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Pediatric asthma incidence rates in the United States from 1980 to 2017

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Background: Few studies have examined longitudinal asthma incidence rates (IRs) from a public health surveillance perspective.
Objective: Our aim was to calculate descriptive asthma IRs in children over time with consideration for demographics and parental asthma history.
Methods: Data from 9 US birth cohorts were pooled into 1 population covering the period from 1980 to 2017. The outcome was earliest parental report of a doctor diagnosis of asthma. IRs per 1,000 person-years were calculated.
Results: The racial/ethnic backgrounds of the 6,283 children studied were as follows: 55% European American (EA), 25.5% African American (AA), 9.5% Mexican-Hispanic American (MA) and 8.5% Caribbean-Hispanic American (CA). The average follow-up was 10.4 years (SD = 8.5 years; median = 8.4 years), totaling 65,291 person-years, with 1789 asthma diagnoses yielding a crude IR of 27.5 per 1,000 person-years (95% CI = 26.3-28.8). Age-specific rates were highest among children aged 0 to 4 years, notably from 1995 to 1999, with a decline in EA and MA children in 2000 to 2004 followed by a decline in AA and CA children in 2010 to 2014. Parental asthma history was associated with statistically significantly increased rates. IRs were similar and higher in AA and CA children versus lower but similar in EA and MA children. The differential rates by sex from birth through adolescence principally resulted from a decline in rates among males but relatively stable rates among females.
Conclusions: US childhood asthma IRs varied dramatically by age, sex, parental asthma history, race/ethnicity, and calendar year. Higher rates in the 0- to 4-year-olds group, particularly among AA/CA males with a parental history of asthma, as well as changes in rates over time and by demographic factors, suggest that asthma is driven by complex interactions between genetic susceptibility and variation in time-dependent environmental and social factors. (J Allergy Clin Immunol 2021;148:1270-80.)

Key words: *Epidemiology, IRs, pediatric asthma, sex, parental history, time, United States*

An incidence rate (IR) is a fundamental epidemiologic measure that, unlike prevalence, is independent of disease duration and remission.[1] As such, IRs are the most valuable data for generating

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Abbreviations used
AA: African American
aIRR: Adjusted IR ratio
CA: Caribbean American
CREW: Children's Respiratory and Environment Workgroup
EA: European American
ECHO: Environmental Influences on Child Health Outcomes
IR: Incidence rate
MA: Mexican American

hypotheses related to disease etiology.[2] In the United States, there are legal requirements to report initial diagnoses of most infectious diseases and cancers to public health authorities, which provide national surveillance systems and detailed descriptive data for these conditions. Routine reporting of IRs according to associated demographic variables from these surveillance systems over time has been the foundation of numerous hypotheses and discoveries.[3] However, there is remarkably little standardized information regarding IRs for either childhood or adult asthma in the United States or worldwide.[4-9] Although some have proposed that asthma become a reportable disease,[10,11] this idea has never been promulgated and there are no long-term established US population–based registries identifying new cases; in contrast, the National Cancer Institute's cancer surveillance system has existed since the early 1970s.[12,13] A careful search of the literature has revealed few studies reporting IRs for pediatric asthma.[14-23] Most are calculated by using data collected for other purposes and cover limited calendar time periods, age groups, geographic areas, and/or racial/ethnic groups.[24-28] These IRs are frequently based on a number of suppositions, such as assuming the timing of diagnoses to be the midpoint between 2 questionnaires administered over a prolonged time interval or using questionnaires not specifically designed, standardized, or validated to collect information on the occurrence of asthma. More studies report cumulative incidence measures,[29-32] which are a measure of the proportion of a population that has developed the disease and which is not a rate but is instead a ratio and a measure of risk.[2]

Several epidemiologic dogmas exist for pediatric asthma; they are based largely on prevalence data. For example, it is inferred from prevalence data[33,34] that Puerto Rican children develop asthma more frequently, followed by Americans of African origin, Americans of European geographic ancestry, and (least frequently) Mexican Americans.[35,36] Reviews of the scientific literature suggest that asthma prevalence is more common in boys than in girls until around puberty, at which time the pattern reverses, presumably because of an increase in asthma IRs among girls.[37] Other research has attempted to evaluate whether the IRs of asthma are changing for children born in more recent decades, which suggests a need to investigate changes in the environment occurring during the relevant time periods. Reports have proposed that in the United States and other developed countries, an increase in asthma occurred in the 1980s and 1990s and has since plateaued or even decreased, but most of the data cited to justify these observations come from health care utilization information or prevalence measures.[38-42]

To address this knowledge gap, we have calculated asthma IRs by using pooled birth cohort data from the Children's Respiratory and Environment Workgroup (CREW), funded through the National Institutes of Health Environmental Influences on Child Health Outcomes (ECHO) program (www.echochildren.org). CREW brings together a dozen demographically diverse asthma-focused birth cohorts from across the United States in an effort to harmonize and subsequently combine data across these study populations.[43] This collaboration allowed retrospective construction of a "surveillance system" for these geographically defined populations of newborns who have been specifically followed for the development of asthma. This approach is complementary to that of another analysis of asthma IRs in 31 ECHO cohorts that include some CREW cohorts,[14] in which cohort-specific IRs were combined in a meta-analysis as opposed to being determined by pooling of individual data. The sample size was larger in the ECHO-wide study; however, its methodologic approach did not permit multivariable modeling or include calendar year of diagnosis (which is basic to surveillance) or detailed racial/ethnic categories. Further, in CREW, all the cohorts were focused on asthma and thus included more frequent survey questions regarding asthma, thereby increasing confidence in the date of asthma diagnosis.

Our goal was to use the harmonized and subsequently pooled data across the CREW cohorts to directly calculate overall and subgroup-specific asthma IRs from 1980 through 2017, with consideration for the fundamental epidemiologic variables of time, place, and person.[2] An advantage relative to a typical surveillance system is that in the CREW studies the parental history of asthma was recorded and used as a surrogate for potential genetic susceptibility.[44]

METHODS

We used data from 9 of the 12 longitudinal US birth cohorts that are part of the CREW consortium within the ECHO program, which has been described in detail by Gern et al,[43] to examine asthma IRs. Three of the CREW cohorts were not included because the youngest children were enrolled in relatively recent years (as late as in 2014, 2016, and 2019, respectively) and could only contribute minimal person-years of follow-up per child at the time when the data were harmonized and pooled across cohorts for these analyses. A data sharing protocol and a data use agreement were approved by the local institutional review boards for each participating cohort. Each cohort provided data to a single biostatistician (S.L.H.), who together with the lead epidemiologist (C.C.J.), worked in accordance with a back-and-forth process among the individual cohort data managers and investigators to address initial differences in the timing and wording of data collection tools and variations in data management, both before and after the data were eventually pooled for harmonization. The follow-up data provided from each cohort were up-to-date as of December 31, 2017.

Demographic variables and definition of outcome

The children included in the IRs were born from 1980 through 2007, and they were followed through the end of 2017; until a date of asthma diagnosis; or until they had been dropped from their respective birth cohort because of loss to follow-up, death, or withdrawal. Geographic locations were classified according to 3 US regions based on cohort location: Northeast (Baltimore, Md; Boston, Mass; and New York, NY), Midwest (Detroit, Mich; Cincinnati, Ohio; Madison, Wis, and St Louis, Mo), and Southwest (Tucson, Ariz). Date of birth and sex at birth were available for all children. Race/ethnicity was classified according to 5 self-identified categories: European American (EA), African American (AA), Caribbean American Hispanic (CA), Mexican American Hispanic (MA), and other. Children were categorized into these groups on the basis of their survey data and, in a few instances, on the basis of further checks with a cohort's research staff regarding available genetic ancestry data or other information helpful for this classification. Parental history of disease was considered positive if either birth parent was reported to have a history of a doctor diagnosis of asthma.

An incident case of asthma was defined as the first occurrence of an asthma diagnosis by a doctor based on the date of diagnosis as reported by a parent (usually the mother). If the exact date of diagnosis was not recalled, it was assumed to be at the median point between the date of administration of the questionnaire on which the diagnosis was reported and the previous questionnaire. Our objective was to retrospectively construct population data and incident cases as they would have been collected by a public health surveillance system that accepts results from physicians and/or associated medical laboratories without future modifications; therefore, we did not place any restrictions on these first reports.

Statistical analyses

IRs per 1000 person-years and 95% CIs derived from 9 CREW cohorts were computed by cohort and across the combined cohorts by calendar time, decade of birth, region, age group (0-4, 5-9, 10-14, 15-19, and 20-35 years), race/ethnicity, child sex, and parental history of asthma. Rates were calculated first in the standard way, which is often referred to as yielding a "crude" IR and is defined by the number of new asthma cases divided by the summed person-years at risk during a defined observation time. Censored subjects were assumed to be disease-free for half of the lost time; for example, a person followed for 1 year but lost to follow-up at year 2 contributed an additional half-year of disease-free time to the denominator. Rates were then calculated for each subcategory of interest (eg, calendar time [ranges of years], decade of birth, geographic region, age, race/ethnicity, sex, and parental history of asthma). Decade born can suggest hypotheses related to environmental changes that may have affected all age groups over the time period followed. Stratified tables are presented for ease of interpretation. Multivariable Poisson regression models involving use of the robust Huber-White sandwich variance estimator were used to calculate adjusted IR ratios (aIRRs) and 95% CIs.[45,46] All adjusted models included the following variables as potential confounders: decade of birth, region, age, race/ethnicity, sex, and parental history of asthma. Parental history of asthma, child sex, race/ethnicity, age, region, and decade of birth were analyzed as potential effect modifiers.

RESULTS

Table I shows the characteristics of the children included in the analyses and crude IRs (for information by individual cohort, see Table E1 and Fig E1 in this article's Online Repository at www.jacionline.org). The 37-year time period of observation for asthma diagnosis ranged from 1980 to 2017 for the 6283 children, with the most person-years of observation between 2000 and 2009. The average person-time contributing to the sample for these analyses, starting at birth (birth years ranged from 1980 to 2007) was 10.4 years (SD = 8.5 years; median = 8.4 years) for a total of 65,291 person-years. At last date of follow-up in 2017, the oldest cohort participants had reached 34.8 years, and the youngest were 12.7 years.

In the combined cohorts at time of birth, 55% of the children were EA, 25.5% were AA, 9.5% were MA, and 8.5% were Puerto Rican or Dominican (CA). Other race/ethnic groups comprised only 1.5% of the population and were excluded from further analyses. Of the 9 cohorts, 4 required a parental allergic history (asthma, allergy, or sensitization) with varying definitions for eligibility (see the section Description of Individual Cohorts in the Online Repository at www.jacionline.org). When the pooled data were used, a parental history of asthma (mother, father, or both) was reported by 37.2% of the parents across all the cohorts.

There were 1798 cases of physician-diagnosed asthma, with an overall crude IR of 27.5 per 1000 person-years (95% CI = 26.3-28.8) (Table I). When calendar period of the diagnoses was considered, the rates were highest from 1995 to 2009, with all of the year categories having an IR of more than 25 per 1000 person-years during this time period and a peak at 41.9 per 1000 person-years in the period from 2005 to 2009 (95% CI = 38.9-45.2). However, whereas the proportions by child sex remained constant in the cohorts over calendar time, the cohorts born earliest came from general population sampling frames (rather than being required to have a family history of asthma or allergies) and were predominantly of European ethnicity (see Fig E2 in this article's Online Repository at www.jacionline.org), with both variables associated with lower IRs (Table I and see Tables E2 and E3 in this article's Online Repository at www.jacionline.org). Therefore, subsequent analyses by calendar time and decade of birth stratified the data by race/ethnicity and parental history.

Interestingly, the IRs were nearly identical and more than doubled for AAs and CAs (51.4 per 1000 person-years [95% CI = 47.0-56.0] and 51.7 per 1000 person-years [95% CI = 44.7-59.5], respectively) as opposed to nearly identical rates in EAs (20.6 per 1000 person-years [95% CI = 19.2-22.1]) and MAs (21.3 per 1000 person-years [95% CI = 18.1-24.9]) (Table I). When the data were stratified by parental history and sex, the IRs in each parallel stratum were similar and higher in AAs and CAs, compared with similarly lower rates in EAs and MAs (see Table E3). We also compared IRs for these 4 race/ethnicity groups by age (Fig 1) and found parallel patterns in the age-specific rates. Thus, for ease of interpretation and to increase the statistical power and precision of the estimates related to other variables, we collapsed these 4 race/ethnic groups into 2, deemed AAs/CAs and EAs/MAs (for sex- and parental history–specific IRs and age- and parental history–specific IRs, respectively, for these 2 combined race/ethnicity groups, see Table E4 and Fig E3 [in this article's Online Repository at www.jacionline.org]).

Analyses of IRs by calendar time and place

The first step in analyzing surveillance data is usually to evaluate IR patterns by year and geographic region (see Figs E4 and E5 in this article's Online Repository at www.jacionline.org). In Fig E4, it is evident that those with a parental history of asthma had higher rates over time for both race/ethnicity categories, and Fig E5, *A-D* shows IRs by Midwest versus Northwest versus Southwest over time, as stratified by parental history and the 2 race/ethnicity categories. However, differences in age distribution of populations being compared affect interpretation if rates vary by age. In this "constructed" population, new birth cohorts were initiated as the years progressed, as a result of which the age distribution of the pooled cohort changed over the years. Therefore, age-specific rates are presented in Fig 2, *A-D*, revealing different patterns by age and calendar year, race/ethnicity, and parental history. The 0- to 4-years age group showed high rates in the period from 1995 to 1999 that were consistent in all race/ethnicity categories and parental history groups. Among the EA/MAs, the 5- to 9-year-olds and 10- to 14-year-olds group rates peaked earlier than did the 0- to 4-years age group and then declined (see also Fig E6, *A* and *B* in the Online Repository at www.jacionline.org). Although unstable before 1995, the IRs in the 0- to 4-year-olds age group were much higher among AAs/CAs with a parental history of asthma than in the other groups. It appears in this AA/CA group that rates peaked in the period from 1990 to 1994, remained high (with IRs higher than 130.0 from 1995 to 2009), but then decreased and were similar to the rates for the other race/ethnic categories after

TABLE I. Overall univariate crude doctor-diagnosed asthma IRs per 1000 person-years, by epidemiologic characteristics

Characteristic	No. (%)	Person-years	No. of asthma cases	IR (95% CI) per 1,000 person-years
All subjects	6,283	65,291	1,798	27.5 (26.3-28.8)
Calendar time of surveillance*				
1980-1984	1,225 (19.5%)	2,860	19	6.6 (4.0-10.4)
1985-1989	1,884 (30.0%)	6,123	123	20.1 (16.7-24.0)
1990-1994	1,777 (28.3%)	7,690	178	23.1 (19.9-26.8)
1995-1999	2,494 (39.7%)	8,609	262	30.4 (26.9-34.3)
2000-2004	3,813 (60.7%)	13,056	357	27.3 (24.6-30.3)
2005-2009	4,628 (73.7%)	16,286	683	41.9 (38.9-45.2)
2010-2014	2,507 (39.9%)	8,761	152	17.3 (14.7-20.3)
2015-2017	1,204 (19.2%)	1,904	24	12.6 (8.1-18.8)
Decade born				
1980-1989	2,058 (32.6)	33,731	562	16.7 (15.3-18.1)
1990-1999	1,098 (17.5)	11,169	390	34.9 (31.5-38.6)
2000-2009	3,127 (49.8)	20,391	846	41.5 (38.7-44.4)
Geographic region				
Northeast	1,535 (24.4%)	13,646	622	45.6 (42.1-49.3)
Midwest	3,044 (48.5%)	25,404	706	27.8 (25.8-29.9)
Southwest	1,704 (27.1%)	26,240	470	17.9 (16.3-19.6)
Child age during follow-up (y)*				
0-4	6,283 (100%)	25,520	1,011	39.6 (37.2-42.1)
5-9	4,365 (69.5%)	17,549	440	25.1 (22.8-27.5)
10-14	2,815 (44,.8%)	10,471	188	18.0 (15.5-20.7)
15-19	1,649 (26.2%)	5,950	77	12.9 (10.2-16.2)
20-35	712 (11.3%)	5,800	82	14.1 (11.2-17.5)
Child race/ethnicity				
EA	3,268 (55.0)	40,184	829	20.6 (19.2-22.1)
AA	1,515 (25.5)	9,813	504	51.4 (47.0-56.0)
MA	563 (9.5)	7,338	156	21.3 (18.1-24.9)
CA	505 (8.5)	3,789	196	51.7 (44.7-59.5)
Other	92 (1.5%)	955	17	17.8 (10.4-28.5)
Child sex				
Male	3,172 (50.5)	30,901	984	31.8 (29.9-33.9)
Female	3,110 (49.5)	34,389	814	23.7 (22.1-25.4)
Parental history of asthma				
None	3,401 (64.5)	41,344	725	17.5 (16.3 -18.9)
Paternal only	645 (12.2%)	6,308	239	37.9 (33.2 -43.0)
Maternal only	1,028 (19.5%)	8,342	422	50.6 (45.9 -55.7)
Both parents	198 (3.8%)	1,248	106	84.9 (69.5-102.7)
Either or both parents	2,017 (37.2)	16,927	831	49.1 (45.8-52.5)

Child sex missing for 1 child, race/ethnicity missing for 432 children, and parental history of asthma missing for 1,011 children.
*The population numbers in the asterisk-prefaced categories are not mutually exclusive; children in the cohorts were followed as they aged over calendar time from the point of enrollment (birth date) until they were censored owing to cessation of follow-up or asthma diagnosis.

2010. Thus, the changes in IRs over calendar time have been greatest in the 0- to 4-year-olds and highest from 1985 to 2009 for AA/CAs with a parental history of asthma. Detailed calendar time–, decade of birth–, age-, sex-, race/ethnicity-, and parental history–specific rates are provided in Table E5 (in this article's Online Repository at www.jacionline.org).

Analyses of IRs by birth decade

IRs were examined next by decade of birth, race/ethnicity, and parental history (Fig 3). Although the IRs by race were similar among those without a parental history of asthma in the decade from 1980 to 1989, they diverged in the 2 subsequent birth decades, with higher IRs for AAs/CAs. For those with a parental history of asthma, the IRs for AAs/CAs were markedly higher than were those for EAs/MAs in all 3 birth decades examined. However, the IRs for EAs/MAs with a positive parental history increased by birth decade, whereas those of the AAs/CAs peaked in the decade from 1990 to 1999.

With regard to age, the most striking changes in rates by decade of birth were found in the 0- to 4-years age groups (Fig 4). Among those without a parental history of asthma, 0- to 4-year-olds from both race/ethnicity groups born in the 1990s had the highest IRs when compared with the IRs among those born in the other 2 decades and all other age groups (Fig 4, *A* and *B*). Among those with a parental history of asthma, the EAs/MAs aged 0 to 4 years once again had the highest IRs during the decade from 1990 to 1999, but the AAs/CAs aged 0 to 4 years had higher IRs in the decade from 1980 to 1989, with their IRs declining dramatically in the subsequent 2 decades, although among the studied cohorts fewer AAs/CAs were enrolled in the 1980s, thus impairing the precision of the IR estimates for that decade. Nevertheless, the rate for AAs/CAs aged 0 to 4 years and born in the 1990s was striking at 150.5 (95% CI = 107.5-204.9) per 1000 person-years, which is nearly 3 times the rate for EAs/MAs of the same age (57.6 [95% CI = 45.9-71.3] per 1000 person years).

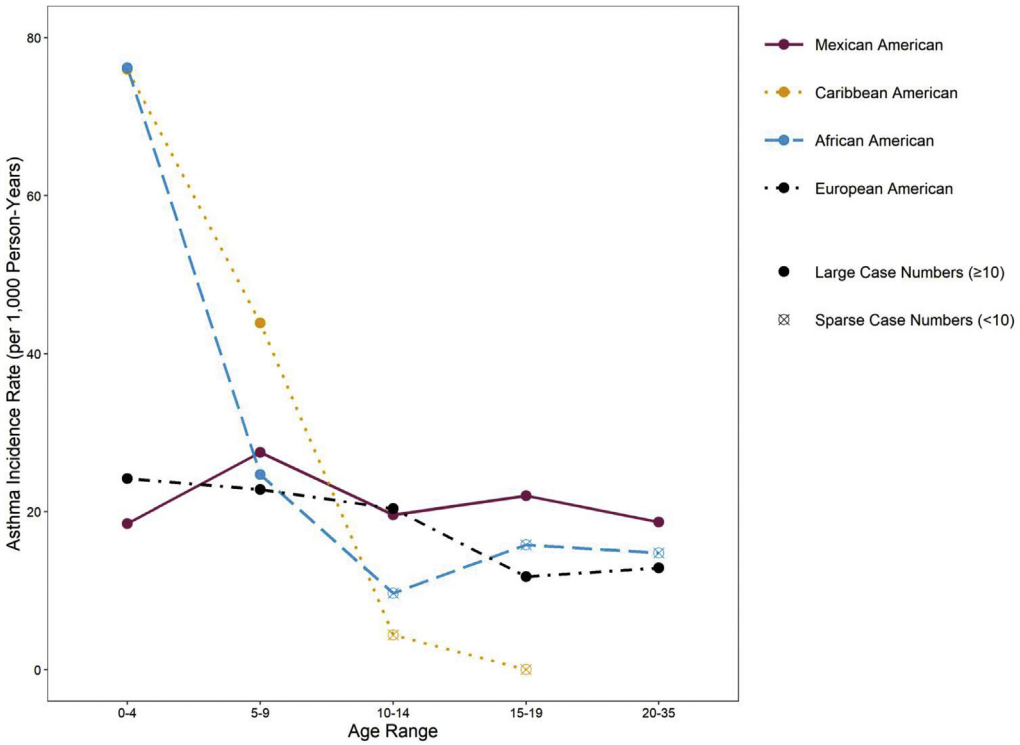

FIG 1. Doctor-diagnosed asthma IRs per 1000 person-years, by age and 4 individual race/ethnicity categories (N = 5035).

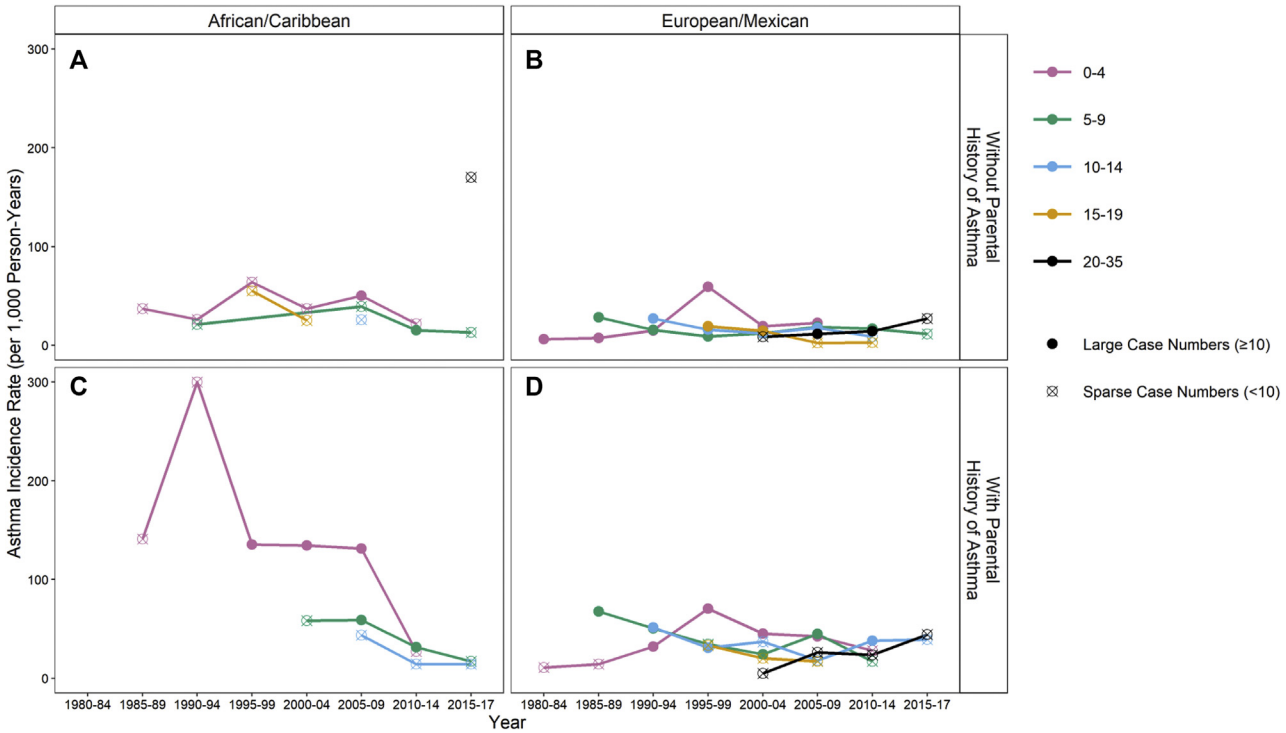

FIG 2. Doctor-diagnosed asthma IRs per 1000 person-years by calendar time (years) and age at diagnosis and by race/ethnicity and parental history of asthma (N = 5035).

Analyses of IRs by age, race, and sex

Differences in asthma patterns by sex and age have been of continuing scientific interest (Fig 5, *A-D*). In subjects without a parental history of asthma (Fig 5, *A* and *B*), the rates among the EA/MA females increased slightly from the age range from 0 to 4 years to the age range from 10 to 14 years, after which they plateaued. The rates among males declined from the age range from 0 to 4 years to the age range from 15 to 19 years, crossing the rates

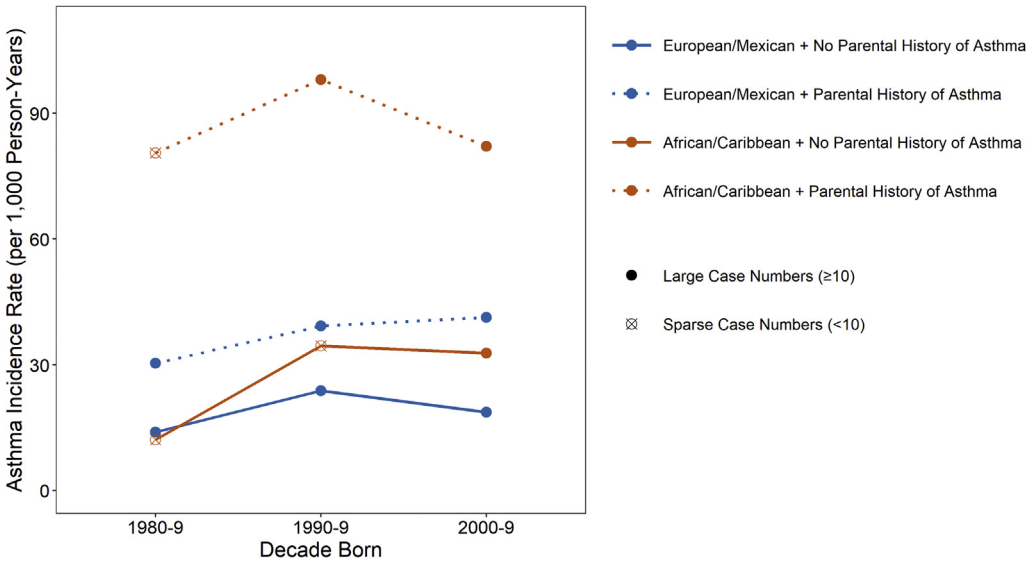

FIG 3. Doctor-diagnosed asthma IRs per 1000 person-years by decade of birth and by race/ethnicity and parental history of asthma (N = 5035).

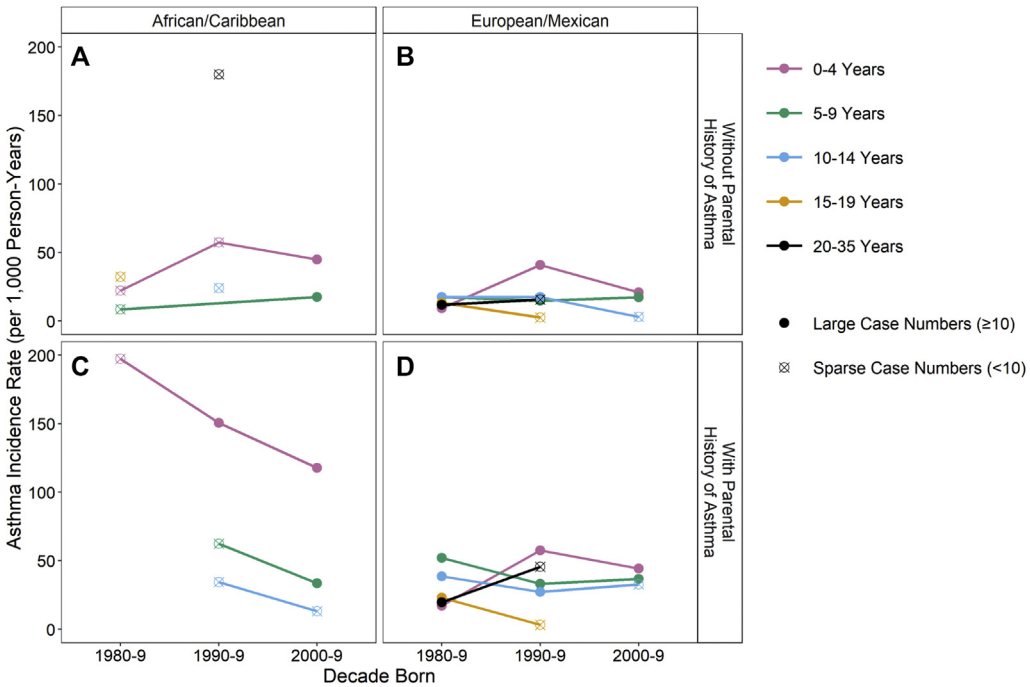

FIG 4. Doctor-diagnosed asthma IRs per 1000 person-years by decade of birth and age at diagnosis and by race/ethnicity and parental history of asthma (N = 5035).

for females during the 10- to 14-year interval. In contrast, the rates for AAs/CAs were highest in 0-year-old to 4-year-old children for both males and females, and although the data are sparse, the trends suggest that the rates initially declined during the interval from 0 to 4 years but then increased in males after 9 years and in females after 14 years. In those with a parental history of asthma (Fig 5, *C* and *D*), the rates were exceedingly high in 0- to 4-year-old AA/CA males (~150 per 1000 person-years) and were also high in AA/CA females in this age group (~100 per 1000 person-years), after which they rapidly declined but did not cross each other. Among the EAs/MAs with a parental history of asthma, there was a crossover in incidence by sex at an older age than found among those without a parental history of asthma and predominately reflected a more rapid decrease in the male rates rather than an increase in the rates among females.

Multivariable analyses

aIRRs were calculated by using Poisson models to account for potential confounders and assess effect modification. The columns devoted to model 1 in Table II display aIRRs for the total population, demonstrating that being born in the 1990s, younger, AA/CA, and male and having a parental history of asthma were all significantly ($P < .001$) associated with higher aIRRs of asthma.

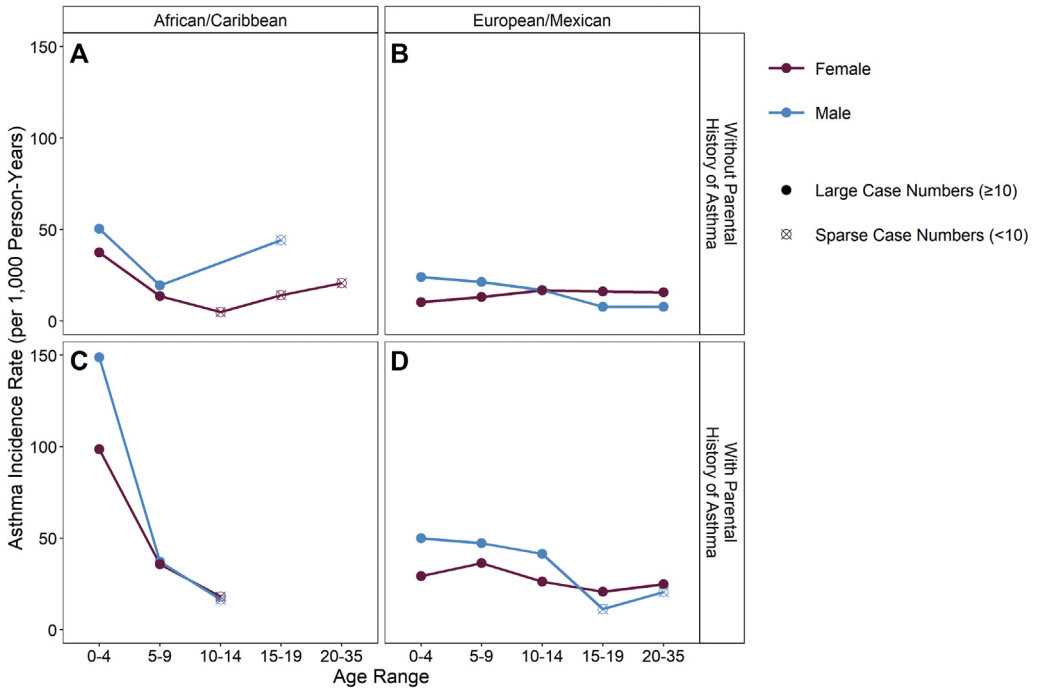

FIG 5. Doctor-diagnosed asthma IRs per 1000 person-years by age and child sex and by race/ethnicity and parental history of asthma (N = 5034).

A sex-by-race/ethnicity term in this model was not significant ($P = .856$), nor was the sex-by–family history term ($P = .496$). However, because the parental history of asthma–by-race/ethnicity interaction term was significant at ($P = .025$), models 2 and 3 assess effect modification by parental history of asthma. AA/CA race/ethnicity is a stronger risk factor in those with a parental asthma history (aIRR = 2.16 [95% CI = 1.76-2.64]), whereas the higher-incidence birth decades (ie, the 1990s and 2000s) seemed more important among individuals without a parental history of asthma. The rate increases in the 0- to 4-years and 5- to 9-years age groups were stronger in those with a parental history of asthma. Models 4 and 5 stratify by decade of birth because the decade born–by-region interaction term was significant at $P < .001$, which was not unexpected, as there were fewer AAs/CAs and northeastern US cohorts born in the 1980s than in the 1990s and 2000s in this study. For those born in the 1980s, the 5- to 9-year-olds and 10- to 14-year-olds groups had the highest rates, rates in the Southwest region were higher than in the Midwest, and the aIRR for parental history of asthma was 2.19 (95% CI = 1.81-2.65). For those born from 1990 to 2009, the aIRR was notably elevated for the 0- to 4-year-olds (aIRR = 5.08 [95% CI = 2.77-9.30]), rates were significantly lower in the Southwest; males and AAs/CAs had increased rates, whereas parental history of asthma maintained a similar association.

DISCUSSION

The IR, which is defined as the number of new cases of a disease over a specified time period occurring in a defined population at risk for the disease, is a fundamental measure in epidemiology because IRs are critical for understanding disease etiology and causality.[47] Other epidemiologic measures, such as mortality rates and prevalence ratios, are less valuable in relation to causality because many factors beyond etiology come into play with these estimates. By measuring childhood asthma IRs over a nearly 40-year period, we found that the rates revealed marked differences over calendar time, as well as by age, racial/ethnic background, sex, and parental history of asthma.

The most highly cited study providing IRs for pediatric asthma in the United States and covering the period from 1964 to 1983 was published in 1992 by Yunginger et al from the Mayo Clinic.[7] The population was 97% White and living in a county of only about 100,000 residents in 1980. This landmark study lacked information on parental history of asthma. Nevertheless, it suggested that the incidence of asthma was increasing in the period just preceding that in which our data collection was initiated, with rates in the early 1980s comparable to those found in our EA/MA population at that time. In addition, the largest increases over calendar time were in children aged 0 to 14 years, particularly in those aged 1 to 4 years, which was similar to our findings (see Fig E6, *A* and *B* for CREW EA–only IRs by calendar time and age comparable to those found in the Yunginger et al[7] study). The peak rate for children aged 1 to 4 years in Olmstead County in 1983 was approximately 10 per 1000 person-years, compared with 6.8 per 1000 person-years in the period from 1980 to 1984 for our EA/MA group, which consisted of children from the earliest Tucson-based cohort. The Mayo group also saw differential IRs over time for males and females depending on age, with the increase in incidence over time greater in males aged 1 to 9 years (and especially in those aged 1 to 4 years) but not in older age groups.

Many questions have been raised regarding the effects of race and ethnicity on epidemiologic and clinical aspects of pediatric asthma. Among the cohorts analyzed in this study, there were minimal differences in IRs among those considering themselves to be predominately EA and those considering themselves to be MA. Similarly, there were minimal differences among those

TABLE II. aIRRs of doctor-diagnosed asthma by Poisson regression model, total and stratified by parental history and birth decade

Characteristic	Model 1* All (N = 5034) aIRR (95% CI)	*P* value	Model 2 Without parental history (n = 3185) aIRR (95% CI)	*P* value	Model 3 With parental history (n = 1849) aIRR (95% CI)	*P* value	Model 4 Born 1980-1989 (n = 1783) aIRR (95% CI)	*P* value	Model 5 Born 1990-2009 (n = 3251) aIRR (95% CI)	*P* value
Decade born										
2000-2009	1.13 (0.95-1.33)	.168	1.29 (1.03-1.62)	.028	0.94 (0.72-1.23)	.670	—	—	—	—
1990-1999	1.32 (1.11-1.59)	.002	1.46 (1.09-1.96)	.012	1.16 (0.89-1.51)	.274	—	—	—	—
1980-1989	Reference		Reference		Reference		—	—	—	—
Region of United States										
Northeast	1.07 (0.88-1.29)	.496	1.18 (0.86-1.62)	.303	1.05 (0.80-1.40)	.706	†	—	1.86 (1.39-2.48)	<.001
Midwest	0.99 (0.85-1.14)	.839	0.96 (0.80-1.16)	.690	1.06 (0.83-1.35)	.621	0.76 (0.62-0.92)	.006	1.51 (1.15-2.00)	.003
Southwest	Reference		Reference		Reference		Reference		Reference	
Age group										
Age (y)										
0-4	1.83 (1.51-2.23)	<.001	1.42 (1.11-1.82)	.005	2.68 (1.87-3.84)	<.001	0.84 (0.65-1.10)	.216	5.08 (2.77-9.30)	<.001
5-9	1.24:(1.01-1.53)	.039	1.14 (0.88-1.47)	.333	1.61 (1.11-2.35)	.012	1.73 (1.37-2.18)	<.001	2.32 (1.25-4.29)	.007
10-14	1.18 (0.94-1.48)	.149	1.18 (0.90-1.56)	.227	1.33 (0.88-2.01)	.173	1.56 (1.21-2.00)	.001	1.71 (0.89-3.30)	.106
15-35	Reference		Reference		Reference		Reference		Reference	
Race/ethnicity										
AA/CA	1.89 (1.62-2.20)	<.001	1.56 (1.24-1.98)	<.001	2.16 (1.76-2.64)	<.001	1.17 (0.64-2.13)	.610	1.58 (1.38-1.80)	<.001
EA/MA	Reference		Reference		Reference		Reference		Reference	
Sex										
Male	1.39 (1.25-1.54)	<.001	1.33 (1.15-1.55)	<.001	1.43 (1.24-1.65)	<.001	1.14 (0.96-1.36)	.136	1.52 (1.33-1.73)	<.001
Female	Reference		Reference		Reference		Reference		Reference	
Parental asthma history										
Yes	2.16 (1.93-2.42)	<.001	—	—	—	—	2.19 (1.81-2.65)	<.001	2.11 (1.83-2.42)	<.001
No	Reference		—	—	—	—	Reference		Reference	

In each model, all variables have been adjusted for all the other variables in the model.
*For model 1, the aIRR of the decade from 2000 to 2009 decade as compared with the decade from 1990 to 1999 decade is 1.10 (95% CI = 0.94-1.29); P =..220.
†There were insufficient numbers to permit an estimate.

considering themselves AA and those identifying as being of CA heritage (in this study, largely children of Dominican or Puerto Rican origin). These findings differ from those of several studies of prevalence reporting that among children, asthma prevalence is highest among Puerto Rican children, followed by Black and White children and lowest among Hispanic children of Mexican heritage.[39,48-52] The apparent differences between the incidence and prevalence findings could be related to variation in remission rates. Some long-term cohort studies have shown that asthma is variably present throughout life, with more remissions during childhood[53-55]; however, there is little information on whether asthma remission varies among racial/ethnic groups.[56] Hispanic populations from the Caribbean in general, and specifically from Puerto Rico and the Dominican Republic, have been shown to have a large percentage of African ancestry, whereas MAs do not.[57,58] These findings, along with the very high IRs in the youngest age group of AA/CA children with parental histories of asthma and the minimal geographic variation, suggest that there may be a factor associated with African ancestry that increases the risk of asthma inception.[59] However, although genetics likely play a role, numerous nongenetic factors associated with race/ethnicity in the United States over multiple generations appear critically important and certainly contribute to the observation that positive asthma family history is a potent influence on IRs. Moreover, the dramatic changes in asthma IRs over just a few decades that vary by race/ethnicity suggest that environmental exposures and social circumstances contribute substantially to disease risk.[60]

An important question arising from monitoring asthma prevalence concerns the increase in prevalence during the 1990s and 2000s followed by an apparent plateau or decline afterward. Our data show a marked decline in the IRs of asthma from the period from 2005 to 2009 to the period from 2010 to 2014 among AA/CA children with parental histories of asthma, which occurred similarly in the 3 areas of the United States considered. This change occurred predominately among children younger than 4 years. The declining incidence during these years is also clearly seen among AA/CA children without a parental history of asthma, and to a lesser degree in the other race/ethnicity–parental history groups. Among EA/MA children, the peak IRs among 0- to 4-year-olds occurred from 1995 to 1999 but took place earlier for the 5- to 9-year-olds group (1985-1989). A study by Engelkes et al examined asthma IRs among 5- to 18-year-old children in The Netherlands from 1999 to 2012 and reported an apparent decline from 2007 to 2012 with a pivot point of 2008-2009, supporting our findings.[20] Another study of asthma IRs in Denmark and Sweden showed an increase in asthma incidence from 1998 to 2006 followed by a similar decline to 2011 in the Danish children that stood in contrast to an increase in incidence from 2006 to 2010 in the Swedish children.[21] Simpson et al in England[61] reported a decline in asthma incidence in all age groups from birth to age 65 years and older from 2001 to 2005 and especially in 2005; similarly, the largest declines were also seen in children aged 0 to 4 years (–38.4%) and in children aged 5 to 14 years (–27.0%).

The pattern of uptick and then decline in asthma IRs over time and by decade born suggests that 1 or more novel external factors were increasingly introduced in the 1980s and more dramatically influenced 0- to 4-year-old children and all racial groups, but especially those of African heritage and those with a parental history of asthma. This factor may have then changed in a way that substantially reduced the number of new childhood asthma diagnoses both in Europe and across the United States, with the decline first witnessed among US children of European origin. It remains for investigators to consider and evaluate possible reasons for such a change. A strong candidate as 1 such factor is the changing use of antibiotics during early infancy in response to antimicrobial stewardship promotion, an exposure that has been examined in the past with respect to risk of allergies and asthma with conflicting results.[62-64] In a 2020 comprehensive article, Patrick et al reported that according to health care administrative data, antibiotic prescribing to children in the province of British Columbia, Canada, who were younger than 1 year had declined by 77% from 1996 to 2016, and from 2000 to 2014, this decline was associated with a significant decrease in asthma diagnoses in children from the age 1 to 4 years.[65] Moreover, in the Canadian CHILD cohort, use of systemic antibiotics before 1 year of age was associated with significantly increased risk for an asthma diagnosis at age 5 years, which was shown to be mediated by the gut microbial community at age 1 year. Interestingly, a US study of claims data across 9 health plans showed a significant decrease (24%) in antibiotic medications dispensed to children in the age group from 3 months to 3 years between 1996 and 2000.[66] Further, over this period of time, many other exposures potentially related to the infant gut microbial community and/or childhood asthma risk have changed; these factors include types and quantities of air pollution, chemicals in foods and on clothing, microbes in food, decreased numbers of early infections and changes in pediatric vaccines, medically based campaigns to alter infant care, drinking water quality, and physical activity levels.[67,68]

One of the more consistent findings in the prevalence data is a decline in the prevalence of asthma in males during the mid-teenage years and an increase in prevalence among females. Many have assumed that this change resulted from an increase in IRs among females related to puberty. However, our data do not show a large increase in IRs among females approaching the teenage years. Among AA/CA children, the incidence for males is always greater or the same as that for females, although our data were limited for AA/CA children in the older age groups. Among the EA/MA subjects, the IRs for males and females do cross between 10 and 19 years for those with and without a parental history of asthma, but the change in IRs is primarily due to a rapid decline in the IRs in males after the first decade, with little change in females. This same pattern of a higher male incidence that declines rapidly between 10 and 20 years of age to fall below the incidence for females has been reported by others.[20,22,28] It has been suggested that older females may be more likely to develop non–IgE-related asthma, which would then be reflected in overall asthma age-specific IRs and prevalence, highlighting the need for more precise asthma phenotyping in epidemiologic studies.[69,70]

Strengths of our study include the large, racially/ethnically and geographically diverse cohorts of subjects who were recruited over the course of more than 30 years and were specifically followed frequently and queried about allergic diseases and asthma. The pooling and harmonization of data from these 9 cohorts allowed relatively robust estimates of asthma IRs over 3 decades, with consideration of the child's age, race/ethnicity, sex, and region of birth within the United States, as well as parental history. Although it is known that the incidence of an asthma diagnosis among children 0 to 4 years of age may often be a transient wheezing phenotype,[71] our intent was to evaluate asthma IRs as they would appear if an asthma diagnosis were a reportable event as part of a routine surveillance system covering all asthma diagnoses and therefore all phenotypes. However, it is reassuring that our results do not conflict with the aforementioned ECHO-wide incidence study,[14] in which a case among children with a diagnosis of asthma or wheeze before the age of 5 years was not considered an incident case at that time point unless there also was sustained evidence of disease after the fifth birthday.

As with all studies, ours had important limitations. There were minor variations between studies in the specific questions asked about asthma diagnosis that had to be reconciled by expert opinion as the data were harmonized. Because these were longitudinal studies of large populations, there were inevitable losses to follow-up in each cohort. Similarly, missing data reduced the numbers of subjects for certain analyses. Just US populations were considered, and they were restricted to only 8 states. Determinations of race and ethnicity were dependent on the parental reports rather than on ancestral DNA markers. As already mentioned, the racial/ethnic makeup of cohorts and their selection criteria varied over the decades of recruitment, making the early-period estimates of IRs for non-EA groups less robust. It is also impossible to ascertain how changes in the diagnostic criteria for asthma over time, by racial group, or by region of the country affected our results. However, it is unlikely that national or local diagnostic trends would have systematically influenced only certain subgroups (particularly by age), as was revealed by our data, suggesting that this may be less of a concern. It would have been valuable to have information on other variables such as allergic sensitization and sequential spirometry to provide more specific phenotypes, but this awaits future analyses, as these data, which are also less widely available, have not yet been harmonized.

In summary, we found that asthma IRs varied dramatically by age, sex, racial/ethnic background, and parental history of asthma. The highest asthma IRs were among AA/CA children 0 to 4 years of age—especially males who had parental histories of asthma. We found that these variables affected rates in both males and females but especially in preschool males. Asthma IRs also varied by decade of birth, with a peak in births in the 1990s. The increase and relatively high IRs for asthma followed by declines suggest that it would be valuable to search for environmental and behavioral changes occurring during the relevant time periods. Importantly, our findings illustrate the potential value of a US asthma surveillance system for discerning patterns and generating etiologic hypotheses that could lead to disease prevention.

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Key messages

- **Childhood asthma IRs in the United States have varied dramatically by age, racial/ethnic background, child sex, and parental history.**
- **Asthma IRs were highest in 0- to 4-year-olds, particularly among AA/CA males with a parental history of asthma, but rates for this race/ethnic category declined after 2009. A defined peak for EA/MA 0- to 4-year-olds occurred in 1995-1999.**

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