



Association between latitude and allergic diseases: a longitudinal study from childhood to middle-age

Vicka Oktaria, MPH^{*,†}; Shyamali C. Dharmage, PhD^{*}; John A. Burgess, PhD^{*}; Julie A. Simpson, PhD^{*}; Stephen Morrison, PhD[‡]; Graham G. Giles, PhD^{*,§}; Michael J. Abramson, PhD^{||}; E. Haydn Walters, DM[¶]; and Melanie C. Matheson, PhD^{*}

^{*} Centre for Molecular, Environmental, Genetic and Analytic Epidemiology, School of Population Health, University of Melbourne, Melbourne, Australia

[†] Faculty of Medicine, Gadjah Mada University, Yogyakarta, Indonesia

[‡] Royal Brisbane and Womens Hospital, Queensland, Australia

[§] Cancer Epidemiology Center, The Cancer Council Victoria, Melbourne, Australia

^{||} School of Public Health & Preventive Medicine, Monash University, Melbourne, Australia

[¶] National Health and Medical Research Council of Australia, Centre of Research Excellence in Chronic Respiratory Disease, Menzies Research Institute Tasmania, Hobart, Australia

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ABSTRACT

Background: Worldwide variations in allergy prevalence suggest that geographic factors may contribute to asthma. Ecologic studies have suggested that latitude, a marker of UV-B exposure and allergen exposures, may be related to clinical allergies.

Objective: To examine the relationship between latitude or UV-B based on self-reported geolocation and allergic sensitization and disease prevalence in Australia.

Methods: The Tasmanian Longitudinal Health Study is a population-based study of respiratory disease spanning childhood to adulthood. The most recent follow-up included a postal survey of 5,729 participants and a clinical substudy of 1,396 participants. Participants' residential addresses were coded for latitude and linked with the UV-B data from satellite-based observations of atmospheric ozone. Multivariable logistic regression analyses were performed to estimate the associations between latitude or UV-B and allergic diseases.

Results: Most northerly latitude, that is, latitude closest to the Equator, and high current UV-B exposure were associated with increased odds of hay fever, food allergy, and skin sensitization to house dust mites and molds. More northerly latitude and higher UV-B exposure were associated with increased odds of current asthma among atopic individuals contrasting with a reduced odds of current asthma among nonatopic individuals.

Conclusion: This is the first study, to our knowledge, to demonstrate a differential effect of atopic status on the relationship between latitude and current asthma. Our study demonstrates in a genetically and culturally similar group of individuals that geographic factors may play a role in the development of allergic disease.

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Introduction

Associations have been described between latitude and allergic diseases.^{1–4} In most studies, latitude was considered a marker for

Reprints: Shyamali C. Dharmage, PhD, Centre for Molecular, Environmental, Genetic & Analytic Epidemiology, Department of Public Health, School of Population Health, The University of Melbourne, Level 3/207 Bouverie St, Carlton, Victoria 3053, Australia; E-mail: s.dharmage@unimelb.edu.au.

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UV-B radiation exposure, which is linked to levels of vitamin D, a factor thought to modify the immune system toward a Th2 bias and an increased risk of allergy.^{5–8} Alternatively, latitude might simply reflect variation in aeroallergens due to climate, housing, social, and cultural differences.^{9,10}

Whether an increase in latitude is a risk or protective factor for allergy has not been established. Ecologic studies correlating latitude and surrogate measures of food allergy found a higher prevalence of infant hypoallergenic formula use and adrenaline prescriptions in the southern, less sunny part of Australia,^{1,2} whereas other international ecologic studies highlighted a higher prevalence of hay fever and asthma in equatorial areas.^{3,4} In contrast, a cross-sectional study reported no association between

participants' residential latitudes, UV-B exposure, and vitamin D levels and asthma.¹¹

To address these inconsistencies, we examined the relationship between latitude and allergic disease using data from the Tasmanian Longitudinal Health Study (TAHS). We used each participant's current residential location at the most recent TAHS follow-up survey and their yearly residential location in the previous 20 years to assign latitude exposure. We used self-reported allergy and results of skin prick tests (SPTs) to a panel of common aeroallergens.

Methods

Study Sample and Population

The sample was drawn from the fifth decade follow-up survey of TAHS, commencing in 2004. This included a postal survey, followed by a laboratory study of a subgroup of the respondents to the postal survey. Briefly, the TAHS started in 1968 when almost all 7-year-old children attending school in Tasmania ($n = 8,583$) were enrolled in a respiratory health study. Their parents completed a questionnaire concerning each child's respiratory symptoms, and the child underwent a clinical examination and lung function tests. Follow-up surveys were completed in 1974, 1981, and 1992. Of the original 1968 cohort, 7,312 (85.2%) were traced to an address in 2004. From those, a completed respiratory questionnaire was returned by 5,729 (78.4%),¹² and a subgroup ($n = 2,387$) was invited to participate in a more detailed clinical study. This subgroup was selected based on participation in previous follow-up studies and enriched for a history of asthma and cough with sputum. Of the 2,387 invited, 1,397 (58.6%) attended the laboratory, another 354 (15%) completed a telephone questionnaire or laboratory visit only, and 636 (26.6%) withdrew. At the clinical visit, participants completed a detailed interviewer-administered questionnaire and underwent comprehensive SPTs for allergy.

The 2004 follow-up studies were approved by the Human Research Ethics Committee at the University of Melbourne (010626 and 040375). Written informed consent was obtained from all participants.

Questionnaires

Participants completed an interviewer-administered questionnaire that collected information on sociodemographic characteristics, asthma and other allergic conditions, smoking history and residence.

Definitions

Current asthma was defined as an affirmative response to the question, "Have you suffered from attacks of asthma or wheezy breathing?" and answered "within the last 12 months" to the question, "How long ago did you have the last attack?" *Ever hay fever* in the postal survey was defined as an affirmative response to the question, "Have you had hay fever (that is sneezing, running, or blocked nose when you do not have a cold or the flu)?" *Childhood eczema* was defined by parent-reported infantile and/or flexural eczema in the 1968 survey. *Allergy to food or dust* was defined as an affirmative response to the question, "Have you ever been allergic to any of food or dust?" *Asthma severity* was defined according to the National Asthma Council classification of asthma for patients with untreated, newly diagnosed asthma and based on self-reported morning, daytime, and nighttime symptoms and number of flare-ups.¹³ *Atopy* was defined by at least one positive SPT result for any tested allergen. *Maternal and paternal asthma* was parent-reported in the 1968 survey. *Socioeconomic status* of each participant was defined by the Australian Standard Classification of Occupations.¹⁴

Skin Prick Tests

SPTs were performed using a standard technique with 8 aeroallergens (Hollister-Stier, EBOS Groups Pty Ltd, Murrarie, Australia): house dust mite (HDM) (*Dermatophagoides pteronyssinus*), cat pelt, molds (*Hormodendrum*, *Alternaria tenuis*, *Penicillium* mix, and *Aspergillus fumigatus*), and pollen (perennial rye grass and mixed grasses No. 7, which included Kentucky bluegrass, orchard, redtop, timothy, sweet vernal grass, meadow fescue, perennial ryegrass). A wheal size diameter 3 mm greater than the negative control was regarded as a positive result.

Current Latitude

Current latitude was defined by the residential address of the participant at the time of the 2004 follow-up. The participant's postcode was used to assign the appropriate latitude and longitude in decimal degrees. Latitude south was presented in absolute values increasing from the Equator.

UV-B Data

UV-B exposure data in the spectral range of 280 to 315 nm was obtained from the National Centre for Atmospheric Research website.¹⁵ The data were available as 12 monthly files of weighted UV-B averaged for the relevant period (1979–2000), for example, the average UV-B exposure levels from 1979 to 2000 for the month of January. These monthly averages were aggregated into an annual UV-B exposure level for the period 1979–2000. This annual UV-B exposure level was available for each latitude and longitude. Each individual was also assigned an annual UV-B exposure level based on latitude and longitude for their place of residence at the time of participation in the 2004 follow-up study.

Cumulative UV-B Exposure

Cumulative UV-B exposure was calculated using the participants' residential history. The residential history was the participants' addresses for the 20 years before the 2004 follow-up study. The postcode for each address was used to assign latitude and longitude, and then the appropriate UV-B exposure level was assigned. This created a UV-B level for each year for the last 20 years. This was then aggregated into a cumulative UV-B exposure for the last 20 years for each participant.

Altitude Data

Each individual was assigned an altitude based on latitude and longitude for their place of residence at the time of participation in the 2004 follow-up study by converting the latitude and longitude data into altitude data through Global Positioning System visualizer website.¹⁶

Statistical Analysis

Data were analyzed using STATA statistical software for Windows, version 11.0 (Stata Corp, College Station, Texas). Multivariable logistic regression was used to examine the association between exposure and outcome as appropriate. A priori confounders included in the models were sex, childhood asthma and eczema, parental allergy, socioeconomic status, and smoking. Month of laboratory visit and altitude were also investigated as potential confounders.

Latitude was analyzed as quartiles based on geolocation toward the Equator and categorized as the most southerly (43.431°, 42.830°), southerly (42.829°, 41.413°), northerly (41.408°, 37.982°), and most northerly (37.976°, 12.185°) quartiles. Current UV-B exposure was categorized as low (<472 kJ/m² per year), moderate (481–518 kJ/m² per year), moderately high (519–594 kJ/m² per

year), or high (>597 kJ/m² per year). Cumulative UV-B exposure was also categorized as low ($<9,441$ kJ/m² per 20 years), moderate (9,450–10,366 kJ/m² per 20 years), moderately high (10,368–11,192 kJ/m² per 20 years), or high ($>11,230$ kJ/m² per 20 y). The association between cumulative UV-B exposure and allergen sensitization (SPTs) was examined for the 1,209 participants who took part in the laboratory study and provided data on place of residence for the previous 20 years. Effect modification by atopic status of the association between latitude or UV-B exposure and self-reported allergic diseases was assessed by fitting interaction terms and tested using the likelihood ratio test. Multinomial logistic regression was used to assess the association between asthma severity and latitude or UV-B exposure. All results are presented as adjusted odds ratios with 95% confidence intervals. *P* value for trend is presented for those with a linear association.

Results

Participant Characteristics

Participants in the postal and laboratory surveys were similar with respect to sex and smoking status. As expected, those who participated in the laboratory study were more likely to have childhood (Table 1) and current asthma, as well as other allergies, than those only in the postal survey.

Self-reported Allergic Disease and Current Latitude–UV-B

The most northerly quartile for latitude, that is, closest to the equator, and the high quartile for current UV-B exposure were significantly associated with the highest odds of hay fever, food, and dust allergy (Tables 2 and 3). Further adjustment for confounders and altitude did not alter these associations. We did not observe any association between ever asthma, current asthma, ever eczema, self-reported animal or pollen allergy, and either latitude or UV-B exposure (data not shown).

SPTs and Current Latitude or UV-B

The most northerly quartile for latitude and the high quartile for current UV-B exposure were significantly associated with HDM sensitization in the same direction as self-reported allergic diseases (Tables 2 and 3). We also observed significant trends of higher prevalence of sensitization to *Alternaria* and *Aspergillus* as latitude

Table 1
Selected characteristics of the study participants

Characteristic	Postal survey, No. (%) (n = 5,729)	Laboratory participants, No. (%) (n = 1,397)
Female sex	2776/5729 (49)	688/1,397 (49)
Childhood asthma	994/5622 (18)	521/1,385 (38)
Childhood eczema		
Infantile eczema	595/5605 (11)	189/1,381 (14)
Flexural eczema	578/5575 (10)	197/1,376 (14)
Maternal history of asthma	591/5473 (11)	186/1,353 (14)
Paternal history of asthma	601/5383 (11)	185/1,326 (14)
Self-reported allergies		
Hay fever	2867/5697 (50)	858/1,391 (62)
Food allergy	634/5729 (11)	205/1,397 (15)
Dust allergy	932/5729 (16)	333/1,397 (24)
Current asthma	638/5720 (11)	332/1,397 (24)
Socioeconomic status		
Manager or administrator	1509/5676 (27)	401/1,387 (29)
Associate professional	609/5676 (11)	166/1,387 (12)
Tradespersons	1105/5676 (20)	280/1,387 (20)
Production, sales, or clerical	1387/5676 (24)	300/1,387 (22)
Laborer/house person	1066/5676 (19)	240/1,387 (17)
Smoking status		
Never	2275/5705 (40)	586/1,392 (42)
Former smoker	1727/5705 (30)	420/1,392 (30)
Current smoker	1703/5705 (30)	386/1,392 (28)

Table 2

Associations between latitude and selected allergic diseases and skin prick test sensitization^a

Allergy	Latitude quartile	No. (%)	OR (95% CI)	P value
Self-reported allergy ^b				
Hay fever	Most southerly	704 (50)	1 (Reference)	
	Southerly	695 (49)	1.00 (0.86–1.18)	.95
	Northerly	668 (47)	0.91 (0.78–1.07)	.25
	Most northerly	795 (56)	1.28 (1.10–1.51)	.002
Food allergy	Most southerly	152 (11)	1 (Reference)	
	Southerly	150 (11)	1.10 (0.85–1.43)	.46
	Northerly	139 (10)	0.99 (0.76–1.29)	.92
	Most northerly	190 (13)	1.34 (1.05–1.71)	.02
Dust allergy	Most southerly	217 (15)	1 (Reference)	
	Southerly	219 (15)	1.08 (0.86–1.34)	.52
	Northerly	221 (15)	1.03 (0.82–1.28)	.82
	Most northerly	273 (19)	1.41 (1.14–1.74)	.002
Skin sensitization ^c				
HDM	Most southerly	179 (39)	1 (Reference)	
	Southerly	148 (39)	0.94 (0.70–1.27)	.70
	Northerly	136 (39)	0.87 (0.64–1.18)	.37
	Most northerly	121 (60)	2.07 (1.44–2.97)	.001
<i>Alternaria</i>	Most southerly	31 (7)	1 (Reference)	
	Southerly	29 (8)	1.18 (0.67–2.08)	.57
	Northerly	30 (9)	1.39 (0.79–2.45)	.25
	Most northerly	28 (14)	1.96 (1.10–3.52)	.02
<i>Aspergillus</i>	Most southerly	8 (2)	1 (Reference)	
	Southerly	13 (3)	1.56 (0.62–3.94)	.35
	Northerly	15 (4)	1.70 (0.67–4.31)	.27
	Most northerly	21 (10)	5.03 (2.10–12.0)	<.001

Abbreviations: CI, confidence interval; HDM, house dust mite; OR, odds ratio.

^aA total of 49 patients were missing in the hay fever group, 17 in the food allergy group, and 17 in the drug allergy group.

^bAdjusted for sex, childhood asthma, childhood eczema, parent history of asthma, socioeconomic status, and smoking status.

^cAdjusted for sex, childhood asthma, childhood eczema, parent history of asthma, socioeconomic status, smoking status, and month of laboratory visit.

came closer to the Equator and current UV-B exposure became higher. No association was found between sensitization to cat, *Hormodendrum*, *Penicillium*, *Aspergillus*, rye grass, or mixed grasses and latitude or UV-B exposure. In addition, no association was found between atopy and either latitude or UV-B exposure (data not shown).

Cumulative UV-B Dose

The association between cumulative UV-B dose was examined for all outcomes. Borderline significant trends were only found between cumulative UV-B exposure and sensitization to HDM (*P* for trend = .09) and *Aspergillus* (*P* for trend = .08) (Fig 1). These trends were consistent with those reported for current UV-B exposure (Table 3).

Atopic and Nonatopic Asthma

Effect modification by atopic status was found for the associations among latitude, current and cumulative UV-B exposure, and asthma (likelihood ratio tests for interaction were 0.03, 0.11, and 0.20, respectively). More northerly latitude, closer to the Equator, and higher current UV-B exposure were associated with borderline trends for higher odds for current asthma among atopic individuals but lower odds among nonatopic individuals after adjustment for confounders (Table 4).

Cumulative UV-B Dose and Asthma Severity

An association was also seen between asthma severity and cumulative UV-B dose (eTable 1) but not latitude or current UV-B exposure. The latitude was related to all asthma severity categories, but no dose response relationship was found.

Table 3Association Between UV-B and selected allergic diseases and skin prick test sensitization^a

Allergy	UV-B quartile	No. (%)	OR (95% CI)	P value
Self-reported allergy^b				
Hay fever	Low	890 (50)	1 (Reference)	
	Moderate	535 (47)	0.92 (0.78–1.08)	.30
	Moderately high	727 (50)	1.03 (0.89–1.20)	.66
	High	710 (54)	1.21 (1.04–1.41)	.02
Food allergy	Low	192 (11)	1 (Reference)	
	Moderate	104 (9)	0.86 (0.66–1.14)	.29
	Moderately high	167 (11)	1.08 (0.85–1.37)	.52
	High	168 (13)	1.24 (0.98–1.57)	.07
Dust allergy	Low	274 (15)	1 (Reference)	
	Moderate	159 (14)	0.92 (0.73–1.16)	.47
	Moderately high	265 (18)	1.25 (1.02–1.53)	.03
	High	232 (18)	1.29 (1.05–1.58)	.02
Skin sensitization^c				
HDM	Low	212 (38)	1 (Reference)	
	Moderate	103 (36)	0.80 (0.58–1.11)	.18
	Moderately high	178 (46)	1.23 (0.92–1.63)	.16
	High	91 (56)	1.83 (1.25–2.68)	.002
<i>Horrendodrum</i>	Low	20 (4)	1 (Reference)	
	Moderate	8 (3)	0.73 (0.30–1.81)	.50
	Moderately high	21 (5)	1.62 (0.83–3.16)	.15
	High	14 (9)	2.51 (1.19–5.28)	.02
<i>Alternaria</i>	Low	33 (6)	1 (Reference)	
	Moderate	26 (9)	1.79 (1.01–3.18)	.047
	Moderately high	35 (9)	1.58 (0.93–2.70)	.09
	High	24 (15)	2.57 (1.40–4.71)	.002
<i>Aspergillus</i>	Low	11 (2)	1 (Reference)	
	Moderate	9 (3)	1.21 (0.44–3.29)	.71
	Moderately high	18 (5)	2.19 (0.96–4.96)	.06
	High	19 (12)	5.93 (2.58–13.65)	<.001

Abbreviations: CI, confidence interval; HDM, house dust mite; OR, odds ratio.

^aA total of 49 patients were missing in the hay fever group, 17 in the food allergy group, and 17 in the drug allergy group.^bAdjusted for sex, childhood asthma, childhood eczema, parent history of asthma, socioeconomic status, and smoking status.^cAdjusted for sex, childhood asthma, childhood eczema, parent history of asthma, socioeconomic status, smoking status, and month of laboratory visit.

Discussion

This is one of the few studies to date using individual latitude and UV-B exposure levels to examine their association with asthma and allergy and the first study, to our knowledge, to examine how these associations might vary with atopy. We found that latitude and UV-B exposure were associated with current asthma and that atopy modified those associations but asthma severity did not. Among atopic persons, proximity to the Equator and high UV-B exposure increased the odds of current asthma, but among non-atopic persons, proximity to the Equator and high UV-B exposure decreased the odds of current asthma. The finding of a differential effect of atopy on the relationship between latitude or UV-B exposure and asthma has not been reported previously. We also found that proximity to the Equator and high UV-B exposure increased the odds of self-reported hay fever, food allergy, and dust allergy and increased the odds of atopy as shown by sensitization to HDM, *Alternaria*, and *Aspergillus*.

Our finding of an increased risk of atopic asthma in the more northerly regions of Australia has some similarity to another Australian study⁴ that used data from the Australia Bureau of Statistics National Health Survey (1995) and found decreasing asthma prevalence with living farther from the Equator. In further support, a recent study by Hughes et al¹¹ demonstrated a reduced incidence of childhood asthma with residence farther from the Equator, a finding that did not persist after adjustment for average daily temperature. Conversely, a study by Krstic¹⁷ that used data from the United States and Australia found a 2% increase in asthma prevalence with a 10° change in both latitude north in the United

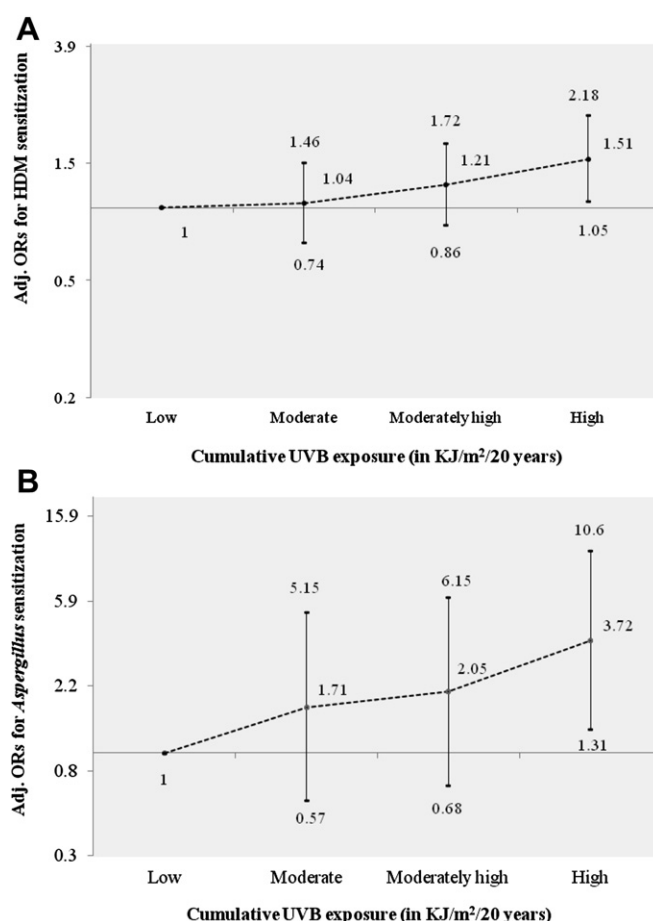


Figure 1. Odds ratio and 95% Confidence interval for the association between (A) cumulative UVB and HDM sensitization and (B) cumulative UVB and *Aspergillus* sensitization.

States (farther from the Equator) and latitude south in Australia (also farther from the Equator). None of these studies examined the effect of atopy, and our observation of effect modification by atopy on the relationship between latitude and asthma might in part explain these discrepant findings.

Vitamin D synthesis is likely to be higher in latitudes closer to the Equator, where daily hours of sunlight exposure are greater. A mechanism to account for the association between latitude or UV-B and asthma and its modification by atopy could lie with the complex relationship among vitamin D, immunity, and atopy. Vitamin D can have apparent contrasting effects on immune responses, on the one hand increasing or decreasing the T_H2 cytokines interleukin 4, interleukin 5, and interleukin 13, depending on dose and life-stage timing,^{18,19} yet also promoting regulatory T cells, which in turn can inhibit T_H2 cytokine responses.²⁰ In an experimental model, vitamin D has been found to reduce airway reactivity by modulating production of various chemokines from airway smooth muscle cells.²¹ On the other hand, a Finnish study found that adults who had received supplementation with vitamin D in childhood had an increased risk of asthma and atopy.⁶ In addition, a possible influence of vitamin D on atopy has been reported by a study that found that both low and high levels of vitamin D were associated with increased IgE production.²² In short, vitamin D can influence asthma by affecting T_H2 immunity and airway smooth muscle reactivity and atopic responses, whereas the exact nature of these effects and how they intermingle are not clear.

Our finding of a increased risk of hay fever with more northerly latitude is consistent with the results of the European Community

Table 4

Associations among latitude, current, and cumulative UV-B Exposure and current asthma by atopic status

Exposure quartile	Current asthma				<i>P</i> _{interaction} value
	Nonatopic		Atopic		
	No. (%)	OR (95% CI) ^a	No. (%)	OR (95% CI) ^a	
Latitude					
Total (100%)	620		776		
Most southerly	39 (19)	1 (Reference)	71 (28)	1 (Reference)	
Southerly	25 (14)	0.67 (0.37-1.21)	57 (28)	1.00 (0.64-1.54)	.30
Northerly	27 (16)	0.84 (0.48-1.49)	54 (31)	1.17 (0.74-1.85)	.37
Most northerly	4 (7)	0.26 (0.08-0.91)	52 (37)	1.51 (0.94-2.40)	.01
Current UV-B					
Total (100%)	620		776		
Low	48 (19)	1 (Reference)	79 (26)	1 (Reference)	
Moderate	24 (16)	0.91 (0.51-1.61)	48 (35)	1.43 (0.89-2.28)	.23
Moderately high	18 (12)	0.68 (0.37-1.26)	68 (29)	1.21 (0.81-1.81)	.13
High	5 (9)	0.43 (0.14-1.26)	39 (37)	1.48 (0.89-2.44)	.04
Cumulative UV-B					
Total (100%)	538		663		
Low	21 (14.4)	1 (Reference)	33 (19.9)	1 (Reference)	
Moderate	27 (15.3)	1.10 (0.55-2.18)	54 (31.2)	1.63 (0.96-2.78)	.37
Moderately high	20 (16.4)	1.42 (0.70-2.90)	53 (30.5)	1.83 (1.08-3.10)	.58
High	8 (8.6)	0.62 (0.24-1.58)	51 (34.0)	1.90 (1.11-3.25)	.04

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

^aAdjusted for sex, childhood eczema, maternal eczema, paternal eczema, and socioeconomic status.

Respiratory Health Study, which also reported that proximity to the Equator increased the likelihood of having hay fever.³ It is also consistent with the results from an Australian multicenter study that found that greater solar exposure in winter was associated with an increased risk of hay fever in children.¹¹

Higher food allergy prevalence with proximity to the Equator in our study contrasts with 2 recent studies that found a higher prevalence of prescriptions for infant hypoallergenic formula and adrenaline autoinjectors (a proxy for food allergy) in the those parts of Australia farthest from the Equator.^{1,2} It is possible that differences in study design may have contributed to the discrepancy in the results. The studies by Mullins et al.^{1,2} were ecologic, whereas ours was a population-based cohort study. Furthermore, these studies were likely to have identified those with more severe food allergy given the nature of the exposure variables examined.

As an alternative to vitamin D-related immune modulations, greater allergic responses nearer to the Equator could simply be due to greater specific aeroallergen exposures. Nonetheless, this alternative mechanism could work in parallel with an increased allergic responsiveness related to vitamin D in atopic individuals.

Latitudinal variation in HDM allergen concentrations has been found in different states in Australia, with higher concentrations in Sydney²³ than in major cities farther from the Equator,^{24,25} a finding consistent with a study from the Northern Hemisphere.²⁶ It is known that HDM sensitization is related to levels of HDM allergen exposure,²⁷ and indeed we found an increasing prevalence of HDM sensitization with increasing UV-B exposure and proximity to the Equator. We also detected a higher prevalence of sensitization to *Hormodendrum* and *Aspergillus* at latitudes closer to the Equator, which have warmer temperatures and higher humidity as reported in an earlier study.⁹ It has been reported that the presence of high levels of *Hormodendrum* and *Aspergillus* increase the risk of sensitization.²⁸ Therefore, it may be that our observed associations between more northerly latitude and sensitization to mold and HDM is due to a higher concentration of these allergens in more northerly regions of Australia. We are unable to

confirm this, however, because we have no measurement of allergen levels.

Strengths of our study are the size of the cohort, the high response rate to the last postal survey, and multiple measurements of allergic disorders. In addition, Australia has a broad span of latitudes that readily allows the study of geographic factors that influence allergic disease risk. In addition, our cohort is all of Anglo-Celtic origin, which limits any genetic or cultural factors that may explain the observed associations. Some differences are found in home heating and cooking appliances between northern and southern Australia; however, adjusting for these factors did not alter the associations observed. The use of parental or participants' reporting of atopic conditions is a limitation. However, the question used to define asthma has been validated against physician diagnosis.²⁹ Another explanation of the observed associations between allergic outcomes and latitude or UV-B exposure is reverse causation (ie, those with allergic disease have moved to more northerly locations). Unfortunately, we do not have age at onset information for SPT sensitivity or the self-reported allergies, so we are unable to exclude this possibility.

A further limitation is that our data did not allow us to examine other environmental factors, including temperature, humidity, and rainfall, that might confound the observed associations. However, adjustment for altitude did not alter the associations. Although we speculate that vitamin D was the factor underlying our observed associations, we acknowledge that this could not be firmly established because serum vitamin D was not measured.

Conclusion

This is the first study, to our knowledge, to demonstrate a differential effect of atopic status on the relationship between latitude and current asthma. Our study demonstrates in a large population-based cohort of genetically and culturally similar individuals that geographic factors may have a role in the development of asthma and allergic disease.

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Supplementary Data

Supplementary data related to this article can be found online at <http://dx.doi.org/10.1016/j.anai.2012.11.005>.

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eTable 1

Association between cumulative UV-B exposure and asthma severity

Cumulative UV-B	Never asthma, No. (%)	Asthma ever but no current asthma		Intermittent asthma		Mild persistent asthma		Moderate to severe persistent asthma	
		No. (%)	OR (95% CI) [<i>P</i> value] ^a	No. (%)	OR (95% CI) [<i>P</i> value] ^a	No. (%)	OR (95% CI) [<i>P</i> value] ^a	No. (%)	OR (95% CI) [<i>P</i> value] ^a
Low	109 (43)	113 (45)	1.0 (Referent)	12 (5)	1.0 (Referent)	7 (3)	1.0 (Referent)	12 (5)	1.0 (Referent)
Moderate	116 (40)	128 (45)	0.95 (0.57–1.57) [.83]	12 (4)	0.70 (0.28–1.75) [.44]	16 (6)	1.61 (0.60–4.28) [.34]	14 (5)	0.72 (0.29–1.80) [.48]
Moderately high	78 (30)	125 (49)	1.33 (0.79–2.25) [.28]	14 (6)	1.44 (0.59–3.52) [.42]	14 (6)	2.62 (0.97–7.09) [.06]	23 (9)	2.14 (0.93–4.95) [.08]
High	61 (27)	107 (47)	1.76 (1.04–2.99) [.04]	24 (11)	3.01 (1.32–6.90) [.009]	17 (7)	3.59 (1.33–9.74) [.01]	18 (8)	2.29 (0.96–5.48) [.06]

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

^aAdjusted for sex, childhood eczema, maternal eczema, paternal eczema, and socioeconomic status.