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Association between birthplace, prevalence, and age of asthma onset in adults: a United States population-based study

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ABSTRACT

Background: Previous studies have found associations between region of birth and asthma prevalence.

Objective: To study the association among birthplace, US prevalence, age of onset, and disease course of adult asthma.

Methods: Data from 447,801 adults from the 1997 to 2011 National Health Interview Survey were reviewed. History of asthma was compared with birthplace using Rao-Scott χ^2 tests, survey logistic, propensity score, and Cox regression. Trends of asthma prevalence were analyzed using logistic regression. Multivariate models controlled for sociodemographics, health care access, smoking history, and body mass index.

Results: Adults born outside the United States had lower odds of ever asthma (adjusted odds ratio [OR] 0.52, 95% confidence interval [CI] 0.49–0.55) or current asthma (OR 0.50, 95% CI, 0.46–0.54). The inverse association between foreign birthplace and asthma prevalence was significant in all regions of birth ($P < .0001$). Adults born outside the United States who resided in the United States for longer than 10 years compared with only 0 to 4 years had higher odds of ever asthma (OR 1.28, 95% CI, 1.18–1.38) and current asthma (OR 1.70, 95% CI, .31–2.19). Foreign-born compared with US-born adults also had delayed onset of asthma (adjusted hazard ratio 0.27, 95% CI, 0.27–0.28). The US prevalence of asthma increased in a linear manner from 1997 (9.1%, 8.77%–9.37%) to 2011 (12.5%, 12.1%–12.8%, $P < .0001$), which paralleled the trend for US-born adults. However, the prevalence of asthma in foreign-born adults was consistently lower and increased to a lesser extent ($P < .0001$).

Conclusion: Foreign-born American adults from all regions of birth have a lower prevalence of asthma, which increases after prolonged US residency. Foreign-born Americans may have a higher risk of adult-onset asthma.

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Introduction

In 2009, the current asthma prevalence was 8.2% of the US population, up from 7.3% in 2001, an increase of 12.3%. In contrast, the prevalence of asthma in the non-Hispanic black population was 11.1%,¹ indicating wide variation of disease prevalence in different US minority groups. Conversely, the prevalences of asthma and allergic disease are much lower in other countries, such as Mexico and China,² indicating wide regional variation of disease prevalence. Some reasons for the varying prevalence rates by race or ethnicity and region include differences of socioeconomic status, urban living, nutritional factors, adiposity, infectious exposures, climate factors, and pollutants, all of which are associated with asthma.^{3–11}

People born and raised outside the United States encounter a different profile of such exposures and would likely have different rates of asthma and allergic disease. Indeed, birthplace outside the United States was recently found to be associated with lower US prevalence of asthma and allergic disease in children, but the disease risk increased with longer than 10 years of US residency.¹² These associations suggest potential gene–environment interactions and perhaps an epigenetic phenomenon in the pathogenesis of childhood asthma and allergic disease. However, it is unknown whether these associations similarly occur in foreign-born American adults or whether lower prevalences occur in all foreign-born Americans or only people who originate from certain countries or regions. In addition, little is known about the effects of foreign birthplace on the disease course and age of asthma onset.

Previous studies have suggested that asthma prevalence increased in the United States by 70% since 1986.¹³ At the same time, rates of foreign-born Americans have dramatically increased

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from 9.7%¹⁴ to 13%¹⁵ of the total population, with more than half of foreign-born Americans coming to the United States since 1990.¹⁵ These increasing rates of foreign-born Americans and racial and ethnic minorities in the United States raise questions about the effects of immigration into the United States on asthma prevalence.

The authors hypothesized that foreign-born Americans have a lower prevalence and a later onset of asthma than US-born adults. If so, delayed onset of asthma in foreign-born Americans has much clinical significance, because these adults may have a different disease course and deny a personal or family history of asthma or atopic disease. However, the disease course and age of asthma onset in foreign-born American adults has not been well studied. The authors further hypothesized that the prevalence of asthma is increasing in US-born and foreign-born Americans, although to a lesser extent in the latter. Further, lower asthma prevalence in foreign-born Americans may deflate the overall nationwide prevalence estimates. However, it is unknown what role foreign birthplace has on the secular trend of adult asthma prevalence in the United States. The goal of this study was to address the effects of birthplace on adult asthma in the United States.

Methods

National Health Interview Survey

The authors used the National Health Interview Survey (NHIS; <http://www.cdc.gov/nchs/nhis.htm>), which was collected by US Bureau of the Census under the supervision of the National Center for Health Statistics. The authors used data from 1997 through 2011 because of consistent sampling methods and survey instruments that allowed for comparison of prevalences and use of complex survey weighting across survey years. The NHIS is the principal source of information on the health of the civilian noninstitutionalized population of the United States. Waiver of informed consent was obtained by the research ethics review board of the National Center for Health Statistics. This study also was approved by the institutional review board at St. Luke's-Roosevelt Hospital Center (New York, New York). The questionnaire included a core module about an adult's health with questionnaires to estimate the prevalence of multiple health issues, including asthma. The survey was administered in person to selected households across all states and districts by the Bureau of the Census using approximately 400 trained interviewers with computer-assisted personal interviewing. One adult was randomly selected for the sample adult questionnaire. Interviews were conducted in English and Spanish.

Using data from the US Census Bureau, sample weights were created that factored age, sex, race, ethnicity, household size, and educational attainment of the most educated household member using a multistage area probability sampling design by the NHIS. These sample weights are needed to provide nationally representative prevalence estimates for each state's population of noninstitutionalized adults. All frequency data are presented as raw values, whereas prevalence estimates presented reflect this complex weighting.

Asthma Outcomes

History of asthma at any time in life and current history of asthma were determined in 1997 through 2011 by separate NHIS questions. Of note, some asthma outcomes were not assessed every survey year (see Table 1 for the list of questions used in this study and the years they were administered). These are referred to throughout the article as ever and current history and lifetime and point prevalence of asthma, respectively. Age of asthma onset was assessed in 2010. In participants with a history of asthma, history of asthma attack, urgent or emergency care for an asthma attack, and overnight hospitalization for an asthma attack in the past year were determined in 1997

Table 1

Questions used in the study

Question	Years
Have you ever been told by a physician or other health professional that you had asthma?	1997–2011
Do you still have asthma?	1997–2011
During the past 12 mo, have you had an episode of asthma or an asthma attack?	1997–2011
During the past 12 mo, have you had to visit an emergency department or urgent care center because of asthma?	1997–2011
During the past 12 mo, have you stayed overnight in a hospital because of asthma?	1999, 2002, 2003, 2008
During the past 3 mo, did you use more than 3 canisters of this type of inhaler?	1999, 2003, 2008
Have you ever taken the preventive kind of asthma medicine used every day to protect your lungs and keep you from having attacks? Include oral medicine and inhalers. This is different from inhalers used for quick relief.	2002, 2003, 2008
Are you currently taking this medication (that protects your lungs) daily or almost daily?	2003, 2008
How old were you when you were first told you had asthma?	2010
Were you born in the United States?	1997–2011
In what country were you born?	2000–2011
In what year did you come to the United States to stay?	1998–2011

through 2011. Further, measurements of asthma control, including the use of at least 3 asthma rescue inhalers in 3 months and ever and current use of long-term asthma control medications, were assessed for participants with current asthma in a subset of study years.

Birthplace

Birthplace in or outside the United States (binary), region of birth (categorical), and duration of residency in the United States (0–4, 5–9, or ≥10 years) were determined. Age at immigration was derived by subtracting the duration of US residency from the current age.

Data Processing and Statistical Methods

All data processing and statistical analyses were performed in SAS 9.2 (SAS Institute, Cary, North Carolina). All statistical analyses, including descriptive statistics, accounted for the complex sample weights generated by the NHIS, such that estimates of prevalence and effect size are reflective of the general population. Univariate associations were tested by Rao-Scott χ^2 tests (Proc Surveyfreq; SAS Institute). Survey logistic regression models were used to determine the effects of birthplace in the United States (binary), region of birth (categorical), and duration of residency in the United States (0–4, 5–9, or ≥10 years) on asthma prevalence (Proc Surveylogistic). Covariates for multivariable models were selected by constructing multiple models that included combinations of sex (male vs female), current age (continuous), race (white, black, American Indian, Asian, multiracial), Hispanic origin (binary and categorical), household income (<100%, 100%–199%, 200%–299%, 300%–399%, or ≥400% family poverty level), family structure (lives alone, married or unmarried couple, other adults in home, and children in home), marital status (lives with spouse or partner, married but not living together with spouse, and not married), current working status (binary), history of health care interaction in the past 12 months (binary), health insurance coverage (binary), lifetime or ever history of smoking (binary), and body mass index (<17, 17–24, 25–29, or ≥30 kg/m²) as binary or categorical variables, and interaction terms between them and US birthplace. These factors were selected based on the authors' a priori hypothesis that they may be potential confounders of the association between foreign birth and asthma and previous published associations with eczema¹⁶ and asthma.¹⁷ The

authors hypothesized these factors do not play a role in the causal pathway of inverse association between foreign birthplace and asthma. Rather, they hypothesized that the causal pathway of association involves environmental exposures early in life, consistent with the “hygiene hypothesis.” Each covariate was manually added to the models and was kept in the final model if it was significant and decreased the overall Bayesian information criteria, which penalize for extra parameters and consider the large sample.¹⁸ Survey year (continuous) also was included as a potentially confounding covariate because the prevalence of asthma and the proportion of foreign-born participants increased steadily during the study years. Complete data analysis was performed (ie, missing values were omitted from analyses).

Propensity score (PS) regression was used to confirm the findings of the results of the survey logistic regression models. In these models, the PS is the conditional probability of birthplace based on all individual covariates and accounts for imbalances in different birthplace groups.¹⁹ The PSs were estimated using survey logistic regression models with and without complex sample weighting²⁰; birthplace was the binary dependent variable and the above-mentioned covariates and Health Resources and Service Administration region were as the independent variables. Then, logistic regression models were constructed with the asthma outcomes as the binary dependent variables and birthplace and PS as the independent variables.

Survival analyses using the Kaplan-Meier method were used to determine whether birthplace outside the United States was associated with delayed asthma onset (for survey year 2010). The time-to-event variable in all models was the time from birth in the United States or immigration to the United States to age at diagnosis of asthma or current age for those without asthma (censored). Models were stratified by history of birthplace in the United States. Log-rank statistics were calculated for testing the homogeneity of survival functions across strata. Similarly, Cox proportional hazards regression models were constructed with several models, including birthplace in the United States as a (1) fixed covariate and (2) adjusted for sex, current age, race, Hispanic origin, household income, family structure, marital status, current working status, history of health care interaction in the past 12 months, health insurance coverage, and lifetime history of smoking as categorical variables. (3) To determine whether foreign birthplace was associated with delayed asthma-free survival for all ages of diagnosis, birthplace in the United States was modeled using time-dependent covariates based on age of asthma diagnosis (0–19, 20–49, and ≥50 years of age).

Several approaches were used to determine the effects of US birthplace on the secular trend of asthma prevalence. In the first approach, logistic regression models were constructed with ever or current history of asthma as the dependent variables using Proc Glimmix. Birthplace in the United States (binary) and year of survey were treated as fixed covariates. Models were tested using linear and polynomial interactions between birthplace and survey year (continuous) and only significant interaction terms were retained in the final model. Various transformations of survey year, such as log, exponential, and square root, were attempted and best-fit models were selected using the Bayesian information criteria. In the second approach, survey year was treated as an ordinal variable for model fitting and was combined into 3 groups (1997–2001, 2002–2005, and 2006–2011) for parsimony and to simplify comparisons of asthma prevalence between years. The a priori plan was to examine all 3 comparisons between the combined groups to test whether there was effect modification for birthplace by survey year. Post hoc comparisons that control for multiple testing and the other covariates were performed using Tukey pairwise comparisons.

Post hoc correction for multiple dependent tests was performed by minimizing the false discovery rate with the approach of Benjamini and Hochberg²¹ and corrected *P* values are presented. Two-

sided *P* values less than or equal to .05 or less were considered significant.

Results

Population Characteristics

Data were collected on 447,801 adults. Prevalence of asthma was significantly associated with younger age, non-Hispanic descent, female sex, lower household income, family structure, not being married, higher level of education, health care interaction and insurance coverage in the past year, ever history of smoking cigarettes, and body mass index of at least 30 kg/m² (Table 2). In contrast, asthma prevalence was lower in whites and Asians and those currently working. Birthplace outside the United States also was significantly associated with all these variables. These were considered potential confounding variables and included in multivariate models.

Survey Logistic Regression Models of Birthplace in United States and Asthma Prevalence

Adults born outside the United States had significantly lower lifetime (6.2% vs 11.6%; survey logistic regression, odds ratio [OR] 0.50, 95% confidence interval [CI] 0.48–0.52, *P* < .0001) and point prevalence (3.0% vs 5.9%; OR 0.48, 95% CI, 0.46–0.51, *P* < .0001) of asthma than those born in the United States (Table 3). These associations remained significant in multivariate logistic regression models. All these covariates remained significant in multivariate models.

There were significant statistical interactions for birthplace by race and Hispanic descent as predictors of lifetime and point prevalence of asthma, but these interactions did not dramatically modify the estimates and were therefore omitted from multivariate models.

In participants with asthma and an attack in the past year, foreign birthplace was associated with a higher odds of urgent or emergency care for such attacks in univariate models (OR 1.70, 95% CI, 1.48–1.98, *P* = .0002) and remained significant in multivariate models (*P* = .03).

There were no associations between foreign birthplace and 1-year prevalence of asthma attacks (*P* = .32), overnight hospitalization for asthma attacks (*P* = .47), use of at least 3 asthma inhalers in the past 3 months (*P* = .34), and ever or current use of long-acting asthma control medications (*P* = .99 and .94, respectively).

Propensity Regression Models of Birthplace in the United States and Asthma Prevalence

Similar results were found using propensity regression models. Adults born outside the United States had significantly lower lifetime (adjusted OR for unweighted PS models 0.56, 95% CI, 0.53–0.58, *P* < .0001) and point prevalence (adjusted OR 0.53, 95% CI, 0.50–0.56, *P* < .0001) of asthma than those born in the United States (eTable 1). Similar results were found for weighted PS models (data not shown).

In propensity regression models, however, there were no significant associations between foreign birthplace and 1-year prevalence of asthma attacks (*P* = .80), urgent or emergency care for asthma attacks (*P* = .06), overnight hospitalization for asthma attacks (*P* = .15), use of at least 3 asthma rescue inhalers in the past 3 months (*P* = .74), and ever or current use of long-acting asthma control medications (*P* = .25 and .58, respectively).

Association between Region of Birth and Asthma Prevalence

Birthplace in all regions outside the United States was associated with lower lifetime and point prevalence of asthma in adults (*P* < .0001; Table 4). These associations remained significant in multivariate models. However, none of the other above-mentioned

Table 2
Participant characteristics (n = 447,801)^a

Variable	Asthma ^b			Birthplace ^c		
	No (n = 399,579)	Yes (n = 47,696)	P value	Inside United States (n = 366,482)	Outside United States (n = 79,420)	P value
Age (yr), mean (95% CI)	45.7 (45.6–45.8)	43.7 (43.6–43.9)	<.0001	45.9 (45.8–46.0)	42.9 (42.7–43.0)	<.0001
Race or ethnicity, n (%)			<.0001			<.0001
African American	57,938 (88.1)	7,879 (11.9)		58,739 (88.7)	6,883 (11.3)	
White	311,766 (89.3)	36,305 (10.7)		293,970 (88.0)	52,988 (12.0)	
Asian	15,309 (92.4)	1,303 (7.6)		3,542 (20.2)	13,031 (70.8)	
American Indian	2,901 (86.3)	459 (13.7)		2,658 (81.7)	694 (18.3)	
Other or mixed	11,328 (86.3)	1,715 (13.7)		7,399 (61.0)	5,629 (39.0)	
Hispanic			<.0001			<.0001
No	329,279 (88.9)	40,974 (11.1)		335,975 (91.2)	33,167 (8.8)	
Yes	70,236 (91.5)	6,714 (8.5)		30,443 (39.2)	46,248 (60.8)	
Sex, n (%)			<.0001			<.0001
Male	178,381 (90.8)	17,324 (9.2)		159,144 (84.3)	35,960 (15.7)	
Female	221,198 (87.8)	30,372 (12.2)		207,338 (85.4)	43,460 (14.6)	
Household income (poverty level), n (%)			<.0001			<.0001
0%–99%	49,817 (85.5)	8,302 (14.5)		42,345 (76.1)	15,637 (23.9)	
100%–199%	63,913 (88.1)	8,210 (11.9)		54,902 (78.9)	17,035 (21.1)	
200%–299%	53,338 (89.1)	6,341 (10.9)		49,646 (85.2)	9,838 (14.8)	
300%–399%	41,722 (89.4)	4,746 (10.6)		40,243 (88.3)	6,091 (11.7)	
≥400%	104,089 (89.7)	11,698 (10.3)		102,407 (89.9)	12,994 (10.1)	
Family structure, n (%)			<.0001			<.0001
Lives alone	125,758 (88.3)	16,219 (11.7)		122,512 (89.0)	19,119 (11.0)	
Lives together with spouse or partner	134,612 (89.3)	15,321 (10.3)		127,101 (87.6)	22,349 (12.4)	
Other adults in home	26,706 (86.4)	4,131 (13.6)		25,486 (87.7)	5,229 (12.3)	
Other adults and children in home	112,503 (89.8)	12,025 (10.2)		91,383 (78.9)	32,723 (21.1)	
Marital status, n (%)			<.0001			<.0001
Not married	187,836 (87.6)	25,550 (12.4)		181,113 (87.2)	31,705 (12.8)	
Married but not living together	6,383 (90.7)	635 (9.3)		3,824 (56.8)	3,167 (43.2)	
Married and living together	203,524 (90.1)	21,367 (9.9)		179,989 (84.0)	44,136 (16.0)	
Highest level of education			<.0001			<.0001
<HS	55,156 (89.7)	6,477 (10.3)		39,014 (66.5)	22,462 (33.5)	
HS or GED	99,209 (89.9)	10,916 (10.1)		93,940 (87.6)	15,818 (12.4)	
>HS	241,810 (88.8)	30,089 (11.2)		231,017 (86.7)	40,030 (13.3)	
Health care interaction in past year, n (%)			<.0001			<.0001
No	80,011 (93.2)	5,524 (6.8)		61,234 (76.3)	24,049 (23.7)	
Yes	312,866 (88.2)	41,426 (11.8)		299,233 (87.0)	53,862 (13.0)	
Health insurance coverage			<.0001			<.0001
No	68,716 (90.0)	6,985 (10.0)		49,247 (70.3)	26,484 (29.7)	
Yes	327,863 (89.0)	40,398 (11.0)		316,039 (87.7)	52,577 (12.3)	
Currently working, n (%)			<.0001			<.0001
No	152,613 (87.7)	20,937 (12.3)		142,965 (85.2)	30,090 (14.8)	
Yes	246,966 (90.0)	26,759 (10.0)		223,517 (84.7)	49,330 (15.3)	
Lifetime smoking history			<.0001			<.0001
No	226,348 (90.1)	24,076 (9.9)		193,298 (80.1)	56,290 (19.9)	
Yes	169,582 (88.0)	23,342 (12.0)		169,995 (90.1)	22,342 (9.9)	
Body mass index (kg/m ²), n (%)			<.0001			<.0001
<17	1,896 (88.0)	259 (12.0)		1,750 (82.0)	397 (18.0)	
17–24	155,942 (90.6)	15,787 (9.4)		138,882 (83.6)	32,275 (16.4)	
25–29	135,853 (90.2)	14,475 (9.8)		121,481 (84.1)	28,344 (15.9)	
≥30	105,888 (86.1)	17,175 (13.9)		104,369 (87.6)	18,404 (12.4)	

Abbreviations: CI, confidence interval; GED, General Education Development certificate; HS, high school.

^aAll frequency data are presented as raw values, whereas prevalence estimates presented reflect the complex weighting defined by the National Health Interview Survey. P values were adjusted by adjusting for the false discovery rate. All variables were analyzed using Rao-Scott χ^2 test, except for age (yr) that was analyzed by survey t-test.^bRow percentages are presented. Frequencies may not total the 447,801 participants included for analysis because of missing values. Of the 447,801 participants, refusal to answer a particular question or a response of “don’t know” occurred for questions pertaining to ever history of asthma in 526 (0.1%), birthplace in the United States in 1,899 (0.4%), age in 0 (0.0%), race in 376 (0.08%), Hispanic descent in 74 (0.02%), sex in 0 (0.0%), household income in 95,382 (21.3%), family structure in 0 (0.0%), marital status in 2,010 (0.4%), highest level of education in 3,701 (0.8%), health care interaction in past year in 7,593 (1.7%), health insurance coverage in 3,345 (0.7%), current working status in 0 (0.0%), lifetime history of smoking in 4,036 (0.9%), and body mass index in 0 (0%).^cColumn percentages are presented.asthma outcomes were associated with region of birth ($P \geq .14$; data not shown).*Prolonged Residency in the United States but not Age of Immigration Increases Asthma in Adults Born Outside the United States*

Adults born outside the United States who lived in the United States for longer than 10 years compared with only 0 to 4 years had significantly higher odds of developing ever asthma (OR 1.28, 95% CI, 1.18–1.38, $P < .0001$) and current asthma (OR 1.70, 95% CI, 1.31–2.19, $P < .0001$; Table 5), whereas US residency for only 5 to 9 years was not associated with increased asthma (OR 0.98, 95% CI, 0.71–1.36, $P = .42$).

Older age at immigration of foreign-born Americans was associated with higher odds of ever and current asthma in univariate models (data not shown), but these associations were no longer significant in multivariable models (Table 5). The association between asthma and duration of US residency remained significant in models that included age at immigration (data not shown).

Association between US Birthplace and Age of Asthma Onset

Kaplan-Meier analysis was used to assess whether birthplace outside the United States was associated with age at onset of asthma. Birthplace outside the United States was found to be

Table 3Association of immigrant status with asthma prevalence, attacks, and long-term control in adults^a

Asthma parameter (sample size for each parameter) ^b	Birthplace								
	Inside United States		Outside United States						
	Frequency	Percentage (95% CI)	Frequency	Percentage (95% CI)	OR (95% CI)	<i>P</i> value	aOR (95% CI)	<i>P</i> value	
Ever history (n = 445,391)									
No	323,670	88.4 (88.2–88.5)	74,208	93.8 (93.6–94.1)	1.00	—	1.00	—	
Yes	42,371	11.6 (11.5–11.8)	5,142	6.2 (5.9–6.4)	0.50 (0.48–0.52)	<.0001	0.52 (0.49–0.55)	<.0001	
Current history (n = 35,147)									
No	10,333	34.7 (34.1–35.4)	1,528	41.3 (39.3–43.3)	1.00	—	1.00	—	
Yes	20,881	65.3 (64.6–6.59)	2,405	58.7 (56.7–607.)	0.48 (0.46–0.51)	<.0001	0.50 (0.46–0.54)	<.0001	
Attack in past year (n = 47,359)									
No	26,801	65.1 (64.6–65.7)	3,278	66.2 (64.5–67.9)	1.00	—	1.00	—	
Yes	15,429	34.9 (34.3–35.4)	1,851	33.8 (32.1–35.5)	0.95 (0.88–1.03)	.32	1.02 (0.92–1.13)	.81	
Urgent or emergency care in past year (n = 17,255)									
No	11,467	76.8 (76.0–77.6)	1,186	66.0 (63.1–69.0)	1.00	—	1.00	—	
Yes	3,940	23.2 (22.4–24.0)	662	34.0 (31.0–36.9)	1.70 (1.48–1.96)	.0002	1.30 (1.04–1.61)	.03	
Overnight hospital stay in past year (n = 3,018)									
No	2,496	93.1 (92.0–94.3)	269	91.6 (88.2–95.0)	1.00	—	1.00	—	
Yes	217	6.9 (5.7–8.0)	36	8.4 (5.0–11.9)	1.24 (0.77–2.02)	.47	1.58 (0.79–3.15)	.28	
Used ≥3 asthma rescue inhalers in past 3 mo (n = 2,821)									
No	1,897	76.4 (74.4–78.3)	176	72.4 (65.5–79.3)	1.00	—	1.00	—	
Yes	661	23.6 (21.6–25.6)	87	27.6 (20.7–34.5)	1.23 (0.86–1.77)	.34	1.04 (0.66–1.63)	.83	
Ever taken long-acting control medications (n = 5,961)									
No	2,241	42.5 (40.9–44.1)	243	42.5 (37.3–47.8)	1.00	—	1.00	—	
Yes	3,028	57.5 (55.9–59.1)	326	57.5 (52.2–62.7)	1.00 (0.80–1.25)	.99	1.17 (0.87–1.57)	.38	
Currently taking long-acting control medications (n = 1,956)									
No	584	36.7 (33.9–39.6)	68	37.3 (27.8–46.8)	1.00	—	1.00	—	
Yes	1,129	63.3 (60.4–66.1)	111	62.7 (53.2–72.2)	0.98 (0.64–1.49)	.94	0.91 (0.44–1.88)	.85	

Abbreviations: aOR, adjusted odds ratio; CI, confidence interval; OR, odds ratio.

^aRefusal to answer a particular question or response of “don’t know” occurred for the questions pertaining to ever history of asthma in 526 (0.1% of participants of whom the question was asked), current history of asthma in 381 (1.1%), asthma attack in the past year in 154 (0.3%), urgent or emergency care for asthma attack in past year in 25 (0.1%), overnight stay in hospital in past year in 1 (0.03%), used at least 3 inhalers in the past 3 months in 38 (1.3%), ever taken long-acting control medications in 40 (0.7%), and currently taking long-acting control medications in 2 (0.1%). The sample sizes listed do not include these missing values. There were significant associations between birthplace by race and Hispanic descent. However, these interactions did not modify the effect sizes of estimates and therefore were omitted from the final models. There were no significant interactions between birthplace and other covariates in the multivariate models.

^bSample sizes for each analysis are listed. The sample sizes for each asthma outcome vary because some asthma outcomes were not assessed every survey year.

associated with significantly prolonged asthma-free survival compared with US-born adults (log-rank test, $P < .0001$; Fig 1A). In multivariate Cox proportional hazards regression models, birthplace outside the United States also was found to be associated with prolonged asthma-free survival (adjusted hazard ratio [HR] 0.27, 95% CI 0.27–0.28, $P < .0001$). Similar results were found in models with time-dependent covariates based on current age (0–19 years old, adjusted HR 0.05, 95% CI, 0.05–0.06, $P < .0001$; 20–49 years old, adjusted HR 0.11, 95% CI, 0.10–0.12, $P < .0001$; ≥50 years old, adjusted HR 0.16, 95% CI, 0.15–0.17, $P < .0001$).

Association between US Birthplace and Secular Trend of Asthma Prevalence

Overall, the US prevalence of asthma increased from 1997 (9.1%, 8.77%–9.37%) to 2011 (12.5%, 12.1%–12.8%; Fig 1B). Using these model fitting approaches, foreign birthplace was found to have a linear interaction with survey year (P for interaction = .002). There were no significant higher-order interaction terms. The best-fitting model, as judged by the Bayesian information criteria, included untransformed survey year, birthplace, and a linear interaction term.

The prevalence of asthma significantly increased over time for US- and foreign-born Americans (Tukey post hoc test, $P < .0001$ for comparisons of survey years 2002–2006 and 2007–2011 vs 1997–2001 and 2007–2011 vs 2002–2006). However, the prevalence of asthma in foreign-born US adults was significantly lower than for US-born adults at all time points and increased over time

to a lesser extent ($P < .0001$). Of note, the percentage of US foreign-born adults steadily increased from 1997 (5.0%, 4.9%–5.2%) to 2011 (8.2%, 8.0%–8.4%; Tukey post hoc test, $P < .0001$ for all comparisons; data not shown).

Discussion

Using a large population-based sample, the authors found that adults born outside the United States have significantly lower lifetime and point prevalence of asthma. These associations were significant for all regions of birth. Further, birthplace outside the United States was associated with delayed onset of asthma. The odds of developing asthma significantly increased in foreign-born adults after residing in the United States for at least a decade. The associations remained significant even after controlling for sex, age, race and ethnicity, socioeconomic status, health care interaction and insurance coverage, and smoking history. However, foreign-born Americans appeared to have significantly more use of urgent or emergency care but an otherwise similar asthma course as their US-born counterparts, with no significant differences of asthma attacks, overnight hospitalization for asthma attacks, use of at least 3 asthma inhalers in the past 3 months, and ever or current use of long-acting asthma control medications in foreign-born vs US-born American adults. Together, these data indicate that foreign-born adults have lower odds of asthma overall but are more likely to have later-onset disease when they develop asthma. Physicians should consider this later onset of disease when treating foreign-born American adults presenting with asthma symptoms,

Table 4Association between region of birth and asthma prevalence in adults^a

Region of birth	History of asthma							
	No		Yes		OR (95% CI)	P value	aOR ^b (95% CI)	P value
	Frequency	Percentage (95% CI)	Frequency	Percentage (95% CI)				
Ever history of asthma (n = 343,989)								
USA	247,761	87.8 (87.7–88.0)	34,307	12.2 (12.0–12.3)	1.00	—	1.00	—
Mexico, Central America, Caribbean	33,851	93.9 (93.6–94.2)	2,389	6.1 (5.8–6.4)	0.47 (0.44–0.49)	<.0001	0.48 (0.44–0.52)	<.0001
South America	3,934	94.2 (93.4–95.0)	273	5.8 (5.0–6.6)	0.44 (0.38–0.51)	<.0001	0.47 (0.40–0.56)	<.0001
Europe	5,577	92.7 (91.9–93.5)	450	7.3 (6.5–8.1)	0.57 (0.51–0.64)	<.0001	0.59 (0.52–0.68)	<.0001
Russia and former USSR	907	95.4 (93.8–96.9)	51	4.6 (3.1–6.2)	0.35 (0.25–0.50)	<.0001	0.35 (0.23–0.52)	<.0001
Africa	1,832	94.2 (92.9–95.5)	107	5.8 (4.5–7.1)	0.44 (0.35–0.56)	<.0001	0.45 (0.35–0.59)	<.0001
Middle East	1,096	93.7 (91.9–95.5)	73	6.3 (4.5–8.1)	0.48 (0.44–0.49)	<.0001	0.49 (0.36–0.70)	<.0001
Indian Subcontinent	2,476	94.8 (93.8–95.9)	134	5.2 (4.1–6.2)	0.40 (0.32–0.49)	<.0001	0.42 (0.31–0.55)	<.0001
Asia	3,567	95.4 (94.5–96.3)	172	4.6 (3.7–5.5)	0.35 (0.29–0.43)	<.0001	0.38 (0.29–0.50)	<.0001
Southeast Asia	4,603	91.6 (90.6–92.6)	429	8.4 (7.4–9.4)	0.66 (0.58–0.75)	<.0001	0.69 (0.57–0.85)	<.0001
Current history of asthma (n = 34,965)								
USA	10,333	34.7 (34.1–35.4)	20,881	65.3 (64.6–65.9)	1.00	—	1.00	—
Mexico, Central America, Caribbean	811	40.5 (37.8–43.3)	1,382	59.5 (56.7–62.2)	0.78 (0.70–0.88)	<.0001	0.68 (0.58–0.80)	.0001
South America	126	49.7 (42.3–57.0)	129	50.3 (43.0–57.7)	0.54 (0.40–0.72)	.0002	0.54 (0.38–0.76)	.001
Europe	153	38.2 (32.6–43.9)	251	61.8 (56.1–67.4)	0.86 (0.68–1.09)	.29	0.94 (0.71–1.24)	.74
Russia and former USSR	11	29.0 (11.8–46.1)	34	71.0 (53.9–88.2)	1.31 (0.57–3.01)	.62	1.02 (0.44–2.38)	.97
Africa	43	43.3 (31.6–55.1)	55	56.7 (44.9–68.4)	0.70 (0.43–1.12)	.20	0.77 (0.45–1.31)	.42
Middle East	22	36.9 (20.7–53.2)	43	63.1 (46.8–79.3)	0.91 (0.45–1.83)	.85	0.76 (0.35–1.66)	.58
Indian Subcontinent	51	37.3 (27.4–47.1)	77	62.7 (52.9–72.6)	0.90 (0.59–1.34)	.71	1.66 (0.98–2.81)	.09
Asia	74	48.0 (37.9–58.2)	87	52.0 (41.8–62.1)	0.58 (0.38–0.87)	.01	0.90 (0.54–1.47)	.74
Southeast Asia	172	45.3 (38.9–51.8)	230	54.7 (48.2–61.1)	0.64 (0.49–0.83)	.002	0.97 (0.67–1.43)	.93

Abbreviations: aOR, adjusted odds ratio; CI, confidence interval; OR, odds ratio.

^aRefusal to answer a particular question or response of “don’t know” occurred for the questions pertaining to ever history of asthma in 526 (0.1%), current history of asthma in 381 (1.1%), and region of birth in 1,778 (0.5%). P values were adjusted by adjusting for the false discovery rate. Sample sizes for each analysis are listed. The sample sizes for ever and current history of asthma vary because the question about current asthma was asked only of participants with ever history of asthma.^bCovariates in multivariable models were selected based on testing in univariate models and minimizing the Bayesian information criteria. No significant multicollinearity was found in multivariate models.

because they may deny any personal or family history of asthma or atopic disease.

The inverse association between foreign birthplace and asthma prevalence does not appear to be related to differences of socioeconomic status or health care usage. First, all associations remained significant even after controlling for these factors. Second, foreign-born Americans who developed asthma reported a similar number of attacks and overnight hospitalization for attacks in the past year. There also were no differences of long-term asthma control as judged by overuse of inhalers and ever or current use of long-acting asthma control medications. These findings suggest that foreign- and US-born Americans had similar health care usage for their asthma. Taken together, the findings of this study suggest

that once foreign-born Americans develop asthma, their disease has a similar phenotype as US-born Americans.

A recent study found that children born outside the United States have a significantly lower prevalence of allergic disorders, including asthma, eczema, hay fever, and food allergies.¹² Moreover, the odds of developing allergic disease significantly increased after residing in the United States for at least a decade. However, in that study, country or region of birth for foreign-born children was not assessed. A previous questionnaire-based study (n = 204) found that children born in the United States had a higher odds of asthma.²² A previous epidemiologic study from the 1994 to 1998 National Health and Nutrition Examination Survey and the 1997 to 2001 NHIS found that US-born Mexican-American adults had more

Table 5Association between duration of residency in the United States and prevalence of adult asthma in foreign-born Americans but not age at immigration^a

Asthma	Frequency	Percentage (95% CI)	Frequency	Percentage (95% CI)	aOR (95% CI)	P value	Frequency	Percentage (95% CI)	aOR (95% CI)	P value
Duration of residence in United States (y)										
Ever history	<5 (n = 10,403)		5–9 (n = 11,710)				>10 (n = 54,501)			
	420	4.3 (3.8–4.8)	470	4.2 (3.7–4.7)	0.89 (0.80–0.98)	.05	3,811	7.1 (6.8–7.4)	1.28 (1.18–1.38)	<.0001
Current history	<5 (n = 339)		5–9 (n = 367)				>10 (n = 1,128)			
	157	45.4 (38.8–52.1)	185	51.1 (44.4–57.7)	0.98 (0.71–1.36)	.42	2,016	61.4 (59.2–63.7)	1.70 (1.31–2.19)	.0001
Age at immigration (y)										
Ever history	<20 (n = 16,741)		20–39 (n = 39,289)				≥40 (n = 20,584)			
	1,073	6.4 (5.9–6.9)	2,222	5.4 (5.1–5.7)	0.94 (0.88–1.01)	.12	1,720	7.6 (7.2–8.1)	0.90 (0.78–1.04)	.20
Current history	<20 (n = 810)		20–39 (n = 1,708)				≥40 (n = 1,332)			
	419	49.0 (44.4–53.7)	1,017	58.3 (55.3–61.2)	0.84 (0.62–1.16)	.38	922	67.0 (63.7–70.4)	0.54 (0.30–0.97)	.06

Abbreviations: aOR, adjusted odds ratio; CI, confidence interval.

^aRefusal to answer a particular question or response of “don’t know” occurred for the questions pertaining to ever history of asthma in 526 (0.1%), current history of asthma in 381 (1.1%), and duration of residency in the United States in 2,495 (3.4%). Sample sizes for each analysis are listed. The sample sizes for ever and current history of asthma vary because the question about current asthma was asked only of participants with ever history of asthma. Data for current history of asthma are presented as the percentage of participants who responded yes to ever having asthma.

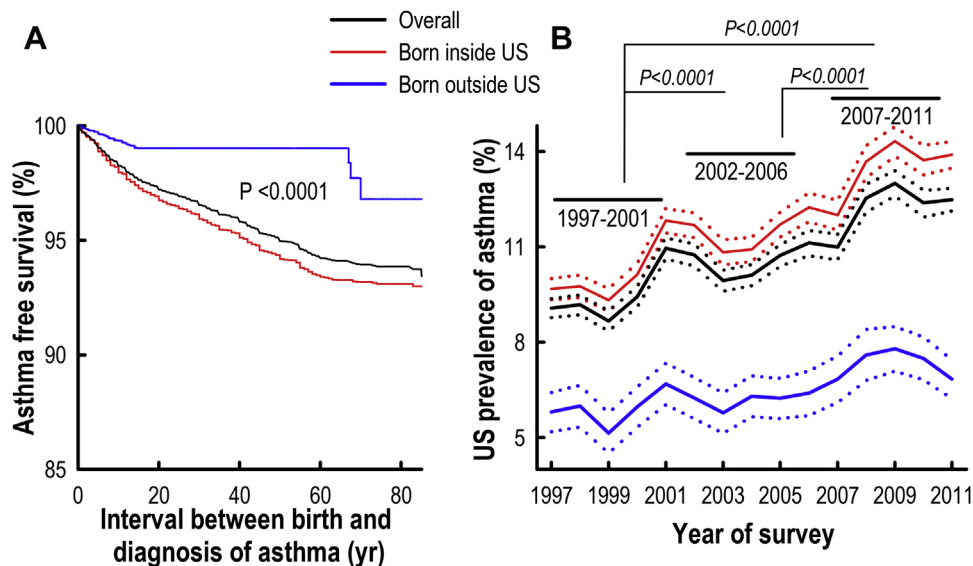


Figure 1. Association between foreign birthplace, asthma-free survival and secular trend of asthma prevalence in the US. (A) Survival analyses using the Kaplan-Meier method was used to determine whether birthplace outside the US delayed the onset of asthma. The time-to-event variable in all models was the time from either birth in the US or immigration to the US to either diagnosis of asthma or censoring, with the censoring variable based on ever history of asthma. Models were stratified by history of birthplace in the US. Log rank statistics were calculated for testing homogeneity of survival functions across strata ($P < .0001$). (B) Logistic regression models were used to determine the effects of US birthplace on secular trend of asthma prevalence. Ever history of asthma was the dependent variable. Birthplace in the US (binary) and year of survey (1997–2001, 2002–2005, and 2006–2011) were treated as fixed covariates. Least squares means with post-hoc comparisons that control for multiple testing and the other covariates were done using Tukey's pair-wise comparisons. $P < .0001$ for all 3 comparisons.

asthma than Mexican-born American adults.²³ In the present study, using the combined power of the 1997 to 2011 NHIS, the authors were able to demonstrate that foreign birthplace in any region is protective compared with being born in the United States. Similarly, previous international studies found that immigrants had lower prevalence of asthma and other allergic disease compared with native-born persons in Italy, Israel, and Australia.^{24–27} However, it is interesting that asthma rates were lower in US adults who were born in European countries. This difference may be attributable to asthma rates being higher in the United States than in European countries. Alternatively, people with greater risk for asthma may be less likely to emigrate from Europe to the United States than those with lower asthma risk. Future international studies are warranted to elucidate this point and to determine whether the prevalence of asthma similarly increases with prolonged duration of residency and whether foreign birthplace affect age of onset.

In the present study, the odds of developing allergic disease increased after residing in the United States for longer than 10 years. Similarly, previous studies found that foreign-born children have increased odds of allergic disease after living in the United States for longer than 10 years.¹² This suggests a greater role for environmental exposures in the United States, such as Western diet, adiposity, climate factors, air quality and airborne pollution, and allergens in later-onset disease. Future studies are needed to identify the dominant triggers for disease in foreign-born Americans.

Previous studies found that the prevalence of asthma has dramatically increased during the past few decades.¹³ The authors found that the rate of increase for asthma prevalence was higher in US-born than in foreign-born Americans (43.7% vs 15.2% from 1997 through 2011, respectively). Moreover, the dominant pattern of asthma increase parallels that of US-born Americans. Of note, the increased odds of asthma observed in US- and foreign-born Americans remained highly significant even after controlling for socioeconomic status, adiposity, smoking history, and other covariates. This suggests that there are additional environmental risk factors and highlights the multifactorial nature of asthma.

This study has several strengths, including being based on a US population with a very large randomly sampled and diverse sample over a 15-year sampling period with sufficient numbers for subset analyses (post hoc power analysis showed $\geq 83.4\%$ power for all subset analyses), and controlled for a large number of potential confounding factors using logistic regression models. There may be some residual confounding owing to a lack of inclusion of all factors related to the outcomes and exposures and misclassification bias. To address these problems, the authors used PS regression, which adjusts for systematic differences between patients and covariate imbalances. PS regression acts as a balancing score such that the covariate distribution is equal for US- and foreign-born adults. This approach minimizes confounding; however, if all confounders are not included in the model or confounders are biased, then the PS may not totally eliminate bias. The random sampling, sampling across all states, with representation of a host of racial and ethnic groups and use of complex weighting and survey-weighted procedures indicate that the results are likely generalizable to the entire US population. However, this study has potential limitations. Asthma history was self-reported and neither assessed clinically nor verified with any diagnostic testing. Self-report of asthma has repeatedly been validated and found to have strong correlation to clinical examination and diagnostic testing.^{28–30} Therefore, this was deemed not to be a major source of bias. Nevertheless, differential validity might be found in immigrant populations, leading to bias. The authors studied long-term residency in the United States as the exposure of interest. However, they were not able to determine the effects of people moving back and forth between the United States and their country of origin as many immigrants do. Foreign-born adults may have less access to health care than US-born adults. Although the authors controlled for health care interaction in the past year in multivariable models, there was still potential for residual confounding. Nevertheless, the lower prevalence and delayed age of onset of asthma in foreign-born Americans are clinically significant. This subgroup differs from many patients with asthma who have a family history and/or a personal history of childhood allergic disease. This suggests that clinicians and health care providers

should be alert to adult onset and perhaps atypical history of disease. Age of asthma onset and immigration to the United States were determined by recall, which may be subject to recall bias. Future longitudinal studies are needed to confirm these findings and determine the effects of short-term travel and related exposures.

In conclusion, foreign-born American adults have significantly lower risk and delayed onset of asthma than their US-born counterparts. However, foreign-born Americans develop increased risk for asthma with prolonged residency in the United States. Further studies are needed to better understand the causative factors for the development of asthma in foreign-born Americans.

Supplementary Data

Supplementary data related to this article can be found at <http://dx.doi.org/10.1016/j.anai.2014.07.006>.

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eTable 1

Propensity regression analysis of association of immigrant status with asthma prevalence, attacks, and long-term control in adults

Asthma parameter	Birthplace outside United States ^a			
	Unweighted PS model		Weighted PS model	
	aOR (95% CI)	P value	aOR (95% CI)	P value
Ever history (n = 445,391)	0.56 (0.53–0.58)	<.0001	0.55 (0.53–0.57)	<.0001
Current history (n = 35,147)	0.85 (0.77–0.93)	.0007	0.83 (0.76–0.92)	.0002
Attack in past year (n = 47,359)	1.02 (0.94–1.10)	.80	1.00 (0.92–1.09)	.97
Urgent or emergency care in past year (n = 17,255)	1.16 (1.01–1.34)	.06	1.14 (0.99–1.31)	.11
Overnight hospital stay in past year (n = 3,018)	1.54 (0.92–2.59)	.15	1.51 (0.90–2.53)	.17
Used ≥3 asthma rescue inhalers in past 3 mo (n = 2,821)	1.10 (0.72–1.69)	.74	1.07 (0.70–1.64)	.82
Ever taken long-acting control medications (n = 5,961)	1.18 (0.93–1.50)	.25	1.16 (0.91–1.47)	.31
Currently taking long-acting control medications (n = 1,956)	0.86 (0.56–1.32)	.58	0.84 (0.55–1.30)	.52

Abbreviations: aOR, adjusted odds ratio; CI, confidence interval; PS, propensity score.

^aPropensity regression models were constructed with asthma outcomes as the binary dependent (outcome) variables. The independent (explanatory) variables were birthplace in the United States (binary) and unweighted or weighted propensity scores (see Methods section for estimation approach). The aOR and 95% CI for asthma outcomes were determined. *P* values were adjusted by adjusting for the false discovery rate.