

Original Paper

The Clinical Registry of Childhood Asthma (CRCA) Elucidating Early-Life Asthma: Cross-Sectional Analysis of a Prospective, Longitudinal, and Digitally Enhanced Real-World Cohort

Juan Li^{1,2}, MD, PhD; Luo Ren^{1,2}, MD, PhD; Jiao Liu¹, MD, PhD; Yuyi Tang¹, MMed; Run Wang^{1,2}, BSc; Peixin Yang¹, BSc; Jing Zhao¹, BSc; Xiao Chen³, BSc; Zheng Xiang², MSc; Wen Zhong^{2,4}, PhD; Na Zang^{1,2}, MD, PhD; Dapeng Chen^{3*}, MD, PhD; Heping Fang^{1,2*}, MD, PhD; Enmei Liu^{1,2*}, MD, PhD

¹Department of Respiratory Medicine, Children's Hospital of Chongqing Medical University, National Clinical Research Center for Child Health and Disorders, Ministry of Education Key Laboratory of Child Development and Disorders, Chongqing Key Laboratory of Child Rare Diseases in Infection and Immunity, Key Laboratory of Children's Important Organ Development and Diseases of Chongqing Municipal Health Commission, Chongqing, China

²Children's Hospital of Chongqing Medical University, Pediatric Research Institute, Chongqing, China

³Department of Clinical Laboratory, Children's Hospital of Chongqing Medical University, Chongqing, China

⁴Guangzhou National Laboratory, Guangzhou, China

*these authors contributed equally

Corresponding Author:

Enmei Liu, MD, PhD

Department of Respiratory Medicine, Children's Hospital of Chongqing Medical University, National Clinical Research Center for Child Health and Disorders

Ministry of Education Key Laboratory of Child Development and Disorders, Chongqing Key Laboratory of Child Rare Diseases in Infection and Immunity

Key Laboratory of Children's Important Organ Development and Diseases of Chongqing Municipal Health Commission

136 Zhongshan Second Road

Yuzhong District

Chongqing, 400014

China

Phone: 86 023 68370223

Email: emliu186@126.com

Abstract

Background: Childhood asthma, particularly in early life, is often underdiagnosed and poorly characterized in real-world outpatient settings due to diagnostic challenges and resource constraints. A pragmatic, scientifically rigorous, prospective cohort model is urgently needed.

Objective: We aimed to establish and present a cross-sectional baseline analysis of the Clinical Registry of Childhood Asthma, a prospective, longitudinal, and digitally enhanced cohort in outpatient settings, focusing on the diagnostic spectrum of early-life asthma.

Methods: We established the Clinical Registry of Childhood Asthma cohort and performed a cross-sectional analysis of its baseline data. We launched the cohort in March 2024 as an ongoing study, enrolling children (<18 years) with persistent cough and wheezing from a tertiary pediatric referral center in Southwest China. The study used a real-world design, integrating symptom-driven recruitment with standardized electronic medical records, structured electronic patient-reported outcomes, and systematic biobanking of residual biospecimens. Participants were classified as having confirmed, suspected, or excluded asthma based on cross-sectional baseline data.

Results: From March 2024 to August 2025, we enrolled 396 children (median age 4.7 years) from 2296 outpatient visits (enrollment rate 17.2%). Follow-up rates were 26.7% and 43.3% at first and second timepoints, respectively. A comprehensive biorepository was established with serum, plasma, PBMCs, and other blood cell samples (average coverage 74.0%). Most children (267/396, 67.4%) were under 6 years. Patients were stratified into confirmed (131/396, 33.1%), suspected (179/396, 45.2%), and excluded asthma (86/396, 21.7%). Suspected and excluded cases were significantly younger than confirmed cases (median 4.1/3.9 vs 6.6 years, $P<.001$). Comorbidity profiles differed significantly: allergic rhinitis prevailed in confirmed asthma (77/131, 58.8%),

while chronic cough (64/86, 74.4%) and bronchitis (39/86, 45.3%) dominated the excluded group. Type 2 inflammation biomarkers also differed across groups, including aeroallergen sensitization, blood eosinophil count, and fractional exhaled nitric oxide ($P<.001$). Physician-parent diagnostic discordance was most pronounced in suspected asthma (76/134, 56.7%, $P<.001$). Multivariable analyses showed suspected asthma (vs excluded) was associated with respiratory infection as wheezing trigger (odds ratio [OR] 4.41, 95% CI 2.16-9.42, $P<.001$), family history of allergic rhinitis (OR 2.27, 95% CI 1.08-4.99, $P=.03$), and higher blood eosinophil count (OR 1.32 per 100 cells/ μ L, 95% CI 1.05-1.73, $P=.02$). Confirmed asthma (vs suspected) was associated with older age (OR 1.29 per year, 95% CI 1.14-1.47, $P<.001$), allergic rhinitis (OR 4.06, 95% CI 1.99-8.31, $P<.001$), and aeroallergen sensitization (OR 3.83, 95% CI 1.91-7.66, $P<.001$). Bronchitis was negatively associated with an asthma diagnosis across models (OR 0.30 for suspected vs excluded; OR 0.21 for confirmed vs suspected; OR 0.13 for confirmed vs excluded).

Conclusions: The Clinical Registry of Childhood Asthma establishes a feasible cohort in outpatient settings that captures the diagnostic uncertainty of early-life asthma. It identifies a distinct suspected asthma subgroup and reveals significant patient-clinician diagnostic discordance, providing a valuable resource for improving disease management.

(*J Med Internet Res* 2025;27:e78693) doi: [10.2196/78693](https://doi.org/10.2196/78693)

KEYWORDS

asthma; early life; digital health; prospective cohort studies; real-world method; patient selection

Introduction

Asthma is a chronic respiratory disease affecting 262 million people worldwide, with children representing a particularly vulnerable population [1]. High prevalence rates have been reported in urban regions of China and India [2]; yet, early-life asthma remains both undermanaged in clinical practice and underrepresented in research [3]. This is due to several challenges, including the fast-paced nature of pediatric outpatient clinics where most children are treated [4], the inherent heterogeneity of asthma [5], and diagnostic difficulties—especially in children under 6 years old [3]. These factors contribute to low rates of diagnostic confirmation and inhaled corticosteroid adherence, exacerbating the overall disease burden [2,6].

To address these issues, the Global Initiative for Asthma (GINA) 2025 report has introduced, for the first time, diagnostic criteria and a definition for suspected asthma in children under 6 years old [3]. Despite this important step, the characteristics of early-life asthma in outpatient settings remain poorly characterized. This gap is particularly critical since the first 5 years of life constitute a key window for allergen sensitization [7], the foremost risk factor for childhood asthma. Therefore, there is an urgent need to establish well-characterized cohorts of young asthmatic children within outpatient settings to improve understanding and management.

To date, 3 primary approaches have been used to study childhood asthma. Large-scale birth cohorts have advanced our understanding of asthma and allergic diseases [8-12] but require substantial resources and yield limited cases due to disease incidence. Small-scale prospective asthma cohorts often include children with established diagnoses (typically over 6 years old) [13-18]; yet, this may restrict exploration of early disease heterogeneity. Retrospective cohorts based on hospital records [19-25] offer real-world insights but are limited by incomplete data and suboptimal biospecimen preservation. Given these limitations, an integrated model that combines prospective and retrospective approaches within routine clinical practice offers a promising alternative.

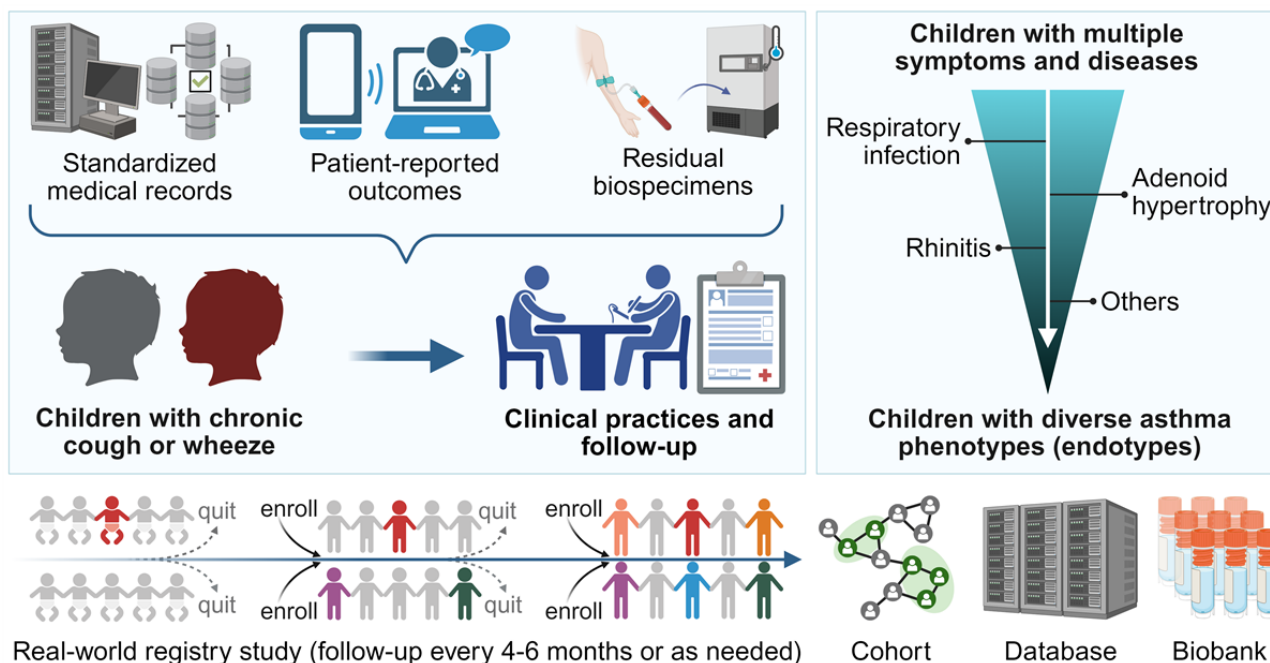
Emerging strategies enhance the feasibility and rigor of such an integrated model. Real-world evidence methodologies and symptom-driven phenotyping enable early identification of children with asthmatic symptoms, even before formal diagnosis [26-29]. Standardized electronic medical records (EMRs) improve data completeness and accessibility [30,31], while electronic patient-reported outcomes (ePROs) capture symptoms and experiences beyond clinical encounters [32-34]. In addition, residual biospecimens from routine testing can be repurposed for molecular endotyping using high-throughput omics technologies, minimizing invasive procedures [35-38]. These tools not only reduce cohort heterogeneity but also facilitate data harmonization and future integration, mirroring successful efforts in major birth cohorts [12,39].

In this study, we developed the Clinical Registry of Childhood Asthma (CRCA)—an outpatient-based integrated research platform that combines symptom-driven recruitment, real-world evidence collection, standardized EMRs, structured ePROs, and residual biospecimens. This framework supports both the establishment of a dynamically updated biorepository and enables phenotyping of early-life asthma. We aimed to characterize children across confirmed, suspected, and excluded asthma categories and identify factors associated with these diagnostic outcomes.

Methods

Study Design

The CRCA is a prospective, longitudinal, digitally enhanced real-world cohort study launched on March 7, 2024, at the Respiratory Clinic of the Children's Hospital of Chongqing Medical University—a tertiary pediatric referral center in Southwest China. Designed to address the critical gap in well-characterized outpatient cohorts for early-life asthma, the CRCA operates as an open, integrated research framework embedded within routine clinical workflows to enable long-term follow-up (Figure 1). This manuscript presents a cross-sectional analysis of the baseline data from this ongoing cohort.

Figure 1. Design and inclusion procedure of the study (created with BioRender.com).

This study used a symptom-driven recruitment strategy to proactively identify and enroll children during visits [27,29]. While this approach may initially include children with a broader spectrum of wheezing illnesses (“off-target” recruitment) [40] and is subject to real-world follow-up challenges [41–43], it is conceptualized not as a limitation but as a fundamental feature enabling the construction of a dynamic, funnel-shaped biorepository for long-term observational research. Through continuous enrollment, the framework accumulates a diverse population, with data collection occurring at scheduled follow-up intervals, which naturally refines over time into a well-characterized cohort of children with confirmed or suspected asthma, while also preserving longitudinal data on the broader natural history of childhood wheezing.

The term “digitally enhanced” refers to our core strategy of synthesizing two complementary data streams collected overtime: (1) hospital-based EMRs for structured clinical data and (2) smartphone-based ePROs for repeatedly capturing symptom and experience data from caregivers beyond clinical encounters. This dual-stream approach ensures comprehensive and continuous longitudinal data acquisition within a high-volume outpatient setting.

The primary outcomes for this article are the detailed cross-sectional characteristics of children with early-life asthma, stratified by diagnostic status (confirmed, suspected, or excluded). Secondary outcomes include metrics related to the implementation of the CRCA study, including the feasibility (>70% ePRO completion and biospecimens collection rates) and sustainability of recruitment efforts. In-depth analysis of longitudinal outcomes is beyond the scope of this initial report, but it is a core purpose of the ongoing cohort. Reporting follows the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines (Multimedia Appendix 1).

Ethical Considerations

The study protocol was approved by the Ethics Committee of the Children’s Hospital of Chongqing Medical University (approval number 2024-37) and registered with China’s National Medical Research Registration and Recording Information System (registration number MR-50-24-049642). Written informed consent was obtained from all participating parents, with additional assent from children aged ≥8 years. No financial compensation was provided. The study imposed no additional diagnostic procedures or financial burdens beyond standard care. All procedures adhered to the Declaration of Helsinki, and participant confidentiality was maintained.

Recruitment and Follow-Up

The longitudinal design of CRCA is implemented through a structured recruitment and follow-up protocol. Eligible participants were children under 18 years of age who presented with persistent or recurrent cough, wheezing, or both, lasting at least 1 month. In addition, asthma needed to be suspected by either the referring practitioner or our study pediatricians. Finally, the child’s clinical assessment or a parental request had to indicate the need for blood tests, such as serum-specific IgE (sIgE) testing. Participants who met the inclusion criteria and elected to continue follow-up at the CRCA clinic were enrolled. It is important to note that while the CRCA registry enrolls children across the entire pediatric age range (<18 years) to establish a comprehensive and longitudinal resource, this initial cross-sectional analysis focuses specifically on the early-life period, where diagnostic uncertainty is greatest.

Enrolled participants are followed prospectively every 4–6 months or as clinically indicated, in accordance with GINA-based management [3]. Study exit was defined as either (1) clinical resolution of symptoms or (2) failure to attend follow-up for over one year. However, given the chronic and relapsing nature of asthma, children who returned to the clinic

after study exit, whether for exacerbations or routine management, were re-eligible for data collection (Figure 1).

Definitions of Asthma Diagnosis

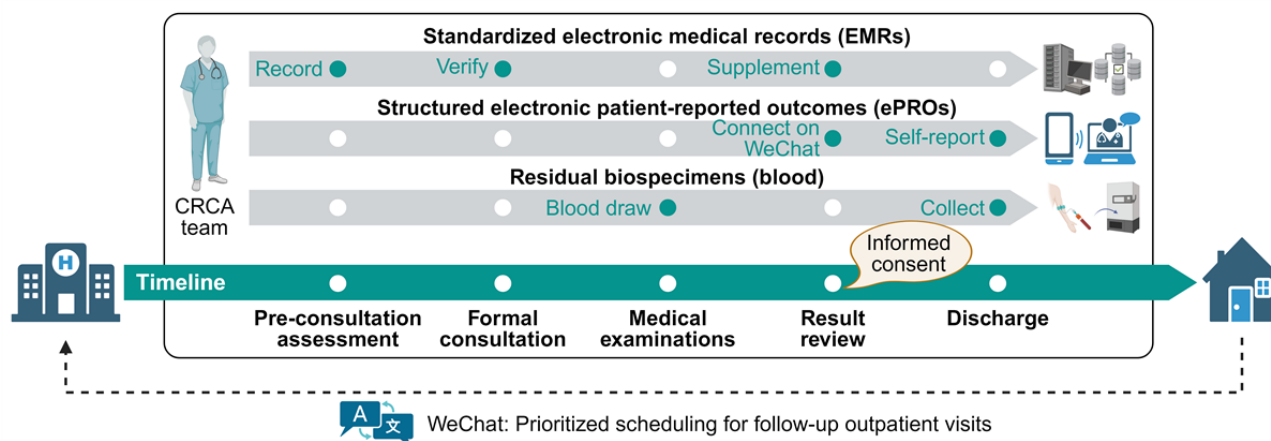
Asthma status was classified for all ages as “confirmed” or “suspected” per GINA 2025 [3]. For children under 6 years, a “confirmed asthma” diagnosis required meeting 3 criteria. First, the child must have had recurrent acute wheezing episodes, which could occur with or without interval symptoms. Second, alternative diagnoses must have been excluded. Third, a timely response to asthma treatment was necessary. A “suspected asthma” classification was applied when there was a highly suggestive clinical history that lacked objective confirmation. This lack of confirmation could be due to the infeasibility of testing or an incomplete treatment response. In such cases, alternative diagnoses were also considered unlikely. For individuals ≥ 6 years, “confirmed asthma” required objective evidence of variable expiratory airflow limitation, demonstrated by positive bronchodilator reversibility, excessive peak expiratory flow variability, or a positive bronchial challenge test. “Suspected asthma” was defined by characteristic symptoms in the absence of confirmatory test results, whether

due to testing infeasibility or negative or equivocal results despite a suggestive history.

Standard EMRs

The CRCA study implemented a standardized EMR template to ensure consistent data collection. The baseline information module captured comprehensive demographic characteristics, including the child’s full name, date of birth, residential address, contact information, and body weight. The clinical assessment module systematically recorded medical data across multiple domains. These included respiratory symptoms, concomitant conditions, and current medications. It also captured treatment responses, physical examination findings, and laboratory results such as complete blood counts and allergen sensitization profiles (serum sIgE tests). Additionally, objective measures like lung function and fractional exhaled nitric oxide (FeNO) were documented. This module also documented complete medical histories, encompassing perinatal events, personal atopy history, previous severe pneumonia episodes, and mechanical ventilation history. Data were initially collected by research staff during preconsultation assessments, then verified and supplemented during formal consultations and test result reviews (Figure 2).

Figure 2. Timeline and workflow of the study (created with BioRender.com). EMR: electronic medical record; ePRO: electronic patient-reported outcome.



ePROs

Parents (primarily mothers) of eligible participants were invited to connect with the official WeChat account of the CRCA study. This account fulfilled 3 essential functions: establishing a direct pediatrician-parent communication channel for clinical inquiries, serving as the platform for ePROs collection, and enabling prioritized scheduling of follow-up outpatient visits.

At enrollment, parents received a voluntary web-based questionnaire administered through WeChat, adapted from our previous and related studies to capture multidimensional quantitative data [44–46]. This instrument collected information across key domains, including sibling composition, family structure, familial atopy history, residential characteristics, pet ownership, indoor air quality, hygiene practices, household chemical usage patterns, health status, asthma risk factors, pharmacological treatment history, and symptom control metrics using age-appropriate Asthma Control Test (ACT) or Childhood Asthma Control Test (C-ACT). Each questionnaire included a

self-rated response quality assessment item to ensure high-quality data collection. The primary analytical objective for this comprehensive environmental exposure data is to determine its associations with key asthma-related outcomes. These outcomes include diagnostic status, symptom control, and exacerbation frequency. Our planned analysis will use multivariate statistical models to quantify these exposure-outcome relationships while adjusting for potential confounders, including demographic and familial risk factors. For longitudinal monitoring, abbreviated follow-up questionnaires collected core demographics alongside age-appropriate ACT or C-ACT measures at each scheduled follow-up time point.

Residual Biospecimens

Residual biospecimens (primarily blood) were collected by CRCA staff through the Clinical Laboratory Department, typically during the afternoon following blood collection. Samples were processed to isolate plasma, serum, peripheral blood mononuclear cells (PBMCs), and other blood cells. Serum

and plasma were aliquoted at 200 μ L per tube, PBMCs at 500 μ L per tube, and other blood cells were stored in one tube per participant. All aliquoted samples were cryopreserved. PBMCs underwent programmed freezing. They were first stored at -80° C for over 12 hours before their final transfer to liquid nitrogen. All samples were ultimately categorized and stored under standardized conditions (-80° C freezers or liquid nitrogen) within our institution's Biobank Center. All associated metadata were tracked electronically. This process followed protocols established by the Western China Birth Cohort study [37]. Residual blood specimens were not used in the present analysis to avoid purposeless consumption. However, the scientific value of these biospecimens is well-established. This is demonstrated by prior multiomics applications in *Mycoplasma pneumoniae* pneumonia research, which used identical specimen collection protocols [38].

Quality Control and Data Security

The CRCA working group comprised trained pediatricians and clinical researchers who met monthly to review and optimize operations. All data were stored locally under anonymized identifiers. Access to data and biospecimens required approval from the principal investigator under stringent security protocols.

A dedicated team managed the EMR data extraction. Initial collection and entry were performed by Juan L and HF, and are now managed by PY and JZ. All EMR data were reviewed and verified by EL. ePROs followed rigorous methodological standards from our previous work [47,48]. Biospecimen handling adhered to stringent Chinese National Standards for human blood biobanking; our group contributed to drafting "Human blood sample biobanking—Part 1: General specifications" (Plan #20253246-T-469) and "Part 2: Peripheral blood mononuclear cells" (Plan #20253247-T-469), publicly accessible on China's National Public Service Platform for Standards Information. This ensures long-term sample quality and readiness for integration with clinical outcomes.

Statistical Analyses

Data analysis and plotting were performed using R 4.4.1, GraphPad Prism 9, and the BioRender website. Categorical variables are presented as frequencies (percentages) while continuous variables are shown as medians (IQRs) following normality assessment. Missing data were not imputed for 2 primary reasons. First, missingness in lung function and FeNO measurements was deemed not missing at random, as it was highly correlated with disease severity and clinical progression. Second, missing questionnaire data typically involved entire unreturned forms; imputation of such large-scale missingness was considered to introduce unacceptable bias. Therefore, all analyses were performed on complete cases.

Participants were stratified by diagnostic category (confirmed, suspected, and excluded asthma). Comparative analyses applied

chi-square tests for categorical variables, and Kruskal-Wallis tests with Bonferroni correction for multiple comparisons. A 2-sided $P < .05$ was considered statistically significant. For multivariable analyses, three logistic regression models were constructed: (1) Model 1 compared suspected versus excluded asthma; (2) Model 2 compared confirmed versus suspected asthma; and (3) Model 3 compared confirmed versus excluded asthma. We used a tiered variable selection strategy to enhance robustness. Univariate screening was conducted at three thresholds ($P < .30$, $P < .20$, and $P < .10$). The model using the strictest threshold ($P < .10$) served as the primary final model, while those using more lenient thresholds ($P < .30$ and $P < .20$) were used in sensitivity analyses to evaluate the stability of core associations. Within each tier, forward stepwise likelihood ratio selection was applied, with age and sex retained in all models irrespective of significance. All models are based on the cross-sectional baseline diagnosis. The stability of these diagnoses overtime and their evolution will be the subject of future longitudinal analyses of this cohort.

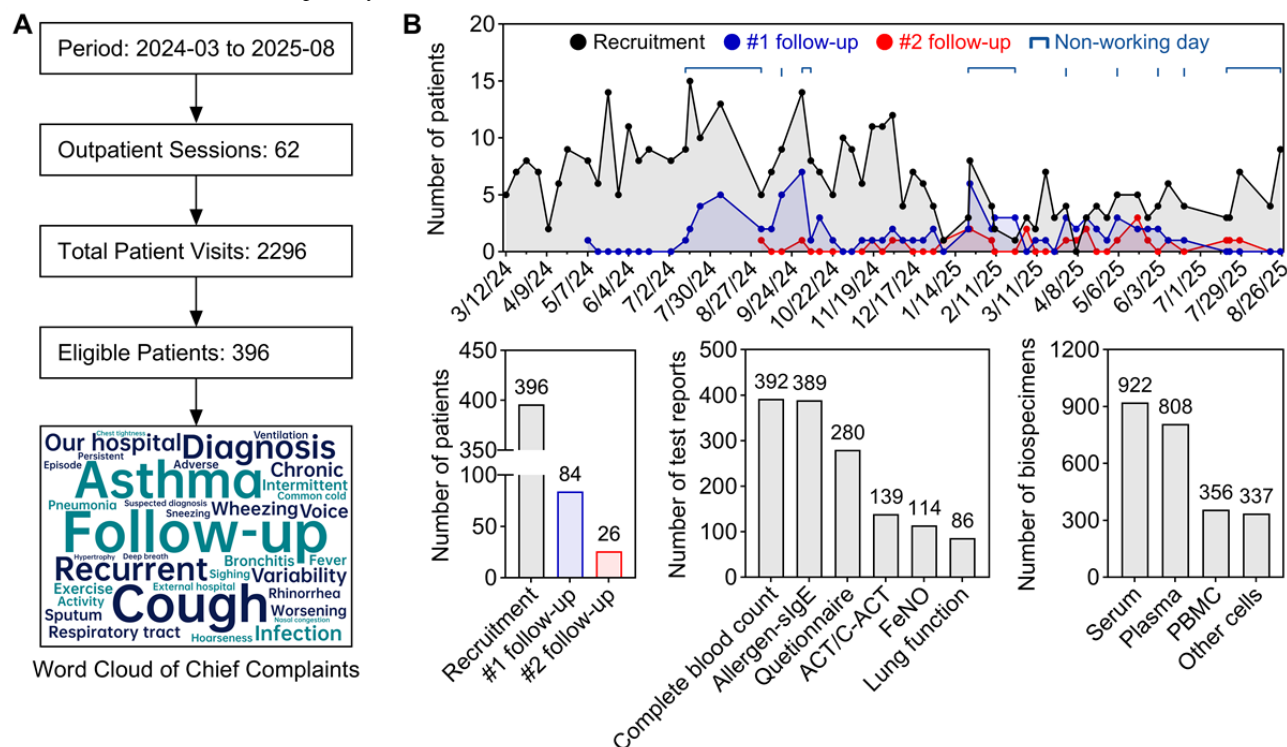
Results

Implementation and Feasibility of the CRCA Study

Between March 2024 and August 2025 (Figure 3A), we organized 62 weekly outpatient sessions, evaluating an average of 37 patients per session (total 2296 visits; mean consultation time: 7.3 minutes). From this population, 396 eligible patients were enrolled (enrollment rate: 17.2%). Initial and second follow-up assessments were completed by 26.7% (84/315) of eligible patients at the first time point and 43.3% (26/60) of those eligible for the second follow-up, respectively (Figure 3B). Temporal patterns indicated that follow-up completion rates peaked during school vacations and national holidays, reaching 1.4 times the baseline. These results demonstrate the feasibility of implementing a comprehensive research framework within the constraints of a high-throughput pediatric clinic, and underscore the need for flexible, family-centered follow-up strategies in real-world studies.

The integrated data and biospecimen repository constitutes a core output of the CRCA study. All enrolled children have standardized EMRs, which include 392 complete blood count reports, 389 allergen-sIgE reports, 86 lung function tests, 114 FeNO measurements, 280 parental questionnaires, and 139 ACT or C-ACT assessments. Furthermore, the biorepository has accumulated 2423 residual biospecimens (Figure 3B), with coverage rates as follows: serum samples from 357 (90.2%) children, plasma from 317 (80.1%), PBMCs from 171 (43.2%), and other blood cell samples from 327 (82.6%), yielding an average coverage of 74.0% across these specimen types. The rate of hemolysis occurrence was 4.0% (16/396). These coverage rates meet the prespecified feasibility indicators for the biorepository component of the study.

Figure 3. Implementation and feasibility of the CRCA study. (A) Enrollment workflow and chief complaint analysis; (B) Recruitment and follow-up timeline, EMRs collection, and biorepository construction. ACT: Asthma Control Test; C-ACT: Childhood Asthma Control Test.



Clinical Characteristics and Diagnostic Patterns

The CRCA successfully captured a predominantly young cohort, with 267 (267/396, 67.4%) children younger than 6 years. Patients were classified into 3 diagnostic categories: confirmed asthma (131/396, 33.1%), suspected asthma (179/396, 45.2%), and excluded asthma (86/396, 21.7%; Figure 4A). Comorbidity profiles differed markedly among groups (Figure 4B). Allergic rhinitis was most prevalent in the confirmed asthma group (77/131, 58.8%). Children in the excluded asthma group were

most frequently diagnosed with chronic cough (64/86, 74.4%) or bronchitis (39/86, 45.3%). In contrast, the suspected asthma group showed a lower prevalence of additional diagnoses, suggesting a clinically distinct, “pure” early wheezing phenotype that is difficult to classify using current criteria.

As shown in Table 1, children with suspected or excluded asthma were significantly younger than those with confirmed asthma ($P < .001$), indicating that the under-6 age group largely comprises uncertain or excluded cases.

Figure 4. Age and diagnosis distribution of the patients. (A) Characteristics of age and diagnosis; (B) Patterns of coexisting conditions across asthma diagnostic groups.

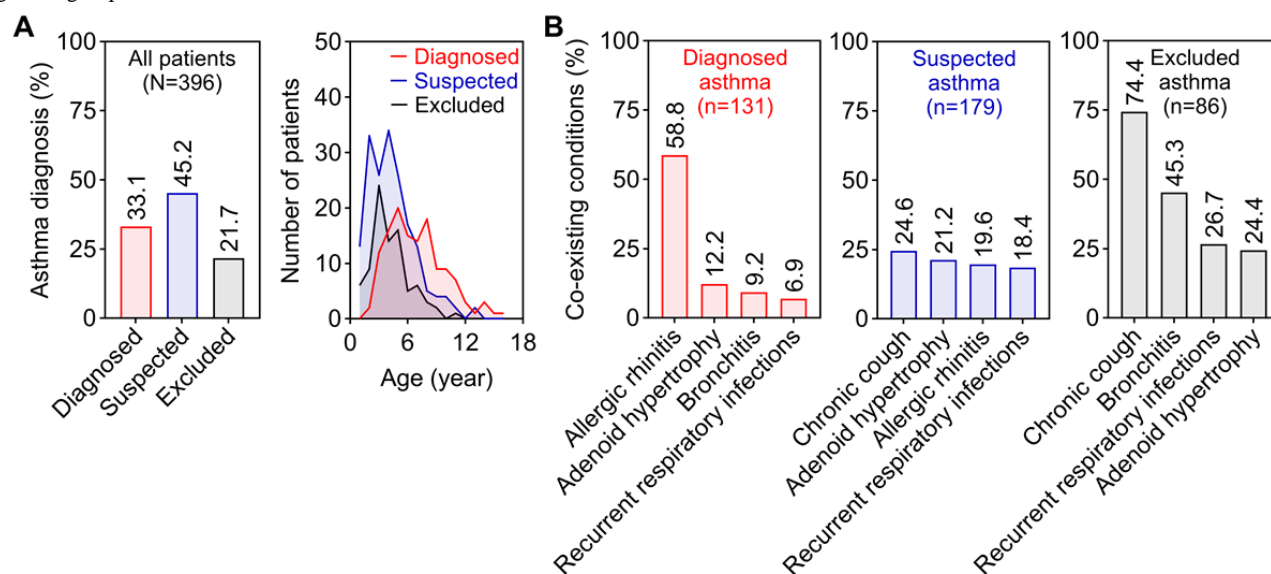


Table 1. Characteristics of the patients according to diagnosis groups.

	Overall (n=396)	Diagnosis groups			P values
		Confirmed	Suspected	Excluded	
Age (year), median (IQR)	4.7 (3.7)	6.6 (3.8) ^{a,b}	4.1 (3.3) ^c	3.9 (2.4) ^a	<.001
Sex, n (%)					.38
Male	237 (59.8)	82 (62.6)	109 (60.9)	46 (53.5)	
Female	159 (40.2)	49 (37.4)	70 (39.1)	40 (46.5)	
Province, n (%)					.26
Sichuan	170 (42.9)	55 (42.0)	74 (41.3)	41 (47.7)	
Chongqing	168 (42.4)	61 (46.6)	75 (41.9)	32 (37.2)	
Guizhou	44 (11.1)	13 (9.9)	24 (13.4)	7 (8.1)	
Others	14 (3.5)	2 (1.5)	6 (3.4)	6 (7.0)	
Term or preterm birth, n (%)					.75
Term	368 (92.9)	120 (91.6)	168 (93.9)	80 (93.0)	
Preterm	28 (7.1)	11 (8.4)	11 (6.1)	6 (7.0)	
Personal history of eczema, n (%)					.01
Yes	230 (58.1)	79 (60.3)	113 (63.1) ^b	38 (44.2) ^a	
No	166 (41.9)	52 (39.7)	66 (36.9)	48 (55.8)	
Personal history of severe pneumonia or invasive mechanical ventilation, n (%)					.95
Yes	26 (6.6)	9 (6.9)	11 (6.1)	6 (7.0)	
No	370 (93.4)	122 (93.1)	168 (93.9)	80 (93.0)	
First visit for this problem, n (%)					<.001
Yes	146 (36.9)	14 (10.7) ^{a,b}	84 (46.9) ^c	48 (55.8) ^c	
No	250 (63.1)	117 (89.3)	95 (53.1)	38 (44.2)	
Completion of initial follow-up, n=315, n (%)					<.001
Yes	84 (73.3)	48 (45.3) ^b	28 (20.3) ^c	8 (11.3) ^c	
No	231 (26.7)	58 (54.7)	110 (79.7)	63 (88.7)	
Coexisting conditions (nonexclusive), n (%)					
Allergic rhinitis	119 (30.1)	77 (58.8) ^{a,b}	35 (19.6) ^c	7 (8.1) ^c	<.001
Chronic cough	113 (28.5)	5 (3.8) ^{a,b}	44 (24.6) ^{b,c}	64 (74.4) ^{b,c}	<.001
Bronchitis	79 (19.9)	12 (9.2) ^b	28 (15.6) ^b	39 (45.3) ^{b,c}	<.001
Adenoid hypertrophy	75 (18.9)	16 (12.2)	38 (21.2)	21 (24.4)	.046
Recurrent respiratory infections	65 (16.4)	9 (6.9) ^b	33 (18.4) ^c	23 (26.7) ^c	<.001
Pneumonia	21 (5.3)	4 (3.1)	10 (5.6)	7 (8.1)	.26
Positive rate of serum allergen-specific IgE (nonexclusive), n=390, n (%)					
Aeroallergens	144 (36. %)	85 (66.9) ^{a,b}	44 (24.7) ^c	15 (17.6) ^c	<.001
Food allergens	110 (28.2)	42 (33.1)	45 (25.3)	23 (27.1)	.32
BEC^d (cells/μL), n=392, median (IQR)	250 (298)	360 (423) ^{a,b}	250 (250) ^{b,c}	170 (145) ^{b,c}	<.001
FEV₁^e %Pred (%), n=83, median (IQR)	100.1 (19.6)	97.3 (14.9)	102.4 (26.5)	109.3 (20.3)	.25
FeNO^f (ppb), n=114, median (IQR)	16.5 (17.0)	22.0 (23.0) ^a	12.0 (7.0) ^c	11.0 (11.8)	<.001

^aAdjusted P value <.05 compared with the suspected asthma group.^bAdjust P value <.05 compared with the excluded asthma group.

^cAdjusted *P* value <.05 compared with the confirmed asthma group.

^dBEC: blood eosinophil count.

^eFEV1%Pred: Forced Expiratory Volume in 1 second as a percentage of Predicted.

^fFeNO: fractional exhaled nitric oxide.

These groups also included more first-time visitors ($P<.001$), highlighting the initial visit as a critical yet uncertain diagnostic window. Significant differences in comorbidity patterns were observed across diagnostic categories. Among children with a previous asthma treatment history ($n=250$), specialist evaluation confirmed asthma in only 46.8% (117/250) and definitively excluded it in 15.2% (38/250), underscoring substantial community-level under- and overdiagnosis. As expected, objective measures of type 2 inflammation and lung function—including aeroallergen sensitization, blood eosinophil counts, and FeNO—differed significantly across groups ($P<.001$), supporting the clinical validity of the diagnostic stratification.

Self-Reported Characteristics and Patient-Physician Discordance

The study achieved a 70.7% (280/396) questionnaire completion rate, with no significant demographic or diagnostic differences between responders and nonresponders. A central finding was a pronounced discordance between physician diagnoses and

parental disease perception ($P<.001$; Table 2). Only 75.6% (68/90) of parents of children with physician-confirmed asthma acknowledged the diagnosis, while merely 57.1% (32/56) of those whose children were ruled out for asthma accepted this conclusion. This difference in diagnostic consistency was most pronounced in the suspected asthma group (discordance rate: 76/134, 56.7%), highlighting a major communication gap in clinical management.

Beyond this discordance, analysis of clinical and environmental factors revealed several patterns more common in the confirmed and suspected asthma groups. Respiratory infections were the predominant wheezing trigger in these groups (62/90, 68.9% and 84/134, 62.7%, respectively). Similarly, seasonal exacerbations in spring and winter were notably more frequent. Inhaled medication use was reported in 60.3% (135/224) of these combined groups, compared to 52.5% (147/280) in the entire cohort. Despite this, 22.3% of patients had uncontrolled symptoms (ACT or C-ACT < 20), indicating a substantial need for improved treatment adherence and effectiveness in real-world practice.

Table 2. Self-reported characteristics of the patient according to diagnosis groups.

	Overall (n=280)	Diagnosis groups			P values
		Confirmed	Suspected	Excluded	
Patient-reported asthma, n (%)					
Confirmed	122 (43.6)	68 (75.6) ^{a,b}	50 (37.3) ^{b,c}	4 (7.1) ^{b,c}	<.001
Suspected	96 (34.3)	18 (20.0)	58 (43.3)	20 (35.7)	
Excluded	62 (22.1)	4 (4.4)	26 (19.4)	32 (57.1)	
Patient-physician discordance, n (%)	122 (43.6)	22 (24.4) ^a	76 (56.7) ^c	24 (42.9)	<.001
Family history of related diseases in first-degree relatives (nonexclusive), n (%)					
Asthma	45 (16.1)	17 (18.9)	24 (17.9)	4 (7.1)	.12
Allergic rhinitis	104 (37.1)	33 (36.7)	56 (41.8)	15 (26.8)	.15
Atopic dermatitis	47 (16.8)	16 (17.8)	27 (20.1)	4 (7.1)	.09
Food allergies	24 (8.6)	11 (12.2)	7 (5.2)	6 (10.7)	.15
Triggers of wheezing episodes (nonexclusive), n (%)					
Respiratory infection	162 (57.9)	62 (68.9) ^b	84 (62.7) ^b	16 (28.6) ^{b,c}	<.001
Cold weather	87 (31.1)	35 (38.9) ^b	42 (31.3)	10 (17.9) ^c	.03
Exercise	57 (20.4)	24 (26.7)	25 (18.7)	8 (14.3)	.16
Inhalation exposure	34 (12.1)	17 (18.9)	13 (9.7)	4 (7.1)	.05
No risk factors	30 (10.7)	10 (11.1)	15 (11.2)	5 (8.9)	.89
Seasonality of respiratory catarrhal symptoms (nonexclusive), n (%)					
Spring	88 (31.4)	35 (38.9) ^b	45 (33.6) ^b	8 (14.3) ^c	.006
Summer	13 (4.6)	5 (5.6)	6 (4.5)	2 (3.6)	.85
Autumn	66 (23.6)	21 (23.3)	39 (29.1) ^b	6 (10.7) ^a	.02
Winter	101 (36.1)	39 (43.3) ^b	51 (38.1) ^b	11 (19.6) ^{b,c}	.01
Indoor environmental factors (nonexclusive), n (%)					
Indoor condensation	71 (25.4)	22 (24.4)	36 (26.9)	13 (23.2)	.85
Humid air	42 (15.0)	14 (15.6)	21 (15.7)	7 (12.5)	.84
Musty smell	20 (7.1)	8 (8.9)	7 (5.2)	5 (8.9)	.49
Water leakage	50 (17.9)	16 (17.8)	29 (21.6)	5 (8.9)	.11
Sunlight exposure	269 (95.7)	88 (97.8)	127 (94.8)	54 (96.4)	.52
Indoor plants	110 (39.3)	32 (35.6)	56 (41.8)	22 (39.3)	.65
Indoor smoking	132 (47.1)	44 (48.9)	59 (44.0)	29 (51.8)	.57
Cockroach present	38 (13.6)	13 (14.4)	19 (14.2)	6 (10.7)	.78
Pets present	28 (10.0)	11 (12.2)	9 (6.7)	8 (14.3)	.20
Stuffed toys	134 (47.9)	40 (44.4)	68 (50.7)	26 (46.4)	.63
Household hygiene products usage (nonexclusive), n (%)					
Air purifier	28 (10.0)	9 (10.0)	14 (10.4)	5 (8.9)	.95
Humidifier	55 (19.6)	13 (14.4)	33 (24.6)	9 (16.1)	.13
Dehumidifier	5 (1.8)	0 (0)	4 (3.0)	1 (1.8)	.26
Vacuum cleaner	54 (19.3)	15 (16.7)	31 (23.1)	8 (14.3)	.28
Fruit detergent	65 (23.2)	18 (20.0)	32 (23.9)	15 (26.8)	.62
Bathroom cleaner	204 (72.9)	68 (75.6)	92 (68.7)	44 (78.6)	.29
Laundry disinfectant	81 (28.9)	23 (25.6)	41 (30.6)	17 (30.4)	.69

	Overall (n=280)	Diagnosis groups			P values
		Confirmed	Suspected	Excluded	
Alcohol spray	91 (32.5)	32 (35.6)	42 (31.3)	17 (30.4)	.75
Medication use (nonexclusive), n (%)					
Inhaled medications	147 (52.5)	65 (72.2) ^{a,b}	70 (52.2) ^{b,c}	12 (21.4) ^{b,c}	<.001
Leukotriene receptor antagonists	67 (23.9)	24 (26.7)	36 (26.9)	7 (12.5)	.08
Antiallergic medications	71 (25.4)	31 (34.4) ^b	35 (26.1) ^b	5 (8.9) ^{b,c}	.003
Allergen immunotherapy	5 (1.8)	3 (3.3)	2 (1.5)	0 (0)	.32
Biologics	0 (0)	0 (0)	0 (0)	0 (0)	—
No medication	34 (12.1)	10 (11.1)	16 (11.9)	8 (14.3)	0.85
ACT^d or C-ACT^e (n=139), n (%)					
Controlled (≥20)	108 (77.7)	54 (74.0)	45 (80.4)	9 (90.0)	.43
Uncontrolled (<20)	31 (22.3)	19 (26.0)	11 (19.6)	1 (10.0)	

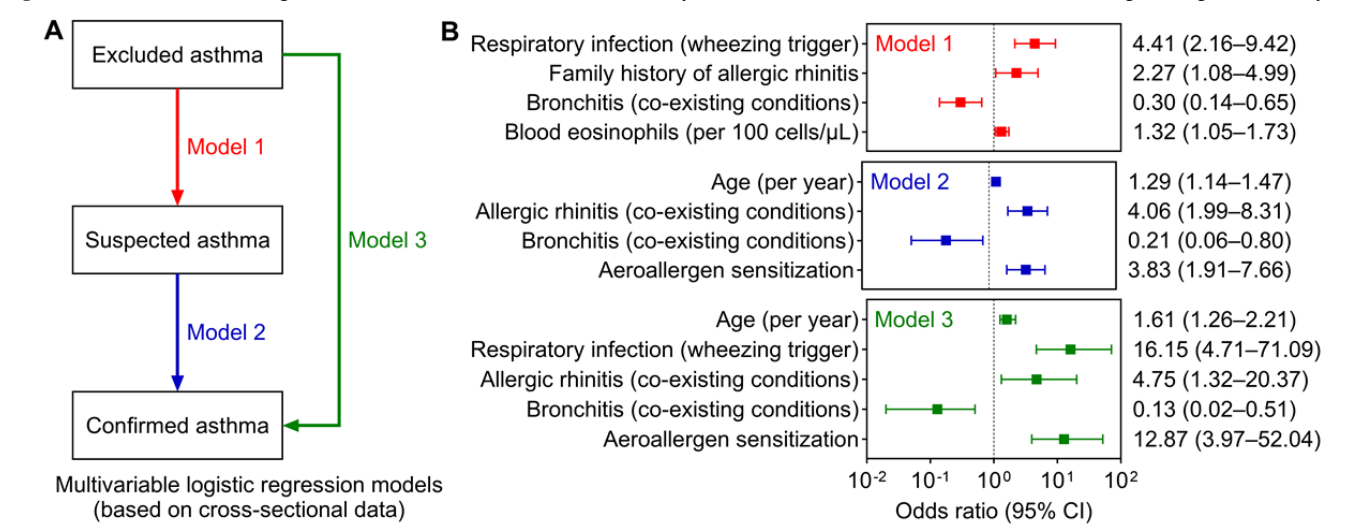
^aAdjusted *P* value <.05 compared with the suspected asthma group.
^bAdjust *P* value <.05 compared with the excluded asthma group.
^cAdjusted *P* value <.05 compared with the confirmed asthma group.
^dACT: Asthma Control Test.
^eC-ACT: Childhood Asthma Control Test.

Determinants of Diagnostic Outcomes

Three multivariable logistic regression models were constructed to identify factors associated with asthma diagnostic categories in this cross-sectional cohort (Figure 5A). In Model 1 (suspected vs excluded asthma), respiratory infection as a wheezing trigger (odds ratio [OR] 4.41, 95% CI 2.16-9.42, *P*<.001), family

history of allergic rhinitis (OR 2.27, 95% CI 1.08-4.99, *P*=.03), and higher blood eosinophil counts (per 100 cells/μL, OR 1.32, 95% CI 1.05-1.73, *P*=.02) were significantly associated with suspected asthma (Figure 5B). In contrast, bronchitis was associated with reduced odds of suspected asthma (OR 0.30, 95% CI 0.14-0.65, *P*=.002).

Figure 5. Determinants of diagnostic outcomes. (A) Schematic of the analytical models; (B) Results of the multivariable logistic regression analysis.



Model 2 (confirmed vs suspected asthma) showed that confirmed asthma was associated with older age (per year, OR 1.29, 95% CI 1.14-1.47, *P*<.001), allergic rhinitis (OR 4.06, 95% CI 1.99-8.31, *P*<.001), and aeroallergen sensitization (OR 3.83, 95% CI 1.91-7.66, *P*<.001). Bronchitis remained negatively associated with confirmed asthma (OR 0.21, 95% CI 0.06-0.80, *P*=.02). These association patterns were consistent in Model 3 (confirmed vs excluded asthma). The robustness of these findings was confirmed through sensitivity analyses

(Multimedia Appendix 2), supporting the clinical validity of the diagnostic stratification and highlighting specific features that distinguish asthma from alternative diagnoses.

Discussion

Principal Findings

This study describes the implementation of a prospective, longitudinal, and digitally enhanced real-world cohort

framework that incorporated symptom-driven recruitment, standardized EMRs, ePROs, and residual biospecimen collection within a routine outpatient setting. Leveraging this framework, we enrolled a diagnostically heterogeneous population of children, with a focus on those younger than 6 years, and characterized their distinct clinical profiles according to categories of confirmed, suspected, or excluded asthma. These findings elucidate the broad spectrum of disease presentation in early life and highlight subgroups that have been historically challenging to systematically study, particularly in outpatient settings.

Characteristics of Early-Life Asthma

The current data from the CRCA study provide an initial insight into the characteristics of young children presenting with asthmatic symptoms in an outpatient clinic. The high proportion of participants classified as suspected asthma (179/396, 45.2%), who were also the youngest at enrollment, reflects the diagnostic uncertainty common in early life. This finding aligns with a previous study using the term “reactive airway disease,” which reported a similarly high prevalence of 61.8% (249/403) in a comparable population [49]. The clinical profile of this group, which showed a lower prevalence of coexisting conditions such as allergic rhinitis and a lower rate of aeroallergen sensitization compared to children with confirmed asthma, yet also differed from the excluded asthma group in features such as lower rates of infectious conditions, suggesting that they may represent a distinct clinical group. This is particularly relevant because although the GINA 2025 criteria provide a definition for suspected asthma in young children, diagnosis remains primarily based on clinical history and lacks reliable biomarkers to support stratification [3]. Thus, the CRCA framework, with its integrated biospecimen repository, is well-positioned to offer future insights in this area. This observation warrants further longitudinal investigation to understand its implications for disease progression and management.

A notable finding was the discrepancy between physician diagnoses and parental perception of the child’s condition. The fact that a substantial proportion of parents did not concur with the physician’s diagnosis, regardless of whether asthma was confirmed or excluded, points to potential challenges in clinical communication and family education [50,51]. This discordance was most pronounced in the suspected asthma group (76/134, 56.7%), which is highly important since misalignment in perception in this particular group may lead to both under- and overtreatment, affecting disease management and medication use. This disconnect may be one factor influencing treatment adherence and outcomes in this age group.

A further focus of the CRCA is on early-life environmental exposures [52], which are currently captured largely through ePROs. Although no statistically significant differences were observed in the current group comparisons, this is likely due to insufficient sample size. Notably, the suspected asthma group showed the highest reported rate of household water leakage (29/134, 21.6%, $P=.11$) as well as the highest frequency of humidifier use (33/134, 24.6%, $P=.13$). These findings are of potentially important given that residential environments in Southwest China are already relatively humid, conditions that

are closely associated with mold sensitization and asthma development in children [53-55]. Furthermore, CRCA’s emphasis on investigating household and personal disinfection and hygiene behaviors aligns with the theoretical frameworks of the hygiene hypothesis and the epithelial barrier hypothesis. As the sample size increases, this focus may support more detailed subgroup analyses in the future. In future phases, in addition to blood specimens, the CRCA plans to include the collection and biobanking of indoor dust samples to further enrich the repository. We also intend to expand our data collection to include maternal health and perinatal factors, thereby providing a more comprehensive assessment of early-life exposures.

To better characterize the distinguishing features of children across diagnostic categories, we constructed three regression models to simulate clinical diagnostic pathways. It must be noted, however, that these models were based on cross-sectional data and thus do not imply causality. We found that infectious triggers of wheezing, a family history of allergic rhinitis, and peripheral blood eosinophil count were the factors most supportive of a suspected asthma diagnosis; these three factors are not currently emphasized in the GINA 2025 guidelines [3]. Moving further along the diagnostic spectrum, older age, comorbid allergic rhinitis, and aeroallergen sensitization were identified as the factors most strongly associated with a confirmed asthma diagnosis. Furthermore, a coexistence of bronchitis was the primary factor arguing against asthma, which is consistent with GINA criteria. These findings align broadly with current clinical understanding [56], yet underscore the particular importance of comorbid allergic rhinitis and sensitization. Moreover, older age emerged as a strongly supportive factor for confirmed asthma, likely reflecting the gradual development of lung function and allergen sensitization throughout childhood. Although this may also be influenced by current diagnostic processes, it reinforces the notion that asthma diagnosis should be viewed through a developmental lens [49], potentially requiring a period of ongoing assessment rather than being considered a binary outcome determined in a single visit.

Methodological Considerations Regarding the CRCA Framework

The CRCA framework demonstrates a practical operational model tailored to high-demand clinical environments like China’s, where implementing research poses substantial challenges [57]. Its shared-responsibility approach, which distributes data and biospecimen collection tasks between clinicians and participants, helps sustain operations within high-volume outpatient workflows. Rather than merely listing its components, the methodological value of CRCA lies in how these features collectively address specific gaps in real-world childhood asthma research. This is evident when contrasted with established international registries (Multimedia Appendix 3), which often prioritize confirmed diagnoses and may lack integrated biospecimen collection, but have substantially larger sample sizes than the CRCA [58-66].

The symptom-driven recruitment strategy, which is seldom used in conventional registries that typically require confirmed diagnoses, enables the enrollment of a heterogeneous patient

population. This approach mirrors the diagnostic uncertainty common in early-life asthma and allows CRCA to capture disease features from the earliest symptomatic stages. Standard EMR systems are designed for clinical rather than research use, which often results in fragmented and incomplete data [67,68]. To address this inherent limitation, CRCA implemented standardized EMR templates and a preconsultation data collection step. This approach helps bridge the gap between clinical efficiency and research data quality in time-constrained environments. Furthermore, while ePROs are often optional or partially implemented in other registries, they constitute a core component of CRCA, which enhances its potential scalability and enables richer patient-centric data capture [32,33]. Similarly, biospecimen collection remains uncommon in large-scale registries due to clinical and logistical burdens; accordingly, CRCA's residual sample-based model offers a pragmatic and scientifically valuable alternative [35-37,69]. This composition of interoperable, standardized modules suggests that portability to other clinical settings is possible.

It is important to position CRCA appropriately among existing studies. While large-scale, resource-intensive cohorts such as COPSAC have generated landmark findings through long-term follow-up and substantial infrastructure [9], CRCA operates within a different context and at a different developmental stage. Its value lies not in direct comparison, but in its seamless integration into routine clinical practice. This integration supports dynamic enrollment and scalable, real-world implementation, aligning with contemporary recommendations for integrating multiomics platforms and target trial methodologies to advance precision medicine under pragmatic conditions [28]. With further refinement, this clinic-embedded model may offer an adaptable framework for real-world evidence generation, especially in resource-constrained settings [39,70].

A challenge observed in this study was the initial follow-up rate (48/106, 45.3% among confirmed cases and 28/138, 20.3% among suspected cases), which reflects broader difficulties in pediatric asthma research. Contributing factors included the geographical dispersion of patients, gaps in parental awareness, and the inherent constraints of a regional referral center operating within a tiered health care system. These issues are not unique to CRCA, as comparable studies in the United States have reported similar follow-up rates (22.6%-55.0%) [41-43]. These realities underscore the importance of developing digital solutions for remote monitoring and self-management—a key future direction for CRCA [71,72]. In response, we have initiated the development of a digital medicine platform within the established CRCA WeChat public account. This platform is designed to integrate educational content, a mini-program for patient reporting, and an AI agent for interactive questions and answers, aiming to improve follow-up adherence and long-term engagement [73]. Additionally, the identification of an “off-day follow-up pattern” also suggests a need for more flexible

scheduling options, such as night clinics, to improve adherence to review visits [74,75].

Looking forward, the “digitally enhanced” framework of CRCA could be positioned to support future innovation. We envision that the integrated data from EMRs and ePROs may serve as a basis for developing AI models that could aid in risk stratification. Similarly, the WeChat platform can be leveraged to extend care beyond the clinic, for instance, through remote monitoring, educational content, and AI-facilitated questions and answers. As these digital tools mature, CRCA could evolve into a testbed for evaluating scalable solutions that may improve asthma care in diverse clinical settings.

Limitations

Several limitations should be considered when interpreting our findings. First, as a single-center study conducted in Southwest China, the CRCA cohort primarily comprises patients from Chongqing and neighboring provinces, which may limit the generalizability of our findings to other geographic or socioeconomic contexts. Second, the symptom-driven, outpatient-based recruitment strategy may introduce selection bias, as enrolled children likely represent a more symptomatic or health-seeking population than the general community. Third, the requirement for blood testing (serum sIgE or other tests), though aligned with the goal of residual biospecimen banking, may have excluded children with already confirmed asthma who were under routine treatment, further contributing to selection bias. Fourth, although the CRCA model successfully addressed recruitment challenges, follow-up rates remained suboptimal, particularly among younger children and those with uncertain diagnoses. This attrition may bias longitudinal analyses if loss to follow-up is associated with disease severity or remission. Finally, while we implemented standardized EMR templates and ePROs to enhance data quality, missingness in certain objective measures (eg, lung function, FeNO) was common and not imputed, which may affect the completeness of phenotypic characterization. This largely reflects age-specific clinical guidelines and efforts to minimize burden; future efforts will therefore prioritize novel, feasible biomarkers to strengthen objective profiling.

Conclusions

The CRCA study demonstrates the feasibility of implementing a prospective, longitudinal, and digitally enhanced real-world cohort within routine pediatric outpatient practice. This initiative successfully captures the diagnostically complex population of children with asthmatic symptoms, with a particular focus on early-life presentations, and delineates a distinct clinical subgroup of children with suspected asthma. By integrating symptom-driven recruitment, standardized digital data collection, and biospecimen banking, the CRCA establishes a scalable platform for real-world evidence generation and may provide a valuable foundation for future research into asthma endotypes and personalized management approaches.

Acknowledgments

The authors thank the nursing staff (Rongli Li and Chaojin Li), Biobank Center staff (Tengteng Zhang and Yue Lu), our traditional asthma cohort team (Xiang Wen, Dan Zeng, Juan Zhou, and Weiguo Li), and the physical examination staff (Kangyi Ren). We

also gratefully acknowledge the Biobank Center at the Children's Hospital of Chongqing Medical University for the professional storage and management of the biospecimens.

This study was supported by the Noncommunicable Chronic Diseases—National Science and Technology Major Project (2024ZD0541100) and Major Program of the National Clinical Research Center for Child Health and Disorders in Children's Hospital of Chongqing Medical University (NCRCCHD-2023-MP-01). The funder had no role in the preparation, review, or approval of the manuscript or decision to submit it for publication.

Authors' Contributions

Juan L, LR, and Jiao L contributed equally to this work and should be considered joint first authors. DC, HF, and EL contributed equally to this work and should be considered joint corresponding authors.

Conceptualization: Juan Li (equal), LR (supporting), Jiao L (supporting), HF (lead), EL (equal).

Data curation: Juan L (lead), Jiao L (equal), RW (supporting), PY (supporting), JZ (supporting), ZX (supporting), HF (equal).

Formal analysis: Juan L (equal), YT (supporting), HF (lead).

Funding acquisition: WZ (equal), HF (equal), EL (lead).

Investigation: Juan L (equal), Jiao L (equal), RW (supporting), PY (supporting), JZ (supporting), XC (supporting), HF (equal), EL (lead).

Methodology: Juan L (equal), LR (equal), Jiao L (equal), YT (supporting), RW (supporting), DC (supporting), HF (lead).

Project administration: DC (equal), EL (lead).

Resources: XC (equal), ZX (equal), NZ (equal), DC (equal), EL (lead).

Supervision: LR (equal), WZ (supporting), NZ (supporting), DC (supporting), EL (lead).

Validation: Jiao L (equal), LR (lead).

Visualization: Juan L (equal), HF (lead).

Writing - Original draft: Juan L (equal), HF (lead).

Writing - Review & editing: LR (supporting), Jiao L (supporting), YT (supporting), EL (lead).

Conflicts of Interest

Non declared.

Multimedia Appendix 1

STROBE checklist.

[\[PDF File \(Adobe PDF File\), 202 KB-Multimedia Appendix 1\]](#)

Multimedia Appendix 2

Multivariable Logistic Regression and Sensitivity Analyses.

[\[PDF File \(Adobe PDF File\), 183 KB-Multimedia Appendix 2\]](#)

Multimedia Appendix 3

Comparison of the CRCA Cohort with Other Registry Studies.

[\[PDF File \(Adobe PDF File\), 175 KB-Multimedia Appendix 3\]](#)

References

1. Shin YH, Hwang J, Kwon R, Lee SW, Kim MS, GBD 2019 Allergic Disorders Collaborators, et al. Global, regional, and national burden of allergic disorders and their risk factors in 204 countries and territories, from 1990 to 2019: A systematic analysis for the global burden of disease study 2019. *Allergy*. 2023;78(8):2232-2254. [\[FREE Full text\]](#) [doi: [10.1111/all.15807](https://doi.org/10.1111/all.15807)] [Medline: [37431853](https://pubmed.ncbi.nlm.nih.gov/37431853/)]
2. Jayasooriya SM, Devereux G, Soriano JB, Singh N, Masekela R, Mortimer K, et al. Asthma: epidemiology, risk factors, and opportunities for prevention and treatment. *Lancet Respir Med*. 2025;13(8):725-738. [doi: [10.1016/S2213-2600\(24\)00383-7](https://doi.org/10.1016/S2213-2600(24)00383-7)] [Medline: [40684789](https://pubmed.ncbi.nlm.nih.gov/40684789/)]
3. Global strategy for asthma management and prevention. Global Initiative for Asthma. 2025. URL: <https://ginasthma.org/> [accessed 2025-10-11]
4. Qi Y, Shi P, Chen R, Zhou Y, Liu L, Hong J, et al. Characteristics of childhood allergic diseases in outpatient and emergency departments in Shanghai, China, 2016-2018: a multicenter, retrospective study. *BMC Pediatr*. 2021;21(1):409. [\[FREE Full text\]](#) [doi: [10.1186/s12887-021-02880-0](https://doi.org/10.1186/s12887-021-02880-0)] [Medline: [34535106](https://pubmed.ncbi.nlm.nih.gov/34535106/)]
5. Fuhlbrigge AL, Sharma S. Unraveling the heterogeneity of asthma: decoding subtypes of asthma. *J Allergy Clin Immunol*. 2025;156(1):41-50. [doi: [10.1016/j.jaci.2025.03.008](https://doi.org/10.1016/j.jaci.2025.03.008)] [Medline: [40118392](https://pubmed.ncbi.nlm.nih.gov/40118392/)]

6. Mohan A, Ludwig A, Brehm C, Lugogo NL, Sumino K, Hanania NA. Revisiting mild asthma: current knowledge and future needs. *Chest*. 2022;161(1):26-39. [doi: [10.1016/j.chest.2021.09.004](https://doi.org/10.1016/j.chest.2021.09.004)] [Medline: [34543667](#)]
7. Howard R, Belgrave D, Papastamoulis P, Simpson A, Rattray M, Custovic A. Evolution of IgE responses to multiple allergen components throughout childhood. *J Allergy Clin Immunol*. 2018;142(4):1322-1330. [FREE Full text] [doi: [10.1016/j.jaci.2017.11.064](https://doi.org/10.1016/j.jaci.2017.11.064)] [Medline: [29428391](#)]
8. Tian F, Zhong X, Ye Y, Liu X, He G, Wu C, et al. Mutual associations of exposure to ambient air pollutants in the first 1000 days of life with asthma/wheezing in children: prospective cohort study in Guangzhou, China. *JMIR Public Health Surveill*. 2024;10:e52456. [FREE Full text] [doi: [10.2196/52456](https://doi.org/10.2196/52456)] [Medline: [38631029](#)]
9. Bisgaard H, Chawes B, Stokholm J, Mikkelsen M, Schoos AM, Bønnelykke K. 25 Years of translational research in the Copenhagen Prospective Studies on Asthma in Childhood (COPSAC). *J Allergy Clin Immunol*. 2023;151(3):619-633. [FREE Full text] [doi: [10.1016/j.jaci.2022.11.022](https://doi.org/10.1016/j.jaci.2022.11.022)] [Medline: [36642652](#)]
10. Rosas-Salazar C, Chirkova T, Gebretsadik T, Chappell JD, Peebles RS, Dupont WD, et al. Respiratory syncytial virus infection during infancy and asthma during childhood in the USA (INSPIRE): a population-based, prospective birth cohort study. *Lancet*. 2023;401(10389):1669-1680. [FREE Full text] [doi: [10.1016/S0140-6736\(23\)00811-5](https://doi.org/10.1016/S0140-6736(23)00811-5)] [Medline: [37086744](#)]
11. Shenhav L, Fehr K, Reyna ME, Petersen C, Dai DL, Dai R, et al. Microbial colonization programs are structured by breastfeeding and guide healthy respiratory development. *Cell*. 2024;187(19):5431-5452.e20. [FREE Full text] [doi: [10.1016/j.cell.2024.07.022](https://doi.org/10.1016/j.cell.2024.07.022)] [Medline: [39303691](#)]
12. Zanolletti A, Ryan P, Coull B, Brokamp C, Datta S, Blossom J. Childhood asthma incidence, early and persistent wheeze, and neighborhood socioeconomic factors in the ECHO/CREW consortium. *JAMA Pediatr*. 2022;176(8):759-767. [doi: [10.1542/peds.2022-059346rr](https://doi.org/10.1542/peds.2022-059346rr)]
13. Wen X, Zhou J, Fang H, Li J, Wang R, Zeng D, et al. Allele-specific micro-RNA-mediated regulation of ADAM33 in childhood allergic asthma. *Respirology*. 2025;30(2):113-123. [doi: [10.1111/resp.14846](https://doi.org/10.1111/resp.14846)] [Medline: [39478322](#)]
14. Zhang J, Zhao L, Zhao D, Chen Z, Li S, Zhang H, et al. Reliability and validity of the Chinese version of the test for respiratory and asthma control in kids (TRACK) in preschool children with asthma: a prospective validation study. *BMJ Open*. 2019;9(8):e025378. [FREE Full text] [doi: [10.1136/bmjopen-2018-025378](https://doi.org/10.1136/bmjopen-2018-025378)] [Medline: [31455696](#)]
15. Rodríguez EM, Pollack CE, Keet C, Peng RD, Balcer-Whaley S, Custer J, et al. Neighborhoods, caregiver stress, and children's asthma symptoms. *J Allergy Clin Immunol Pract*. 2022;10(4):1005-1012.e1. [FREE Full text] [doi: [10.1016/j.jaip.2021.08.043](https://doi.org/10.1016/j.jaip.2021.08.043)] [Medline: [34626856](#)]
16. Nkoy F, Fassl B, Wilkins V, Johnson J, Unsicker E, Koopmeiners K, et al. Ambulatory management of childhood asthma using a novel self-management application. *Pediatrics*. 2019;143(6):e20181711. [doi: [10.1542/peds.2018-1711](https://doi.org/10.1542/peds.2018-1711)] [Medline: [31097465](#)]
17. Kasuga S, Kabata D, Sakaguchi T, Kudoh S, Nishigaki S, Higa Y, et al. Usefulness of serum bioprotein as a predictive biomarker for childhood asthma control: A prospective cohort study. *Allergol Int*. 2019;68(1):96-100. [FREE Full text] [doi: [10.1016/j.alit.2018.08.012](https://doi.org/10.1016/j.alit.2018.08.012)] [Medline: [30297096](#)]
18. Olaniyan T, Jeebhay M, Rössli M, Naidoo RN, Künzli N, de Hoogh K, et al. The association between ambient NO₂ and PM_{2.5} with the respiratory health of school children residing in informal settlements: A prospective cohort study. *Environ Res*. 2020;186:109606. [doi: [10.1016/j.envres.2020.109606](https://doi.org/10.1016/j.envres.2020.109606)] [Medline: [32371276](#)]
19. Zhang L, Fu Z, Deng H, Xie Q, Wu W. Identification and treatment of persistent small airway dysfunction in paediatric patients with asthma: a retrospective cohort study. *BMC Pulm Med*. 2024;24(1):94. [FREE Full text] [doi: [10.1186/s12890-024-02907-z](https://doi.org/10.1186/s12890-024-02907-z)] [Medline: [38395894](#)]
20. Zhao Y, Patel J, Xu X, Zhang G, Li Q, Yi L, et al. Development and validation of a prediction model to predict school-age asthma in preschool children. *Pediatr Pulmonol*. 2023;58(5):1391-1400. [doi: [10.1002/ppul.26331](https://doi.org/10.1002/ppul.26331)] [Medline: [36698223](#)]
21. Zhang Q, Xu F, Chen F. Construction and validation of a predictive model for allergic rhinitis complicating children with bronchial asthma. *Allergol Immunopathol (Madr)*. 2025;53(1):131-138. [doi: [10.15586/aei.v53i1.1242](https://doi.org/10.15586/aei.v53i1.1242)] [Medline: [39786886](#)]
22. Liu S, Zhou X, Wang W, Zhang M, Sun Y, Hu X, et al. The risk of asthma in singletons conceived by ART: a retrospective cohort study. *Hum Reprod Open*. 2024;2024(3):hoae041. [doi: [10.1093/hropen/hoae041](https://doi.org/10.1093/hropen/hoae041)] [Medline: [39040637](#)]
23. Li L, Li J, Hu C, Di Nardo M, Srinivasan V, Adamko DJ, et al. Effectiveness of polyvalent bacterial lysate for pediatric asthma control: a retrospective propensity score-matched cohort study. *Transl Pediatr*. 2022;11(10):1697-1703. [FREE Full text] [doi: [10.21037/tp-22-489](https://doi.org/10.21037/tp-22-489)] [Medline: [36345454](#)]
24. Wei X, Xue M, Yan J, Han Y, Liu Y, Liu M, et al. Effect of diagnosis delay on pulmonary function in children with asthma. *Allergy Asthma Clin Immunol*. 2022;18(1):92. [FREE Full text] [doi: [10.1186/s13223-022-00731-w](https://doi.org/10.1186/s13223-022-00731-w)] [Medline: [36261858](#)]
25. Lang J, Tang M, Zhao C, Hurst J, Wu A, Goldstein B. Well-child care attendance and risk of asthma exacerbations. *Pediatrics*. 2020;146(6):e20201023. [doi: [10.1542/peds.2020-1023](https://doi.org/10.1542/peds.2020-1023)] [Medline: [33229468](#)]
26. Verkerk K, Voest E. Generating and using real-world data: A worthwhile uphill battle. *Cell*. 2024;187(7):1636-1650. [FREE Full text] [doi: [10.1016/j.cell.2024.02.012](https://doi.org/10.1016/j.cell.2024.02.012)] [Medline: [38552611](#)]
27. Gunatilleke NJ, Fleuriot J, Anand A. A literature review on the analysis of symptom-based clinical pathways: Time for a different approach? *PLOS Digit Health*. 2022;1(5):e0000042. [FREE Full text] [doi: [10.1371/journal.pdig.0000042](https://doi.org/10.1371/journal.pdig.0000042)] [Medline: [36812546](#)]

28. Liang X, Zhang D, Wang H, Tahir MF, Chen L, Zhao X, et al. Importance of cohort and target trial emulation in clinical research. *Cell Rep Med*. 2025;6(4):102081. [FREE Full text] [doi: [10.1016/j.xcrm.2025.102081](https://doi.org/10.1016/j.xcrm.2025.102081)] [Medline: [40239630](https://pubmed.ncbi.nlm.nih.gov/40239630/)]
29. Reyna ME, Dai R, Tran MM, Breton V, Medeleanu M, Lou WYW, et al. Development of a symptom-based tool for screening of children at high risk of preschool asthma. *JAMA Netw Open*. 2022;5(10):e2234714. [FREE Full text] [doi: [10.1001/jamanetworkopen.2022.34714](https://doi.org/10.1001/jamanetworkopen.2022.34714)] [Medline: [36201211](https://pubmed.ncbi.nlm.nih.gov/36201211/)]
30. Yuan Y, Mei Y, Zhao S, Dai S, Liu X, Sun X, et al. Data flow construction and quality evaluation of electronic source data in clinical trials: pilot study based on hospital electronic medical records in China. *JMIR Med Inform*. 2024;12:e52934. [FREE Full text] [doi: [10.2196/52934](https://doi.org/10.2196/52934)] [Medline: [38973192](https://pubmed.ncbi.nlm.nih.gov/38973192/)]
31. Santos-Beneit G, Fuster V, Fernández-Jiménez R. Use of primary care electronic medical records for research purposes: is it taking off? *Rev Esp Cardiol (Engl Ed)*. 2022;75(4):288-290. [doi: [10.1016/j.rec.2021.10.018](https://doi.org/10.1016/j.rec.2021.10.018)] [Medline: [34953765](https://pubmed.ncbi.nlm.nih.gov/34953765/)]
32. Bele S, Paolucci EO, Johnson DW, Quan H, Santana M. Implementing paediatric patient-reported outcome measures in outpatient asthma clinics: a feasibility assessment study. *BMJ Open*. 2023;13(11):e073260. [FREE Full text] [doi: [10.1136/bmjopen-2023-073260](https://doi.org/10.1136/bmjopen-2023-073260)] [Medline: [37945296](https://pubmed.ncbi.nlm.nih.gov/37945296/)]
33. Lin JH, Huang E, Rauch B, Young LR, Allen J, Myers JS. Improving asthma control test completion rates across a multi-site pediatric pulmonary clinic network: a quality improvement initiative. *J Asthma*. 2024;61(12):1629-1637. [doi: [10.1080/02770903.2024.2371004](https://doi.org/10.1080/02770903.2024.2371004)] [Medline: [38913112](https://pubmed.ncbi.nlm.nih.gov/38913112/)]
34. Bousquet J, Shamji M, Anto J, Schünemann H, Canonica G, Jutel M. Patient-centered digital biomarkers for allergic respiratory diseases and asthma: The ARIA-EAACI approach - ARIA-EAACI task force report. *Allergy*. 2023;78(7):1758-1776. [doi: [10.22541/au.160916124.47621341/v1](https://doi.org/10.22541/au.160916124.47621341/v1)]
35. Mandal S, Simmons R, Ireland G, Charlett A, Desai M, Coughlan L, et al. Paediatric acute hepatitis of unknown aetiology: a national investigation and adenoviraemia case-control study in the UK. *Lancet Child Adolesc Health*. 2023;7(11):786-796. [FREE Full text] [doi: [10.1016/S2352-4642\(23\)00215-8](https://doi.org/10.1016/S2352-4642(23)00215-8)] [Medline: [37774733](https://pubmed.ncbi.nlm.nih.gov/37774733/)]
36. Bourgeois F, Avillach P, Kong SW, Heinz M, Tran T, Chakrabarty R, et al. Development of the precision link biobank at boston children's hospital: challenges and opportunities. *J Pers Med*. 2017;7(4):21. [FREE Full text] [doi: [10.3390/jpm7040021](https://doi.org/10.3390/jpm7040021)] [Medline: [29244735](https://pubmed.ncbi.nlm.nih.gov/29244735/)]
37. Li X, Wu Y, Yi B, Chen M, Zhang G, Shao X, et al. A multi-centered prospective birth cohort study in Western China. *Imeta*. 2025;4(3):e70049. [doi: [10.1002/imt2.70049](https://doi.org/10.1002/imt2.70049)] [Medline: [40469506](https://pubmed.ncbi.nlm.nih.gov/40469506/)]
38. Tang Y, Fu X, Li X, Fang H, Yang F, Wang R, et al. Multi-omics analysis of human plasma reveals reprogramming of tryptophan metabolism associated with inflammation in *Mycoplasma pneumoniae* pneumonia in children. *J Infect*. 2025;91(1):106525. [FREE Full text] [doi: [10.1016/j.jinf.2025.106525](https://doi.org/10.1016/j.jinf.2025.106525)] [Medline: [40456320](https://pubmed.ncbi.nlm.nih.gov/40456320/)]
39. Lee S, Nakano T, Shimojo N, Yamamoto-Hanada K, Fukuie T, Ohya Y, et al. A2BC network. Asian birth cohort studies on allergic diseases: The A2BC network initiative. *Pediatr Allergy Immunol*. 2024;35(11):e14280. [doi: [10.1111/pai.14280](https://doi.org/10.1111/pai.14280)] [Medline: [39560177](https://pubmed.ncbi.nlm.nih.gov/39560177/)]
40. Irvine A, Chey W, Ford A. Screening for celiac disease in irritable bowel syndrome: an updated systematic review and meta-analysis. *Am J Gastroenterol*. 2017;112(1):65-76. [FREE Full text] [doi: [10.1038/ajg.2016.466](https://doi.org/10.1038/ajg.2016.466)] [Medline: [27753436](https://pubmed.ncbi.nlm.nih.gov/27753436/)]
41. Bardach NS, Harder VS, McCulloch CE, Thombley R, Shaw JS, Hart VC, et al. Follow-up after asthma emergency department visits and its relationship with subsequent asthma-related utilization. *Acad Pediatr*. 2022;22(3S):S125-S132. [doi: [10.1016/j.acap.2021.10.015](https://doi.org/10.1016/j.acap.2021.10.015)] [Medline: [35339239](https://pubmed.ncbi.nlm.nih.gov/35339239/)]
42. Ruffner MA, Henrickson SE, Chilutti M, Grundmeier R, Spergel JM, Brown-Whitehorn TF. Improving allergy office scheduling increases patient follow up and reduces asthma readmission after pediatric asthma hospitalization. *Ann Allergy Asthma Immunol*. 2018;121(5):561-567. [FREE Full text] [doi: [10.1016/j.anai.2018.08.015](https://doi.org/10.1016/j.anai.2018.08.015)] [Medline: [30170026](https://pubmed.ncbi.nlm.nih.gov/30170026/)]
43. Hall K, Barry F, Thompson LR, Ravandi B, Hall JE, Chang TP, et al. Feasibility of text message follow-up for pediatric asthma care after an emergency department visit. *J Asthma*. 2024;61(2):140-147. [doi: [10.1080/02770903.2023.2248507](https://doi.org/10.1080/02770903.2023.2248507)] [Medline: [37610221](https://pubmed.ncbi.nlm.nih.gov/37610221/)]
44. Zhou J, Li W, Wen X, Zeng D, Lin J, Chen S, et al. Establishing a patient registry study database of dust mite allergic asthma in children: design, methodology and preliminary exploration. *Ann Transl Med*. 2021;9(12):993. [FREE Full text] [doi: [10.21037/atm-21-2566](https://doi.org/10.21037/atm-21-2566)] [Medline: [34277793](https://pubmed.ncbi.nlm.nih.gov/34277793/)]
45. Wang L, Guo R, Yang H, Yuan X. Analysis between indoor environment and childhood asthma and family nursing interventions in Chongqing. *Chinese General Practice*. 2019;22(12):1405-1412.
46. Zhang Y, Feng L, Chen R, Hao Y. Chinese version of Pediatric Quality of Life Inventory™ (PedsQL™) 3.0 asthma module parent report: reliability and validity. *Journal of Sun Yat-Sen University (Medical Sciences)*. 2010;31(5):710-714.
47. Fang H, Xian R, Ma Z, Lu M, Hu Y. Comparison of the differences between web-based and traditional questionnaire surveys in pediatrics: comparative survey study. *J Med Internet Res*. 2021;23(8):e30861. [FREE Full text] [doi: [10.2196/30861](https://doi.org/10.2196/30861)] [Medline: [34319240](https://pubmed.ncbi.nlm.nih.gov/34319240/)]
48. Fang H, Lv Y, Chen L, Zhang X, Hu Y. The current knowledge, attitudes, and practices of the neglected methodology of web-based questionnaires among chinese health workers: web-based questionnaire study. *J Med Internet Res*. 2023;25:e41591. [FREE Full text] [doi: [10.2196/41591](https://doi.org/10.2196/41591)] [Medline: [36533302](https://pubmed.ncbi.nlm.nih.gov/36533302/)]
49. Frey SM, Goldstein NP, Kwiatkowski V, Reinish A. Clinical outcomes for young children diagnosed with asthma versus reactive airway disease. *Acad Pediatr*. 2022;22(1):37-46. [doi: [10.1016/j.acap.2021.06.009](https://doi.org/10.1016/j.acap.2021.06.009)] [Medline: [34153535](https://pubmed.ncbi.nlm.nih.gov/34153535/)]

50. Korsten K, Naaktgeboren CA, Bont LJ, van der Ent CK, de Hoog ML. Defining asthma in children: how well do parents, doctors and spirometry agree? *ERJ Open Res*. 2020;6(4):00348-02019. [FREE Full text] [doi: [10.1183/23120541.00348-2019](https://doi.org/10.1183/23120541.00348-2019)] [Medline: [33043055](https://pubmed.ncbi.nlm.nih.gov/33043055/)]
51. Yang F, Chen C, Deng X, Hu T, Bi D, Li H. Perspectives and experiences of mothers of school-age children with asthma: a qualitative study. *J Asthma*. 2024;61(5):444-452. [FREE Full text] [doi: [10.1080/02770903.2023.2288322](https://doi.org/10.1080/02770903.2023.2288322)] [Medline: [38009785](https://pubmed.ncbi.nlm.nih.gov/38009785/)]
52. Celebi Sozener Z, Ozdel Ozturk B, Cerci P, Turk M, Gorgulu Akin B, Akdis M, et al. Epithelial barrier hypothesis: effect of the external exposome on the microbiome and epithelial barriers in allergic disease. *Allergy*. 2022;77(5):1418-1449. [FREE Full text] [doi: [10.1111/all.15240](https://doi.org/10.1111/all.15240)] [Medline: [35108405](https://pubmed.ncbi.nlm.nih.gov/35108405/)]
53. Cai J, Li B, Yu W, Yao Y, Wang L, Li B, et al. Associations of household dampness with asthma, allergies, and airway diseases among preschoolers in two cross-sectional studies in Chongqing, China: repeated surveys in 2010 and 2019. *Environ Int*. 2020;140:105752. [FREE Full text] [doi: [10.1016/j.envint.2020.105752](https://doi.org/10.1016/j.envint.2020.105752)] [Medline: [32371306](https://pubmed.ncbi.nlm.nih.gov/32371306/)]
54. Du C, Li B, Yu W, Yao R, Cai J, Li B, et al. Characteristics of annual mold variations and association with childhood allergic symptoms/diseases via combining surveys and home visit measurements. *Indoor Air*. 2022;32(9):e13113. [doi: [10.1111/ina.13113](https://doi.org/10.1111/ina.13113)] [Medline: [36168229](https://pubmed.ncbi.nlm.nih.gov/36168229/)]
55. Fang H, Li J, Li X, Wen X, Zeng D, Tang Y, et al. High sensitization to in children with allergic asthma in Southwest China: A microfluidic chip and proteomics study. *World Allergy Organ J*. 2025;18(8):101097. [FREE Full text] [doi: [10.1016/j.waojou.2025.101097](https://doi.org/10.1016/j.waojou.2025.101097)] [Medline: [40822752](https://pubmed.ncbi.nlm.nih.gov/40822752/)]
56. Donath H, Klenner H, Hutter M, Meoli A, Trischler J, Schulze J. Severe bronchial hyperresponsiveness along with house dust mite allergy indicates persistence of asthma in young children. *Pediatr Allergy Immunol*. 2023;34(12):e14047. [doi: [10.1111/pai.14047/v2/response1](https://doi.org/10.1111/pai.14047/v2/response1)]
57. Fang H, Xian R, Li J, Li Y, Liu E, Zhao Y, et al. Urban-suburban differences in public perspectives on digitalizing pediatric research: cross-sectional survey study. *J Med Internet Res*. 2025;27:e60324. [FREE Full text] [doi: [10.2196/60324](https://doi.org/10.2196/60324)] [Medline: [39773676](https://pubmed.ncbi.nlm.nih.gov/39773676/)]
58. Agache I, Torres M, Eguiluz-Gracia I, Bradatan E, El Abd K, Bilo MB, Cuenda, et al. HEAD Study Group. Economic impact of allergic diseases and asthma-the HEAD pan-european registry. *Allergy*. 2025;80(6):1677-1701. [doi: [10.1111/all.16596](https://doi.org/10.1111/all.16596)] [Medline: [40391774](https://pubmed.ncbi.nlm.nih.gov/40391774/)]
59. Shelef DQ, Badolato GM, Badh R, Owotomo O, Kachroo N, Weissman M, et al. Creation and validation of a citywide pediatric asthma registry for the district of Columbia. *J Asthma*. 2022;59(5):901-909. [doi: [10.1080/02770903.2021.1895213](https://doi.org/10.1080/02770903.2021.1895213)] [Medline: [33635727](https://pubmed.ncbi.nlm.nih.gov/33635727/)]
60. ISAR Study Group. International severe asthma registry: mission statement. *Chest*. 2020;157(4):805-814.
61. Hansen S, Hoffmann-Petersen B, Sverrild A, Br  uner EV, Lykkegaard J, Bodtger U, et al. The Danish national database for asthma: establishing clinical quality indicators. *Eur Clin Respir J*. 2016;3:33903. [FREE Full text] [doi: [10.3402/ecrj.v3.33903](https://doi.org/10.3402/ecrj.v3.33903)] [Medline: [27834178](https://pubmed.ncbi.nlm.nih.gov/27834178/)]
62. Gall R, Jain N, Soong W, Settupane RA, Xia C, Zhang Y, et al. Dupilumab-treated patients with asthma in the real world: the RAPID global registry. *Adv Ther*. 2023;40(3):1292-1298. [FREE Full text] [doi: [10.1007/s12325-022-02399-5](https://doi.org/10.1007/s12325-022-02399-5)] [Medline: [36626107](https://pubmed.ncbi.nlm.nih.gov/36626107/)]
63. D'Urzo KA, Tamari IE, Chapman KR, Maleki-Yazdi MR, Greiver M, Upshur RE, et al. Primary care severe asthma registry and education project (PCSAR-EDU): Phase 1 - an e-Delphi for registry definitions and indices of clinician behaviour. *BMJ Open*. 2022;12(3):e055958. [FREE Full text] [doi: [10.1136/bmjopen-2021-055958](https://doi.org/10.1136/bmjopen-2021-055958)] [Medline: [35332043](https://pubmed.ncbi.nlm.nih.gov/35332043/)]
64. Chen Q, Chen J, Zhou Y, Huang L, Tang Y, Li J, et al. Natural history and associated early life factors of childhood asthma: a population registry-based cohort study in Denmark. *BMJ Open*. 2021;11(11):e045728. [FREE Full text] [doi: [10.1136/bmjopen-2020-045728](https://doi.org/10.1136/bmjopen-2020-045728)] [Medline: [34824103](https://pubmed.ncbi.nlm.nih.gov/34824103/)]
65. Liu NM, van Aalderen W, Carlsen KC, Coleman C, Chalmers JD, Cunningham S, et al. Severe paediatric asthma collaborative in Europe (SPACE): protocol for a European registry. *Breathe (Sheff)*. 2018;14(2):93-98. [FREE Full text] [doi: [10.1183/20734735.002018](https://doi.org/10.1183/20734735.002018)] [Medline: [29875828](https://pubmed.ncbi.nlm.nih.gov/29875828/)]
66. Braido F, Blasi F, Canonica GW, Paggiaro P, Begh   B, Bonini M, MANI Network, et al. Mild/Moderate asthma network in Italy (MANI): a long-term observational study. *J Asthma*. 2022;59(9):1908-1913. [FREE Full text] [doi: [10.1080/02770903.2021.1968895](https://doi.org/10.1080/02770903.2021.1968895)] [Medline: [34469268](https://pubmed.ncbi.nlm.nih.gov/34469268/)]
67. Lawrentschuk N. Electronic medical records - a disappointing mirage for clinicians and research. *BJU Int*. 2023;131 Suppl 4:4-5. [doi: [10.1111/bju.16082](https://doi.org/10.1111/bju.16082)] [Medline: [37346011](https://pubmed.ncbi.nlm.nih.gov/37346011/)]
68. Declerck J, Lee J, Sen A, Palmeri A, Oostenbrink R, Giannuzzi V, et al. The potential to leverage real-world data for pediatric clinical trials: a proof-of-concept study. *J Med Internet Res*. 2025;27:e72573. [FREE Full text] [doi: [10.2196/72573](https://doi.org/10.2196/72573)] [Medline: [40446289](https://pubmed.ncbi.nlm.nih.gov/40446289/)]
69. Wachter F, Regensburger A, Antonia Sophia Peter, Knieling F, Wagner A, Simon D, et al. Continuous monitoring of SARS-CoV-2 seroprevalence in children using residual blood samples from routine clinical chemistry. *Clin Chem Lab Med*. 2022;60(6):941-951. [FREE Full text] [doi: [10.1515/ccbm-2022-0037](https://doi.org/10.1515/ccbm-2022-0037)] [Medline: [35218170](https://pubmed.ncbi.nlm.nih.gov/35218170/)]
70. Xing Y, Yang X, Li Z, Zou Q, Yang P, Wang Q, et al. Advancing understanding of childhood asthma: lessons learned from birth cohort studies. *Clin Rev Allergy Immunol*. 2024;66(1):50-63. [doi: [10.1007/s12016-024-08979-3](https://doi.org/10.1007/s12016-024-08979-3)] [Medline: [38324179](https://pubmed.ncbi.nlm.nih.gov/38324179/)]

71. Gupta R, Fierstein J, Boon K, Kanaley M, Bozen A, Kan K, et al. Sensor-based electronic monitoring for asthma: a randomized controlled trial. *Pediatrics*. 2021;147(1). [FREE Full text] [doi: [10.1542/peds.2020-1330](https://doi.org/10.1542/peds.2020-1330)] [Medline: [33386336](https://pubmed.ncbi.nlm.nih.gov/33386336/)]
72. van der Kamp M, Hengeveld V, Willard N, Thio B, de Graaf P, Geven I, et al. Remote patient monitoring and teleconsultation to improve health outcomes and reduce health care utilization of pediatric asthma (ALPACA study): protocol for a randomized controlled effectiveness trial. *JMIR Res Protoc*. 2023;12:e45585. [FREE Full text] [doi: [10.2196/45585](https://doi.org/10.2196/45585)] [Medline: [37399066](https://pubmed.ncbi.nlm.nih.gov/37399066/)]
73. Ma Y, Zhang X, Jin L, Liu S, Liang X, Ye Q, et al. Social media interventions and postoperative follow-up in congenital ectopia lentis: a randomized clinical trial. *JAMA Ophthalmol*. 2025;143(5):438-445. [doi: [10.1001/jamaophthalmol.2025.0526](https://doi.org/10.1001/jamaophthalmol.2025.0526)] [Medline: [40208617](https://pubmed.ncbi.nlm.nih.gov/40208617/)]
74. Pandey S, Goldberg JI, Kapoor-Hintzen N, Stabler S, Nelson JE. Beyond 9 to 5: expansion of an inpatient specialist palliative care service to 24/7 onsite presence. *J Hosp Palliat Nurs*. 2022;24(5):E233-E239. [FREE Full text] [doi: [10.1097/NJH.0000000000000892](https://doi.org/10.1097/NJH.0000000000000892)] [Medline: [35666762](https://pubmed.ncbi.nlm.nih.gov/35666762/)]
75. Hu B, Li X. Study on effectiveness of price policy of consultation fees in evening outpatient services in pediatrics of jiangsu. *Chinese Health Economics*. 2020;39(5):17-19.

Abbreviations

ACT: Asthma Control Test

C-ACT: Childhood Asthma Control Test

CRCA: Clinical Registry of Childhood Asthma

EMR: electronic medical record

ePRO: electronic patient-reported outcome

FeNO: fractional exhaled nitric oxide

GINA: Global Initiative for Asthma

OR: odds ratio

PBMC: peripheral blood mononuclear cell

sIgE: specific IgE

STROBE: Strengthening the Reporting of Observational Studies in Epidemiology

Edited by J Sarvestan; submitted 08.Jun.2025; peer-reviewed by S Chetty-Mhlanga, L Chen; comments to author 25.Aug.2025; revised version received 11.Sep.2025; accepted 03.Oct.2025; published 30.Oct.2025

Please cite as:

Li J, Ren L, Liu J, Tang Y, Wang R, Yang P, Zhao J, Chen X, Xiang Z, Zhong W, Zang N, Chen D, Fang H, Liu E
The Clinical Registry of Childhood Asthma (CRCA) Elucidating Early-Life Asthma: Cross-Sectional Analysis of a Prospective, Longitudinal, and Digitally Enhanced Real-World Cohort

J Med Internet Res 2025;27:e78693

URL: <https://www.jmir.org/2025/1/e78693>

doi: [10.2196/78693](https://doi.org/10.2196/78693)

PMID:

©Juan Li, Luo Ren, Jiao Liu, Yuyi Tang, Run Wang, Peixin Yang, Jing Zhao, Xiao Chen, Zheng Xiang, Wen Zhong, Na Zang, Dapeng Chen, Heping Fang, Enmei Liu. Originally published in the Journal of Medical Internet Research (<https://www.jmir.org>), 30.Oct.2025. This is an open-access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work, first published in the Journal of Medical Internet Research (ISSN 1438-8871), is properly cited. The complete bibliographic information, a link to the original publication on <https://www.jmir.org/>, as well as this copyright and license information must be included.