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Social Determinants of Childhood Asthma Symptoms: An Ecological Study in Urban Latin America

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Abstract Asthma is an important public health problem in urban Latin America. This study aimed to analyze the role of socioeconomic and environmental factors as potential determinants of asthma symptoms prevalence in children from Latin American (LA) urban centers. We selected 31 LA urban centers with complete data, and an ecological analysis was performed. According to our theoretical framework, the explanatory variables were classified in three levels: distal, intermediate, and proximate. The association between variables in the three levels and prevalence of asthma symptoms was examined by bivariate and multivariate linear regression analysis weighed by sample size. In a second stage, we fitted several linear regression models introducing sequentially the variables according to the predefined hierarchy. In the final hierarchical model Gini Index, crowding, sanitation, variation in infant mortality rates and homicide rates, explained great part of the variance in asthma prevalence between centers ($R^2 = 75.0$ %). We found a strong association between socioeconomic and environmental variables and prevalence of asthma symptoms in LA urban children, and according to our hierarchical framework and the results found we suggest that social inequalities (measured by the Gini Index) is a central determinant to explain high prevalence of asthma in LA.

Keywords Asthma · Social inequalities · Urban · Children

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Introduction

While recent studies from many industrialized countries suggest that the prevalence of asthma, while high, may be reaching a plateau, consistent observations from the International Study of Asthma and Allergies in Childhood (ISAAC) have also reported a high prevalence of asthma symptoms in Latin American urban centers, and there are evidences that it continues an upward trend [1.] The likelihood of environmental and life-style changes being important in the asthma upward trend is evident from the rapid concomitant temporal increase in their occurrences, which in Latin America have been closely associated with urbanization and acquisition of a 'modern' lifestyle [2, 3.]

Asthma in Latin America disproportionately affects disadvantaged urban communities, with a greater burden of disease among children in low socio-economic groups [2, 4]. In these populations atopy does not seem to be a key factor in the large burden of asthma symptoms. In fact, the most common phenotype of asthma observed in this region is likely to be non-atopic [5, 6].

Diverse conditions might be related to the high prevalence of asthma symptoms among poor Latin America children. Epidemiological studies have identified a few important risk factors for non atopic asthma linked to poverty and urban life like exposure to environmental dirt, infection and psychosocial stress [6–11].

Overall, Latin America is not the poorest but certainly is the most unequal region in the world [12]. It is composed by 21 countries with substantial variability in their size, development level, urbanization level, income distribution and life styles. Environmental and social disadvantages may play a role in the significant variation in the prevalence of asthma symptoms in this region.

Thence, this study aims at investigating the relationship between socioeconomic and environmental determinants and the prevalence of asthma symptoms in children aged 6–7 years old living in Latin American urban centers according to a predefined hierarchical conceptual framework.

Methods

Study Area and Design

An ecological analysis was conducted using data available from Latin American urban centers that had surveys for asthma symptoms in the period 2000–2003 as part of the ISAAC phase III [13]. It is an epidemiological research program established to study the global increasing of asthma and allergies prevalence. The simple questionnaire used enabled the collection of comparable data from children from different countries and examine time trends in the prevalence of asthma symptoms and related disorders providing information on how these prevalence varies across the world.

ISAAC defined two different age groups for its surveys, the 13–14 and the 6–7 years-old. The 6–7-year-old group was selected for this analysis, and the 31 Latin American urban centers that participated were included. Two centers were excluded because of the large amount of missing data for exposure variables (Fig. 1).

Study Variables and Data Source

Asthma symptoms prevalence was calculated by dividing the number of children with wheeze in the past 12 months by the number of completed questionnaires for each center.

Variables measuring different exposures were selected according to a hierarchical framework similar to that proposed by other authors [14]. The model was built in accordance with knowledge of the social and biological determination of asthma, emphasizing the importance of developing models that integrate the complex determinants of health conditions (Fig. 2).

Fig. 1 ISAAC participating Latin American urban centers

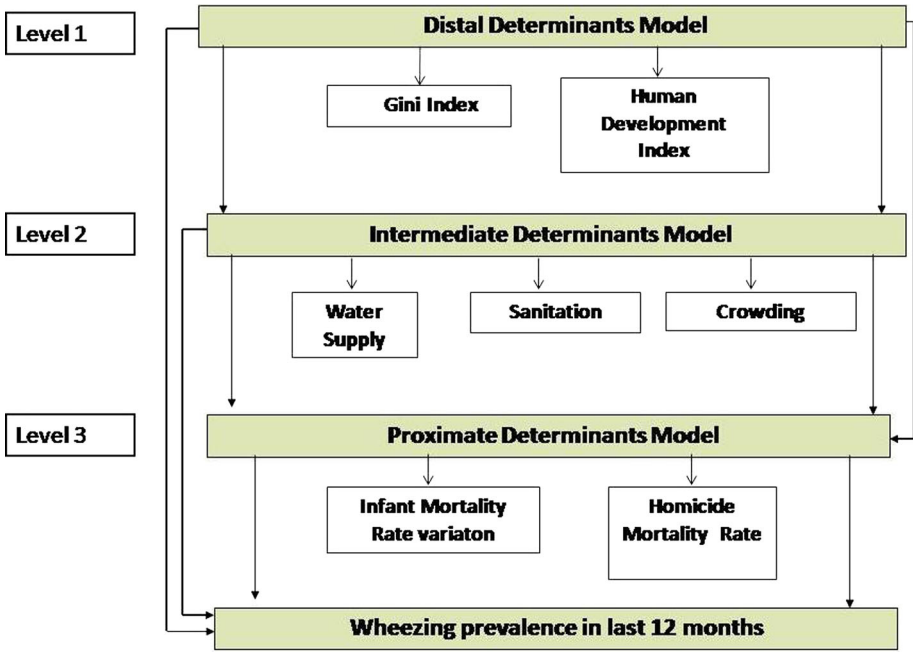

Fig. 2 Socioeconomic and environmental determinants of the prevalence of wheezing in children from Latin American urban centers: a conceptual framework

The socioeconomic variables placed in the distal level included: Gini Index (measure of statistical dispersion, used as a measure of income distribution inequality) and Human Development Index (composite statistic of life expectancy, education level and gross national income per capita) (HDI). The environmental variables in the intermediate level were: water supply (percentage of households with connection to piped water system), sanitation (percentage of households connected to sewage system or septic tank) and crowding (average inhabitants per household). Proximate level included two health related variables: homicide mortality rate (number of homicide deaths as classified by ICD-10 in the entire population per 100,000), which was used as a proxy of the level of psychosocial stress [15]; and variation in infant mortality rates between 1990 and 2000 using the following formula: IMR variation (2000,1990) = 100*[(IMR 1990 − IMR 2000)/IMR 1990], which was selected because it would express the living conditions and healthcare across the population in the period. Data source was obtained from the Human Development Report of each country, the National census database, and Census Office of each country.

Statistical Analysis

We performed a descriptive analysis of the variables to observe differences between the units of analysis. To determine the nature of the relationship between asthma symptoms prevalence and each covariates we constructed scatter plots. The nonlinearity of homicide mortality rate was corrected using logarithmic transformation, and the average inhabitants per household were turned into categorical from the median. Afterwards, we adjusted the linear regression line to visualize the slope of the relationship.

In the bivariate and multivariate analyses, the prevalence of asthma symptoms was modeled through simple and multiple linear regressions. We computed a normal regression with a robust estimate of variance to correct the cluster effect (country) observed between the units of analysis. An analytical weight was employed to correct for heteroskedasticity on data.

To account for the hierarchical framework, first, three sets of bivariate and intra-level multivariate linear regression models was fitted. The variables at the intra-level model were introduced together since they operate at the same level, and those significant ($p \leq 0.10$) were selected.

In a second stage, in order to assess how much of the effect of the distal variables are mediated by intermediate and proximate variables, we fitted several linear regression models introducing sequentially the variables according to the predefined framework. Thereby we performed the model A, which included the significant variables of level 1 and 2 and estimated the effect of the socioeconomic variables not mediated by environmental variables as the overall effects of level 2.

Finally, the model B was performed by the model A plus the significant variables of level 3, which estimated the effect of the socioeconomic variables not mediated simultaneously by the variables of level 2–3, as well as the overall effects of level 3.

We performed a complete regression diagnosis to check linear regression assumptions. We considered the removal of an influential point which resulted in improving the

model and the corroboration of the regression assumptions. The statistical analysis was done using Stata, version 10 (StataCorp, College Station, TX, USA).

Results

The average prevalence for current wheezing among children in the 31 studied urban centers was 17.6 %, with a minimum of 5.1 % and a maximum of 37.6 %. In eleven centers (32.3 %) the prevalence was above 20 %. General characteristics of the units of analysis are shown in Table 1.

Significant correlation was observed between current wheezing and Gini Index ($r = 0.42$, $p = 0.01$), HDI ($r = -0.47$, $p = 0.008$), crowding ($r = -0.48$, $p = 0.005$), water supply ($r = 0.35$, $p = 0.04$) and homicide mortality rate ($r = 0.32$, $p = 0.07$) (Fig. 3).

In the intra-level analysis, both distal variables were singly correlated with asthma prevalence [Gini Index ($\beta = 0.67$, $p = 0.001$) HDI ($\beta = -76.8$, $p = 0.01$)]. When both variables were included simultaneously, the HDI lost statistical significance ($p = 0.21$), but the Gini Index ($\beta = 0.55$, $p = 0.05$) remained, explaining 48.1 % of the variation in the observed asthma prevalence (Table 2).

Correlation between asthma prevalence and intermediate variables shows statistical significance for water supply ($\beta = 0.22$, $p = 0.06$) and crowding ($\beta = -7.4$, $p = 0.01$).

Table 1 Socioeconomic factors, living conditions and health conditions for 31 Latin American urban centers, 2002

	Mean	SD	Minimum	Maximum
Dependent variable				
Asthma symptoms prevalence	17.6	7.7	5.1	37.6
Distal variables				
Gini Index[a]	52.6	7.0	41.5	68.0
Human Development Index[a]	0.79	0.04	0.7	0.9
Intermediate variables				
% households with piped water supply	83.8	12.3	58.9	98.6
% households with adequate sanitation	87.4	12.4	47.8	99.5
Crowding (average inhabitants per household)	3.9	0.5	2.9	5.2
Proximate variables				
Infant mortality rate variation (%)	25.6	12.7	−6.4	46.0
Homicide rate (per 100,000)[a]	24.4	24.3	1.5	92.0

[a] One city excluded for missing data

However, in the intra-level multivariate analysis all variables were statistically associated. The analysis for the proximate determinants shows a direct association for IMR variation ($\beta = 0.20$, $p = 0.045$) and homicide mortality rates ($\beta = 0.19$, $p = 0.01$), which remained unchanged when both variables were added together.

Table 3 summarizes the results of the hierarchical approach performed to estimate model A and B. Since we postulate that the effects of the socioeconomic level can be mediated by the environmental level, from the distal variable that remained significant in the intra-level analysis (Gini Index) we introduced the intermediate variables. It reduced the strength of the association for Gini Index ($\beta = 0.39$, $p = 0.032$) and crowding ($\beta = -5.81$, $p = 0.01$), accentuate the association for sanitation ($\beta = -0.23$, $p = 0.01$) while water supply stayed outside the model (model A).

Finally, using the significant variables of model A, the proximal variables were added to perform the model B. The Gini Index did not change substantially after adjusting for health related variables ($\beta = 0.31$, $p = 0.024$), and crowding ($\beta = -5.12$, $p = 0.01$) and sanitation ($\beta = -0.19$, $p = 0.001$) declined slightly. Both the IMR variation ($\beta = 0.13$, $p = 0.01$) and homicide mortality rate ($\beta = 0.10$, $p = 0.000$) reduced their strength but remained significant in the final model. This three-level model explained 75 % of the variance in the asthma prevalence in these centers.

Discussion

In this ecological analysis, conducted in a large sample of urban centers we found evidence that social and environmental factors are associated with asthma prevalence at ecological level. High level of income inequality, lack of adequate sanitation, less crowding households, greater reduction in the infant mortality rates and high homicide rates were main determinants of asthma symptoms in Latin American urban 6–7 years-old children.

According to our findings, income inequality was a central determinant of asthma prevalence in Latin America. Income distribution and the development of the societies would determine the community resources such as the access to basic services and to health care. Also, community features could define the distribution of the level of psychosocial factors. The level of income inequality would be a proxy of the degree of social class stratification, and it has been suggested that wider income differences are particularly harmful and damage the quality of social relationships which are marked by more violence, hostility and mistrust [16]. It has been hypothesized that living in hierarchical societies promote status competition and cause

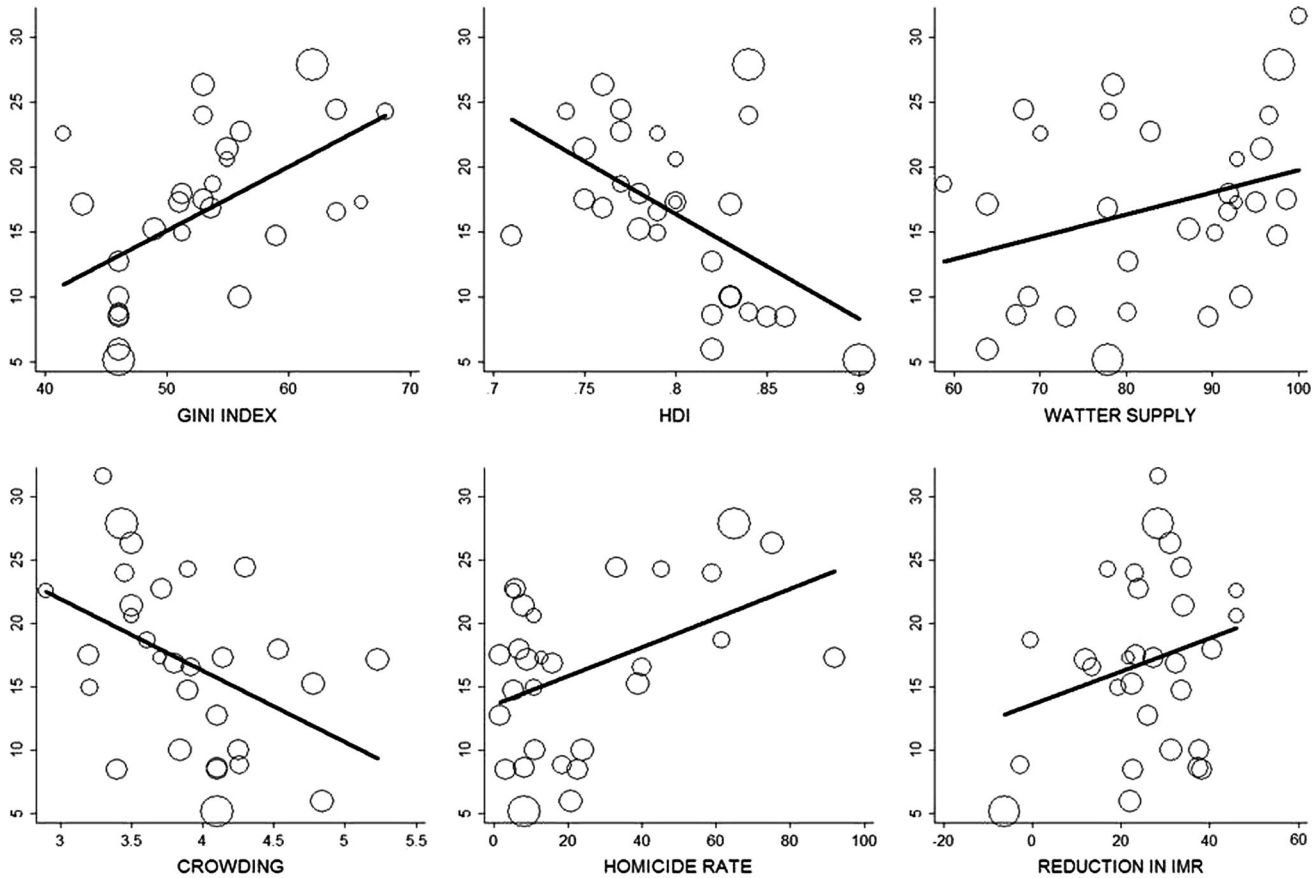

Fig. 3 Scatter plots of the prevalence of wheezing in the last 12 months in children aged 6–7 and selected socioeconomic indicators

Table 2 Bivariate and multivariate intra-level analysis of socioeconomic and environmental determinants of wheezing in children aged 6–7 years in Latin America

Bivariate analysis				Multivariate analysis (by level)		
Variables	β (SD)	*p* value	R^2 (%)	β (SD)	*p* value	R^2 (%)
Level I: distal determinants						
Gini index[a]	0.67 (0.17)	0.001	42.85	0.55 (0.25)	0.05	48.1
Human development index[a]	−76.8 (29.7)	0.01	25.82	− 39.2 (35.5)	0.21	
Level II: Intermediate determinants						
Water supply	0.22 (0.11)	0.06	13.3	0.27 (0.08)	0.017	52.9
Crowding	−7.4 (2.6)	0.01	18.7	−7.03 (2.01)	0.008	
Sanitation	−0.12 (0.09)	0.18	4.17	−0.34 (0.07)	0.001	
Level III: proximate determinants						
Infant mortality rate variation	0.20 (0.09)	0.045	13.6	0.10 (0.05)	0.001	51.5
Homicide rate	0.19 (0.04)	0.010	35.9	0.19 (0.03)	0.001	

[a] One city excluded for missing data

stress, and it is well known that stressful experiences contribute to the development and exacerbation of asthma symptoms [10]. In addition, other measure of socioeconomic inequality like homicide rate, was strongly associated with asthma symptoms in our study. This topic is particularly important in Latin America, where interpersonal violence has become a major cause of morbidity and mortality [17].

These associations may reflect the effect of multiple and adverse social conditions characteristic of the urban poor. Indicators of community-level stressors like high crime/violence rates, limited social capital, deprivation, social

Table 3 Hierarchical analysis of socioeconomic and environmental determinants of wheezing grouped by levels in children aged 6–7 years in Latin America

Model A[a] (block I–II)				Model B[a] (block I–II–III)		
Variables	β (SD)	*p* value	R^2 (%)	β (SD)	*p* value	R^2 (%)
Level I: distal determinants						
Gini index	0.39 (0.16)	0.032		0.31(0.12)	0.024	
Level II: intermediate determinants						
Water supply	0.10 (0.08)	0.22				
Crowding	−5.81 (2.04)	0.01		−5.12 (1.4)	0.01	
Sanitation	−0.23 (0.07)	0.01		−0.19 (0.05)	0.001	
			61.7			
Level III: proximate determinants						
Infant mortality rate Variation				0.13(0.04)	0.01	
Homicide mortality rate				0.10(0.02)	0.000	
						75.0

[a] One city excluded for missing data

exclusion and others, have been characterized as neighborhood disadvantage, expressing the level of chronic stressors in communities [18, 19].

Our results are in line with other studies conducted in urban Latin American settings that reported a very high prevalence of wheezing among children living in poor neighborhoods [4], and associated with population measures of socio-economic inequality [20], poverty [21], and violence [22, 23] suggesting that environmental exposures related to poverty and stress increases the risk of having asthma.

Moreover, it is known that living condition is an important determinant of population health. Residential exposure was linked with asthma by being the physical environment for people's lives. Thus, poor quality housing related to crowding, inadequate ventilation and lack of clean water were identified as important risk factor for asthma symptoms [24].

In addition, places may be related to health independently of individual-level characteristics, and substandard housing conditions would represent the degree of social development of the urban centers where individual lives.

However, in our study living condition indicators were distinctly associated with asthma symptoms. Higher asthma prevalence was found in centers with less household crowding and lower coverage of adequate sanitation. In those urban centers poor sanitation would reflect several unhealthy housing conditions and chronic hazards that expose population to known risk factor to the disease [25].

The fact that we found wheezing prevalence increasing with decreasing crowding while apparently contradict the previous finding is according with the hygiene hypothesis [26], it could reflect an increase of atopic wheezing as result of socioeconomic and housing improvement [27, 28]. Latin America changes towards an highly urbanized population, process that is usually associated with economic growth and development. However, the improvement in living conditions is not uniform [17] then, different patterns of exposure and hence different immunological profiles are expected.

Unexpectedly, according to our results, the greater the reduction in infant mortality rates in the past decade, the higher the asthma prevalence in urban centers. The infant mortality rate is universally considered an indicator of health status, and it reflects the relation among the causes of infant mortality and those structural factors such as economic development, living conditions and social well-being manifested in the health of the population. Improvements in socioeconomic and health conditions may introduce new environmental stimuli and modulate the immunological response toward the development of atopy [29]. However, despite the apparent improvement in child health, inequities between the rich and the poor persist and have even increased, [30] and it could reflect not only different living conditions but even differential availability and utilization of public health interventions, especially in developing countries. Therefore, and considering the prevalence of non-atopic asthma in Latin American countries, we would expect the coexistence of exposure factors associated with both atopic and non-atopic asthma, leading to a progressive increase of allergies and to an overlapping of the two phenotypes in urban centers.

The main strength of this study lies in the assessment of some socioeconomic determinants of asthma in such a large region as Latin America, using urban centers as units of analysis. Some global associations could be explored with the ecological approach which is an appropriate way to examine the relation between prevalence of disease and social and economic conditions through a hierarchical framework.

Nevertheless, this study has some limitations. First, it is an ecological study which limits the establishment of causal relationships. The fundamental problem with the ecological analysis is that it cannot distinguish the effect of the variable on the individual level from its contextual effect. Especially, with some measures used in our analysis, like those related to infrastructure factors, we cannot differentiate the extent to which individuals who are exposed in fact develop the disease. However, other variables used, like Gini index, IMR variation or homicide rate are intrinsically aggregated measures and operate at population level; their effect are not restricted to the poor but extends to all social strata, so the exposure is expected to be shared by all members of the society.

Secondary data from diverse sources were used with the consequent variability in information quality. Notwithstanding, to ensure validity, they were extracted in all cases from official sources. The existence of an expected correlation observed between independent variables sustains the adequacy of the collected data.

In conclusion, we found strong evidence of the association between inequalities and asthma symptoms in urban Latin America, one of the most unequal regions in the world [15]. Rural Latin American populations have migrated intensely in the past 3–4 decades into large urban settlements, drawing a pattern of rapid and unplanned urbanization with profound effects on people's living conditions and health status. The correlations observed in our study may reflect the deep demographic changes and consequent living conditions, and their impact on lung development and immune responses. In Latin America non-atopic asthma phenotype is dominant but the frequency of atopy is also high. The determinants of non-atopic asthma are related to poverty, lack of cleanliness and psychosocial factors while a decreased burden of infection is related to high frequency of atopy. As the social and environmental situation improves in Latin America it is possible to hypothesize that atopy is increasing and non-atopic asthma is decreasing. While there is no evidence that atopic asthma is increasing in Latin America, there is some evidence suggesting its increase in other parts of the world. Therefore, the findings from this cross-sectional ecological analysis could reflect the complex dynamic of asthma and allergies in this region of the world.

From a public health perspective the findings may be of interest, especially considering the social determination of the disease and the potential to remove the underlying causes that make the disease so common. We consider it relevant to conduct studies that explore this relationship in depth, discriminating the different phenotypes of asthma, addressing both the geographic area and the individual level, and incorporating other variables related to urbanization and the socioeconomic dimension.

Conflict of interest The authors declare that they have no competing interests.

References

1. Pearce, N., Aït-Khaled, N., Beasley, R., Mallol, J., Keil, U., Mitchell, E., et al. (2007). Worldwide trends in the prevalence of asthma symptoms: Phase III of the International Study of Asthma and Allergies in Childhood (ISAAC). *Thorax, 62*, 758–766.
2. Cooper, P. J., Rodrigues, L. C., Cruz, A. A., & Barreto, M. L. (2009). Asthma in Latin America: A public heath challenge and research opportunity. *Allergy, 64*, 5–17.
3. Rodríguez, A., Vaca, M., Oviedo, G., Erazo, S., Chico, M. E., Teles, C., et al. (2011). Urbanisation is associated with prevalence of childhood asthma in diverse, small rural communities in Ecuador. *Thorax, 66*, 1043–1050.
4. Mallol, J. (2000). Childhood asthma in developing countries. Low income aspects and related matters. *Allergologia et Immunopathologia, 28*(5), 283–286.
5. Pereira, M. U., Sly, P. D., Pitrez, P. M., Jones, M. H., Escouto, D., Dias, A. C. O., et al. (2007). Nonatopic asthma is associated with helminth infections and bronchiolitis in poor children. *European Respiratory Journal, 29*, 1154–1160.
6. Cunha, S. S., Barreto, M. L., Fiaccone, R. L., Cooper, P. J., Alcantara-Neves, N. M., Simões, S. M., et al. (2010). Asthma cases in childhood attributed to atopy in tropical area in Brazil. *Revista Panamericana de Salud Publica, 28*(6), 405–411.
7. Chatkin, M. N., Menezes, A. M., Victora, C. G., & Barros, F. C. (2003). High prevalence of asthma in preschool children in Southern Brazil: A population-based study. *Pediatric Pulmonology, 35*, 296–301.
8. Lara, M., Akinbami, L., Flores, G., & Morgenstern, H. (2006). Heterogeneity of childhood asthma among Hispanic children: Puerto Rican children bear a disproportionate burden. *Pediatrics, 117*, 43. doi:10.1542/peds.2004-1714.
9. Celedón, J. C., Soto-Quiros, M. E., Silverman, E. K., Hanson, L., & Weiss, S. T. (2001). Risk factors for childhood asthma in Costa Rica. *Chest, 120*, 785–790.
10. Wright, R. J. (1998). Review of psychosocial stress and asthma: An integrated biopsychosocial approach. *Thorax, 53*, 1066–1074.
11. Cooper, P. J., Rodrigues, L. C., & Barreto, M. L. (2012). Influence of poverty and infection on asthma in Latin America. *Current Opinion in Allergy and Clinical Immunology, 12*, 171–178.
12. Hoffman, K., & Centeno, M. A. (2003). The lopsided continent: Inequality in Latin America. *Annual Review of Sociology, 29*, 363–390.
13. Pearce, N., Aït-Khaled, N., Beasley, R., Mallol, J., Keil, U., Mitchell, E., Robertson, C., & the ISAAC Phase Three Study Group. (2009). Global variation in the prevalence and severity of asthma symptoms: Phase Three of the International Study of Asthma and Allergies in Childhood (ISAAC). *Thorax,* 64, 476–483.
14. Victora, C. G., Huttly, S. R., Fuchs, S. C., & Olinto, M. T. (1997). The role of conceptual frameworks in epidemiological analisis: A hierarchical approach. *International Journal of Epidemiology, 26*(1), 224–227.
15. Wilkinson, R. G., Kawachi, I., & Kennedy, B. P. (1998). Mortality, the social environment, crime and violence. *Sociology of Health and Illness, 20*(5), 578–597.
16. Wilkinson, R. G. (2000). Inequality and the social environment: A reply to Lynch et al. *Journal of Epidemiology and Community Health, 54*, 411–413.
17. Fay, M. (Ed.). *The urban poor in Latin America/2005*. Washington, DC: The World Bank.

18. Williams, D. R., Sternthal, M., & Wright, R. J. (2009). Social determinants: Taking the social context of asthma seriously. *Pediatrics, 123*, S174.
19. Yonas, M. A., Lange, N. E., & Celedón, J. C. (2012). Psychosocial stress and asthma morbidity. *Current Opinion in Allergy and Clinical Immunology, 12*(2), 202–210.
20. Cunha, S. S., Pujades-Rodriguez, M., Barreto, L. M., Genser, B., & Rodriguez, L. C. (2007). Ecological study of socio-economic indicators and prevalence of asthma in schoolchildren in urban Brazil. *BMC Public Health, 7*, 205.
21. Barreto, M. L., Cunha, S. S., Fiaccone, R., Esquivel, R., Amorin, L. D., Alvim, S., et al. (2010). Poverty, dirt, infections and non-atopic wheezing in children from a Brazilian urban center. *Respiratory Research, 11*, 167.
22. Wright, R. J., Mitchell, H., Visness, C. M., et al. (2004). Community violence and asthma morbidity: The Inner-City Asthma Study. *American Journal of Public Health, 94*, 4.
23. Alves, G. C., Santos, D. N., Feitosa, C. A., & Barreto, M. L. (2012). Community violence and childhood asthma prevalence in peripheral neighborhoods in Salvador, Bahia State, Brazil. *Cadernos de Saúde Pública, 28*(1), 86–94.
24. Krieger, J., & Higgins, D. L. (2002). Housing and health: Time again for public health action. *American Journal of Public Health, 92*(5), 758–768.
25. Corburn, J., Osleeb, J., & Porter, M. (2006). Urban asthma and the neighbourhood environment in New York City. *Health and Place, 12*(2), 167–179.
26. Schaub, B., Lauener, R., & von Mutius, E. (2006). The many faces of the hygiene hypothesis. *Journal of Allergy and Clinical Immunology, 117*(5), 969–977.
27. Corvalán, C., Amigo, H., Bustos, P., & Rona, R. (2005). Socioeconomic risk factors for asthma in chilean young adults. *American Journal of Public Health, 95*(8), 1375–1381.
28. da Costa Lima, R., Victora, C. G., Menezes, A. M., & Barros, F. (2003). Do risk factors for childhood infections and malnutrition protect against asthma? A study of Brazilian male adolescents. *American Journal of Public Health, 93*, 1858–1864.
29. Figueiredo, C. A., Alcantara-Neves, N. M., Amorim, L. D., Silva, N. B., Carvalho, L. C., Cooper, P. J., et al. (2011). Evidence for a modulatory effect of IL-10 on both Th1 and Th2 cytokine production: The role of the environment. *Clinical Immunology, 139*(1), 57–64.
30. Victora, C. G., Vaughan, J. P., Barros, F. C., Silva, A. C., & Tomasi, E. (2000). Explaining trends in inequities: Evidence from Brazilian child health studies. *The Lancet, 356*(9235), 1093–1098.