

Do Risk Factors for Childhood Infections and Malnutrition Protect Against Asthma? A Study of Brazilian Male Adolescents

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Asthma is a major health problem among children and adolescents.^{1,2} According to the International Study of Asthma and Allergy in Childhood (ISAAC),³ which involved 155 study sites in 56 different countries, prevalence rates of reported asthma (measured as “wheezing”) in the past year among children aged 13 and 14 years ranged from 6.6% in Southeast Asia to 29.7% in Australia and New Zealand.⁴ Rates tended to be higher in developed countries. In addition, several other studies from different countries have shown increasing frequencies of asthma.^{5–8}

Although genetic factors play an important role in an individual’s risk of asthma, these factors probably do not account for large differences among populations.⁹ Thus, social, environmental, and behavioral factors must play an important role, an assertion that is confirmed by the increasing prevalence rates that have been observed. Many studies have assessed the roles of passive smoking and air pollution,^{10,11} dietary changes¹² (including changes in breastfeeding patterns^{13,14}), and reduced exposure to infections.¹¹ The latter factor has been conceptualized in the “hygiene hypothesis”: early exposure to infectious agents increases the production of T_H1 lymphocytes, providing protection against IgE-mediated atopic diseases.

A mixture of different conditions¹⁵ with distinct etiologies and risk factors combine to cause childhood wheezing. It is important, therefore, to study the presence of wheezing among individuals of older ages, among whom atopic conditions prevail. Prospective birth cohort studies provide the ideal design for understanding the role of social, environmental, and behavioral factors in adolescent health. Few such studies have been conducted in developing countries, and the study described here is, to our knowledge, the first large cohort investigation to assess the influence of early risk factors on adolescent asthma.

Objectives. We studied the association between early life conditions and asthma in adolescence.

Methods. We conducted a population-based birth cohort study involving 2250 male 18-year-olds residing in Brazil.

Results. Approximately 18% of the adolescents reported having asthma. Several childhood factors were found to be significantly associated with increased asthma risk: being of high socioeconomic status, living in an uncrowded household, and children being breastfed for 9 months or longer.

Conclusions. The present results are consistent with the “hygiene hypothesis,” according to which early exposure to infections provides protection against asthma. The policy implications of our findings are unclear given that risk factors for asthma protect against serious childhood diseases in developing countries. (*Am J Public Health.* 2003; 93:1858–1864)

METHODS

Pelotas is a city of 320 000 inhabitants in southern Brazil. In 1982, all 5914 newborns in the city’s 3 hospitals (accounting for more than 99% of all deliveries occurring in the city) were enrolled in the Pelotas Birth Cohort Study. Mothers were interviewed, and their infants were examined. The cohort was followed up on several occasions. In 1983, when the cohort’s average age was 12 months, one third of the sample was studied; in 1984 (mean age: 20 months) and 1986 (mean age: 42 months), attempts were made to locate all of the cohort children. Follow-up rates were 87% in 1984 and 84% in 1986. Details regarding the methodology of the early stages of the study have been provided elsewhere.¹⁶

In 2000, all cohort boys who still resided in Pelotas were legally required to undergo a Brazilian Army medical examination. On this occasion, they were invited to participate in the present study; if they agreed to take part, they signed an informed consent form. They then completed a standardized questionnaire and underwent anthropometric and physical examinations.

Information on the following variables was collected in the 1982 interview: monthly family income; maternal age, edu-

cation level, skin color, weight gain and smoking status during pregnancy, and parity; parental tobacco use; type of delivery; gestational age; and birthweight. We assessed intrauterine growth retardation using the 10th percentile of the birthweight-by-gestational age curve.

In 1984, data regarding several other variables were collected via maternal reports: history of “asthma or bronchitis,” expulsion of intestinal worms, or pneumonia; diphtheria–pertussis–tetanus, polio, and measles immunization status; number of persons per bedroom; whether or not other children resided in the home; and presence of piped water and a flush toilet in the home. Also, an asset index was constructed; this variable involved a factor analysis of 5 household assets, type of residence, and number of rooms. In the case of children who could not be located in 1984, information on these variables was obtained from the 1986 questionnaire. In addition, all hospital admissions reported during the 3 interviews were recorded.

Also during the 1984 visit, children were weighed with portable scales, and their height was measured. We calculated weight-for-age, length-for-age, and weight-for-length z scores according to the standards of the National Center for Health Statistics.¹⁷

Information on breastfeeding was collected during all visits. If the child was seen in 1983 and had already been weaned, information from this interview was used; otherwise, information from the 1984 interview was used. If the child had not been seen in 1984 but was seen in 1986, the latter information was used. Few children were exclusively breastfed at any age, in that other fluids were typically introduced very early.

When children were aged 3 months, they were categorized into one of the following groups: exclusively or predominantly breastfed (breast milk in combination with water or tea), partially breastfed (breast milk in combination with nutritive fluids or semisolids), or not breastfed. Since children were seldom exclusively or predominantly breastfed after 3 months of age, we characterized feeding at older ages according to type of milk received: breast, nonbreast, or both.

In 2000, information was collected on adolescents' schooling and skin color, and the scale developed for the ISAAC study was used in assessing prevalence rates of respiratory symptoms.³ This questionnaire was translated from English to Portuguese and validated by Sole et al.¹⁸ Presence of asthma was determined via a positive answer to the question "Have you ever had wheezing or whistling in the chest in the last 12 months?" We repeated all analyses using a cutoff of 6 or more positive ISAAC scale responses, the cutoff validated in Brazil.¹⁸ Our study was designed to have 80% power in terms of detecting a prevalence ratio (PR) of 1.3, at the 5% significance level, for exposures present in a 20% to 70% range of the sample.

We estimated prevalence ratios and their associated 95% confidence intervals (CIs) using Poisson regression¹⁹; we used the robust variance option in Stata 6.0²⁰ in this analysis, which allowed for the inclusion of maternal schooling, monthly family income, and the assets index. In the case of the breastfeeding variables, we included additional confounding factors in the analyses: crowding, maternal age, parental smoking, birthweight, gestational age, intrauterine growth retardation, parity, and type of delivery. When applicable, we used linear trend tests to assess ordinal variables. All statistical tests were 2 sided.

RESULTS

Of the 3037 boys born in 1982, 143 had died and 2294 were located in the year 2000, among whom 2250 were interviewed. The 44 participants who could not be interviewed included 10 who had severe mental handicaps and 34 who did not respond despite several attempts. Those interviewed or known to have died accounted for 78.8% of the original cohort. Interviews took place between July 2000 and January 2001, and all but 3 respondents provided information on the outcomes under study.

Response rates were analyzed according to variables for which information was collected during the 1982 baseline interview (income, maternal education level, birthweight, preterm delivery, and intrauterine growth retardation). More than three quarters of respondents in the study categories were traced with the exception of those in the lowest family income group, of whom 72.5% were located (data available on request).

Among the respondents, 18.6% (95% CI=17.0%, 20.2%) reported experiencing "wheezing in the chest" in the past year. When asthma was defined according to the ISAAC scale cutoff (6 or more positive responses), 16.1% (95% CI=14.6%, 17.7%) of the respondents were classified as having asthma. This classification identified more severe cases than the general question on wheezing.

All 3 socioeconomic indices—family income, maternal education, and the asset index—were positively associated with asthma prevalence rates in the crude analyses; when these variables were adjusted for one another, only the asset index remained significant. Two variables related to crowding were significantly associated with asthma in both the crude and adjusted analyses; children living in a home with a high number of persons per bedroom or living in a home with other children had lower asthma risks (Table 1).

Presence of piped water and type of flush toilet in the home were not associated with risk of asthma after adjustment for socioeconomic status. Likewise, no association was found between asthma and maternal smoking during pregnancy (PR=0.97; 95% CI=0.80,

1.18) or between asthma and overall parental smoking (PR=0.98; 95% CI=0.81, 1.19).

Table 2 shows the effects of variables related to gestation and type of delivery. After adjustment, only type of delivery remained significant, with a 29% increase in asthma rates among babies delivered via cesarean delivery. Birthweight was not associated with risk of asthma, even when it was coded as an ordinal variable with several categories; also, there was no association with intrauterine growth retardation. Neither maternal age nor maternal skin color was associated with asthma risk (data not shown).

Several variables related to breastfeeding were investigated. The data presented in Table 3 reveal no significant association between feeding pattern at 3 months and risk of asthma. Likewise, type of milk consumed at 3 and 6 months failed to show significant effects. However, at older ages, children who were breastfed, particularly those consuming both breast milk and other milk, had higher risks of asthma than those who had stopped breastfeeding.

An additional analysis (data not shown in Table 3) indicated that, after adjustment for socioeconomic variables, children breastfed for at least 9 months were 42% (95% CI=13%, 77%) more likely than those breastfed for less than 3 months to have asthma. Results related to breastfeeding remained unchanged when other potential confounding factors (crowding, maternal age, parental smoking, birthweight, gestational age, intrauterine growth retardation, parity, and type of delivery) were included in the model.

Table 4 shows that children who were underweight or stunted at the age of 20 months exhibited reduced asthma prevalence rates; after adjustment, however, this association was no longer significant. Table 4 also shows data relating to morbidity. A history of having expelled intestinal worms and a history of pneumonia were not associated with later risk of asthma; however, children whose mothers reported as experiencing "asthma or bronchitis" exhibited a 40% increased risk of asthma as adolescents.

Several other variables related to childhood infections were studied but were not found to be significant. These variables included all-cause hospital admissions and completion of

TABLE 1—Asthma Prevalence Ratios (PRs) and 95% Confidence Intervals (CIs), According to Various Socioeconomic and Environmental Factors: Pelotas, Brazil

	No. ^a	Prevalence, %	Crude PR (95% CI)	Adjusted PR (95% CI)
Monthly family income, \$ (1982) ^b				
<50	420	16.4	1.00	1.00
50–149	1102	17.1	1.04 (0.81, 1.34)	0.94 (0.72, 1.23)
150–299	448	21.2	1.29 (0.98, 1.71)	1.09 (0.80, 1.50)
≥ 300	269	23.8	1.45 (1.07, 1.96)	1.10 (0.73, 1.65)
<i>p</i> ^c			.02	.66
Maternal education, y (1982) ^d				
0–4	698	17.0	1.00	1.00
5–8	987	17.3	1.02 (0.82, 1.26)	0.99 (0.78, 1.24)
9–11	243	21.8	1.28 (0.96, 1.71)	1.12 (0.81, 1.55)
≥ 12	315	23.2	1.36 (1.05, 1.76)	1.05 (0.73, 1.50)
<i>p</i> ^c			.04	.86
Assets index (1984) ^e				
1	370	13.2	1.00	1.00
2	383	18.5	1.40 (1.00, 1.96)	1.40 (0.99, 1.95)
3	464	19.2	1.45 (1.05, 2.00)	1.39 (1.00, 1.95)
4	532	18.8	1.42 (1.04, 1.94)	1.30 (0.93, 1.84)
5	318	26.1	1.97 (1.43, 2.71)	1.78 (1.24, 2.55)
<i>p</i> ^c			.001	.02
No. of persons per bedroom (1984) ^f				
<2	409	26.7	1.00	1.00
≥ 2	1753	16.8	0.63 (0.52, 0.76)	0.67 (0.53, 0.86)
<i>p</i> ^c			.0000	.001
No. of other children living in the home (1984) ^f				
0	556	23.6	1.00	1.00
≥ 1	1580	17.2	0.73 (0.61, 0.88)	0.72 (0.60, 0.87)
<i>p</i> ^c			.0008	.0007

^aTotals may not sum to 2247 owing to missing data.

^bAdjusted for maternal education and assets index.

^c χ^2 heterogeneity test for variables with 2 categories; χ^2 trend test for variables with 3 or more categories.

^dAdjusted for family income and assets index.

^eAdjusted for family income and maternal education.

^fAdjusted for family income, maternal education, and assets index.

DISCUSSION

To our knowledge, the present study is the first population-based birth cohort investigation conducted in a developing country to report on risk factors for asthma in adolescence. Approximately 4 of every 5 study respondents were traced after 18 years, and more than 70% of the individuals grouped in each risk category were traced.

Limitations of the study include its restriction to male participants, the lack of information on familial history of asthma, and the absence of data on sera immunoglobulins. The finding of a direct association between wealth indicators and asthma prevalence raised the possibility of reporting bias; however, such bias was not likely in that adolescents at higher education levels were slightly less likely to report asthma.

We found a prevalence rate of 18.6% in terms of wheezing reported in the previous 12 months, while the mean prevalence among 17 Latin American studies using the same criterion as that used here was 17%. When we used the ISAAC scale cutoff, the asthma prevalence rate was 16.1%. The only other Brazilian study involving use of the same criteria employed here revealed a 22.5% prevalence rate among São Paulo adolescents aged 13 or 14 years. Air pollution levels are high in São Paulo but very low in Pelotas, which may partly account for this difference.¹⁸

Our analyses showed that high socioeconomic status, living in an uncrowded household, and children being breastfed for 9 months or longer were associated with higher asthma risks. In addition, when the stricter definition of asthma was used, individuals of adequate weight and those not having expelled worms were both at risk for asthma. All of these variables are well-known protective factors against childhood infections. Our findings are consistent with the earlier-described “hygiene hypothesis,” according to which early exposure to infections protects one against asthma.¹¹ However, other variables associated with exposure to infectious agents, including history of pneumonia, hospital admissions, and immunizations, were not associated with asthma risk.

Mallol et al.^{21(p444)} argued that the high prevalence rates of asthma found in 17

diphtheria–pertussis–tetanus, polio, and measles immunizations (data not shown).

To investigate the possibility of reporting bias, we analyzed the association between education history and asthma. Relative to boys with fewer than 6 years of schooling, those with 6 to 9 years of schooling exhibited a 15% decrease in asthma risk, and those with 10 or more years exhibited a 25% decrease ($P=.19$).

We repeated all analyses using the ISAAC scale cutoff (according to which 16.1% of the respondents had asthma; these individuals were included among the 18.6% who re-

ported having experienced wheezing in the past year). In the adjusted analyses, the associations with the asset index, number of persons per bedroom, number of other children living in the home, type of delivery, breastfeeding pattern, and report of asthma in 1984 remained significant. Two variables that were not associated with respondents' reports of wheezing in the past year—normal or high weight for age ($PR=2.17$; 95% $CI=1.06, 4.43$) and report of expulsion of worms ($PR=0.76$; 95% $CI=0.60, 0.96$)—were significantly associated with ISAAC scale score.

TABLE 2—Asthma Prevalence Ratios (PRs) and 95% Confidence Intervals (CIs), According to Variables Related to Gestation and Delivery: Pelotas, Brazil

	No. ^a	Prevalence, %	Crude PR (95% CI)	Adjusted ^b PR (95% CI)
Maternal weight gain during pregnancy, kg (1982)				
< 9.6	572	15.4	1.00	1.00
≥ 9.6	1158	19.5	1.27 (1.01, 1.59)	1.13 (0.90, 1.42)
<i>p</i> ^c			.04	.29
Type of delivery (1982)				
Vaginal	1591	16.9	1.00	1.00
Cesarean	656	22.6	1.33 (1.12, 1.60)	1.29 (1.07, 1.55)
<i>p</i> ^c			.002	.007
Multiple births (1982)				
No	2211	18.4	1.00	1.00
Yes	36	27.8	1.51 (0.88, 2.57)	1.45 (0.84, 2.51)
<i>p</i> ^c			.13	.18
Gestational age, wk (1982)				
< 37	214	22.0	1.00	1.00
≥ 37	1605	18.6	0.85 (0.65, 1.11)	0.81 (0.61, 1.06)
<i>p</i> ^c			.24	.12
Birthweight, g (1982)				
< 2500	132	17.4	1.00	1.00
≥ 2500	2115	18.6	1.07 (0.73, 1.57)	1.07 (0.72, 1.58)
<i>p</i> ^c			.73	.75
Intrauterine growth retardation (1982)				
No	1546	19.5	1.00	1.00
Yes	273	16.1	0.83 (0.62, 1.10)	0.84 (0.62, 1.14)
<i>p</i> ^c			.19	.26

^aTotals may not sum to 2247 owing to missing data.

^bAdjusted for family income, maternal education, and assets index.

^c χ^2 test for heterogeneity.

Latin American studies contradict the hygiene hypothesis: “factors that appear to protect against asthma . . . do not seem to play a protective role in this region.” However, this statement was based on an ecological comparison of prevalence rates between Latin American studies and other investigations. No individual-level analyses were presented. Furthermore, the study sites were mostly in national capitals or other large polluted cities, and the samples were restricted to children attending school; thus, the results may not be representative of the poorest populations in these countries. Our results show that when a population-based sample of adolescents is analyzed at the individual level, it is possible to detect several associations supporting the hygiene hypothesis.

An interesting finding related to type of delivery. After adjustment for socioeconomic variables, babies delivered via cesarean delivery exhibited a 29% increase in asthma prevalence. Moreover, this association persisted after adjustment for breastfeeding patterns. The study of Annesi-Maesano et al.²² conducted in France produced similar results, and the authors speculated that intrauterine conditions, if adverse, could affect lung development. However, in Brazil, cesarean deliveries appear to be more strongly associated with socioeconomic status than with gestational risk.²³ In a Finnish study, Kero et al.²⁴ recently reported an association that they attributed to lower microbial exposures in surgically delivered babies. In our study, the possibility of residual confounding according to social status cannot be dismissed.

Of particular interest was the positive association between breastfeeding duration and asthma. The analyses comparing different durations of breastfeeding and those examining feeding patterns at different ages (Table 3) produced consistent results. These findings may be regarded as counterintuitive, in that it has been proposed that breast milk may protect against atopic disorders.¹³ In a 1988 review, Kramer¹⁴ discussed methodological requirements for studies involving analyses of breastfeeding, including a short recall period for information on breastfeeding and the need for (1) interviewers unaware of breastfeeding history, (2) at least a 2-month assessment of breastfeeding patterns, and (3) inclusion of infants who have been exclusively breastfed (or nearly so). All of these criteria were met in the present study.

Two recent reviews assessed breastfeeding and childhood asthma. Gdalevich et al.¹³ carried out a meta-analysis of 12 prospective studies conducted in developed countries. The summary odds ratio for the protective effect of breastfeeding was 0.70 (95% CI = 0.60, 0.81). The effect was greater when a family history of asthma was present. Takemura's et al.²⁵ review of asthma and other atopic conditions included 3 studies showing protective effects,^{26–28} 10 showing no association, and 2 reporting an increased risk.

The 2 studies that revealed an increased risk were those of Martin et al.²⁹ and Savilahti et al.³⁰ The Martin et al. Australian study, which involved respondents aged 7 to 21 years, showed that those with severe asthma had been breastfed longer than those with mild or moderate asthma and those without asthma. Savilahti et al.³⁰ reported a higher frequency of atopic conditions in Finnish infants who were exclusively breastfed for 9 months or longer. The Takemura et al. results from their own study showed that, after adjustment for several confounding variables, Japanese children breastfed at the age of 3 months exhibited a 20% increase in asthma prevalence at the ages of 6 to 15 years.

However, as some authors have pointed out,^{15,31} results from childhood studies cannot necessarily be extrapolated to adolescents, in that infectious wheezing conditions

TABLE 3—Asthma Prevalence Ratios (PRs) and 95% Confidence Intervals (CIs), According to Breastfeeding Status: Pelotas, Brazil

	No. ^a	Prevalence, %	Crude PR (95% CI)	Adjusted ^b PR (95% CI)
Feeding pattern at 3 months (1983–1986)				
Exclusive	578	20.9	1.26 (1.02, 1.54)	1.22 (0.99, 1.51)
Partial	541	20.0	1.20 (0.97, 1.48)	1.18 (0.95, 1.47)
Not breastfed	1128	16.7	1.00	1.00
<i>p</i> ^c			.06	.13
Type of milk received at 3 months (1983–1986)				
Breast	679	20.9	1.25 (1.03, 1.53)	1.22 (1.00, 1.50)
Mixed	440	19.8	1.19 (0.94, 1.49)	1.17 (0.93, 1.47)
Nonbreast	1128	16.7	1.00	1.00
<i>p</i> ^c			.06	.13
Type of milk received at 6 months (1983–1986)				
Breast	353	22.1	1.27 (1.02, 1.58)	1.26 (1.00, 1.58)
Mixed	264	20.8	1.20 (0.92, 1.55)	1.19 (0.91, 1.54)
Nonbreast	1630	17.4	1.00	1.00
<i>p</i> ^c			.07	.09
Type of milk received at 9 months (1983–1986)				
Breast	207	22.7	1.30 (0.99, 1.71)	1.34 (1.02, 1.75)
Mixed	204	24.5	1.41 (1.08, 1.83)	1.41 (1.08, 1.83)
Nonbreast	1836	17.4	1.00	1.00
<i>p</i> ^c			.01	.009
Type of milk received at 12 months (1983–1986)				
Breast	138	21.0	1.18 (0.84, 1.65)	1.26 (0.90, 1.77)
Mixed	185	24.3	1.36 (1.04, 1.79)	1.39 (1.06, 1.82)
Nonbreast	1924	17.8	1.00	1.00
<i>p</i> ^c			.06	.03

^aTotals may not sum to 2247 owing to missing data.

^bAdjusted for family income, maternal education, and assets index.

^c χ^2 test for trend.

and atopic asthma are combined in these studies³²; since breastfeeding may protect against the former, an overall protective effect may be found. The pair of reviews just described identified 2 studies—those of Takemura et al.²⁵ and Martin et al.²⁹—including adolescents. We were able to identify another 6 recent studies focusing on this issue. Of the 8 combined studies, 4 reported a positive association between breastfeeding and asthma (Martin et al.,²⁹ Takemura et al.,²⁵ Wright et al.,³³ and Sears et al.³⁴), 2 reported a negative association (Saarinen and Kajosaari³⁵ and Schwartz et al.³⁶), and 2 reported no association (Gustafsson et al.³⁷ and Lewis et al.³⁸).

In the Wright et al. study, the association between breastfeeding and asthma was re-

stricted to adolescents whose mothers had a history of asthma. The authors provided an extensive discussion of the possible biological mechanisms behind this association.³³ First, the breast milk of allergic mothers may differ from that of nonallergic mothers in ways that affect infants' subsequent susceptibility to allergens. Second, according to the hygiene hypothesis, breastfeeding may hamper the development of immune responses as a result of reduced exposure to pathogens in infancy.

As mentioned, our study is the first investigation conducted outside of a developed country to focus on risk factors for adolescent asthma. If the hygiene hypothesis is correct, factors that protect against infections are likely to be stronger risk factors for asthma in less developed countries, since the infectious

burden will be greater. Further—and better—studies are needed on this issue.

The policy implications of the current findings are not clear cut. A number of countries are undergoing epidemiological and nutritional transitions, and changes involving the social, environmental, and behavioral factors that protect against childhood infections and malnutrition may increase the risk of chronic diseases later in life. An example of this dilemma is our recent research³⁹ showing that rapid growth in infancy protects against early morbidity and mortality but leads to overweight and obesity in adolescence. The results described here may represent another example of this trade-off.

There is no question that breastfeeding, avoidance of malnutrition and crowding, and reductions in the presence of infections are highly beneficial for infants and children, but there may be mixed consequences later in life. Moreover, given current knowledge, there is no question that childhood risk factors should be curtailed, since the benefits for young children far outweigh later risks. ■

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Contributors

All of the authors participated in the design, analysis, and writing of this study. C. G. Victora and F. C. Barros contributed to study coordination. R. C. Lima coordinated the field work for this phase of the study.

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TABLE 4—Asthma Prevalence Ratios (PRs) and 95% Confidence Intervals (CIs), According to Nutritional and Morbidity Variables: Pelotas, Brazil

	No. ^a	Prevalence, %	Crude PR (95% CI)	Adjusted ^b PR (95% CI)
Weight-for-age z score (1984)				
< -2	102	10.8	1.00	1.00
≥ -2	1962	19.4	1.80 (1.02, 3.17)	1.59 (0.90, 2.80)
p ^c			.04	.11
Length-for-age z score (1984)				
< -2	231	13.9	1.00	1.00
≥ -2	1833	19.6%	1.42 (1.01, 1.98)	1.24 (0.88, 1.75)
p ^c			.04	.23
Weight-for-length z score (1984)				
< -1	228	17.1	1.00	1.00
≥ -1	1836	19.2	1.12 (0.83, 1.52)	1.03 (0.76, 1.40)
p ^c			.45	.84
Expulsion of intestinal worms (1984)				
No	1414	20.4	1.00	1.00
Yes	648	15.7	0.77 (0.63, 0.95)	0.85 (0.69, 1.05)
p ^c			.01	.14
Pneumonia (1984)				
No	1699	19.1	1.00	1.00
Yes	368	18.2	0.95 (0.75, 1.21)	1.04 (0.82, 1.33)
p ^c			.68	.73
Asthma or bronchitis (1984)				
No	1654	17.8	1.00	1.00
Yes	413	23.7	1.33 (1.09, 1.63)	1.40 (1.14, 1.72)
p ^c			.005	.001

^aTotals may not sum to 2247 owing to missing data.

^bAdjusted for family income, maternal education, and assets index.

^cχ² test for heterogeneity.

Human Participant Protection

The Medical Research Board of the Federal University of Pelotas, which is affiliated with the National Commission on Research Ethics of the Brazilian Ministry of Health, approved the study protocol. All respondents provided written informed consent.

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