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Impact of specific sensitization on asthma and rhinitis in young Brazilian and Chilean adults

R. J. Rona*, C. Vargas†, E. O. Vianna‡, P. Bustos†, H. Bettiol§, H. Amigo†, J. Mackenney¶ and M. A. Barbieri§

*Department of Psychological Medicine, King's College London, London, UK, †Department of Nutrition, Faculty of Medicine, University of Chile, Chile, Departments of

‡Medicine, §Paediatrics, Medical School of Ribeirão Preto, University of São Paulo, São Paulo, Brazil and ¶Department of Paediatrics, Faculty of Medicine, University of Chile, Chile

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Summary

Background The pattern of associations and the attributable fractions (AF) of atopic conditions due to specific sensitizations vary between countries.**Objective** To assess the level of associations and AF between sensitization to five allergens and atopic conditions in two settings.**Methods** We studied 2063 Brazilians and 1231 Chileans of both sexes using representative samples selected at birth in the 1970s. Information on asthma and rhinitis was based on the European Community Respiratory Health Survey questionnaire. We assessed bronchial hyperresponsiveness (BHR) to methacholine and sensitization to *Dermatophagoides pteronyssinus*, cat, dog, grass blend and *Alternaria alternata*.**Results** The prevalence of sensitization to one or more allergens was 50% in Brazilians and 22% in Chileans. The level of associations varied according to the outcome used. Strong associations between sensitization and asthma, defined as wheeze or awakening with breathlessness at night and positive BHR, were found for each of the five allergens in Chileans [varying from odds ratio (OR) 3.24, 95% confidence interval (CI) 1.47, 7.15 for *D.**pteronyssinus* to 8.44, 95% CI 3.82, 18.66 for cat], whereas the level of associations was restricted to *D. pteronyssinus*, cat and dog in Brazilians and was somewhat weaker (highest OR 3.90, 95% CI 2.80–5.44). The AF of sensitization on asthma was 54% in Brazil and 44% in Chile. *D. pteronyssinus* and cat made an independent contribution to asthma in the two samples. The patterns of associations between sensitization and rhino-conjunctivitis were similar to those for asthma.**Conclusion** The associations between sensitization, and asthma and rhinitis were high in Chile and moderately high in Brazil, but the AF were higher in Brazil, reflecting a higher prevalence of sensitization. In Brazil, dust mite had the greatest impact on atopic conditions while in Chile several allergens had an impact. Sensitization is as serious a problem in Chile and Brazil as in developed countries.**Keywords** asthma, attributable fraction, bronchial responsiveness to methacholine, rhino-conjunctivitis, skin prick test

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Correspondence:

Prof. Roberto J. Rona, Department of Psychological Medicine, King's College London, Weston Education Centre, Cutcombe Rd, London SE5 9RJ, UK.
E-mail: roberto.rona@iop.kcl.ac.uk

Introduction

Atopy is an important risk factor of asthma, rhinitis and bronchial hyperresponsiveness (BHR) to challenge [1–7]. The asthma attributable fraction (AF) due to atopy, a measure of the proportion who would not have the condition if no one in the population had been sensitized, ranges from 0% to 63%, although the majority of esti-

mates are between 25% and 50% [2, 5, 7, 8]. There has been increasing interest in the geographical variation of the effect of specific allergens on asthma [1, 7, 8]. This interest has been stimulated by the difference in the geographical pattern of associations between sensitization to allergens and asthma. It has been shown in the European Community Respiratory Health Survey (ECRHS) that house dust mite (HDM) and cat sensitizations may

have a greater impact on asthma in Europe, in New Zealand rye grass is an additional important contributor, whereas in the USA *Alternaria alternata* (*Alternaria*), cat and white oak may be more important [1, 6, 7]. Another issue that has puzzled researchers is the large variation in the association between specific allergens not only between countries but also within country [7].

Findings from developing countries seem to indicate that the level of association between sensitization and asthma is lower than in developed countries [8–10]. So far, the reports of effects of specific atopy on asthma have been restricted to only a few allergens [8, 10].

Few studies have described the pattern of association between specific allergen, and allergic rhinitis or BHR [2–4]. Sensitization to grass and eggs was highly associated with rhinitis [4], while several allergens such as cat, timothy grass and HDM were associated with BHR [2, 3].

The aim of this study was to assess the relationship between five specific allergens using skin prick tests (SPT), and asthma, BHR, and rhinitis in two studies in young adults in Ribeirão-Preto, Brazil, and Limache, Chile [11–13]. We also assessed whether *Dermatophagoides pteronyssinus*, *Alternaria*, cat, dog and a blend of grass pollens explained most of the sensitizations in the two studies and their AF regarding the outcomes indicated above. The two studies were planned collaboratively, used the same methodology with respect to the atopic conditions and measurements assessed and were carried out between 2001 and 2004 in subjects of similar age.

Methods

Samples

The two studies have been described previously [11–14]. The Brazilian study was carried out in 2063 men and women born between 1 June 1978 and 31 May 1979. This sample was selected from 5665 singleton births, alive by the age of 20 years, and living in Ribeirão Preto and was based on the sample size required to find a 12% difference with a power of 80% for a prevalence of 10%. The sample was stratified according to neighbourhood into three socio-economic groups ensuring participation from all social groups [15].

The Chilean sample was made up of 1231 men and women randomly selected from a total of 3096 births occurring between 1974 and 1978 in the Hospital of Limache, as most deliveries take place in hospitals. The sample size, based on a paper by Rona *et al.* [16], was estimated to detect, at the 5% significance level with a power of 80%, a correlation of 0.085 between birth weight and forced expiratory volume in 1 s (FEV₁).

12.8% of the Brazilian sample and 21% of the Chilean sample were replaced using the same sampling approach

because of unwillingness to take part in the study, emigration, death or custodial sentence [11–14].

Ribeirão Preto is one of the wealthiest cities of Brazil with approximately 550 000 inhabitants, is 250 miles from the sea, latitude 21°11 min South and longitude 47°49 min West [13, 15]. Limache has approximately 53 000 inhabitants, and its poverty level is near the median for the country. It is 20 miles from the sea, latitude 33°1 min South, Longitude 71°16 min West [12, 17].

Questionnaire and measurements

Symptoms and conditions. Atopic symptoms were assessed using the ECRHS questionnaire. We used the asthma items wheeze in the last 12 months, waking up with breathlessness in the last 12 months, and asthma ever diagnosed. Rhinitis was defined as nasal discharge and blockage in the absence of cold in the last 12 months and for rhino-conjunctivitis the participants also had to indicate red eyes and itching. We used two definitions of asthma: wheezing or breathlessness at night plus positive BHR [Asthma (algorithm)], and asthma ever, mostly physician-diagnosed asthma (Asthma ever) [11].

Skin prick tests. We assessed sensitization to *D. pteronyssinus*, cat, dog, *Alternaria* and a blend of grass pollens. The blend of grass pollens included oat, crested dog's tail, cocksfoot, rye, meadow, vernal, bent, brome grass, meadow foxtail, Timothy, meadow fescue and Yorkshire fog. There were three different allergens used in each country. They were *Dermatophagoides farinae*, *Penicillium notatum* and *Aspergillus fumigatus* in Brazil and cockroach, a blend of trees and a blend of weeds and shrubs common in Chile. We assessed the prevalence to sensitization to at least one of the five common allergens and one out of the eight allergens. Allergens were obtained from Allergy Therapeutics (Worthing, West Sussex). We considered a mean welt size of 3 mm or more as positive [12, 13]. Five Brazilians and 14 Chileans who reacted to the negative control were omitted. Data on response to allergens were missing in 147 participants in Brazil and two in Chile.

Bronchial hyperresponsiveness to methacholine and forced expiratory volume in 1 s. BHR was measured using the tidal breathing method. Increasing concentrations of methacholine were used from 0.5 to 16 mg/mL using a nebulizer for 2 min at each concentration [11–13]. FEV₁ was assessed at baseline and FEV₁ 2 min after each increasing concentration. Although the methodology was the same in the two countries, the equipment differed in that the Brazilian team used a DeVilbiss 646 nebulizer and the Chilean team used a Hudson nebulizer (Hudson RCI, Temecula, CA, USA). The Brazilians used a Koko Digidoser System (PDS Instrumentation, Louisville, CO, USA), an

integrated system that also assesses lung function, and the Chileans used a Vitalograph 2120 (Vitalograph Ltd, Buckingham, UK) and software Spirotrac IV. An FEV₁ decrease of 20% in comparison with baseline FEV₁ at any concentration up to 8 mg/L was considered to be a positive BHR. Further details are available elsewhere [11–13].

The studies were approved by the Ethics Committees of the Faculty of Medicine of the University of Chile and the Faculty of Medicine of the University of São Paulo in Ribeirão Preto. The participants were asked to sign a consent form after reading or listening to explanatory notes about the research.

Analysis

Odds ratios (OR) were estimated using multiple logistic regressions for the outcomes wheeze, waking up with breathlessness, each asthma definition, BHR status, rhinitis and rhino-conjunctivitis in relation to five specific allergens. In each of the analyses, we used two models: In model 1, we adjusted for sex, age, smoking, obesity and years of full-time education and in model 2 additional adjustments were made for the other allergens in the study. The analysis was carried out by country, but we also assessed an interaction between country and sensitization on atopic outcomes combining the two data sets. The AF for each allergen was estimated and its 95% confidence interval (95% CI) was calculated using the method of the bias-corrected percentiles based on bootstrap methodology. [18] Most analyses were carried out using SPSS version 14.0, but the combined analysis and the AF analysis were carried out using STATA version 9.0.

Results

The Chilean sample was slightly older than the Brazilian sample, but the percentage by sex was similar (Table 1). Full-time education over 12 years was more common in Brazilians. Smoking was far more prevalent in Chileans and this difference was not accounted for education level. Although asthma symptoms were more common in the Chilean sample, positive BHR, rhinitis and rhino-conjunctivitis were more common in Brazilians. Asthma (algorithm) and asthma ever were more common in Brazilians. Although there were some differences between sexes regarding the characteristics in Table 1, within each of the countries, these were minor in comparison with the differences between countries.

Sensitization to *D. pteronyssinus* was the most common among the allergens studied in the two countries, especially Brazil (Table 2). Cat and dog sensitizations were more common in Brazil, but sensitization to a blend of grass pollens was more common in Chile. Sensitization to *Alternaria* was uncommon in the two countries. Sensitization to any of the five common allergens was more

Table 1. Characteristics of the Brazilian and Chilean samples

	Brazil (n = 2063)	Chile (n = 1231)
Males (%)	995 (48.2)	557 (45.2)
Age years, mean (SD)	23.9 (0.71)	24.8 (1.59)
Full-time education in years (%)		
1–8	320 (15.5)	256 (20.8)
9–11	1039 (50.4)	654 (53.2)
> 12	704 (34.1)	320 (26.0)
Smoking status (%)		
Never	1555 (75.4)	394 (32.0)
Ex-smoker	153 (7.4)	127 (10.3)
<5 cigarettes/day	128 (6.2)	426 (34.6)
≥5 cigarettes/day	227 (11.0)	284 (23.1)
Wheeze in last 12 months (%)	401 (19.4)	337 (27.4)
Awaking with breathlessness at night in the last 12 months (%)	185 (9.0)	169 (13.7)
Rhinitis (%)	1125 (54.5)	4444 (36.1)
Rhino-conjunctivitis (%)	493 (23.9)	169 (14.1)
Asthma (algorithm)* (%)	214 (10.6)	44 (3.6)
Asthma ever† (%)	324 (16.2)	56 (4.5)
Positive BHR <8 mg/mL (%)	601 (31.3)	96 (8.1)

*Wheeze or awakening with breathlessness and positive BHR.

†Asthma ever mostly physician diagnosed asthma.

Minimal denominator for the Brazilian sample was 1922 (BHR status), but for most respiratory variables 1997 subjects or more, minimal denominator for the Chilean sample 1190 subjects (BHR status) and 1217 subjects for all other respiratory variables. Other variables as indicated in the heading.

BHR, bronchial hyperresponsiveness.

prevalent in Brazil, reflecting the high frequency of sensitization to *D. pteronyssinus*. Only a marginal increase in sensitization to at least one of the five allergens or one of the eight allergens was observed. There was an increase in the prevalence of sensitization for most outcomes in the study in comparison with the total sample, reflecting their contribution to atopic conditions. The greater contributions to sensitization came from asthma (algorithm) and asthma ever in Brazil and asthma (algorithm) in Chile and, to a lesser degree, positive BHR and rhino-conjunctivitis. The prevalence of sensitization in those waking up with breathlessness at night was only marginally above that of the total sample in the two countries.

Tables 3 and 4 give OR of sensitization for each of the outcomes by country unadjusted and adjusted for the other common allergens. Sensitization to *D. pteronyssinus* was associated with most outcomes in Brazil and Chile and the effect sizes were moderately high, especially for asthma (algorithm) and asthma ever (Table 3). Likewise, sensitization to cat and dog was associated with most outcomes, especially in Chile. *Alternaria* and grass pollens were associated with some of the outcomes but only in Chileans. The level of association of sensitization for at

least one of the five common allergens was similar to those for *D. pteronyssinus* for each outcome and also similar to that of at least one of eight allergens (not shown). In the assessment of interactions, there was evidence for cat, dog and *Alternaria* that the association between sensitization, and rhino-conjunctivitis and asthma (algorithm) was higher in Chile than Brazil (P varying between 0.049 and 0.002). We also found indications that the association between grass pollens and BHR status was higher in the Chilean sample ($P=0.021$). There were not significant interactions for *D. Pteronyssinus* and country on any of the outcomes. Only sensitization to *D. Pteronyssinus*, cat and, to a lesser extent, dog were associated with many of the outcomes after adjustment for the rest of the allergens in the study (Table 4).

The AF, unadjusted for the effect of other sensitizations, showed that *D. pteronyssinus* had the highest impact on the atopic conditions in the Brazilian sample and, to a lesser degree, in the Chilean sample (Table 5). With the exception of wheeze, the AF of *D. pteronyssinus* was only marginally lower to sensitization to at least one of the five allergens in Brazilians. The AF for the Chilean sample was higher for sensitization to at least one allergen for asthma (algorithm), rhino-conjunctivitis and positive BHR. The AF was of the same magnitude for cat and dog allergens in the two countries. The AF was substantial for sensitization to a blend of grass pollens in the Chilean sample, especially asthma (algorithm) and asthma ever, rhino-conjunctivitis and positive BHR.

We assessed whether the selection of the common five allergens in each of the countries would have left unaccounted part of the effect of sensitization on selected outcomes in our study. In multiple logistic regressions, sensitization to any of eight allergens was not associated with the outcomes rhino-conjunctivitis, asthma (algorithm) and BHR positive when adjustment for the five allergens studied was included in the model, indicating that the other allergens used did not make an additional contribution (not shown).

Discussion

There was a substantial degree of variation in the level of association and AF between sensitization and atopic conditions. The associations were higher for asthma (algorithm), based on symptoms and BHR status, asthma ever based on diagnosed asthma, BHR status on its own and rhino-conjunctivitis. Sensitization showed a stronger association with asthma (algorithm) than asthma ever in Chile but not in Brazil, possibly reflecting a better health-care service in Ribeirão Preto, which is the wealthiest city in Brazil, than Limache, which is a small city with only basic health facilities. Thus, asthma (algorithm) would be the most suitable outcome to use for comparison between these two samples as it is less affected by cultural back-

ground, health service provision and includes subjective (symptoms) and objective (BHR status) criteria.

The AF for asthma (algorithm) was above 46% for the Brazilian sample and 44% for the Chilean sample. These two AF estimates are among the highest, similar to those reported in the Third National Health and Nutrition Examination Survey (NHANES III) and the centres with the highest AF in the ECRHS and International Study of Asthma and Allergies in Childhood (ISAAC) [1, 7, 8]. The AF were higher in our study than those from other Latin-American countries [8, 9]. AF of sensitization regarding rhino-conjunctivitis was also substantial in the two countries, but higher in Brazil than Chile.

Sensitization to inhalant allergens played an important role in the aetiology of asthma, BHR and rhinitis following a pattern more similar to developed countries [1, 2, 4, 7, 19, 20] than developing countries [8, 9]. Our results do not confirm the recent study from ISAAC that non-affluent countries have a lower AF than affluent countries [8]. There are two possible reasons for this discrepancy. First, in the ISAAC study middle-income countries, such as Brazil and Chile with a gross national income per capita in 2006 of US\$4730 and US\$6980, respectively, equivalent to a purchasing power parity of US\$8800 and US\$11 270, were under-represented [21]. Second, our conclusion was drawn using the outcome asthma (algorithm), which was not available in the other studies including less affluent countries [8, 9]. If wheeze on its own were used, the AF would have declined in the Brazilian and Chilean samples, but the Brazilian sample would have still remained at levels commonly seen in developed countries [8, 9]. Some differences between countries may be due to the difficulty that participants had in grasping the meaning of wheeze in a self-completed questionnaire. Such a difficulty may vary according to country, economic development and education level [13, 22]. Thus, cultural factors may account for the differences in AF when using wheeze as an outcome and may also account for differences between outcomes when comparing studies using different methodologies.

In Ribeirão Preto and Limache sensitization to *D. pteronyssinus* was highly associated with asthma and BHR, but cat and dog allergens also made a meaningful contribution, especially in Chile. The AF regarding sensitization to *D. pteronyssinus* was overwhelming in comparison with other allergens in Brazil but not in Chile. Dust mites are widespread in humid and warm environments; thus, the opportunity for dust mite sensitization would be higher in Ribeirão Preto climate than in Limache. In the two countries, clinical series of patients with atopic conditions have shown a high prevalence of sensitization to dust mites [23–26]. Dust mites are usually highly associated with asthma and BHR [2, 4, 7, 27, 28], but in some studies cat and dog sensitizations are more strongly associated with asthma although with similar AF

Table 2. Percentage of sensitized subjects according to symptoms, condition or positive BHR in Brazil and Chile

Symptoms	<i>Dermatophagoides pteronyssinus</i>				Cat				Dog				<i>Alternaria alternata</i>				Grass				One of five allergens				One of eight allergens			
	Brazil (891)		Chile (172)		Brazil (203)		Chile (65)		Brazil (147)		Chile (25)		Brazil (46)		Chile (20)		Brazil (79)		Chile (115)		Brazil (951)		Chile (263)		Brazil (993)		Chile (306)	
	%	%	%	%	%	%	%	%	%	%	%	%	%	%	%	%	%	%	%	%	%	%	%	%	%	%	%	
Wheeze	57.4	20.1	15.0	9.3	7.0	9.8	2.7	3.6	3.9	4.6	11.7	61.5	28.8	63.9	32.4													
Rhinitis	52.1–62.5	15.9–24.8	11.5–19.1	6.4–12.9	7.0–13.3	1.2–5.0	1.9–6.0	2.1–6.6	2.7–7.3	8.5–15.7	56.3–66.5	24.0–34.0	58.8–68.9	27.4–37.7														
	53.5	19.2	14.2	8.4	8.7	3.9	2.7	3.2	4.2	11.0	56.3	26.3	58.8	29.9														
Rhino-conjunctivitis	50.5–56.5	15.6–23.2	12.2–16.3	6.0–11.4	7.0–10.4	2.3–6.1	1.7–3.7	1.8–5.3	3.0–5.4	8.2–14.3	53.3–59.3	22.2–30.6	55.9–61.8	25.6–34.4														
	64.2	26.0	18.1	14.8	11.1	7.7	2.4	5.3	4.0	16.0	66.7	36.7	68.9	41.4														
Wake up with breathlessness	59.6–68.5	19.6–33.3	14.6–21.7	9.8–21.0	8.4–14.4	4.2–12.8	1.2–4.3	2.5–9.9	2.4–6.2	10.8–22.3	62.1–71.0	29.4–44.4	64.4–73.1	33.9–49.2														
	53.9	14.3	11.4	7.1	8.4	1.8	1.8	2.4	3.0	11.3	56.9	24.4	59.9	28.6														
Asthma (algorithm)*	46.0–61.6	9.4–20.5	7.0–17.2	3.7–12.1	4.6–13.7	0.4–5.1	0.4–5.1	0.6–6.0	1.0–6.8	6.9–17.1	49.0–64.5	18.1–31.6	52.0–67.4	21.9–36.0														
	71.4	40.5	21.4	26.2	13.6	9.5	3.4	11.9	5.8	21.4	73.8	54.8	74.8	54.8														
Asthma ever †	64.7–77.4	25.6–56.7	16.0–27.6	13.9–42.0	9.2–19.0	2.7–22.6	1.4–6.9	4.0–25.6	3.0–9.9	10.3–36.8	67.2–79.6	38.7–70.1	68.2–80.5	38.7–70.1														
	75.3	32.7	19.9	16.4	12.9	7.3	3.5	5.5	5.9	18.2	76.7	36.4	79.1	40.0														
Positive BHR	69.8–80.1	20.7–46.7	15.4–25.0	7.8–28.8	9.2–17.3	2.0–17.6	1.7–6.3	1.1–15.1	3.5–9.3	9.1–30.9	71.3–81.4	23.8–50.4	73.9–83.6	27.0–54.1														
≤ 8 mg/mL	65.9	31.9	17.2	16.0	13.2	6.4	4.0	6.4	5.1	22.3	68.4	45.7	69.4	47.9														
Sensitized in the total sample	61.8–69.8	22.7–42.3	14.2–20.6	9.2–24.9	10.5–16.2	2.4–13.4	2.6–6.0	2.4–13.4	3.4–7.2	14.4–32.1	64.4–72.2	35.4–56.3	65.7–73.1	37.4–58.4														
	46.6	14.1	10.6	5.3	7.7	2.1	2.4	2.4	4.1	9.4	49.8	21.6	52.1	25.2														
	44.4–48.9	12.2–16.2	9.3–12.1	4.1–6.7	6.5–9.6	1.3–3.0	1.8–3.2	1.6–3.4	3.3–5.1	7.9–11.2	47.5–52.0	19.3–24.0	49.7–54.2	22.7–27.7														

*Wheeze or awakening with breathlessness and positive BHR.

†Asthma ever mostly physician diagnosed asthma.

In brackets in the heading number of sensitised participants in the sample (Brazil N = 1911; Chile N = 1217). BHR, bronchial hyperresponsiveness.

Table 3. Odds ratio due to sensitization to each allergen for each atopic symptom or condition, or BHR by country unadjusted for other allergens

Symptoms	<i>Dermatophagoides pteronyssinus</i>				Cat		Dog		<i>Alternaria alternata</i>		Blend of grass pollens		Five allergens	
	Brazil	Chile	Brazil	Chile	Brazil	Chile	Brazil	Chile	Brazil	Chile	Brazil	Chile	Brazil	Chile
	OR	OR	OR	OR	OR	OR	OR	OR	OR	OR	OR	OR	OR	OR
	95% CI	95% CI	95% CI	95% CI	95% CI	95% CI	95% CI	95% CI	95% CI	95% CI	95% CI	95% CI	95% CI	95% CI
Wheeze	2.07	1.88	1.75	2.64	1.56	1.57	1.61	2.17	1.28	1.45	2.16	1.74		
	1.62–2.64	1.33–2.60	1.23–2.49	1.56–4.48	1.02–2.38	0.67–3.65	0.81–3.22	1.02–4.70	0.72–2.28	0.95–2.20	1.69–2.78	1.29–2.35		
Rhinitis	1.98	1.88	2.69	2.31	1.70	3.81	1.71	1.73	1.28	1.37	1.96	1.53		
	1.64–2.40	1.35–2.61	1.94–3.74	1.38–3.88	1.19–2.44	1.61–8.98	0.92–3.16	0.82–3.64	0.80–2.04	0.92–2.05	1.62–2.36	1.16–2.03		
Rhino-conjunctivitis	2.98	2.70	2.76	4.27	2.10	7.85	1.10	2.98	1.15	2.33	2.94	2.57		
	2.37–3.76	1.81–4.02	2.01–3.78	2.48–7.38	1.43–3.09	3.44–17.87	0.54–2.23	1.32–6.71	0.66–2.01	1.45–3.75	2.33–3.72	1.80–3.66		
Wake up with breathlessness	1.65	1.08	1.19	1.43	1.22	0.93	0.60	1.01	0.78	1.43	1.63	1.26		
	1.18–2.30	0.67–1.73	0.71–1.99	0.74–2.79	0.67–2.23	0.27–3.19	0.18–2.03	0.34–2.97	0.30–2.01	0.84–2.43	1.17–2.28	0.86–1.85		
Asthma (algorithm)*	3.90	5.10	2.81	8.44	2.23	6.60	1.19	7.13	1.53	3.24	3.78	5.10		
	2.80–5.44	2.64–9.90	1.91–4.14	3.82–18.66	1.39–3.57	2.00–21.74	0.51–2.79	2.41–21.13	0.79–2.96	1.47–7.15	2.69–5.30	2.69–9.66		
Asthma ever†	4.67	3.18	2.59	3.91	2.37	4.01	1.79	2.30	1.71	2.37	4.35	2.16		
	3.48–6.26	1.75–5.78	1.84–3.65	1.77–8.67	1.56–3.59	1.29–12.42	0.86–3.73	0.66–7.96	0.97–3.01	1.14–4.90	3.23–5.86	1.22–3.83		
Positive BHR	3.55	3.90	2.54	4.58	2.65	4.66	1.80	3.62	1.26	3.73	3.36	3.94		
≤ 8 mg/mL	2.86–4.40	2.38–6.38	1.87–3.46	2.37–8.84	1.84–3.80	1.72–12.64	0.98–3.30	1.38–9.53	0.77–2.06	2.14–6.49	2.70–4.18	2.52–6.17		

Adjusted by age, smoking, BMI, years of school and sex.

*Wheeze or awakening with breathlessness and positive BHR.

†Asthma ever mostly physician diagnosed asthma.

OR, odds ratio; CI, confidence interval; BHR, bronchial hyperresponsiveness, BMI, body mass index.

to *D. pteronyssinus* [7, 29] or other allergens such as *Alternaria* and white oak [1]. The Chilean pattern has also been shown in the ECRHS and New Zealand [7, 30]. Sears *et al.* [30] demonstrated that dust mite, cat and rye grass

were the most important allergens in relation to BHR as in our Chilean sample, perhaps reflecting the similar climate in the study areas. *Alternaria* was only associated with atopic conditions and positive BHR in Chile. Sensitizations

Table 4. Odds ratio due to sensitization to each allergen for each atopic symptom or condition, or BHR by country adjusted for sensitization to the other allergens in the table

Symptoms	<i>Dermatophagoides pteronyssinus</i>				Cat		Dog		<i>Alternaria alternata</i>		Blend of grass pollens	
	Brazil	Chile	Brazil	Chile	Brazil	Chile	Brazil	Chile	Brazil	Chile	Brazil	Chile
	OR	OR	OR	OR	OR	OR	OR	OR	OR	OR	OR	OR
	95% CI	95% CI	95% CI	95% CI	95% CI	95% CI	95% CI	95% CI	95% CI	95% CI	95% CI	95% CI
Wheeze	1.96	1.59	1.25	2.06	1.08	0.86	1.27	1.57	0.96	0.97		
	1.51–2.53	1.09–2.33	0.84–1.86	1.14–3.73	0.66–1.77	0.33–2.20	0.61–2.67	0.69–3.54	0.51–1.82	0.60–1.57		
Rhinitis	1.75	1.60	2.07	1.70	1.01	2.70	1.23	1.04	0.91	0.89		
	1.44–2.14	1.12–2.30	1.43–2.98	0.95–3.06	0.67–1.53	1.08–6.75	0.64–2.38	0.46–2.32	0.54–1.52	0.56–1.41		
Rhino-conjunctivitis	2.65	1.83	1.78	2.46	1.31	4.06	0.70	1.23	0.76	1.09		
	2.09–3.38	1.16–2.89	1.25–2.58	1.29–4.68	0.84–2.03	1.62–10.21	0.32–1.53	0.48–3.13	0.41–1.42	0.61–1.97		
Wake up with breathlessness	1.66	0.98	0.96	1.32	1.17	0.73	0.57	0.92	0.77	1.39		
	1.18–2.35	0.57–1.63	0.54–1.70	0.63–2.78	0.60–2.30	0.20–2.73	0.16–2.06	0.30–2.86	0.28–2.11	0.78–2.51		
Asthma (algorithm)*	3.48	2.97	1.66	4.12	1.23	1.98	0.70	2.62	1.07	0.92		
	2.46–4.91	1.38–6.42	1.07–2.57	1.63–10.87	0.71–2.15	0.49–8.00	0.27–1.78	0.76–8.99	0.51–2.24	0.33–2.56		
Asthma ever†	4.28	2.36	1.37	2.05	1.33	1.90	1.07	1.01	1.10	1.20		
	3.16–5.79	1.19–4.66	0.93–2.01	0.80–5.27	0.82–2.14	0.54–6.64	0.48–2.38	0.26–3.91	0.59–2.08	0.50–2.87		
Positive BHR	3.20	2.71	1.37	2.00	1.67	1.64	1.15	1.44	0.73	1.89		
≤ 8 mg/mL	2.56–4.02	1.46–4.51	0.97–1.94	0.89–4.14	1.10–2.53	0.53–4.84	0.59–2.25	0.49–4.08	0.42–1.29	1.00–3.75		

Adjusted by age, smoking, BMI, years of school and sex and for the other allergens in the table.

*Wheeze or awakening with breathlessness and positive BHR.

†Asthma ever mostly physician diagnosed asthma.

OR, odds ratio; CI, confidence interval; BHR, bronchial hyperresponsiveness

Table 5. Attributable fractions due to sensitization to each allergen for each atopic symptom or condition, or BHR by country unadjusted for sensitization to other allergens

Symptoms	<i>Dermatophagoides pteronyssinus</i>			Cat			Dog			<i>Alternaria alternata</i>			Blend of grass pollens			Five allergens		
	Brazil AF	Chile AF	95% CI	Brazil AF	Chile AF	95% CI	Brazil AF	Chile AF	95% CI	Brazil AF	Chile AF	95% CI	Brazil AF	Chile AF	95% CI	Brazil AF	Chile AF	95% CI
Wheeze	29.6	9.4	4.1–15.2	6.4	5.8	2.4–9.5	3.54	1.0	–0.7–3.12	1.4	2.1	–0.9–3.4	1.0	3.6	–0.46–8.1	33.1	12.3	5.36–19.5
Rhinitis	26.5	9.0	4.1–15.2	8.9	4.8	2.4–9.5	3.6	2.9	–0.2–7.2	1.2	1.4	–0.1–4.81	0.9	3.0	–0.46–8.1	29.4	9.1	5.36–19.5
Rhino-conjunctivitis	42.7	16.4	4.46–13.8	11.5	11.3	1.76–8.0	5.8	6.7	1.16–4.9	0.2	3.5	–0.1–2.3	0.5	9.1	–0.8–2.8	44.0	22.4	22.8–36.0
Wake up with breathlessness	34.4–49.6	8.5–23.6	5.6–16.9	7.5–15.6	5.6–16.9	5.6–16.9	2.8–9.8	3.0–10.9	–0.1–1.5	–1.3–2.0	0.1–7.2	–0.8–2.9	–1.6–2.9	3.0–16.3	35.3–50.8	22.0	13.4–31.6	5.0
Asthma (algorithm)*	53.1	32.5	–4.9–8.1	13.8	23.1	–3.2–8.2	7.5	8.1	–3.2–6.5	5.4	10.2	–3.1–1.4	2.0	14.8	–3.1–3.1	54.3	44.0	–4.3–14.3
Asthma ever†	59.2	22.4	16.1–51.1	12.2	12.2	2.4–29.6	7.5	5.5	0.8–18.9	1.6	3.1	–1.9–3.9	2.5	10.5	–1.6–6.0	59.04	19.5	23.1–60.6
Positive BHR	47.3	23.7	6.0–36.7	10.4	12.5	2.2–23.0	8.2	5.0	–0.1–12.9	–0.6–4.2	–1.4–9.4	–0.4–5.5	–0.4–5.5	–0.3–22.0	49.5–67.5	48.0	34.2	3.2–36.6
≤ 8 mg/mL	40.6–53.7	13.3–34.2	7.1–14.5	7.1–14.5	5.0–21.1	5.0–21.1	5.1–11.5	0.81–11.7	–0.3–4.0	0.5–10.4	–1.4–3.4	7.3–25.6	40.4–54.6	20.9–47.0				

Adjusted by age, smoking, BMI, years of school and sex.

In italic: AF based on non-significant OR thus AF is likely to be zero.

*Wheeze or awakening with breathlessness and positive BHR.

†Asthma ever mostly physician diagnosed asthma.

OR, odds ratio; CI, confidence interval; BHR, bronchial hyperresponsiveness.

were consistently associated with asthma 2 and the effect sizes of the associations were moderately high for each allergen in the Chilean sample. The significant interactions between country and sensitization to cat, dog and *Alternaria* on asthma (algorithm) and other outcomes would indicate that there is a difference in the magnitude of the effect of these allergens on atopic conditions, the association being higher in Chile than Brazil.

An important feature to note is that 31.8% of those in the Brazilian sample and 9.4% in the Chilean sample were sensitized to dust mite but did not report symptoms of any atopic conditions. The same occurred, but to a lesser degree, for the other allergens. The same feature has been reported in studies carried out in Africa [10]. Thus, sensitization, although an important factor in the development of an atopic condition, may require another factor to cause an individual to experience asthma or rhinitis, confirming Sunyer *et al*'s [7] assertion that although sensitization may be aetiologically important it may not be sufficient on its own.

Some researchers have assessed the independent effect of a specific sensitization after adjusting for other allergens [1, 3, 30] but others have not [2, 7]. Adjusting for other allergens may be appropriate when the population is sensitized at a moderate level to several allergens. We wonder about its appropriateness when the level of sensitization to one of the allergens (*D. pteronyssinus*) is as high as that found in the Brazilian sample. With such an approach, the high prevalence of *D. pteronyssinus* would hide the possible effect of any other allergens. However, such an approach may be appropriate for countries, such as Chile, with a lower prevalence of sensitization for any single allergen. We believe that it would be more appropriate to show results with model adjusted and unadjusted for other allergens to allow comparisons between studies.

In our study, we could not see a distinctive pattern to sensitization to allergens and rhino-conjunctivitis or asthma as shown by Arshad *et al.* [2], but we did not assess food allergens in our study. In our analyses, we did not distinguish between seasonal and perennial rhinitis. Our rationale was to consider a gradation of symptoms to assess whether there was an increase in the association with an increase in the specificity of the condition. This was confirmed as combined nasal and eye involvement was strongly associated with sensitization.

The limitations of our study are that it is a cross-sectional study as are many of the previous contributions [1–8], but as SPT is a semi-quantitative objective test the risk of recall bias is minimal, especially because the participants in our studies completed the questionnaire before the SPT assessment. As indicated by Chinn *et al.* [4], the level of agreement between specific IgE and specific SPT is satisfactory, but not optimal and thus it is not certain that we are comparing like with like in studies

using IgE and those using SPT. We assessed a limited number of allergens to explore sensitization and atopic conditions. It is possible that other allergens could fulfil an important role. However, in the ECRHS most sensitization was accounted by five allergens, with only marginal increases when additional allergens were included [31]. In our study, four of the five allergens with the highest prevalence of sensitization in the ECRHS were included. We have also demonstrated in our logistic analysis of sensitization to five and eight allergens that five allergens provided a fair assessment of total sensitization in the population. We could not assess sensitization and severity of asthma in our study. We cannot be sure that an assessment of one city is a fair representation of the situation in Brazil or Chile, but the ISAAC study has shown that differences between countries are larger than differences between centres in the same country [32].

We conclude that the associations between sensitization and asthma and rhinitis were very high in Chile and high in Brazil, but the AF were higher in Brazil than Chile, reflecting the higher prevalence of sensitization in Brazilians. There were two different patterns in terms of the effect of sensitization on atopic conditions: in Brazil dust mite is the predominant sensitization causing asthma and rhinitis while in Chile dust mite, followed by cat, dog and, possibly, grass and *Alternaria* were also important. Atopy and atopic conditions are as serious a problem in Brazil and Chile as in many developed countries.

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