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Epidemiology of Childhood Asthma in the UK

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Purpose: Global prevalence of pediatric asthma and associated morbidity and mortality has continuously increased. Asthma is the most common chronic illness in children in the UK; however, recent epidemiology data are lacking. This analysis describes the overall prevalence and burden of illness of asthma in children.

Methods: This was a retrospective, longitudinal, database analysis using the Clinical Practice Research Datalink database. Primary care records of 19,330 patients (6–11 years) between January 1 and December 31, 2017, were analyzed. Asthma prevalence was assessed by severity (as described by Global Initiative for Asthma 2017 guidelines), and symptoms, comorbidities, and treatments were compared between asthma patients and matched non-asthmatic controls. Results are presented descriptively; logistic regression analyses were performed for asthma symptoms.

Results: The estimated prevalence of pediatric asthma was 6.5% (95% CI: 6.4–6.5) in the UK (mild: 74.2%; moderate: 15.0%; severe: 10.8%). All patients with moderate or severe asthma and 72.5% of patients with mild asthma were prescribed drug therapy. Most patients with moderate or severe asthma were prescribed a short-acting β2-agonist (94.9% and 96.0%, respectively), compared with 69.2% of mild asthma patients. Daytime symptoms were reported by 78.1% in those with severe asthma; 34.9% reported night-time symptoms and 30.8% reported an impact on usual activities. Asthma patients had a higher baseline prevalence of comorbidities compared with non-asthmatic controls, notably atopic dermatitis (47.8% in severe asthma versus 20.8% in controls) and allergic rhinitis (13.3% in severe asthma versus 2.0% in controls).

Conclusion: This analysis confirmed that asthma remains a common morbidity among children in the UK. Increasing asthma severity was associated with worsening symptoms, and asthma patients had significantly more comorbidities compared with non-asthmatic controls.

Keywords: asthma, pediatric, epidemiology, United Kingdom

Introduction

The global prevalence of pediatric asthma and associated morbidity and mortality has continuously increased over the past 40 years.[1] However, the prevalence of childhood asthma varies considerably by geographic region;[1,2] the highest rates are reported in Southeast Asia, North America, and Latin America.[1] In the UK, asthma is the most common chronic illness in children, but more recent epidemiology data are needed to characterize asthma in children.[3] Pediatric asthma has a significant economic impact on the National Healthcare System: there were over 6000 inpatient admissions in England in 2020/2021 for asthma in children aged ≤9 years,[4] and over 1 million children received treatment for asthma across the UK.[5]

Asthma symptoms differ between children, because risk factors and clinical burden depend on specific asthmatic phenotypes; atopic asthma and episodic viral wheeze are most commonly observed in children.[6] Disease management is specific to each phenotype and consists of drug therapy (which also includes rescue therapy, such as short-acting β2-agonists [SABAs]), additional maintenance medication, and avoiding asthma triggers.[7,8] Additionally, diagnosing and managing asthma in children is more difficult than in adults.[9,10] However, reviews in low income populations have shown indications of under-diagnosis or misdiagnosis of asthma across age groups, while studies in high income populations suggest over-diagnosis of asthma.[11–14] A potential reason for this is the lack of a gold standard for the diagnosis of asthma.[15]

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This study aimed to address the lack of recent data on epidemiology and characteristics of asthma in children in order to better understand the clinical burden of this heterogenous disease.[16] The primary objective of this study was to estimate the overall prevalence of asthma in children aged 6 to 11 years in the UK and to characterize the burden of illness (symptoms, comorbidities, and treatment patterns) in children with asthma using data from a real-world UK database, the Clinical Practice Research Datalink (CPRD). Prevalence and treatment patterns were further stratified by level of disease severity based on the Global Initiative for Asthma (GINA) 2017 guidelines.[8]

Methods

Study Design

This was a retrospective, case-matched analysis of data from the CPRD GOLD primary care dataset. CPRD (formerly the General Practice Research Datalink) is a longitudinal, anonymized research database that contains patient records for more than 13 million patients from nearly 700 primary care practices across the UK.[17] Studies using the CPRD dataset are covered by the ethics approval granted by Trent Multicentre Research Ethics Committee (reference 05/MRE04/87). CPRD Independent Scientific Advisory Committee approval was also granted for this study (ISAC 19_268). The study population consisted of patients aged 6 to 11 years with a recorded diagnosis of asthma, as indicated by Read or ICD-10 classification codes, either in the index year (2017) or in the previous year (2016; Tables S1 and S2). The index date was either the date of first diagnosis of asthma in 2017 or, for patients diagnosed before the index year, January 01, 2017; patients were followed until 31st December 2017. A control group of individuals with no history of asthma during or prior to the study period were matched on age, sex, primary care practice, and concurrent practice registration. Prevalence of asthma symptoms and treatment patterns were assessed in patients with mild, moderate, and severe asthma. Comorbidities were compared between patients with asthma and matched non-asthmatic controls.[8]

Data Analysis

Prevalence

The period prevalence of asthma was calculated for the year 2017. All included asthma patients formed the numerator, with the midpoint (30th June 2017) CPRD age-specific population forming the denominator. The prevalence rates and confidence intervals (CI) based on the mid-p exact test were also calculated. Mid-p values are defined as half of the conditional probability of the observed statistic combined with the conditional probability of more extreme values.

Asthma Therapies

Asthma specific therapies prescribed during the index year were extracted from the CPRD therapy table and classified as SABA, inhaled corticosteroids (ICS; presented overall and by low, medium and high dose, as defined by GINA 2017[8]), long-acting bronchial beta-agonists (LABA), ICS/LABA combination, long-acting muscarinic antagonist (LAMA), and leukotriene receptor antagonists (LTRA). Systemic corticosteroid (SCS) were reported for <3 days (short-term use), 3 to 29 days (medium-term use), and ≥30 days (chronic use) total annual exposure. Patients receiving any of these asthma-related prescriptions during 2017 were included in the analysis.

GINA Severity Classification

Asthma severity was categorized as mild, moderate or severe based on medication received, in line with GINA 2017 guidelines, which were the latest GINA guidelines available at the time of data collection (Table S3). [8] This approach is in line with previous studies focused on asthma severity.[18–20] For patients classified within different severity categories during 2017, the highest level of severity reported was considered in this analysis. A stepwise approach was taken to categorize the patients: asthma that was treated with step 1 or step 2 therapies was considered to be mild, and treatment with step 3 therapies was considered to indicate moderate asthma. Severe asthma was defined as receipt of step 4 or 5 treatment.[8] In this analysis, once patients with asthma had been categorized by severity, the patient population in each severity category was matched to control individuals.

Asthma Symptoms

Asthma symptoms were classified according to the following Royal College of Physicians 3 Questions (RCP-3Q) for Asthma, as recorded in CPRD: "Have you had difficulty sleeping because of your asthma symptoms (including cough)?" "Have you had your usual asthma symptoms during the day (cough, wheeze, chest tightness, or breathlessness)?" and, "Has your asthma interfered with your usual activities (eg, housework, work/school)?" Descriptive analyses were provided for each symptom reported by patients during 2017 for the overall patient sample and by severity. For each question, a logistic regression model, in which presence of each symptom was classified as the binary outcome variable, was performed. Odds ratios with 95% CIs were presented for each GINA severity classification, and mild cases were used as the reference category.[8] The regression model was adjusted for age, sex, and presence of selected comorbidities (allergic rhinitis, allergic conjunctivitis, atopic dermatitis, and chronic rhinosinusitis). The CPRD clinical symptoms of respiratory infection, cough, and wheeze during baseline were reported by GINA severity classification and were compared with rates in non-asthmatic control individuals using chi-squared tests.[8]

Comorbidities

Baseline comorbidities from the CPRD clinical table were defined as occurring prior to the index date. The following baseline comorbidities were recorded: allergic rhinitis, allergic conjunctivitis, atopic dermatitis, chronic rhinosinusitis without nasal polyps, and food allergy. Rates of comorbidities were reported by GINA classification and compared with non-asthmatic control individuals using chi-squared test.[8]

Results

Baseline Characteristics

Overall, 19,330 pediatric patients with asthma aged 6 to 11 years were registered in the CPRD dataset during 2017; baseline characteristics of the prevalent asthma population are presented in Table 1. The mean age of patients was 8.7 years, and approximately 60% were male. Most patients (43%) were from England. The estimated point prevalence of pediatric asthma in 2017 was 6.5% (95% CI 6.4–6.5%); 15.0% of these prevalent cases were classified as moderate asthma cases and 10.8% as severe (Table 1).

Table 1 Baseline Characteristics of the Prevalent Asthma Population and Proportion of the Population Classified as Having Mild, Moderate, or Severe Asthma (Based on the 2017 GINA Guidelines)[8]

Characteristic[a]	N = 19,330
Age, mean (SD), years	8.7 (1.7)
Follow-up, days	
Mean (SD)	323.6 (91.8)
Median (IQR)	365.0 (206–365)
Sex	
Male	11,568 (59.8)
Nation/region	
England	8329 (43.1)
Scotland	5115 (26.5)
Wales	4271 (22.1)
Northern Ireland	1615 (8.4)
GINA severity classification	
Mild	14,346 (74.2)
Moderate	2903 (15.0)
Severe	2081 (10.8)

Note: [a]n (%) unless otherwise stated.
Abbreviations: GINA, Global Initiative for Asthma; IQR, interquartile range; SD, standard deviation.

Treatment Patterns

Overall, 79.6% of patients with an asthma diagnosis had a prescription for an asthma-related medication in 2017 (Table 2). All patients classified with moderate or severe asthma were prescribed an asthma-related therapy during 2017, as per GINA 2017 guidelines.[8] Among patients classified as having mild asthma, 72.5% were prescribed asthma medication. The majority of patients classified as having moderate or severe asthma were prescribed a SABA (94.9% and 96.0%, respectively), compared with 69.2% of patients with mild asthma. A short-term SCS (<3 days) was prescribed to 14 patients (0.7%) with severe asthma, five patients (0.2%) with moderate asthma, and 20 patients (0.1%) with mild asthma. Treatment with SCS for 3 to 29 days was recorded for 744 patients (5.2%), 330 patients (11.4%), and 411 patients (19.8%) classified as having mild, moderate, and severe asthma, respectively. SCS use was considered chronic (≥30 days) in <5 patients with severe asthma (no patients with mild or moderate asthma recorded chronic SCS use).

Asthma Symptoms

Of those with available responses to the RCP-3Qs for Asthma, 78.1% of patients with severe asthma reported daytime symptoms, 34.9% reported night-time symptoms, and 30.8% reported an impact on usual activities (Table S4). However, for each symptom category across severities, responses were missing for approximately 50% of patients, with over 60% of

Table 2 Proportion of Pediatric Patients with Asthma Prescribed Asthma Therapies During 2017, by Level of Severity of Asthma (Based on GINA 2017 Guidelines)[8]

	Mild (n=14,346)		Moderate (n=2903)		Severe (n=2081)	
	n	%	n	%	n	%
SABA	9922	69.2	2755	94.9	1998	96.0
Low dose ICS	6913	48.2	1445	49.8	471	22.6
Medium dose ICS	0	0	1480	51.0	1556	74.8
High dose ICS	0	0	0	0	428	20.6
All ICS	6934	48.3	2623	90.4	2001	96.2
LTRA	299	2.1	1175	40.5	1333	64.1
LABA	0	0	340	11.7	1617	77.7
LAMA	0	0	0	0	0	0
SCS <3 days	20	0.1	5	0.2	14	0.7
SCS 3–29 days	744	5.2	330	11.4	411	19.8
Chronic (>30 days) SCS	0	0	0	0	<5	<5
ICS/LABA	0	0	308	10.6	1609	77.3
Low	0	0	308	10.6	497	23.9
Medium	0	0	0	0	1134	54.5
High	0	0	0	0	348	16.7
Any treatment	10,398	72.5	2903	100.0	2081	100.0

Note: Biologic therapies are routinely administered in secondary care, but granular data were not available.

Abbreviations: GINA, Global Initiative for Asthma; ICS, inhaled corticosteroids; LABA, long-acting beta2-agonist; LAMA, long acting muscarinic antagonist; SABA, short-acting β2-agonist; SCS, systemic corticosteroid.

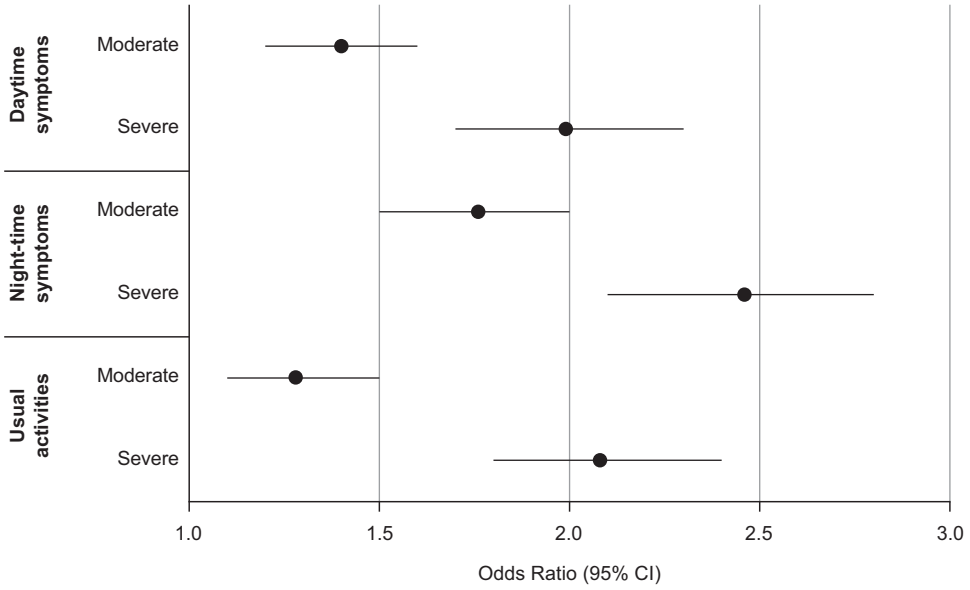

Figure 1 Logistic regression model[a] predicting responses to the Royal College of Physicians 3 Questions for Asthma symptoms for pediatric patients with asthma, by Level of Severity of Asthma (Based on GINA 2017 Guidelines).[8]
Notes: Mild n = 14,346; moderate n = 2903; severe n = 2081. [a]Adjusted for age, sex, baseline allergic rhinitis, conjunctivitis, atopic dermatitis, and Index of Multiple Deprivation.

responses missing from patients with mild asthma. In a logistic regression model (Figure 1), presence of symptoms was significantly associated with asthma severity. Compared with patients with mild asthma, patients with moderate asthma were 1.41 (95% CI 1.2–1.6) times more likely to experience daytime symptoms and 1.76 (95% CI 1.5–2.0) times more likely to experience night-time symptoms. Patients with severe asthma were 1.99 (95% CI 1.7–2.3) times more likely to experience daytime symptoms and 2.46 (95% CI 2.1–2.8) times more likely to experience night-time symptoms than patients with mild asthma. Across asthma severities, significantly more patients with asthma reported respiratory infection, cough, and wheeze compared with non-asthmatic control individuals (Table 3). Cough was the most frequently occurring symptom, reported by 20.5%, 34.0%, and 37.5% of patients with mild, moderate, and severe asthma, respectively.

Table 3 Symptoms Recorded by Pediatric Patients with Asthma, by Level of Severity of Asthma (Based on GINA 2017 Guidelines)[8]

	Patients With Asthma	Control Individuals	*P*-value
	n (%)		
Mild (n = 14,279)			
Respiratory infection	214 (1.5)	48 (0.3)	<0.001
Cough	2928 (20.5)	672 (4.7)	<0.001
Wheeze	159 (1.1)	18 (0.1)	<0.001
Moderate (n = 2895)			
Respiratory infection	53 (1.8)	11 (0.4)	<0.001
Cough	984 (34.0)	144 (5.0)	<0.001
Wheeze	51 (1.8)	5 (0.2)	<0.001
Severe (n = 2071)			
Respiratory infection	33 (1.6)	9 (0.4)	<0.001
Cough	777 (37.5)	103 (5.0)	<0.001
Wheeze	49 (2.4)	<5	<0.001

Note: Patients without recorded symptom information at baseline are removed.
Abbreviation: GINA, Global Initiative for Asthma.

Table 4 Number of Patients with Recorded Comorbidity at Baseline Compared with Control Individuals, by Level of Severity of Asthma (Based on GINA 2017 Guidelines)[8]

	Patients With Asthma	Control Individuals	*P*-value
	n (%)		
Mild (n = 14,279)			
Atopic dermatitis	6441 (45.1)	3045 (21.3)	<0.001
Allergic rhinitis	1007 (7.1)	290 (2.0)	<0.001
Food allergy	963 (6.7)	189 (1.3)	<0.001
Allergic conjunctivitis	331 (2.3)	113 (0.8)	<0.001
Moderate (n = 2895)			
Atopic dermatitis	1405 (48.5)	604 (20.9)	<0.001
Allergic rhinitis	274 (9.5)	46 (1.6)	<0.001
Food allergy	230 (7.9)	33 (1.1)	<0.001
Allergic conjunctivitis	79 (2.7)	19 (0.7)	<0.001
Severe (n = 2071)			
Atopic dermatitis	990 (47.8)	431 (20.8)	<0.001
Allergic rhinitis	275 (13.3)	41 (2.0)	<0.001
Food allergy	211 (10.2)	25 (1.2)	<0.001
Allergic conjunctivitis	71 (3.4)	13 (0.6)	<0.001

Note: Patients without recorded comorbidity information at baseline are removed.
Abbreviation: GINA, Global Initiative for Asthma.

Comorbidities

Patients with asthma had a significantly higher prevalence of all comorbidities assessed compared with the non-asthmatic group (Table 4). The most common comorbidity was atopic dermatitis, reported by 45.1%, 48.5%, and 47.8% of patients with mild, moderate, and severe asthma, respectively. Allergic rhinitis was reported by 7.1%, 9.5%, and 13.3% of patients with mild, moderate, and severe asthma, respectively. There were fewer than five deaths in each severity group; therefore, there was insufficient statistical power to conduct a mortality analysis.

Discussion

In this UK retrospective primary care dataset, the prevalence of asthma was 6.5% in patients aged 6 to 11 years in the UK. This is similar to the findings of the 2018 Health Survey for England, in which the self-reported prevalence of current asthma was, respectively, 7% and 5% for those aged 4 to 6 years and 7 to 9 years.[21] Most prevalent patients (60%) were male, consistent with data indicating that prepubescent boys have a higher asthma incidence than pre-pubescent girls.[22,23]

A considerable proportion (10.8%) of patients from the dataset were classified as having severe disease. This appears relatively high compared with previous reports from other regions (2% in a Swedish study and 5% in a Norwegian study).[24,25] The majority of patients classified as having moderate or severe asthma were prescribed rescue medication (94.9% and 96.0%, respectively), compared with SABA prescriptions for 69.2% of patients with mild asthma. The severity of asthma was associated with a considerable increase in the proportion of patients reporting symptoms across all categories (daytime, night-time, and impacting on usual activities). The odds of experiencing daytime and night-time symptoms were 2.0 and 2.5 times higher in those with severe asthma compared with mild.

In the comparison of a priori selected comorbidities, there was a significant difference in rates of all comorbidities among patients with asthma versus non-asthmatic control individuals, and this was observed for all severity categories. There was little difference in the prevalence between severity classifications (eg, approximately 45–49% of all patients reported atopic dermatitis), but the prevalence of allergic rhinitis appeared to be slightly higher in the severe group than in the mild and moderate groups (13.3% versus 7.1% and 9.5%, respectively). However, severity of comorbidities was not assessed in this study; therefore, we cannot determine any association between asthma severity and the severity of comorbidities. In general,

there are currently limited data on the reporting of the prevalence of specific comorbidities of asthma in children in other studies.[26] A US study, in which information was provided by an adult proxy respondent, has reported allergies as the most common category of comorbidity in children with current asthma, including hay fever/respiratory allergy (45%), eczema/skin allergy (25%), and food/digestive allergy (15%).[26] The most notable differences in comorbidities between children with asthma versus those without asthma were also found within these categories in our analysis. A potential reason for this difference in comorbidities may be the increased clinician contact due to the asthma diagnosis.[26] It should further be noted that atopic dermatitis was the most prevalent comorbidity, which stands in contrast to previous findings in which the most common comorbidities for asthma were allergic rhinitis and rhinosinusitis.[27–29] A potential reason for this variability is the current lack of standardisation of rhinitis diagnoses.[30]

A strength of this study is that the quality of CPRD data is monitored at a practice- and patient-level, depending on whether the data are recorded within a prespecified expected range based on practice size and demographics. Patient data are classified as eligible for inclusion in research only if the patient has a valid recorded code for sex and birth year. Patients are also required to be permanently registered at the practice in order to be deemed research eligible.[17] These criteria ensure that the data are adequate for research purposes. It should be noted that this analysis used a substantially larger sample (n=19,330) compared with previous studies (n=329 in the Swedish study and n=616 in the Norwegian study); this study also employed a different methodology compared to these birth cohort studies and the 2018 Health Survey for England, which presents patient-reported data.[21,24,25] Therefore, any comparisons to these previous studies should be made in the context of these differences and our analysis addresses a high unmet need for large-scale epidemiological studies of asthma in children.

Limitations

The CPRD database collects data predominantly for the administration and financial reimbursement of the healthcare system; therefore, data collection cannot be controlled as rigorously as in a prospective observational or interventional study. Within the CPRD, only primary care prescriptions were available in the datasets. However, certain therapies (such as biologics) are administered solely within the hospital setting. CPRD derives data from the National Healthcare System, which treats the vast majority of the UK population. While the database was representative of the UK in terms of age and sex in 2017, just under 60% of the contributing practices in the database were based in Northern Ireland, Scotland, and Wales, whereas these nations make up around 15% of the UK population. It should furthermore be noted that low response rates (~50%) for each item of the RCP-3Qs for Asthma were observed, which potentially represents a selection bias. These findings may not be generalizable to other countries and geographical regions, as disease severity may vary widely between countries, and this variation may be obscured further by different definitions used to describe disease severity.[22]

Conclusion

This study, using 2017 CPRD data, confirmed that pediatric asthma is a relatively common morbidity in the UK. A high proportion of patients with moderate (15.0%) and severe (10.8%) asthma was observed. Patients across all asthma severity categories had significantly increased baseline prevalence of comorbidities compared with non-asthmatic control individuals, suggesting a high clinical burden. The majority of patients with moderate or severe asthma were prescribed rescue medication, indicating an unmet need in this population. To the best of the authors' knowledge, this analysis represents the largest assessment of childhood asthma in UK clinical practice and demonstrates that pediatric asthma prevalence and clinical burden are slightly higher than previously estimated. These findings indicate a requirement for improved clinical management of childhood asthma in the UK.

Abbreviations

CI, confidence intervals; CPRD, Clinical Practice Research Datalink; GINA, Global Initiative for Asthma; SABA, short-acting β2-agonist; SCS, systemic corticosteroid.

Data Sharing Statement

This study is based in part on data from the CPRD obtained under license from the UK Medicines and Healthcare Products Regulatory Agency. The data is provided by patients and collected by the NHS as part of their care and support.

The interpretation and conclusions contained in this study are those of the authors alone. Due to the license arrangements with CPRD, it is not possible to share data used in this study.

Ethics Approval and Informed Consent

Studies using the CPRD dataset are covered by the ethics approval granted by Trent Multicentre Research Ethics Committee (reference 05/MRE04/87). CPRD Independent Scientific Advisory Committee approval was also granted for this study (ISAC 19_268).

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; contributed to drafting, revising or critically reviewing the article; have agreed on the journal to which the article has been submitted; gave final approval of the version to be published; and agree to take responsibility and to be accountable for all aspects of the work.

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Disclosure

Imène Gouia, Asif H Khan, and Florence Joulain are employees and stockholders of Sanofi. Yi Zhang is a former employee and stockholder of Regeneron Pharmaceuticals, Inc. Christopher Ll Morgan is an employee of Pharmatelligence Ltd, which has received funding from Sanofi and Regeneron Pharmaceuticals, Inc, for this analysis. The authors report no other conflicts of interest in this work.

References

1. Serebrisky D, Wiznia A. Pediatric asthma: a global epidemic. *Ann Glob Health*. 2019;85(1):6. doi:10.5334/aogh.2416
2. Ferrante G, La Grutta S. The burden of pediatric asthma. *Front Pediatr*. 2018;6:186. doi:10.3389/fped.2018.00186
3. Simpson CR, Sheikh A. Trends in the epidemiology of asthma in England: a national study of 333,294 patients. *J R Soc Med*. 2010;103(3):98–106. doi:10.1258/jrsm.2009.090348
4. Office for Health Improvement and Disparities [homepage on the Internet]. Public health profiles, England; 2023. Available from: https://fingertips.phe.org.uk/search/asthma%20admission. Accessed March 23, 2022.
5. NHS England [homepage on the Internet]. Childhood asthma. Available from: https://www.england.nhs.uk/childhood-asthma/. Accessed February 3, 2022.
6. Townshend J, Hails S, Mckean M. Diagnosis of asthma in children. *BMJ*. 2007;335(7612):198–202. doi:10.1136/bmj.39234.651412.AE
7. Global Initiative for Asthma (GINA) [homepage on the Internet]. Pocket guide for asthma management and prevention (for adults and children older than 5 years); 2020. Available from: https://ginasthma.org/wp-content/uploads/2020/04/Main-pocket-guide_2020_04_03-final-wms.pdf. Accessed September 8, 2023.
8. Global Initiative for Asthma (GINA) [homepage on the Internet]. Global strategy for asthma management and prevention; 2017. Available from: https://ginasthma.org/wp-content/uploads/2019/04/wmsGINA-2017-main-report-final_V2.pdf. Accessed September 8, 2023.
9. Papadopoulos NG, Čustović A, Cabana MD, et al. Pediatric asthma: an unmet need for more effective, focused treatments. *Pediatric Allergy and Immunology*. 2018.
10. Golebski K, Dankelman LHM, Björkander S, et al. Expert meeting report: towards a joint European roadmap to address the unmet needs and priorities of paediatric asthma patients on biologic therapy. *ERJ Open Res*. 2021;7(4):00381–2021. doi:10.1183/23120541.00381-2021
11. Wjst M, Boakye D. Asthma in Africa. *PLoS Med*. 2007;4(2):e72. doi:10.1371/journal.pmed.0040072
12. Musafiri S, Joos G, Van Meerbeeck JP. Asthma, atopy and COPD in sub-Saharan countries: the challenges. *East Afr J Public Health*. 2011;8(2):161–163.
13. van Gemert F, van der Molen T, Jones R, Chavannes N. The impact of asthma and COPD in sub-Saharan Africa. *Prim Care Respir J*. 2011;20(3):240–248. doi:10.4104/pcrj.2011.00027
14. Mphahlele REM, Masekela R. A historical overview of childhood asthma in Southern Africa: are we there yet? *Afr J Thorac Crit Care Med*. 2021;27(4):163–167.
15. Saglani S, Menzie-Gow AN. Approaches to asthma diagnosis in children and adults. *Front Pediatr*. 2019;7:148. doi:10.3389/fped.2019.00148
16. Grigg J. Management of paediatric asthma. *Postgrad Med J*. 2004;80(947):535–540. doi:10.1136/pgmj.2003.014936
17. Herrett E, Gallagher AM, Bhaskaran K, et al. Data resource profile: Clinical Practice Research Datalink (CPRD). *Int J Epidemiol*. 2015;44(3):827–836. doi:10.1093/ije/dyv098

18. Song HJ, Blake KV, Wilson DL, Winterstein AG, Park H. Medical costs and productivity loss due to mild, moderate, and severe asthma in the United States. *J Asthma Allergy*. 2020;13:545–555. doi:10.2147/JAA.S272681
19. Tognella S, Micheletto C, Roggeri A, et al. Organization, clinical and management indicators on the first year of activity of an outpatient clinic dedicated to the diagnosis and treatment of severe asthma in Italy. *J Asthma Allergy*. 2021;14:1011–1018. doi:10.2147/JAA.S309740
20. Rönnebjerg L, Axelsson M, Kankaanranta H, et al. Severe asthma in a general population study: prevalence and clinical characteristics. *J Asthma Allergy*. 2021;14:1105–1115. doi:10.2147/JAA.S327659
21. Fuller E, Mindell J, Prior G Health Survey for England 2018, London: NHS Digital. Available from: https://digital.nhs.uk/data-and-information/publications/statistical/health-survey-for-england/2018. Accessed 12, January, 2022.
22. Dharmage SC, Perret JL, Custovic A. Epidemiology of asthma in children and adults. *Front Pediatr*. 2019;7:246. doi:10.3389/fped.2019.00246
23. Poyser MA, Nelson H, Ehrlich RI, et al. Socioeconomic deprivation and asthma prevalence and severity in young adolescents. *Eur Respir J*. 2002;19(5):892–898. doi:10.1183/09031936.02.00238402
24. Lang A, Carlsen KH, Haaland G, et al. Severe asthma in childhood: assessed in 10 year olds in a birth cohort study. *Allergy*. 2008;63(8):1054–1060. doi:10.1111/j.1398-9995.2008.01672.x
25. Nordlund B, Melén E, Schultz ES, Grönlund H, Hedlin G, Kull I. Prevalence of severe childhood asthma according to the WHO. *Respir Med*. 2014;108(8):1234–1237. doi:10.1016/j.rmed.2014.05.015
26. Mirabelli MC, Hsu J, Gower WA. Comorbidities of asthma in U.S. children. *Respir Med*. 2016;116:34–40. doi:10.1016/j.rmed.2016.05.008
27. Kumar P, Singh G, Goyal JP, Khera D, Singh K. Association of common comorbidities with asthma in children: a cross-sectional study. *Sudan J Paediatr*. 2019;19(2):88–92. doi:10.24911/SJP.106-1544873451
28. Onubogu U, West B. The pattern of comorbidities of childhood asthma as seen in the rivers state university teaching hospital, Nigeria. *Open J Resp Dis*. 2021;11(01):1–18. doi:10.4236/ojrd.2021.111001
29. Nyenhuis SM, Akkoyun E, Liu L, Schatz M, Casale TB. Real-world assessment of asthma control and severity in children, adolescents, and adults with asthma: relationships to care settings and comorbidities. *J Allergy Clin Immunol Pract*. 2020;8(3):989–996.e1. doi:10.1016/j.jaip.2019.10.032
30. Mortada MM, Kurowski M. Challenges in local allergic rhinitis diagnosis, management, and research: current concepts and future perspectives. *Medicina*. 2023;59(5):929. doi:10.3390/medicina59050929