

Prevalence of Asthma in School Children on the Arizona-Sonora Border



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What is already known about this topic? Population-based studies have previously shown that Mexican-born children living in the United States have a lower prevalence of asthma than children not born in Mexico. However, the causality of this remains unclear.

What does this article add to our knowledge? Using the International Study of Asthma and Allergy in Children questionnaire, we found a significantly higher prevalence of asthma in school children of Mexican descent in Arizona, compared with those in Sonora, Mexico, despite proximity and common ancestry.

How does this study impact current management guidelines? This difference in asthma prevalence may be attributable in part to environmental influences. Understanding these differences may identify modifiable risk factors for asthma.

BACKGROUND: Mexican-born children living in the United States have a lower prevalence of asthma than other US children. Although children of Mexican descent near the Arizona (AZ)-Sonora border are genetically similar, differences in environmental exposures might result in differences in asthma prevalence across this region.

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This work was supported in part by Health Resources and Services Administration (HRSA)/Maternal & Child Health Bureau (MCHB) T76MC04925, P30 ES006694, K25 HL103970, T32 ES007091 and the México Section of the US-Mexico Border Health Commission.

Conflicts of interest: T. F. Carr has received consultancy fees from Aimmune National Advisory Board; has provided expert testimony for the law offices of Joel L. Herz; and has received lecture fees and payment for manuscript preparation from the North American Rhinology and Allergy Conference. P. I. Beamer has received research support from the National Institutes of Health (NIH), Sonoran Environmental Research Institute and Environmental Protection Agency. L. B. Gerald has received research support from HRSA/MCHB. Y. O. Van Horne has received research support from the NIH T32 (# ES007091). D. Vercelli has received research support from Johnson & Johnson (UA009253-0001). F. D. Martinez has received consultancy fees from Copeval; and has received research support from the NIH/National Heart Lung and Blood Institute (HL098112, HL09501, HL064307, HL30045, and HL0981889, HL056177), NIH/National Institute of Environmental Health Sciences (ES006694), and Johnson & Johnson (UA009253-0001). A. L. Wright has received research support from the NIH and has received fees for participation in review activities from NIH. The rest of the authors declare that they have no relevant conflicts of interest.

Received for publication March 7, 2016; revised June 29, 2016; accepted for publication July 1, 2016.

Available online August 17, 2016.

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2213-2198

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<http://dx.doi.org/10.1016/j.jaip.2016.07.001>

OBJECTIVE: The objective of this study was to determine if the prevalence of asthma and wheeze in these children varies across the AZ-Sonora border.

METHODS: The International Study of Asthma and Allergy in Children written and video questionnaires were administered to 1753 adolescents from 5 middle schools: Tucson (school A), Nogales, AZ (schools B, C), and Nogales, Sonora, Mexico (schools D, E). The prevalence of asthma and symptoms was compared, with analyses in the AZ schools limited to self-identified Mexican American students.

RESULTS: Compared with the Sonoran reference school E, the adjusted odds ratio (OR) for asthma was significantly higher in US schools A (OR 4.89, 95% confidence interval [CI] 2.72-8.80), B (OR 3.47, 95% CI 1.88-6.42), and C (OR 4.12, 95% CI 1.78-9.60). The adjusted OR for wheeze in the past year was significantly higher in schools A (OR 2.19, 95% CI 1.20-4.01) and B (OR 2.67, 95% CI 1.42-5.01) on the written questionnaire and significantly higher in A (OR 2.13, 95% CI 1.22-3.75), B (OR 1.95, 95% CI 1.07-3.53), and Sonoran school D (OR 2.34, 95% CI 1.28-4.30) on the video questionnaire compared with school E.

CONCLUSIONS: Asthma and wheeze prevalence differed significantly between schools and was higher in the United States. Environmental factors that may account for these differences could provide insight into mechanisms of protection from asthma. © 2016 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2017;5:114-20)

Key words: Asthma; Bacterial Load; Environment; Mexican Americans; Socioeconomic Factors; Wheezing

Asthma is a chronic disease for which an individual's early life exposures may be critically important as preventive or modulating factors.¹ Although the prevalence of asthma in Hispanic children across the United States is similar to the prevalence of

Abbreviation used

ISAAC- *International Study of Asthma and Allergy in Children*

asthma in non-Hispanics, there is variability among Hispanics, with the risk of asthma in children of Mexican descent being very low compared with other subgroups.²⁻⁵ Evidence supports an effect of nativity on this risk.⁶ Children who were born in and emigrated from Mexico have been shown to have a lower prevalence of asthma than Mexican American children born in the United States.⁶⁻¹¹ Degree of acculturation, age of immigration to the United States, immigrant generation, and duration of time lived in the United States have all been associated in a dose-dependent manner with the prevalence of asthma.^{9,12-15} Much of this prevalence data, however, is acquired through national surveys. In contrast, cross-sectional analyses of socioeconomically distinct but geographically and ethnically similar regions can provide unique insight into the impact of social and economic factors on disease prevalence.¹⁶

The US-Mexico border spans more than 3000 km, with the “border region” extending 100 km on each side of the border, as defined by the La Paz Agreement. Most of the region’s population reside in 14 city pairs straddling the border, one of which comprises the sister cities of Nogales, Arizona, USA, and Nogales, Sonora, Mexico. Once a large shared city and environment where people easily traversed the US-Mexico border, this region has gradually separated into discrete cities following the adoption of stricter border controls. Nogales, Sonora, is the larger city, housing 90% of the region’s population (approx. 241,129). Although the population of Nogales, Arizona, is 95% Hispanic, societal infrastructure is consistent with US standards and contrasts with that of Sonora in sanitation, access to clean drinking water, access to health care, and traffic density. The extent to which the border partition has impacted disparities between the environments, populations, and disease prevalence is not yet clear.¹⁷ Tucson, Arizona, is located approximately 110 km north of Nogales, Arizona, along the Interstate 19 corridor. Although the general population of Tucson is reported to be 41.6% Hispanic,¹⁸ some census tracts within Tucson are more than 90% Hispanic.

We hypothesized that as a result of environmental and/or social differences in these areas, the prevalence of asthma is lower in Sonora than in Arizona, and that these differences would be detected across this region, despite the proximity of the areas studied. We therefore sought to compare the prevalence of asthma and asthma symptoms among middle school aged children in 3 cities within this unique border location: Tucson, Arizona; Nogales, Arizona; and Nogales, Sonora, Mexico.

METHODS

We conducted a cross-sectional study of asthma and asthma symptoms among adolescents from 5 schools near the US-Mexico border: 1 school in Tucson, Arizona (school “A”), 2 in Nogales, Arizona (schools “B” and “C”); and 2 in Nogales, Sonora (schools “D” and “E”) (Figure 1). The Arizona schools were chosen for the high proportion of Hispanic children. The schools in Sonora were chosen to represent children from higher (school D) and lower (school E) socioeconomic status. Characteristics of each school are shown in Table I. To capture students in the 13- to 14-year-old age range, seventh and eighth grades were invited to participate. Parental

consent was obtained through forms or school-facilitated opt-out notifications, and a statement of assent read before questionnaires were distributed. Surveys were completed during a 4-week span in late spring 2015, during a single school day for each school, except for the Tucson school, which was surveyed over 2 days. Study documents were translated by a professional translator familiar with regional Spanish from English to Spanish, and then backtranslated by our bilingual study staff and investigators. The study was approved and monitored by the University of Arizona Human Subjects Protection Program.

Written questionnaire

Survey questions were taken directly from the International Study of Asthma and Allergy in Children (ISAAC), a questionnaire to assess asthma prevalence that has been validated in multiple populations around the world.¹⁹⁻²³ Children were asked to report if they “ever had asthma,” “ever had wheezing or whistling in the chest,” and “wheezing in the past 12 months.” Subjects also recorded age, gender, and primary language spoken at home. In US schools, questionnaires were offered in both English and Spanish. In Mexican schools, questionnaires were offered in Spanish.

Video questionnaire

The ISAAC video questionnaire was administered to all participants. Students were instructed to watch 5 separate scenarios depicting asthma symptoms. After each scene, the students were instructed to answer the corresponding question of whether they have had these symptoms, and whether and how frequently the symptoms occurred in the past 12 months. Wheeze was defined based on responses to the first scenario, which depicts a person wheezing at his or her desk. Questions were asked in English in Arizona schools and Spanish in Sonora.

Dust collection

Dust sampling methods are reported in this article’s Online Repository at www.jaci-inpractice.org.

Bacterial DNA extraction and quantitation

Bacterial DNA extraction and quantitation methods are reported in this article’s Online Repository at www.jaci-inpractice.org.

Statistical methods

Demographic characteristics by school were compared by Fisher’s exact test and one-way analysis of variance. Differences in asthma prevalence and reported wheeze were initially compared across schools by Fisher’s exact test. We then calculated odds ratios for asthma and wheeze using mixed-effects logistic regression models to adjust for age and gender, and to control for within class-period correlation. The strength of agreement between written and video questionnaires was assessed by kappa coefficient, defined as follows²⁴: poor (<0.20), fair (0.21-0.40), moderate (0.41-0.60), good (0.61-0.80), or very good (0.81-1.0). Statistical significance was defined as $P < .05$. All tests were performed using Stata version 10.0 (StataCorp, College Station, Tex).

RESULTS

A total of 1753 students participated in this survey. Participant characteristics are presented in Table II. A high proportion of students from Arizona schools self-identified as Hispanic of Mexican origin (Table II). All participants in Mexico were assumed to be Hispanic of Mexican origin. As our hypothesis focused on students of Mexican origin, all further analyses

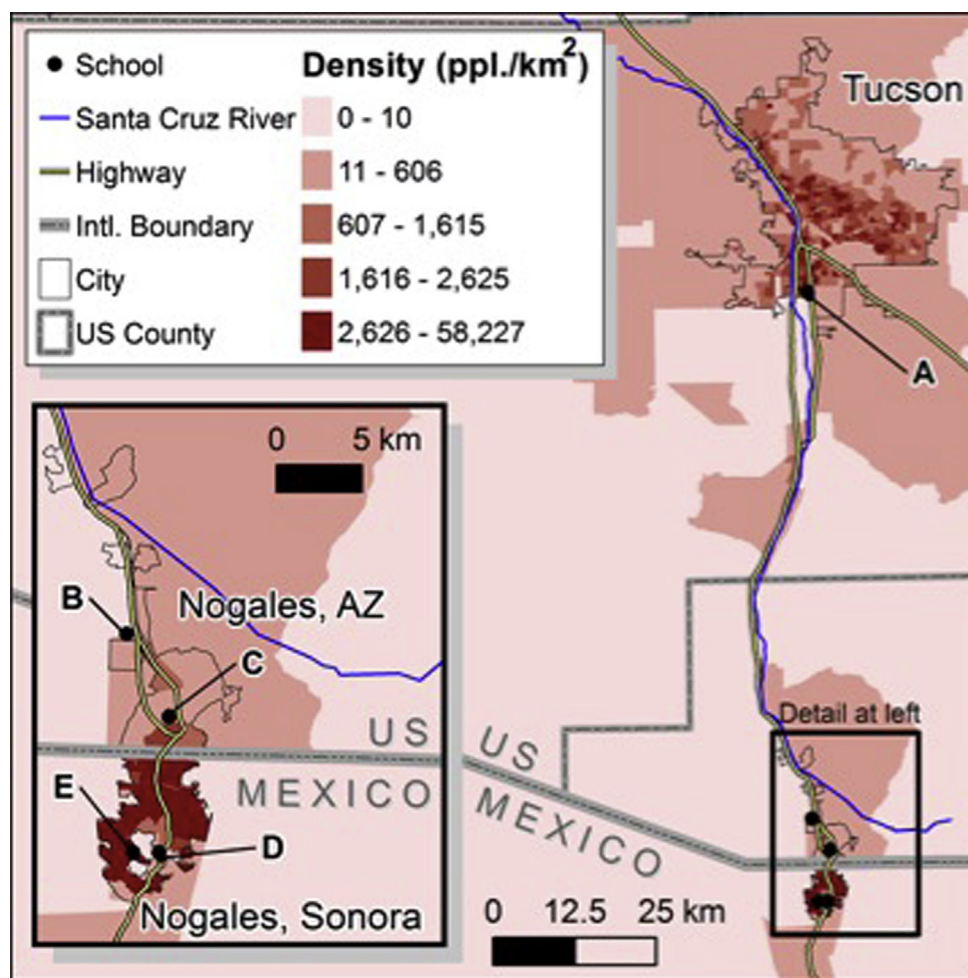


FIGURE 1. Map of school location with population density (people per square kilometer) by quintiles.

exclude the US students who did not identify as being of Mexican origin. Table II shows the distribution of languages spoken in the home for each school. The proportion of households speaking English without Spanish was greater for schools in the United States, with the highest proportion in the school located furthest from the US-Mexico border.

Rates of reported asthma and asthma symptoms from each school are displayed in Table III. Children in Arizona schools reported significantly higher rates of ever having asthma compared with children in Sonora schools (25.8% vs 8.4%, respectively, $P < .001$). This was also true for wheeze in the past year as reported on the written questionnaire (16.9% vs 9.6%, $P < .001$).

A slightly different pattern was evident from the video questionnaire. Although students in the Arizona schools and school E reported similar rates of wheeze in the past year to those reported on the written questionnaire, children in school D reported double the rate of wheeze in response to the wheezing video scene (Table III) compared with what they reported on the written questionnaire. Although rates of wheeze reported on the video questionnaire are higher in the United States compared with Mexico, this was not statistically significantly different (16.5% vs 14.2%, respectively, $P = .27$). The inter-rater agreement (kappa

value) between an affirmative response to the written and video questionnaire on the wheeze question was moderate for schools A and B, and only fair in schools C, D, and E.

The odds ratios for asthma and wheeze in each school, adjusting for age, gender, and class period, are presented in Table IV, using school E in Sonora as a reference. Schools A and B had higher odds ratios for asthma and wheeze in the past year as reported both on written and video questionnaires. School C had a higher odds ratio for reported asthma, compared with school E. Interestingly, the odds ratio for wheeze in the past year on the video questionnaire was also significantly higher for school D.

Adjustment for language spoken in the home was not performed in the logistic models shown in Table IV, because there was no variability of language spoken in the Mexican schools. However, among US participants, the odds ratio for asthma was 1.71 (1.14-2.55, $P = .009$) for those who spoke English only and 0.88 (0.61-1.28, $P = .52$) for those who spoke both English and Spanish, compared with those who spoke Spanish only in the home (Table E1, available in this article's Online Repository at www.jaci-inpractice.org). Similarly, wheeze in the past year showed a similar language gradient among participants in the United States, with odds ratios for ever wheeze on the written

TABLE 1. Demographic and socioeconomic characteristics of each middle school

	Total school enrollment, all grades	Ethnicity	Estimate of socioeconomic status
Arizona schools			
A	931	89% Hispanic 10% Native American <1% White	Free and reduced lunch 84%
B	783	98% Hispanic <1% Native American <1% White	Free and reduced lunch 100%
C	621	98% Hispanic <1% Native American <1% White	Free and reduced lunch 100%
Sonora schools			
D	593	n/a	High urbanization Low marginalization 15 students/computer 16 students/teacher
E	463	n/a	Low urbanization High marginalization 31 students/computer 17 students/teacher

questionnaire being 1.88 (1.15-3.08, $P = .01$) and 1.30 (0.82-2.05, $P = .27$) for those who spoke English only or both English and Spanish, respectively, compared with exclusive Spanish speakers. Inter-rater statistics for agreement between the written and video questionnaire by home languages were moderate for all groups, with kappa of 0.53 for English no Spanish, 0.41 for English and Spanish, and 0.42 for Spanish no English.

The average mass of dust per square meter varied by school. The dust load, measured as grams of dust per square meter, was markedly lower in Arizona schools A and B compared with schools D and E (Figure E1 and Table E2, available in this article's Online Repository at www.jaci-inpractice.org). The bacterial load, measured as bacterial DNA copies per square meter, was substantially higher in schools D and E (Figure E1 and Table E2).

DISCUSSION

Our study shows a lower prevalence of asthma and wheeze reported in children of Mexican origin attending school in Nogales, Sonora, Mexico, compared with Nogales, Arizona, and Tucson, Arizona. Rates of lifetime asthma were 3-fold higher in children from the Arizona schools. Symptoms reported in the past year, a marker of current asthma, were also substantially higher in children from Arizona compared with those from Sonora when reported in response to the written questionnaire.

Our results are consistent with the few studies of asthma in the US-Mexico border zone that collectively suggest higher rates of asthma and allergic disease on the US side of the Texas-Mexico border,^{14,25} and along the California-Mexico border,²⁶ particularly among those who are Hispanic. In 1996, Stephen et al²⁷ compared respiratory symptoms in primary school-aged children in Nogales, Arizona, and Nogales, Sonora.

In this study, the frequency of wheeze was significantly higher in the Arizonan students, which is similar to our findings. A high rate of asthma hospitalization has also been observed on the US side compared with the Mexican side of the border, and reducing this rate is an objective of both the Healthy Border 2010 initiative²⁸ and the Healthy Border 2020 initiative.²⁹

Although the overall rate of asthma among children in Mexico is estimated at 13%,³⁰ rates of asthma in Mexico vary widely by geographic region, even when utilizing the same ISAAC questionnaire that was used in this study.³¹⁻³⁴ This regional variability supports the hypothesis that environmental and/or sociocultural factors differentially impact the development of asthma among groups in Mexico. Further, this variability creates the potential to identify low risk areas, and to investigate the lifestyle characteristics that are associated with lower asthma prevalence, as has been done for farming communities in Europe.^{1,35,36}

Tucson and both cities of Nogales are officially grouped as a combined statistical area, based on their social and economic ties.³⁷ However, there are a number of social and environmental differences between the Arizona cities and Nogales, Sonora. There has been substantial population growth in Nogales, Sonora, estimated at 40% from 2000 to 2010,³⁸ compared with only 20% in the Arizona region.³⁷ Population density is also substantially greater in Nogales, Sonora (Figure 1). The average number of people per household is 2.5 in Tucson, 3.1 in Nogales, Arizona, and 3.8 in Nogales, Sonora.^{39,40} The rapid population growth in Nogales, Sonora, has resulted in increased traffic and development of neighborhoods that lack sanitation and access to clean drinking water.^{41,42} The neighborhood that feeds into school E is one of these, with only 20% of the population having access to sewers or sanitation.^{43,44} Further, air pollution as a result of increased traffic and industrial emissions is also higher on the Mexican side of Nogales than on the US side.⁴⁵ There are multiple other differences between the communities (eg, prenatal care,^{46,47} breastfeeding,⁴⁸ and cesarean-section rates⁴⁹), which may contribute to differences in the prevalence of asthma and wheeze. Bacterial exposure, utilizing endotoxin measurement as proxy, has been previously inversely associated with atopy and asthma, particularly in farming communities.^{50,51} The notable differences of dust load and bacterial load were identified among the schools in this study, whereas a rough estimate of the overall environmental exposures of these children likely reflects meaningful differences in community exposures. In the context of different asthma rates among the schools, this is consistent with the possibility that environmental microbial exposures may impact asthma risk and development.^{36,52}

The difference in asthma reporting and symptoms between the 2 Nogales, Sonora, schools may reflect differences in exposures and populations represented in those schools. Although children in both schools have equal access to medical care through state health systems, schools D and E represent very different populations and environments within the city of Nogales, Sonora. School D is physically located in the middle of the *maquiladora* park (ie, industrial complex with multiple manufacturing factories), where there may be industrial emissions.¹ This school also functions as a magnet school, attracting children of higher socioeconomic status who live in neighborhoods across the city, requiring separate application, entrance examinations, and external endorsement for admission. In contrast, school E is in a *colonia* that originated as a squatters' settlement for *maquiladora* workers. This *colonia* has limited access to sanitation and infrastructure despite a very high

TABLE II. Demographic characteristics of participants, by school

	Total participants	Gender	Age, y	Hispanic, Mexican Origin	Languages spoken at home (Hispanic, Mexican origin only)		
	n*	Male	Mean (range)	% (n)	English, no Spanish	English and Spanish	Spanish, no English
Tucson, Ariz							
A	783	47.6 (369/776)	13.4 (11-16)	79.9 (622/779)	34.3 (211/615)	44.2 (272/615)	21.5 (132/615)
Nogales, Ariz							
B	384	50.5 (191/378)	13.3 (12-16)	93.2 (357/383)	14.8 (51/345)	55.4 (191/345)	29.9 (103/345)
C	72	37.5 (27/72)	12.7 (10-16)	81.9 (59/72)	12.1 (7/58)	70.7 (41/58)	17.2 (10/58)
Nogales, Sonora							
D	302	45.0 (130/289)	13.6 (12-16)	NA	2.1 (6/284)	4.9 (14/284)	92.7 (265/284)
E	212	52.3 (104/199)	13.5 (11-15)	NA	0.0 (0/198)	2.0 (4/198)	98.0 (194/198)
P values		.15	<.001†	<.001	<.001		

NA, Hispanic ethnicity and of Mexican origin question not applicable to children in Sonoran schools.

Unless indicated, values are expressed as percentage, with number per total responses received.

*Total participants n reflects the number of students in each classroom on the day of survey administration. Reported denominators for each variable reflect the number of students responding to that question.

†P values assessed by ANOVA. All groups were significantly different from each other in post hoc testing.

TABLE III. Student report of ever having asthma and wheeze in the past year

School	Written questionnaire		Video questionnaire	Agreement of written, video wheeze Kappa, P value
	Asthma, ever % (proportion)	Wheeze, past year % (proportion)	Wheeze, past year % (proportion)	
Tucson, Ariz				
A	28.0 (169/603)	16.0 (97/603)	17.3 (106/613)	0.45, <.001
Nogales, Ariz				
B	22.0 (76/346)	18.6 (66/354)	15.7 (56/357)	0.45, <.001
C	26.0 (14/54)	14.3 (8/56)	14.0 (8/57)	0.41, .001
Nogales, Sonora				
D	9.6 (28/292)	9.5 (28/295)	18.5 (56/302)	0.29, <.001
E	6.8 (14/206)	7.7 (16/209)	8.0 (17/212)	0.26, <.001
P value	<.001	<.001	.008	

TABLE IV. Odds ratio from mixed-effect logistic regression models for ever having asthma and wheeze in the past year

School	Written questionnaire				Video questionnaire	
	Asthma, ever		Wheeze, past year		Wheeze, past year	
	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
Tucson, Ariz						
A	4.89 (2.72-8.80)	<.001	2.19 (1.20-4.01)	.01	2.13 (1.22-3.75)	.008
Nogales, Ariz						
B	3.47 (1.88-6.42)	<.001	2.67 (1.42-5.01)	.002	1.95 (1.07-3.53)	.03
C	4.13 (1.78-9.60)	.001	1.67 (0.63-4.42)	.30	1.60 (0.63-4.07)	.32
Nogales, Sonora						
D	1.36 (0.68-2.71)	.32	1.26 (0.62-2.54)	.52	2.34 (1.28-4.30)	.006
E	ref	ref	ref		ref	ref
P value	<.0001		.0003		.058	

CI, Confidence interval; OR, odds ratio.

population density (Figure 1), and is highly marginalized as measured by the Mexican National Council for Population.⁵³ Social differences are also evident in the higher proportion of English spoken in the home among children of school D, compared with those of school E. The differences in reported asthma symptoms between these schools may therefore reflect both environmental and socioeconomic differences.

One limitation of this study is the reliance on self-reporting of asthma and symptoms. This is a limitation of all studies utilizing the ISAAC questionnaire, which was validated in mixed ethnic populations.²³ Children with a personal or family history of asthma may better understand the asthma-specific terms used in the survey. However, health care in Nogales, Sonora, is available to everyone through 1 of 3 state-run health care systems. In fact,

residents of Arizona are more likely to lack access to health care, and even under the Affordable Care Act, Hispanics in Arizona are among the most under-enrolled groups.⁵⁴ In addition, schools A, B, and C are in medically underserved areas with limited access to care. Therefore, rates of reported asthma in Arizona in this study may be underestimated.

An assumption underlying our hypothesis in conducting this study is that the children surveyed were born in the catchment area for their school. In fact, some students who live in Mexico cross the border to attend school in Arizona and some Arizona students may have been born or raised in Mexico and immigrated to the United States. Asking children where they were born would have provided this information. However, given the current political climate in Arizona regarding illegal immigration,⁵⁵ we opted not to ask about birthplace because it may have made participants feel uncomfortable despite the confidential and deidentified nature of the questionnaires, particularly in a public school setting. In either case, misclassification of birthplace would bias toward no difference between the cities. Maternal nativity may affect asthma reporting, with children of foreign-born mothers being less likely to report asthma,⁵⁶ but this too would bias toward no difference. Further, although we assume genetic similarity among the participants, we acknowledge the lack of information documenting genetic admixture.

Language spoken in the home may be utilized as a surrogate marker of acculturation and shows a predicted gradient of English to Spanish from Tucson to Mexico (Table II), supporting the previously reported effect of acculturation on regression to the local mean of disease status.⁶ Within the Arizona schools, we see a gradient of asthma prevalence that varies by language spoken in the home.

The lack of concordance between response to the written and video questionnaires identified in this study, being only fair to moderate, is consistent with previously published literature for ISAAC.^{23,57} Although ISAAC has been utilized in Spanish-speaking or Latin American countries,^{58,59} with sensitivity and specificity of the wheeze question at 44.2% and 90%, respectively,⁵⁸ one ISAAC validation study noted relative underreporting of wheeze in Spanish-speaking adolescents when compared with a video vignette depicting a child wheezing.⁶⁰ Wheeze may, however, be the best symptom indicator of asthma in Mexican school children.³⁰ With binational and bilingual studies such as this, the terminology used to assess asthma symptoms may not translate accurately. Specifically, the term “wheeze” may be misunderstood in non-English languages.⁶¹ We recognized that our results may therefore be confounded by translation and choice of words. The differences in video questionnaire results between schools D and E may also have resulted from methodological issues. Administration of the video questionnaire in school D was challenging due to the lack of student engagement, behavioral issues, and technical difficulties that made it hard to hear the video.

This study shows that asthma prevalence reflects a gradient spanning Tucson to Sonora, with rates particularly low in regions of low socioeconomic status in Sonora. These differences, in a population of adolescents from similar ethnic background, suggest that environmental factors contribute to this gradient in a complex way, potentially mediated by socioeconomic status, education, and acculturation. Further study is warranted to assess the environmental and social factors that contribute to these differences in prevalence in a single population of common ancestry who live on both sides of the US-Mexico border.

Acknowledgments

We are extremely thankful to the school leadership for their support of this study, and to the students and their families for their participation. We would also like to thank James Roebuck for designing and scanning the questionnaires; Celina Valencia, BA, Nicolas Galvez Lopez, MPH, for helping with data collection; Aimee Snyder, MPH, who recruited and coordinated data collection volunteers, and those volunteers: Rachelle Begay, MPH, Shelby Calvillo, Briana Chavez, Marie Culver, Jayelle Harrison, Ashley Lowe, and Emily Waldron, MPH.

T.F.C. and P.I.B. contributed equally to writing the manuscript. T.F.C., P.I.B., J.R., and D.A.S. participated in data analysis. P.I.B., J.R., C.B.R., L.B.G., D.V., M.G., and A.L.W. participated in data collection. Y.O.V. and O.N.P. conducted experiments and participated in experimental design and writing. M.H., F.D.M., and all other authors participated in the conception and design of the study, data interpretation, revisions of draft for critically important intellectual content, and approval of the final version of the manuscript. All authors agree to be accountable for all aspects of the work.

REFERENCES

1. Bousquet J, Gern JE, Martinez FD, Anto JM, Johnson CC, Holt PG, et al. Birth cohorts in asthma and allergic diseases: report of a NIAID/NHLBI/MeDALL joint workshop. *J Allergy Clin Immunol* 2014;133:1535-46.
2. Canino G, Koinis-Mitchell D, Ortega AN, McQuaid EL, Fritz GK, Alegría M. Asthma disparities in the prevalence, morbidity, and treatment of Latino children. *Soc Sci Med* 2006;63:2926-37.
3. Akinbami LJ, Moorman JE, Bailey C, Zahran HS, King M, Johnson CA, et al. Trends in asthma prevalence, health care use, and mortality in the United States, 2001-2010. *NCHS Data Brief* 2012;(94):1-8.
4. Leong AB, Ramsey CD, Celedón JC. The challenge of asthma in minority populations. *Clin Rev Allergy Immunol* 2012;43:156-83.
5. Moorman JE, Zahran H, Truman BI, Molla MT. Centers for Disease Control and Prevention (CDC). Current asthma prevalence—United States, 2006-2008. *MMWR Surveill Summ* 2011;60(Suppl):84-6.
6. Barr RG, Aviles-Santa L, Davis SM, Aldrich T, Gonzalez F 2nd, Henderson AG, et al. Pulmonary disease and age at immigration among Hispanics: results from the Hispanic Community Health Study/Study of Latinos (HCHS/SOL). *Am J Respir Crit Care Med* 2016;193:386-95.
7. Eldeirawi K, McConnell R, Freels S, Persky VW. Associations of place of birth with asthma and wheezing in Mexican American children. *J Allergy Clin Immunol* 2005;116:42-8.
8. Holguin F, Mannino DM, Antó J, Mott J, Ford ES, Teague WG, et al. Country of birth as a risk factor for asthma among Mexican Americans. *Am J Respir Crit Care Med* 2005;171:103-8.
9. Eldeirawi KM, Persky VW. Associations of acculturation and country of birth with asthma and wheezing in Mexican American youths. *J Asthma* 2006;43:279-86.
10. Iqbal S, Oraka E, Chew GL, Flanders WD. Association between birthplace and current asthma: the role of environment and acculturation. *Am J Public Health* 2014;104(Suppl 1):S175-82.
11. Subramanian SV, Jun HJ, Kawachi I, Wright RJ. Contribution of race/ethnicity and country of origin to variations in lifetime reported asthma: evidence for a nativity advantage. *Am J Public Health* 2009;99:690-7.
12. Eldeirawi KM, Persky VW. Associations of physician-diagnosed asthma with country of residence in the first year of life and other immigration-related factors: Chicago asthma school study. *Ann Allergy Asthma Immunol* 2007;99:236-43.
13. Cagney KA, Browning CR, Wallace DM. The Latino paradox in neighborhood context: the case of asthma and other respiratory conditions. *Am J Public Health* 2007;97:919-25.
14. Svendsen ER, Gonzales M, Ross M, Neas LM. Variability in childhood allergy and asthma across ethnicity, language, and residency duration in El Paso, Texas: a cross-sectional study. *Environ Health* 2009;8:55.
15. Balcazar AJ, Grineski SE, Collins TW. The Hispanic health paradox across generations: the relationship of child generational status and citizenship with health outcomes. *Public Health* 2015;129:691-7.
16. Haahela T, Laatikainen T, Alenius H, Auvinen P, Fyhrquist N, Hanski I, et al. Hunt for the origin of allergy-comparing the Finnish and Russian Karelia. *Clin Exp Allergy* 2015;45:891-901.

17. Casey ES, Watkins M. *Up Against the Wall: Re-Imagining the U.S.-Mexico Border*. Austin, Tex: University of Texas Press; 2014.
18. United States Census Bureau. QuickFacts; 2016. Available from: <http://www.census.gov/quickfacts/table/PST045215/0477000, 0477000>. Accessed January 21, 2016.
19. Shaw RA, Crane J, Pearce N, Burgess CD, Bremner P, Woodman K, et al. Comparison of a video questionnaire with the IUATLD written questionnaire for measuring asthma prevalence. *Clin Exp Allergy* 1992;22:561-8.
20. Shaw RA, Crane J, O'Donnell TV, Lewis ME, Stewart B, Beasley R. The use of a videotaped questionnaire for studying asthma prevalence. A pilot study among New Zealand adolescents. *Med J Aust* 1992;157:311-4.
21. Lai CK, Chan JK, Chan A, Wong G, Ho A, Choy D, et al. Comparison of the ISAAC video questionnaire (AVQ3.0) with the ISAAC written questionnaire for estimating asthma associated with bronchial hyperactivity. *Clin Exp Allergy* 1997;27:540-5.
22. Asher MI, Keil U, Anderson HR, Beasley R, Crane J, Martinez F, et al. International Study of Asthma and Allergies in Childhood (ISAAC): rationale and methods. *Eur Respir J* 1995;8:483-91.
23. Gibson PG, Henry R, Shah S, Toneguzzi R, Francis JL, Norzila MZ, et al. Validation of the ISAAC video questionnaire (AVQ3.0) in adolescents from a mixed ethnic background. *Clin Exp Allergy* 2000;30(8):1181-7.
24. Altman D. *Practical Statistics for Medical Research*. London: Chapman & Hall/CRC; 1991.
25. Ramos IN, Davis LB, He Q, May M, Ramos KS. Environmental risk factors of disease in the Cameron Park Colonia, a Hispanic community along the Texas-Mexico border. *J Immigr Minor Health* 2008;10:345-51.
26. English PB, Von Behren J, Hamly M, Neutra RR. Childhood asthma along the United States/Mexico border: hospitalizations and air quality in two California counties. *Rev Panam Salud Publica* 1998;3:392-9.
27. Stephen GA, McGill C, Mack MD, O'Rourke MK, Flood TJ, Lebowitz MD. Assessment of respiratory symptoms and asthma prevalence in a U.S.-Mexico border region. *Arch Environ Health* 2003;58:156-62.
28. United States-Mexico Border Health Commission. Healthy border 2010: an agenda for improving health on the United States-Mexico border; 2013. Available from: http://www.borderhealth.org/files/res_63.pdf. Accessed November 9, 2015.
29. United States-Mexico Border Health Commission. Healthy border 2020: a prevention and health promotion initiative; 2015. Available from: http://www.borderhealth.org/files/res_2805.pdf. Accessed November 17, 2015.
30. Mancilla-Hernández E, Medina-Ávalos M, Barmica-Alvarado R, Soto-Candia D, Guerrero-Venegas R, Zecua-Nájera Y. Prevalence of asthma and determinants of symptoms as risk indicators. *Rev Alerg Mex* 2015;62:271-8.
31. Barraza-Villalreal A, Sanin-Aguirre LH, Tellez-Rojo MM, Lacasana-Navarro M, Romieu I. [Prevalence of asthma and other allergic diseases in school children from Juarez City, Chihuahua]. *Salud Publica Mex* 2001;43: 433-43 [in Spanish].
32. Tatto-Cano MI, Sanin-Aguirre LH, Gonzalez V, Ruiz-Velasco S, Romieu I. Prevalence of asthma, rhinitis and eczema in school children in the city of Cuernavaca, Mexico [in Spanish]. *Salud Publica Mex* 1997;39:497-506.
33. Mendoza-Mendoza A, Romero-Cancio JA, Pena-Rios HD, Vargas MH. [Prevalence of asthma in schoolchildren from the Mexican city Hermosillo]. *Gac Med Mex* 2001;137:397-401 [in Spanish].
34. Rojas Molina N, Legorreta Soberanis J, Olvera Guerra F. [Prevalence and asthma risk factors in municipalities of the State of Guerrero, Mexico]. *Rev Alerg Mex* 2001;48:115-8 [in Spanish].
35. Illi S, Depner M, Genuneit J, Horak E, Loss G, Strunz-Lehner C, et al. Protection from childhood asthma and allergy in Alpine farm environments-the GABRIEL Advanced Studies. *J Allergy Clin Immunol* 2012;129:1470-1477.e1476.
36. Ege MJ, Mayer M, Normand AC, Genuneit J, Cookson WO, Braun-Fahrlander C, et al. Exposure to environmental microorganisms and childhood asthma. *N Engl J Med* 2011;364:701-9.
37. US Census Bureau. Arizona - Core Based Statistical Areas (CBSAs) and counties; 2013. Available from: http://www2.census.gov/geo/maps/metroarea/stcbsa_pg/Feb2013/cbsa2013_AZ.pdf. Accessed November 9, 2015.
38. Coyle EA. Carondelet Holy Cross Hospital community health needs assessment: Santa Cruz County, Arizona; 2013. Available from: http://www.carondelet.org/Portals/0/docs/community-benefit/HolyCrossCHNA_final.pdf. Accessed November 17, 2015.
39. US Census Bureau. 2009-2013 ACS 5 year summary files and data profiles; 2013. Available from: <http://www.census.gov/data/developers/updates/acs-5-yr-summary-available-2009-2013.html>. Accessed November 17, 2015.
40. Instituto Nacional de Estadística y Geografía. Populations, households, and housing [in Spanish]; 2016. Available from: <http://www3.inegi.org.mx/sistemas/temas/default.aspx?s=est&c=17484>. Accessed July 29, 2016.
41. Norman L, Feller M, Guertin D. Forecasting urban growth across the United States-Mexico border. *Comput Environ Urban Syst* 2009;33:150-9.
42. Norman LM, Donelson A, Pfeifer E, Lam AH; US Geological Survey. Colonia development and land use change in Ambos Nogales, United States—Mexican border; 2006. Available from: <http://pubs.usgs.gov/of/2006/1112>. Accessed December 1, 2015.
43. Austin D, Trujillo F; Border Environment Cooperation Commission, US Environmental Protection Agency. Composting toilets and water harvesting: alternatives for conserving and protecting water in Nogales, Sonora; 2010. Available from: http://server.cocfec.org/Final_Reports_B2012/20047/20047_Final_Report_EN.pdf. Accessed December 1, 2015.
44. Wilder M, Scott C, Pineda-Pablos N, Varady R, Garfin G; Udall Center for Studies in Public Policy, The University of Arizona. Moving forward from vulnerability to adaptation: climate change, drought, and water demand in the urbanizing southwestern United States and northern Mexico; 2012. Available from: <http://udallcenter.arizona.edu/sarp/pdf/Casebook.pdf>. Accessed December 1, 2015.
45. Smith LA, Mukerjee S, Monroy GJ, Keene FE. Preliminary assessments of spatial influences in the Ambos Nogales region of the US-Mexican border. *Sci Total Environ* 2001;276:83-92.
46. Casteucci BC, Piña Carrizales LE, D'Angelo DV, McDonald JA, Foulkes H, Ahluwalia IB, et al. Attempted breastfeeding before hospital discharge on both sides of the US-Mexico border, 2005: the Brownsville-Matamoros Sister City Project for Women's Health. *Prev Chronic Dis* 2008;5:A117.
47. Frank R, Heuveline P. A crossover in Mexican and Mexican-American fertility rates: evidence and explanations for an emerging paradox. *Demogr Res* 2005; 12:77-104.
48. Harley K, Stamm NL, Eskenazi B. The effect of time in the U.S. on the duration of breastfeeding in women of Mexican descent. *Matern Child Health J* 2007;11:119-25.
49. McDonald JA, Mojarro Davila O, Sutton PD, Ventura SJ. Cesarean birth in the border region: a descriptive analysis based on US Hispanic and Mexican birth certificates. *Matern Child Health J* 2015;19:112-20.
50. Simpson A, John SL, Jury F, Niven R, Woodcock A, Ollier WE, et al. Endotoxin exposure, CD14, and allergic disease: an interaction between genes and the environment. *Am J Respir Crit Care Med* 2006;174:386-92.
51. Braun-Fahrlander C, Riedler J, Herz U, Eder W, Waser M, Grize L, et al. Environmental exposure to endotoxin and its relation to asthma in school-age children. *N Engl J Med* 2002;347:869-77.
52. Fujimura KE, Demoor T, Rauch M, Faruqi AA, Jang S, Johnson CC, et al. House dust exposure mediates gut microbiome *Lactobacillus* enrichment and airway immune defense against allergens and virus infection. *Proc Natl Acad Sci USA* 2014;111:805-10.
53. Secretaria De Gobernacion, Estados Unidos Mexicanos. Indices de Marginacion; 2010. Available from: http://www.conapo.gob.mx/es/CONAPO/Indices_de_Marginacion. Accessed December 1, 2015.
54. Office of the Assistant Secretary for Planning and Evaluation, US Department of Health and Human Services. Survey data on health insurance coverage for 2013 and 2014; 2014. Available from: <http://aspe.hhs.gov/pdf-report/survey-data-health-insurance-coverage-2013-and-2014>. Accessed December 1, 2015.
55. Simpson J. Judge upholds Arizona's 'show your papers' immigration law. Reuters. September 5, 2015. Available at: <http://www.reuters.com/article/2015/09/05/us-usa-arizona-immigration-idUSKCN0R50WD20150905?WkGdiVWJJBk111.97>. Accessed December 1, 2015.
56. Camacho-Rivera M, Kawachi I, Bennett GG, Subramanian SV. Revisiting the Hispanic health paradox: the relative contributions of nativity, country of origin, and race/ethnicity to childhood asthma. *J Immigr Minor Health* 2015; 17:826-33.
57. Hong SJ, Kim SW, Oh JW, Rah YH, Ahn YM, Kim KE, et al. The validity of the ISAAC written questionnaire and the ISAAC video questionnaire (AVQ 3.0) for predicting asthma associated with bronchial hyperactivity in a group of 13-14 year old Korean schoolchildren. *J Korean Med Sci* 2003;18:48-52.
58. Lukrafka JL, Fuchs SC, Moreira LB, Picon RV, Fischer GB, Fuchs FD. Performance of the ISAAC questionnaire to establish the prevalence of asthma in adolescents: a population-based study. *J Asthma* 2010;47:166-9.
59. Mata Fernández C, Fernández-Benítez M, Pérez Miranda M, Guillén Grima F. Validation of the Spanish version of the Phase III ISAAC questionnaire on asthma. *J Investig Allergol Clin Immunol* 2005;15:201-10.
60. Crane J, Mallol J, Beasley R, Stewart A, Asher MI. International Study of Asthma and Allergies in Childhood Phase I study group. Agreement between written and video questions for comparing asthma symptoms in ISAAC. *Eur Respir J* 2003;21:455-61.
61. Ellwood P, Williams H, Ait-Khaled N, Björkstén B, Robertson C, Group IPIS. Translation of questions: the International Study of Asthma and Allergies in Childhood (ISAAC) experience. *Int J Tuberc Lung Dis* 2009;13:1174-82.

SUPPLEMENTAL METHODS

Dust collection

Dust samples were obtained in schools A, B, D, and E. School C had not granted permission for dust collection at the time of the study. In schools A and B, dust was collected from the science classrooms in which the children were surveyed. In schools D and E, dust was collected from science classrooms and the auditorium in which the children were surveyed. Dust was collected using a 12 AMP Eureka 3670G Mighty Mite canister vacuum cleaner (Eureka, Peoria, Ill) equipped with a preweighed X-Cell 100 dust collection sock (Midwestern Filtration, West Chester Township, Ohio) inserted in the crevice tool.²³ A 1 m² template was laid on the floor in each room and vacuumed for 5 minutes. Dust samples from each school were combined, dried in an oven at 105°C-110°C for 24 hours, and then homogenized for each school and sieved using an electrical shaker (Ro-tap, Tyler, Mentor, Ohio) to particle size <150 µm.

Bacterial load assessment

DNA was extracted from 43-112 mg of dust using the Fast DNA spin kit for soil (MP Biomedicals, Solon, Ohio) following standard manufacturer protocols. Extracted DNA was quantified using a Qubit 2.0 Fluorometer (Life Technologies, Carlsbad, Calif). DNA yields ranged from 0.53 to 14.9 ng/µL.

qPCR was performed using the SensiMix SYBR Hi-ROX Kit (Bioline USA, Boston, Mass). Concentrations of bacterial 16S rRNA genes were estimated using primers ACT CCT ACG GGA GGC AGC AG and ATT ACC GCG GCT GCT GG.⁶⁰ Quantification standards were generated from a pGEM-T Easy

TABLE E1. Prevalence of asthma and symptoms among US students, by language spoken at home among children self-identified as Hispanic or Mexican origin

Language spoken at home	Asthma (ever)	Wheeze past year, written	Wheeze past year, video
English, no Spanish	35.4 (91/257)	21.5 (57/265)	19.3 (51/263)
English and Spanish	22.0 (108/491)	17.0 (83/489)	16.8 (85/501)
Spanish, no English	24.3 (57/235)	12.9 (31/240)	14.0 (34/243)
P value	<.001	.04	.27

TABLE E2. Dust and bacterial load, by school

School	Dust load (g/m ²)	Bacterial DNA concentration (million copies/g dust)	Bacterial DNA load (million copies/m ²)
A	0.033	635	21
B	0.092	963	89
D	1.206	7004	8450
E	1.399	773	1080

plasmid (Promega, Madison, Wis) containing the bacterial 16S rRNA gene fragment of *Escherichia coli* JM109. A standard curve was created using 10-fold dilutions ranging from 3×10^{-7} to 300 copies and calculations were performed according to the Applied Biosystems protocol (Applied Biosystems, Foster City, Calif).

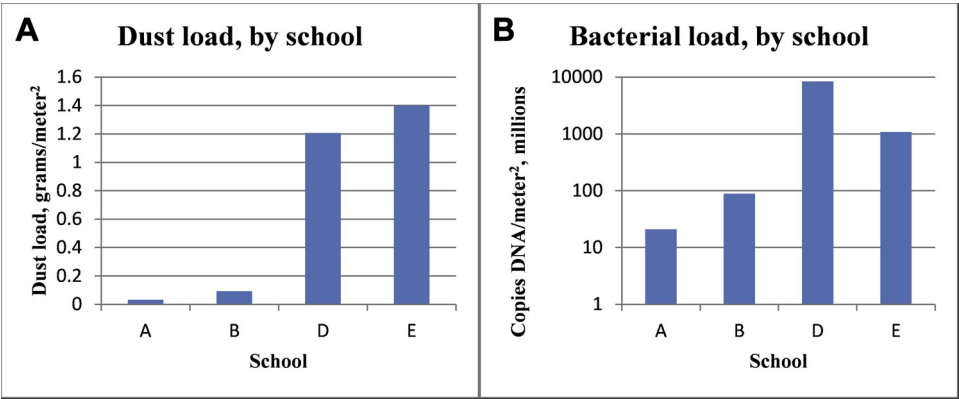


FIGURE E1. Bacterial load and dust load, by school. **A**, Load of dust from pooled samples collected from schools A, B, D, and E, calculated as grams of dust per square meter vacuumed. **B**, Bacterial load of pooled dust samples collected from schools A, B, D, and E, calculated as copies of bacterial DNA per square meter vacuumed, in millions.

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