Original research

Recent trends in asthma diagnosis, preschool wheeze diagnosis and asthma exacerbations in English children and adolescents: a SABINA Jr study

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ABSTRACT

Background Asthma-related burden remains poorly characterised in children in the UK. We quantified recent trends in asthma prevalence and burden in a UK population-based cohort (1–17-year-olds).

Methods The Clinical Practice Research Datalink Aurum database (2008–2018) was used to assess annual asthma incidence and prevalence in 1–17-year-olds and preschool wheeze in 1–5-year-olds, stratified by sex and age. During the same period, annual asthma exacerbation rates were assessed in those with either a diagnosis of preschool wheeze or asthma.

Results Annual asthma incidence rates decreased by 51% from 1403.4 (95% CI 1383.7 to 1423.2) in 2008 to 688.0 (95% CI 676.3 to 699.9) per 10^5 person-years (PYs) in 2018, with the most pronounced decrease observed in 1–5-year olds (decreasing by 65%, from 2556.9 (95% CI 2509.8 to 2604.7) to 892.3 (95% CI 866.9 to 918.3) per 10^5 PYs). The corresponding decreases for the 6–11- and 12–17-year-olds were 36% (1139.9 (95% CI 1110.6 to 1169.7) to 739.9 (95% CI 720.5 to 759.8)) and 20% (572.3 (95% CI 550.4 to 594.9) to 459.5 (95% CI 442.9 to 476.4)) per 10^5 PYs, respectively. The incidence of preschool wheeze decreased over time and was slightly more pronounced in the 1–3 year-olds than in the 4-year-olds. Prevalence of asthma and preschool wheeze also decreased over time, from 18.0% overall in 2008 to 10.2% in 2018 for asthma. Exacerbation rates increased over time from 1.33 (95% CI 1.31 to 1.35) per 10 PYs in 2008 to 1.81 (95% CI 1.78 to 1.83) per 10 PYs in 2018.

Conclusion Paediatric asthma incidence decreased in the UK since 2008, particularly in 1–5-year-olds; this was accompanied by a decline in asthma prevalence. Preschool wheeze incidence also decreased in this age group. However, exacerbation rates have been increasing.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Despite the considerable burden of asthma in the UK, asthma remains poorly characterised in the paediatric population.

WHAT THIS STUDY ADDS

⇒ Using routinely collected data from primary care practice in the UK (2008–2018), our findings show that the decrease in asthma incidence continues in the paediatric population but was accompanied by an increase in exacerbation rate, particularly in the 1–5-year-old age group. During the same period, preschool wheeze decreased in the paediatric asthma population.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ The increasing asthma exacerbation rates represent a growing burden for families and the health system. Research is needed to identify how exacerbations can be reduced and health systems pivoted to implement these interventions.

INTRODUCTION

Asthma, a chronic heterogeneous, fluctuating, inflammatory, respiratory disease,[1] is common across Europe, with approximately 30 million diagnosed cases among children and adults aged under 45 years.[2] In the UK, it is estimated that 5.4 million people currently receive treatment for asthma, including 1.1 million children.[3] Asthma accounts for ~3% of all primary care consultations, 60 000 hospital admissions and 200 000 bed days each year[4] and costs the UK ~£1.1 billion in prescriptions, general practitioner (GP) visits, hospital care and benefits.[5]

Despite the high healthcare burden, the epidemiology of asthma, especially in the UK paediatric population, remains poorly characterised. There is some evidence to suggest that the rate of new asthma diagnoses in children has been in a steady decline since 2000, particularly among younger children.[6] Similar trends have been observed in other high-income countries, with evidence suggesting that asthma prevalence in children may be beginning to plateau, and in some age groups even starting to fall.[7]

Investigating these trends using more recent data is crucial to determining whether the decrease in incidence and prevalence, if persisting, is real and/ or whether it is associated with changes in diagnostic practices over time. Additionally, understanding the incidence and prevalence of preschool wheeze and how these have changed over time may prove insightful, given that it is considered by some to be a precursor to an asthma diagnosis. In light of the significant burden of exacerbations, it is also imperative to understand how rates of asthma exacerbations

are changing over time; this will not only inform disease control and healthcare utilisation at a population level but may also provide some clues on why asthma deaths have increased by around a third in the last decade.[8]

Therefore, the main objectives of this study were to describe recent trends in the incidence and prevalence of asthma and asthma exacerbation rates, categorised by age group, sex and area deprivation level in a paediatric population aged 17 years and under. We also investigated trends in the epidemiology of preschool wheeze in children aged 1–5 years.

METHODS
Data sources
This study accessed routinely collected primary care data from GP practices using the EMIS Web software, that is, data curated by the UK Clinical Practice Research Datalink (CPRD) service and furnished to researchers as the CPRD Aurum database. As of October 2020, CPRD Aurum had archived longitudinal health data for nearly 12 million living patients, representing approximately 18% of the UK population. Aurum data have been shown to be representative of the national demographic, including age and sex.[9] CPRD Aurum data include information on clinical diagnoses, healthcare consultations, medications prescribed by primary care providers, laboratory tests and referrals to medical specialists. Linked socioeconomic data (from the Index of Multiple Deprivation (IMD) dataset) and secondary care data spanning accident and emergency (A&E) visits and admissions (from the Hospital Episode Statistics (HES) dataset) were provided for this study by CPRD. Approximately 75% of CPRD practices in England are eligible for HES data linkage.[9]

Study design
We described the incidence and prevalence of asthma in the population between 2008 and 2018, year-on-year, both overall and stratified by age (1–5, 6–11 and 12–17 years) and sex. Person-time started accruing either on the observation period start date (ie, 1 January of the year of interest) or once the patient had met the eligibility criteria (excluding asthma diagnosis), whichever came last. Person-time accrued until the patient left the practice, the last day the practice submitted data to CPRD, the patient died or the end of the study period (31 December of the year of interest), whichever was earlier. Incidence rates were reported per 10^5 person-years (PYs) at risk. Prevalence was also calculated for each calendar year of the study period, with stratification by age group and sex. Additionally, we described the incidence and prevalence of preschool wheeze in the 1–5 years age group and 1–3-year-olds and 4-year-olds alone, and the rate of asthma exacerbations across all age groups in those with either a diagnosis of preschool wheeze or asthma. We also described the proportion of asthma exacerbations by IMD quintile in each age group. IMD quintile 1 corresponds to the least deprived Lower Super Output Areas (LSOAs) and IMD quintile 5 corresponds to the most deprived LSOAs.

Patient population
The study population comprised children and adolescents (aged 1–17 years) registered at GP practices and participating in the CPRD's HES/Office of National Statistics linkage scheme who met CPRD's data quality criteria and our study inclusion criteria. In terms of the latter, participants had to have a clinical code indicative of an asthma/preschool wheeze diagnosis and at least 1 day of follow-up during the study period (1 January 2008 to 31 December 2018). Children aged at least 6 years had to have an asthma code, while those under the age of 5 years could have either an asthma

or a preschool wheeze diagnosis. Patients with less than 12 months of research-acceptable data prior to their asthma/preschool wheeze code and those with prior diagnoses of other chronic respiratory diseases, such as cystic fibrosis, bronchiectasis or primary ciliary dyskinesia, chronic upper airway cough syndrome or bronchopulmonary dysplasia were excluded from the study.

Exposure, outcomes and covariates
The codes used to identify asthma and preschool wheeze are available at https://github.com/NHLI-Respiratory-Epi/SABINA_Jr_codelists/ The definition of asthma used in this study has been validated previously for adults by comparing the CPRD GOLD database against a reference standard of physician-reviewed patient notes and exhibits a high positive predictive value (>86%).[10]

The analysis included GP-managed asthma exacerbations (defined as symptomatic worsening necessitating a short course of oral corticosteroids (OCS), an A&E department visit or a hospital admission). A short course of OCS was defined as a prescription for either oral prednisolone (prescribed for 3–5 days) or dexamethasone as a single dose (below a given threshold dose of 20 mg in the case of prednisolone), not administered on the same day as the annual asthma review. Hospital admissions for asthma as a primary diagnosis were identified by the International Classification of Diseases, 10th Revision codes (J45 and J46), whereas A&E visits were identified by a diagnostic code highly suggestive of an emergency department attendance for asthma (251). Events dated 14 days or less apart were assumed to represent ongoing treatment for the same event rather than sequential, new events. Where this occurred, the event was categorised based on its highest level of urgency (in the order of hospital admission, A&E visit and GP visit).

Statistical analysis
The incidence rate was calculated separately for incident or 'new' cases of asthma or preschool wheeze for each calendar year of the study period (2008–2018), and further stratified by sex and age group (1–5, 6–11 and 12–17 years). The numerator consisted of patients who were newly diagnosed with asthma (during the time period of interest) and the denominator comprised the person-time (in years) when the patient was at risk of developing the disease (during the time period of interest). Patients were only considered to have incident disease once over the study period.

For prevalence, we estimated a percentage point prevalence, such that the numerator consisted of patients with a diagnosis of asthma or preschool wheeze at the time of assessment or at any point prior. The denominator comprised all patients who met the inclusion criteria for our study at a certain time point. We chose 1 July, the mid-year point, as the basis for our estimation of point prevalence.

To investigate the change in asthma incidence over the study period, incidence rate ratios (IRRs) for the incidence rate linear trend were estimated for the overall study population and for each age group (1–5, 6–11 and 12–17 years). This effect estimate corresponded to the average annual change in the incidence rate (in per cent per year). To allow for overdispersion in IRR estimates (which can occur if the variance is greater than the mean of the incidence rates), negative binomial regression models were used. A similar approach was adopted to estimate the rate of change in prevalence. Thus, for prevalence, we constructed binomial regression models to estimate the odds ratios (ORs) and set the scale parameter to the deviance divided by the residual degrees of freedom to account for overdispersion.

The annual asthma exacerbation rates were estimated overall and by age group and sex. For these estimates, asthma exacerbations during the study period were considered as the
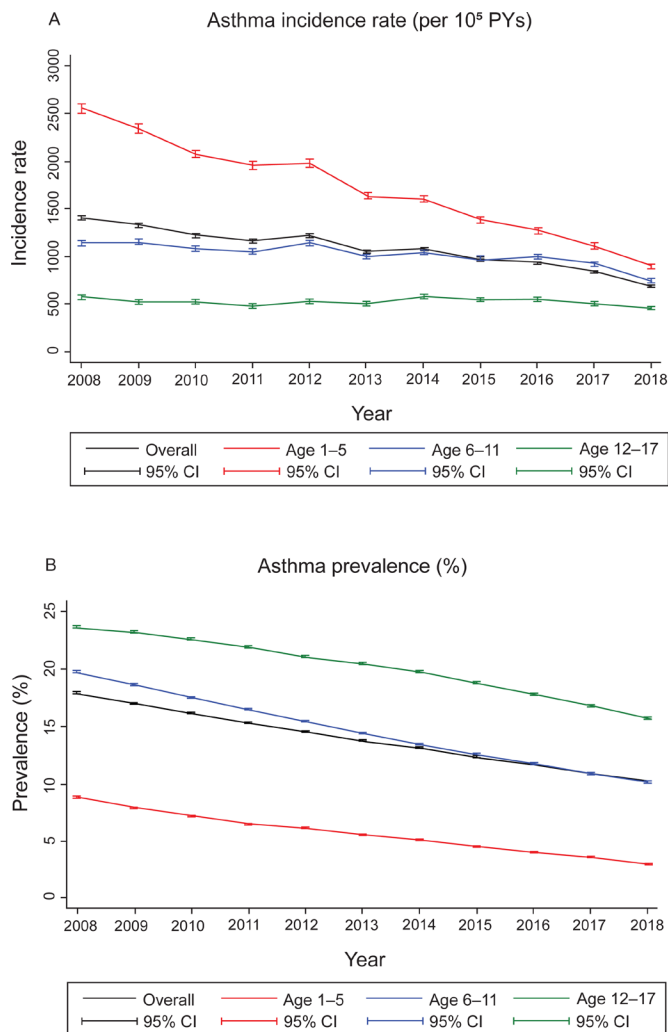
Figure 1 Trends in (A) incidence rate (per 10^5 PYs) and (B) prevalence (%) of asthma in UK children by age group during the study period (2008–2018). PY, person-year.

corresponding numerator, while patients with asthma during the same time period were considered as the denominator. An exact Poisson distribution procedure was employed to estimate asthma exacerbation rates per 10 PYs with corresponding 95% CIs. To investigate changes in asthma exacerbations over the study period, a similar approach to that used to estimate changes in asthma incidence rates was implemented. All analyses were performed using STATA statistical software, V.17 (StataCorp. 2021. Stata Statistical Software: Release 17; StataCorp).

RESULTS
Incidence and prevalence of asthma
A total of 498 503 children and adolescents (aged 1–17 years) met the inclusion criteria and were included in this study. During the study period (2008–2018), 190 986 incident cases of asthma were identified. For the overall study population, asthma incidence decreased from 1403.4 (95% CI 1383.7 to 1423.2) per 10^5 PYs in 2008 to 688.0 (95% CI 676.3 to 699.9) per 10^5 PYs in 2018, representing a 51% decline (figure 1A). Although asthma incidence decreased across all age groups, this decrease was most marked in the 1–5 years age group (decreasing by 65% from 2556.9 (95% CI 2509.8 to 2604.7) per 10^5 PYs to 892.3 (95% CI 866.9 to 918.3) per 10^5 PYs). The corresponding decreases for the 6–11- and

12–17-year-olds were 36% (1139.9 (95% CI 1110.6 to 1169.7) to 739.9 (95% CI 720.5 to 759.8)) and 20% (572.3 (95% CI 550.4 to 594.9) to 459.5 (95% CI 442.9 to 476.4)) per 10^5 PYs, respectively.

For the whole cohort, the annual rate of decrease averaged 6% per year (assuming a linear trend) (IRR 0.94; 95% CI 0.93 to 0.95; p<0.001). The IRR for the youngest age group, the 1–5-year-olds, was estimated to be 0.91 (95% CI 0.90 to 0.92; p<0.001), or 9% per year; for the 6–11-year-olds the annual percentage decline in incidence was lower, just 3% (IRR 0.97; 95% CI 0.96 to 0.98; p<0.001). In this age group, the decrease in the rate of new diagnoses of asthma was most marked from 2016 to 2018. Conversely, in the oldest age group, the 12–17-year-olds, the annual rate of decrease was not statistically significant (IRR 0.99; 95% CI 0.98 to 1.01; p=0.300).

Asthma prevalence also decreased over the period of our study, from 18.0% in 2008 to 10.2% in 2018 (figure 1B). The average prevalence change (assuming a linear trend) for the whole study population was 6% per year (OR 0.94; 95% CI 0.94 to 0.94; p<0.001). Again, we found a higher annual average rate of decline in the 1–5 years age group (10% per year) (OR 0.90; 95% CI 0.89 to 0.90; p<0.001) and slightly slower rate of decline in the older age groups, 8% per year in the 6–11 years age group (OR 0.92; 95% CI 0.92 to 0.93; p<0.001) and 5% per year in the 12–17 years age group (OR 0.95; 95% CI 0.95 to 0.96; p<0.001). The incidence and prevalence of asthma were consistently higher in boys than in girls and decreased over time across both sexes (online supplemental table S1).

Incidence and prevalence of preschool wheeze
There were 102 150 incident cases of preschool wheeze during the study period. The average preschool wheeze incidence rate change IRR for the overall group was 0.98 (95% CI 0.97 to 0.99; p=0.001); similar rates were found for the two separate age groups, the 1–3-year-olds (IRR 0.98; 95% CI 0.97 to 0.99; p=0.002) and 4-year-olds (IRR 0.98; 95% CI 0.97 to 1.00; p=0.037) (figure 2A). The average preschool wheeze prevalence change OR for the overall group was 0.98 (95% CI 0.98 to 0.99; p<0.001), or 2% per year, which was comparable across both age groups (for 1–3-year-olds, OR 0.98; 95% CI 0.97 to 0.99; p<0.001; for 4-year-olds, OR 0.99; 95% CI 0.98 to 0.99; p<0.001; figure 2B). Decreases in both incidence and prevalence of preschool wheeze were most marked between 2016 and 2018. Compared with girls, the incidence and prevalence of preschool wheeze were higher in boys and decreased over time across both sexes (online supplemental table S2).

Asthma exacerbation rates
Overall, the exacerbation rates increased over time across all age groups in both boys and girls (figure 3A,B; online supplemental table S3). Compared with other age groups, children aged 1–5 years experienced the highest rate of exacerbations. In the overall population, the IRR for linear trend was 1.04 (95% CI 1.02 to 1.05; p<0.001), implying an average increase in exacerbation rate of 4% per year over the study period. Similar values were obtained for individual age groups and sexes.

Analysis of the proportion of exacerbations across socioeconomic status categories, using IMD quintiles as our measure, revealed a higher proportion of exacerbations in children in the most deprived quintile of IMD (figure 4A–C).

DISCUSSION
This study, using routinely collected primary care data, showed that the incidence of asthma decreased steadily by 51% from 2008 to 2018; the rate of decline was similar in boys and girls, with the
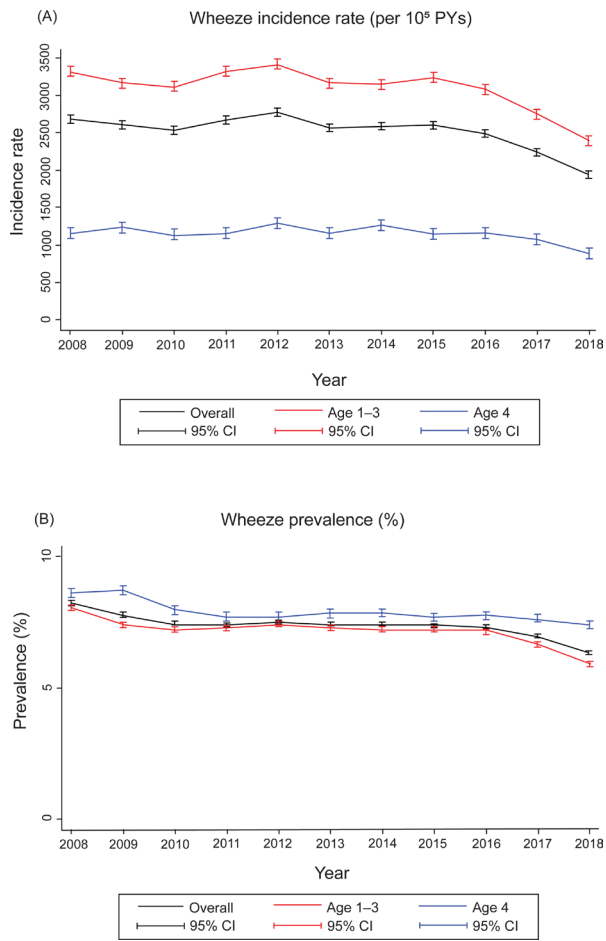
Figure 2 Trends in (A) incidence rates (per 10^5 PYs) and (B) prevalence (%) of preschool wheeze among children in the UK aged 1–4 years during the study period (2008–2018). PY, person-year.
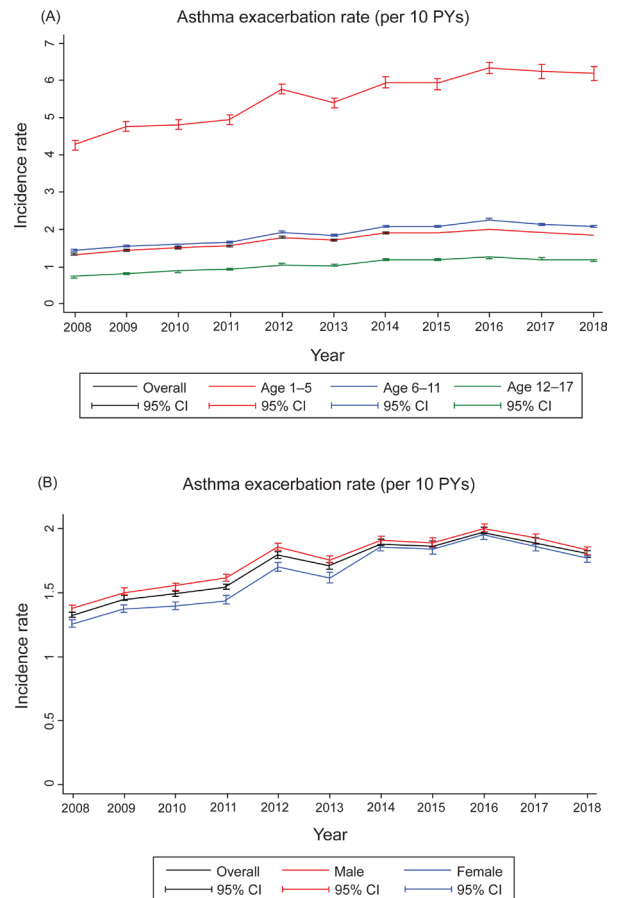

Figure 3 Trends in exacerbation rates (per 10 PYs) in UK children stratified by (A) age group and (B) sex during the study period (2008–2018). PY, person-year.

most pronounced decrease observed in the 1–5-year-olds. Overall, a 6% decline per year in the incidence rate was observed in the study population, with the decline being statistically significant in the 1–5 years and 6–11 years age groups (averaging 9% and 3% per year, respectively), but not in the 12–17-year-old age group. The incidence and prevalence were consistently higher in boys than in girls. The decrease in prevalence was statistically significant in all age groups, and as in the case of incidence, was most pronounced in the 1–5-year-olds. Among the 1–5-year-olds, the incidence of preschool wheeze decreased, particularly from 2015 onwards, driven largely by a decrease in the 1–3 years age group. The prevalence of preschool wheeze also decreased over time in both boys and girls. In contrast, exacerbation rates increased over time among both boys and girls and in all age groups, and higher proportions of children and adolescents exacerbating were those from socioeconomically deprived groups.

With respect to asthma diagnosis, the most pronounced decline in the 1–5 years age group may be due to a change in diagnostic decision-making for asthma, likely due to previous overdiagnosis of childhood asthma in primary care.[11] Interestingly, an increase in diagnoses of preschool wheeze was not observed in the same age group, suggesting that it is not as simple as children being given a diagnosis of preschool wheeze instead of asthma.[11 12] Nor do our findings suggest that asthma diagnoses are being delayed until children are at least 5 or 6 years old, as incidence is also decreasing in the 6–12-year-olds. Both observations are consistent with the possible historical overdiagnosis of asthma in preschoolers in

the UK.[11] Our data suggest that overdiagnosis of asthma may be more likely in very young children, as no reduction in incidence rates in the 12–17-year-olds was observed. The magnitude of our observed decreases is also suggestive of overdiagnosis (and not real change), as it would be unlikely that we would see such a change in asthma incidence and prevalence over the past 10 years due to changing risk factors alone. For instance, while the prevalence of smoking has decreased in the UK,[13] it has not been accompanied by a decrease in other risk factors for asthma, such as allergy, obesity and air pollution. Obesity continues to increase among children in the UK,[14] particularly in the most socioeconomically deprived groups.[15] Additionally, although breast feeding confers protection against wheezing in early life,[16] rates have not improved in the UK.[17] The smoking ban in 2007[18] may have had an impact on the development of asthma, given that it has had an impact on hospitalisation rates[19]; however, this is difficult to ascertain from these data. Historically, physicians were more likely to diagnose interval symptoms as asthma (cough, wheeze, dyspnoea), whereas today, perhaps, we are being more discerning when it comes to calling it 'asthma'.

The trends observed in this study are broadly consistent with those of previous studies using older data. A study using data from 2001 to 2005 found a decrease in asthma incidence over time, with the largest reduction seen in those under 5 years of age.[6] This study reported an increase in the prevalence of asthma, but in lifetime prevalence, which is not directly comparable to point prevalence reported here.[6] Work undertaken by the British Lung Foundation using data from 2004 to 2012 also found a decrease in incidence and a stable lifetime asthma prevalence.[20] Similarly, a health survey
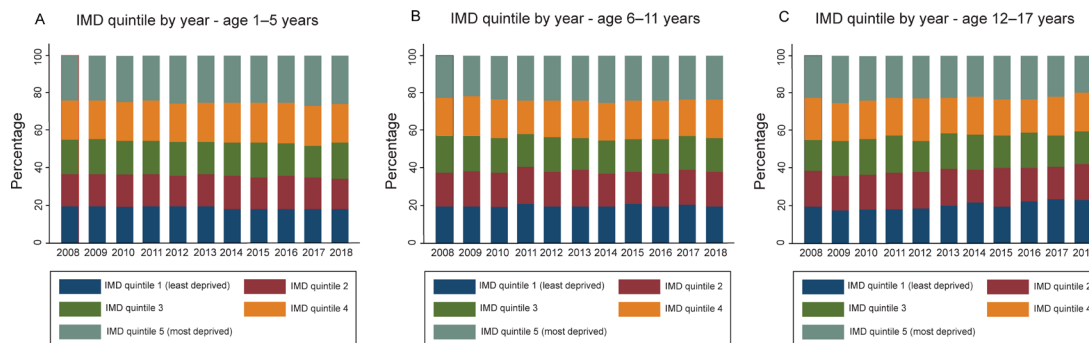
Figure 4 Proportion of exacerbations in UK children in (A) 1–5, (B) 6–11 and (C) 12–17-year-olds, stratified by IMD. IMD, Index of Multiple Deprivation.

for England observed that the proportion of children aged 0–15 years with an asthma diagnosis decreased from 20% in 2001 to 10% in 2018.[21] This trend is also in keeping with historical studies.[22]

Other explanations for our findings may include possible changes in coding practices, healthcare behaviours and healthcare utilisation. Interestingly, we found a small increase in asthma exacerbations over time. This may be related to a fall in asthma diagnoses; if a diagnosis is made less frequently, probably due to more stringent criteria, it is more likely to reflect real disease. Thus, patients with a diagnosis are more likely to exacerbate. The rate of exacerbations was the highest in very young children, approximately 3–4 times higher than in other age groups, perhaps reflecting the experience of those at the start of their asthma journey, who have not yet had the opportunity to achieve adequate asthma control through optimal medication. Another explanation may be lower thresholds for treating asthma attacks with OCS or a better understanding among parents about when to take their child to the doctor.

As with all epidemiological studies of this nature, our analysis has some strengths and limitations. The strength of this study is the large cohort size that used data generally representative of the paediatric asthma population in England and the use of validated clinical code sets to define GP-diagnosed asthma cases. In terms of limitations, this study did not evaluate additional clinical characteristics of asthma, including phenotypes, or perform clinical evaluations, such as lung function tests. Moreover, the potential impact of variations in diagnostic criteria on asthma prevalence was also not considered. Our study also did not evaluate the association between trends in influenza or pneumococcal vaccinations and prescribing patterns of asthma medications. However, neither coverage for the influenza or pneumococcal vaccinations[23 24] nor asthma prescribing patterns[25] substantially varied during the 10-year study period; therefore, this is unlikely to have impacted our study findings. We are aware that there are difficulties in estimating prevalence slopes using aggregate-level data, particularly where there are repeated measures from some patients in different years. While we can accurately report trends in the data, we can only make assumptions about why these trends occur. The introduction of the Quality and Outcomes Framework in the UK in 2004, a pay-for-performance scheme for general practices based on meeting targets for the quality of clinical care, has improved certain aspects of the management of chronic diseases, including the multidisciplinary management of chronic conditions and a reduction in socioeconomic inequalities in the delivery of care.[26 27] Therefore, our findings should be interpreted in light of advancements in the quality of asthma care.[26]

Overall, this work suggests that perhaps asthma is on the decline or at least is being diagnosed less frequently, which is in line with previous studies.[20–22] However, the perception remains that asthma is a large problem. Indeed, asthma mortality remains an issue in the UK, with the UK having some of the highest mortality rates in Europe.[28] Equally, there is still a high lifetime prevalence—perhaps related to the asthma 'epidemic' of the 1980s and 1990s.[22] It is plausible that the high rates of diagnoses then have resulted in a proportion of adults now being labelled with asthma, despite the fact they may have 'grown out of it'. This is certainly something that the calculation of lifetime prevalence would not take into account.

CONCLUSION

The incidence of asthma has decreased over time, particularly in younger age groups, and has been accompanied by a decrease in prevalence. The diagnosis of preschool wheeze also decreased over the period of our study, but at a more modest rate. In contrast, exacerbation rates have increased over our 10-year time span, suggesting that while fewer children are diagnosed with asthma, asthma exacerbations remain an important issue.

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