriate and inclusive measure for our analysis. Fifth, in the absence of adequate relevant data, we were not able to address some of the prespecified objectives, namely, to compare the viral loads of respiratory viruses during stable and acute asthma and to describe the seasonality of various respiratory viruses. Sixth, low-income countries were absent from our sample, with only two studies originating from lower-middle-income economies per World Bank classifications, and African populations were notably underrepresented. Last, studies conducted after the onset of the COVID-19 pandemic were deliberately excluded to avoid pandemic-related confounding. A future update of this review will be necessary to investigate any shifts in respiratory viral epidemiology attributable to the pandemic.

However, this meta-analysis of 111 studies from six continents has several strengths, including a prospective and transparent design that aligns with Cochrane guidance, ensuring methodological rigour, a highly sensitive search strategy, comprehensive quality assessments of the included studies and body of evidence for each outcome, and the application of robust statistical methods.

Future research must address the complexities of viral pathogen assessment in asthma through large-scale, prospective cohorts that capture seasonal variability and clinical burden. International collaboration, standardised viral assessments and robust data sharing are essential to build a comprehensive evidence base. Meanwhile, an individual participant data meta-analysis could offer detailed, cost-effective insights to inform targeted preventive and therapeutic strategies, including vaccines and antivirals, ultimately improving global asthma outcomes.

In conclusion, this study quantifies respiratory virus prevalence in both acute and stable asthma among adults and children, providing the first aggregate data on stable asthma, and reveals a notable prevalence, with adults exhibiting higher rates compared to healthy individuals. It also offers indirect evidence linking certain viruses to more severe acute attacks, underscoring the complexities of viral involvement in asthma. By integrating stratified analyses and applying a rigorous, prospectively registered methodology, this work enhances the evidence base and identifies key areas for future investigation, ultimately supporting more precise and effective approaches to asthma care.

**Points for clinical practice**

- Respiratory viruses are common in both stable and acute asthma, in children and adults.
- Rhinovirus is the most frequently detected virus, particularly during an acute asthma attack.
- Influenza virus B and adenovirus may be associated with more severe acute asthma in children.
- Influenza virus A and parainfluenza 4 may be associated with more severe acute asthma in adults.
- The diagnostic value of a positive viral test during acute episodes may be limited and could benefit from complementary biomarkers to improve interpretation.

Data availability: All data extracted from the included studies will be made available on request.

Provenance: Submitted article, peer reviewed.

The systematic review protocol was registered with PROSPERO (https://www.crd.york.ac.uk/prospero/) with identifier: CRD42023375108.

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