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INPLASY

Predictors of persistence of childhood asthma into adulthood: A systematic review and meta-analysis (Protocol)

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ADMINISTRATIVE INFORMATION

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Review Stage at time of this submission - Preliminary searches.

Conflicts of interest - The authors declare no competing interests. The funders had no role in study design, data collection, data analysis, data interpretation, or the decision to submit the protocol for registration.

INPLASY registration number: INPLASY2026110001

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 1 November 2026 and was last updated on 1 November 2026.

INTRODUCTION

Review question / Objective To identify baseline characteristics measured in childhood that predict persistence of asthma into adulthood, and to estimate the proportion of children with asthma who still have active asthma in adulthood.
Population: children and adolescents younger than 18 years with physician-diagnosed asthma who are followed longitudinally into adulthood, with the outcome assessed at 18 years or older. Population-based, outpatient and inpatient recruitment settings are all eligible.
Exposure: baseline clinical, demographic and paraclinical characteristics measured in childhood, including but not limited to sex, family history of asthma, allergic rhinitis, eczema, allergic sensitization assessed by specific IgE or skin prick testing, airway hyperresponsiveness, baseline lung function including FEV1 and FEV1/FVC, blood eosinophil count, asthma severity, early-life respiratory infections, breastfeeding, and exposure to tobacco smoke.
Comparator: participants with versus without each candidate predictor, or higher versus lower levels for continuous predictors.
Outcome: the primary outcome is the association between each baseline predictor and persistence of asthma into adulthood, expressed as a pooled adjusted odds ratio. The secondary outcome is the proportion with persistence of asthma into adulthood, defined as active asthma present at the outcome assessment time point and including participants who relapse after a period of remission.
Study design: prospective or retrospective longitudinal cohort studies with at least five years

of follow-up that report extractable 2×2 counts or adjusted effect estimates with 95% confidence intervals.

Rationale Asthma is one of the most common chronic respiratory diseases in children. A substantial proportion of affected children continue to have active asthma after reaching adulthood, and reported persistence proportions vary widely across cohorts depending on the population studied, the remission definition applied, and the length of follow-up. Persistence into adulthood carries long-term consequences, including accelerated decline in lung function, an increased risk of chronic obstructive pulmonary disease, and ongoing treatment burden.
Knowing which children are likely to have persistent disease would allow earlier risk stratification, closer monitoring, and better-targeted long-term management. Individual cohort studies have examined a range of candidate predictors, including sex, family history of asthma, allergic rhinitis, eczema, allergic sensitization, airway hyperresponsiveness, baseline lung function, and blood eosinophil count. Their findings are not consistent: reported estimates differ in magnitude and, for some predictors, in direction.
Preliminary searches identified no published meta-analysis that has pooled these effect estimates, and the available evidence has not been examined for sources of between-study heterogeneity. A systematic review with meta-analysis is therefore needed to obtain pooled estimates for each predictor and to establish whether the observed inconsistencies reflect real differences between populations or variation in study methods. The findings are intended to support prognostic counselling in clinical follow-up and to inform the design of future longitudinal studies.Asthma is one of the most common chronic respiratory diseases in children. A substantial proportion of affected children continue to have active asthma after reaching adulthood, and reported persistence proportions vary widely across cohorts, from roughly 25% to 85%, depending on the population studied, the remission definition applied, and the length of follow-up. Persistence into adulthood carries long-term consequences, including accelerated decline in lung function, an increased risk of chronic obstructive pulmonary disease, and ongoing treatment burden.
Knowing which children are likely to have persistent disease would allow earlier risk stratification, closer monitoring, and better-targeted long-term management. Individual cohort studies have examined a range of candidate predictors, including sex, family history of asthma, allergic rhinitis, eczema, allergic sensitization, airway hyperresponsiveness, baseline lung function, and blood eosinophil count. Their findings are not consistent. Reported estimates differ in magnitude and, for some predictors, in direction; the association between female sex and persistence is positive in several cohorts and reversed in others.
Preliminary searches identified no published meta-analysis that has pooled these effect estimates, and the available evidence has not been examined for sources of between-study heterogeneity. A systematic review with meta-analysis is therefore needed to obtain pooled estimates for each predictor and to establish whether the observed inconsistencies reflect real differences between populations or variation in study methods. The findings are intended to support prognostic counselling in clinical follow-up and to inform the design of future longitudinal studies.

Condition being studied Asthma is a chronic inflammatory disorder of the airways. It is defined by a history of respiratory symptoms such as wheeze, cough, dyspnoea and chest tightness that vary in intensity and over time, together with evidence of variable expiratory airflow limitation and airway hyperresponsiveness. Symptoms are often worse at night or in the early morning and may be triggered by exercise, viral infection, allergen exposure or cold air.
Asthma with onset in childhood is one of the most common chronic diseases seen in paediatric practice. The diagnosis rests on a compatible symptom pattern combined with objective evidence obtained through spirometry, bronchodilator reversibility testing or bronchial challenge testing. In younger children who cannot perform reproducible spirometry, diagnosis depends more heavily on clinical judgement, the pattern of symptoms over time, and the response to a trial of asthma treatment.
The condition carries a considerable burden through day-to-day symptoms, acute exacerbations, and the need for long-term controller therapy. Its course differs between individuals: symptoms remit in some patients, whereas in others active disease continues from childhood into adult life and is associated with progressive impairment of lung function and a higher risk of fixed airflow obstruction later on.

METHODS

Search strategy Searches will be run in six electronic databases: PubMed/MEDLINE, Embase, Scopus, Web of Science Core Collection, the Cochrane Central Register of Controlled Trials

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(CENTRAL), and the Cochrane Database of Systematic Reviews. The search is restricted to English-language publications, with no restriction on publication date.
MEDLINE and Embase form the core biomedical searches, using MeSH and Emtree subject headings respectively alongside free-text terms. Scopus and Web of Science are searched to broaden journal coverage and to allow citation tracking. CENTRAL is searched because Cochrane reviews conventionally include it and because trials may report extended follow-up data. The Cochrane Database of Systematic Reviews is searched to identify existing reviews and to screen their reference lists.
ProQuest Dissertations and Theses Global will also be searched to identify unpublished cohort follow-up data. Dissertations that meet the eligibility criteria will be assessed with the same risk of bias tool as journal articles. Where a dissertation and a later journal publication describe the same cohort, the journal publication will be used as the primary source and the dissertation retained only for supplementary data.
The strategy combines controlled vocabulary and free-text terms in three conceptual blocks. The first covers asthma, childhood asthma and related terms. The second covers remission, persistence, resolution, relapse and their derivatives. The third covers cohort, longitudinal, follow-up, prospective and observational study terms. Terms within each block are combined with OR, and the blocks are combined with AND. Reference lists of included studies and of relevant reviews will be screened for additional records. The full search strategy for each database will be reported following the PRISMA-S statement.

Participant or population Children and adolescents younger than 18 years with asthma who are followed longitudinally into adulthood, with the outcome assessed at 18 years or older. Participants recruited from population-based cohorts, outpatient clinics and hospital settings are all eligible. Studies of asthma with onset in adulthood and cross-sectional surveys without longitudinal follow-up are excluded.

Intervention No intervention is evaluated; this is a prognostic review of baseline predictors. The exposures of interest are baseline clinical, demographic and paraclinical characteristics measured in childhood, including sex, family history of asthma, allergic rhinitis, eczema, allergic sensitization, airway hyperresponsiveness, baseline lung function including FEV1 and FEV1/FVC, blood eosinophil count, asthma severity, early-life respiratory infections, breastfeeding and tobacco smoke exposure. Any additional baseline predictor reported by an included study will also be considered.

Comparator Absence of the predictor under assessment, or a lower level for continuous predictors. Each predictor is examined by comparing subgroups defined by presence versus absence, or higher versus lower level where the predictor is continuous.

Study designs to be included Included: prospective or retrospective longitudinal cohort studies with at least 5 years of follow-up that report extractable 2x2 counts or adjusted effect estimates (OR/RR/HR with 95% CI). Excluded: randomised trials, cross-sectional surveys without longitudinal follow-up, case series, narrative reviews, conference abstracts, and animal or laboratory studies.

Eligibility criteria Additional inclusion criteria: English-language publications only; no restriction on publication date or publication status, so journal articles and dissertations are both eligible; the study must report a binary outcome of asthma persistence or remission assessed at 18 years or older, or report an adjusted effect estimate for a predictor with its 95% confidence interval.
Additional exclusion criteria: studies reporting only continuous lung function measures without a binary persistence or remission classification; studies in which the outcome cannot be linked to a defined assessment time point; duplicate reports of the same cohort, from which the report with the largest sample size and longest follow-up is retained; studies whose essential data remain unavailable after contacting the authors.

Information sources Electronic databases: PubMed/MEDLINE, Embase, Scopus, Web of Science Core Collection, the Cochrane Central Register of Controlled Trials, and the Cochrane Database of Systematic Reviews. Searches are restricted to English-language records with no date limit.
Grey literature: ProQuest Dissertations and Theses Global will be searched for unpublished cohort follow-up data.
Other sources: reference lists of all included studies and of relevant reviews will be screened. Authors of primary studies will be contacted where necessary to obtain missing or unclear information such as numerators, denominators, or adjusted estimates. No trial registers will be searched, since the review includes cohort studies rather than trials.

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Main outcome(s) Primary outcome: the association between each baseline predictor measured in childhood and persistence of asthma into adulthood. Outcome assessment occurs at the final follow-up, when participants are aged 18 years or older. The effect measure is the odds ratio, taken from multivariable models when reported, and pooled across studies with 95% confidence intervals. Estimates reported toward remission will be inverted so that all express the odds of persistence.

Additional outcome(s) Secondary outcome: the proportion of participants with persistence of asthma into adulthood. Persistence means active asthma present at the outcome assessment time point, when participants are aged 18 years or older. It includes those with continuous symptoms since childhood and those who remitted and later relapsed. The proportion will be pooled with 95% confidence intervals.
Relapse after remission will be described narratively where studies report it, since too few studies are expected to permit pooling.

Quality assessment / Risk of bias analysis Risk of bias in included studies will be assessed with the Quality In Prognostic Studies (QUIPS) tool. It covers six domains: study participation, study attrition, prognostic factor measurement, outcome measurement, study confounding, and statistical analysis and reporting. Two reviewers will assess each study independently, and disagreements will be resolved by discussion or arbitration by a third reviewer.
Each domain will be rated as low, moderate or high risk of bias, and an overall judgement recorded for each study. Studies judged at high risk of bias will be retained in the main analysis but excluded in sensitivity analysis so that their influence can be examined. The certainty of evidence for each predictor may additionally be assessed with the GRADE framework adapted for prognostic factor studies.

Strategy of data synthesis Data will be analysed with random-effects meta-analysis using the DerSimonian-Laird estimator. For each predictor with at least two contributing studies, adjusted odds ratios will be pooled and reported with 95% confidence intervals. Where a study reports both unadjusted and adjusted estimates, the adjusted estimate will be used, and estimates reported toward remission will be inverted so that all express the odds of persistence.
Heterogeneity will be quantified with the I^2 statistic, τ^2 and Cochran Q. A 95% prediction interval will be reported for any outcome with at least three contributing studies. Forest plots will be produced for each predictor.
For the binary outcome of persistence, proportions will be pooled after Freeman-Tukey double-arcsine transformation under a random-effects model, with 95% confidence intervals. Between-study heterogeneity is expected to be substantial for proportions, so pooled estimates will be interpreted descriptively.
Analyses will be performed in R using the metafor package, or equivalent software.

Subgroup analysis Prespecified subgroup analyses will be performed according to: recruitment setting (population-based versus clinical); outcome age (younger than 25 years versus 25 years or older); remission definition (symptom-based, clinical or complete); and type of effect estimate (adjusted versus crude).
Differences between subgroups will be tested with the between-subgroup Q statistic. A subgroup analysis will be undertaken only where at least two studies contribute to each subgroup; where this condition is not met, the comparison will not be performed and will be reported as not feasible. Subgroup findings will be interpreted cautiously, since subgroups are defined by study-level characteristics rather than by individual patient data.

Sensitivity analysis Sensitivity analyses address decisions where the main analysis and the alternative analysis differ. Criteria already fixed in the eligibility criteria, namely retaining one report per cohort and requiring outcome assessment at 18 years or older, are therefore not repeated as sensitivity analyses.
Sensitivity analyses will (1) add crude estimates to the adjusted estimates used in the main analysis, (2) exclude studies at high risk of bias, (3) restrict the analysis to prospective designs, (4) exclude studies of selected severe inpatient populations, and (5) exclude grey literature including dissertations.

Language restriction Searches and inclusion are restricted to English-language publications.

Country(ies) involved China.

Other relevant information This is a prognostic review; no intervention is evaluated. The protocol follows the PRISMA 2020 statement, and the search is reported according to PRISMA-S. Where a cohort is described in more than one publication, a single report is retained, as specified in the eligibility criteria. Any post-registration amendment to this protocol will be recorded with the date and

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the reason for the change. Extracted data will be made available with the final publication.

Keywords childhood asthma; asthma; asthma persistence; asthma remission; prognosis; predictor; prognostic factor; risk factor; longitudinal cohort; meta-analysis.

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