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Eczema, atopy and allergen exposure in adults: a population-based study

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Clinical and Experimental Allergy

Summary

Background There are few published studies on geographical variation in prevalence of eczema in adults or its association with recognised risk factors for allergic disease.

Objective To describe the geographical variation in prevalence of eczema in adults, assess the associations with sociodemographic risk factors, serum-specific IgE and IgG, and exposure to allergen.

Methods A community-based sample of 8206 adults aged 27–56 years, in 25 European centres and Portland, USA, provided questionnaire information on symptoms of eczema.

Serum-specific IgE to house dust mite (HDM), cat, grass and *Cladosporium*, and IgG and IgG4 to HDM and cat were measured. Mattress levels of mite and cat allergen were assessed.

Results Overall prevalence of eczema was 7.1% (range between countries of 2.2–17.6%). Eczema was associated with female gender [odds ratio (OR) 1.25; 95% confidence interval (CI) (1.01–1.55)], family history of atopic disease (OR 1.43; 95% CI 1.18–1.74), IgE sensitization to at least one allergen (OR 1.50; 95% CI 1.19–1.90), particularly *Cladosporium* (OR 3.65; 95% CI 1.81–7.37), and total IgE. Eczema was negatively associated with age and no clear associations were observed with sibship size, mattress mite and cat allergen levels or with cat and HDM-specific IgG or IgG4.

Conclusions There is geographical variation in the prevalence of eczema in adults both within and between countries. Although the disease is associated with IgE sensitization, in this study it was not related to mattress mite or cat allergen levels.

Keywords atopic dermatitis, ECRHS, eczema, epidemiology

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Introduction

Most published research on eczema [1] has been carried out in children. The geographical variation in prevalence of disease in children [2] has been described and risk factors identified [3–5]. Less is known about the disease in adults, despite suggested persistence rates after puberty of 40–60% [3] and an increasingly recognized burden in terms of morbidity and healthcare costs [6]. There have been country-specific studies on eczema in adults [7–11] but differing disease definitions and study methodologies make

international comparisons between these studies problematic. Although it is recognized that adult eczema may be associated with IgE sensitization to environmental allergen, associations with allergen exposure and IgG have not often been widely reported in population-based surveys.

This report from a multi-centre study, of 8206 adults in 26 centres across 12 countries, describes the prevalence of eczema in adults, assesses the association with sociodemographic risk factors and with IgE and IgG sensitization, and determines whether there is evidence that exposure to allergen is linked to disease.

Methods

Study design and population

The methodology of the European Community Respiratory Health Survey (ECRHS) has been described previously [12, 13] (Fig. 1). In brief, for ECRHS I a community-based sampling frame was used in each centre to identify at least 1500 men and 1500 women aged between 20 and 44 years, who were sent a postal questionnaire. A random sub-sample of 600 responders were invited to a local clinic to undergo a clinical interview (including response to the question 'Have you ever had eczema or any kind of skin allergy?') and tests, including measurements of total and specific IgE. Participants in the clinical phase were re-contacted about 9 years later for ECRHS II and asked to provide more detailed information on the presence of eczema ($n=8206$). Information on smoking behaviour, sibship size, occupational group and dampness and mould in the home was also collected. Blood samples were taken for measurement of serum total IgE and specific IgE to house dust mite (HDM), grass, cat and *Cladosporium* ($n=6496$). A further subsample ($n=2897$) was identified for a home visit, at which dust samples were taken. In 2778 of these participants serum-specific IgG and IgG4 to HDM and cat were also measured. IgE, IgG and IgG4 were

measured using the Pharmacia CAP System (Pharmacia Diagnostics AB, Uppsala, Sweden).

Measurement of cat and dust mite allergen

When participants were visited at home a sample of dust was taken from the participant's mattress by vacuuming an area of 1 m² for a period of 2 min using an Electrolux 'Mondo' 1150 vacuum cleaner (1300 W) with an attached ALK dust collection filter (ALK-Abello, Horsholm, Denmark). These samples were sealed in a plastic bag, frozen for 24 h at -20°C and then forwarded to a central laboratory for measurement of HDM (Der p 1 and Der f 1) and cat allergen (Fel d 1), by a standardized ELISA technique [14].

Disease definition

In ECRHS II the presence of eczema was determined following expert recommendations [15]. Eczema was defined as a positive response to 'Have you ever had an itchy rash that was coming and going for at least 6 months?' AND 'Have you had this itchy rash in the last 12 months?' AND 'Has this itchy rash at any time affected any of the following places: the folds of the elbows, behind the knees, in front of the ankles, under the buttocks or around the neck, ears or eyes?'

Atopic eczema was defined as the presence of both eczema and specific IgE to any of the tested allergens.

Statistical analysis

This analysis is based on information provided at ECRHS II. However, to determine whether responders to ECRHS II were representative of those initially selected for ECRHS I in all centres, factors at baseline associated with completion of ECRHS II were identified through multivariable logistic regression. The 12-month period prevalence of eczema in ECRHS II in each centre and country was determined and direct standardization for age and sex carried out to the European standard population (equal numbers of men and women in three age groups 27–36.9, 37–46.9, 47–57 years).

Three analyses were conducted. The first analysis examined the association of eczema with gender, age group, occupational group (defined by the first digit of the ISCO code of the longest held occupation during the period of follow-up) [16], smoking status (never, smoked in past but not in last month, current), number of siblings, maternal and paternal history of atopic disease (asthma, hayfever, eczema, skin or nasal allergy), visible damp (wet or damp spots on surfaces inside the home other than in the basement over the last 12 months: yes or no), and visible mould on any indoor surface in the last 12 months (yes or no). A second analysis examined the association of eczema with specific IgE values (positive test defined as $\text{IgE} > 0.35 \text{ kU}_A/\text{L}$). A third analysis examined the

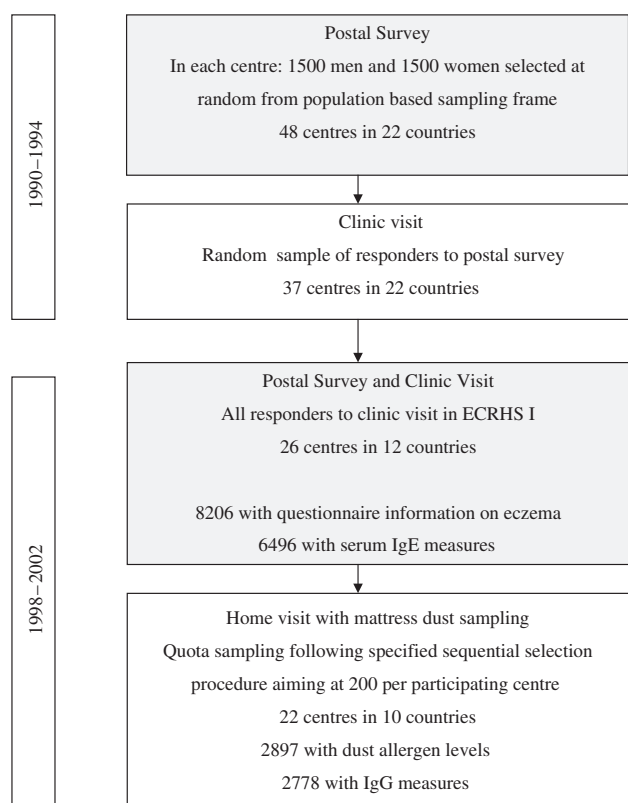


Fig. 1. Flow diagram of the European Community Respiratory Health Survey (ECRHS).

association of eczema with IgG and IgG4 values, exposure to HDM (Der f 1, Der p 1 and total Der 1) and to Fel d 1. As these measures were skewed they were analysed in quartile groups (HDM analyses) and tertile groups (cat analyses). As it is often hypothesised that allergen exposure is only of relevance in those who are IgE sensitized the associations of eczema with allergen exposure are presented stratified by IgE status.

Meta-analysis was carried out to examine the heterogeneity in associations between countries [17]. All analyses were conducted using STATA 9.0 [18].

Permission to conduct the study was granted from local ethical committees.

Results

Response

The sample consisted of 8206 adults aged 27–56 years. Overall, 57.6% of participants who took part in ECRHS I took part in the administered interview in ECRHS II. Responders were older, less likely to come from lower social classes and less likely to be ex- or current smokers (Table 1). However, there was no significant difference in the prevalence of reported 'eczema or skin allergy ever' at ECRHS I in those who did and did not take part in ECRHS II, with no evidence that this association varied between

centres (P for heterogeneity = 0.78), although in Spanish centres (in particular Barcelona), response was more strongly associated with a positive answer to this question than elsewhere. Response was not associated with IgE sensitization to HDM, cat, grass or *Cladosporium*.

Prevalence and geographical variation

The 12-month period prevalence of eczema ranged from 2.2% in Switzerland to 17.6% in Estonia, with an overall prevalence of 7.1% [95% confidence interval (CI) 6.6–7.7%] (Table 2). Prevalence in Switzerland, Spain (4.2%) and Germany (5.1%) was significantly lower than the country median value of 7.7%, and in Estonia (17.6%) was significantly higher. Variation between centres within countries was observed. The twelve-month period prevalence of atopic eczema varied from 0.3% in Switzerland to 6.2% in Estonia.

Risk factors for eczema

In participants taking part in the interviewer-administered questionnaire (Table 3), eczema was associated with being female. Any parental history of atopic disease was associated with an increased risk of eczema (OR 1.43; 95% CI 1.18–1.74) and this was seen most clearly for maternal history (see Table 3). Older people had less eczema (after adjustment, P for trend across age groups = 0.005).

Table 1. Characteristics of responders and non-responders to ECRHS II (1999–2001) assessed in the frame of ECRHS I (1991–1993)

	Non-responders	Responders	OR (95% CI) for response*	OR (95% CI) for response†
	<i>n</i> = 6046	<i>n</i> = 8206	<i>n</i> = 14 249	<i>n</i> = 10 852
Reported 'eczema or any kind of skin allergy ever' in ECRHS I (%)	37.1	39.5	1.06 (0.99–1.15)	1.00 (0.91–1.09)
Female gender (%)	52.0	52.0	1.01 (0.94–1.08)	1.01 (0.92–1.10)
Mean age (years)	33.0	34.0	1.02 (1.02–1.03)	1.03 (1.02–1.03)
UK social class (%)				
I	6.5	7.0	1.00	1.00
II	20.5	22.2	1.08 (0.92–1.27)	1.06 (0.88–1.29)
III	15.7	18.9	1.01 (0.85–1.20)	1.02 (0.84–1.25)
IV	16.6	16.5	0.83 (0.70–0.98)	0.83 (0.69–1.01)
V	10.3	9.6	0.73 (0.61–0.88)	0.81 (0.65–1.01)
Unknown	30.4	25.9	0.86 (0.72–1.02)	0.88 (0.72–1.07)
Smoking status (%)				
Lifetime non-smoker	38.4	44.3	1.00	1.00
Ex-smoker	19.7	21.1	0.90 (0.81–0.99)	0.85 (0.75–0.95)
Current smoker	42.0	34.7	0.69 (0.63–0.75)	0.67 (0.61–0.74)
Serum specific IgE	<i>n</i> = 4054	<i>n</i> = 6819	<i>n</i> = 10 871	
House dust mite (%)	19.6	16.1	0.95 (0.85–1.06)	0.94 (0.83–1.06)
Cat (%)	9.6	9.2	1.03 (0.89–1.20)	0.97 (0.82–1.14)
Grass (%)	19.8	17.9	1.09 (0.98–1.22)	1.07 (0.95–1.21)
<i>Cladosporium</i> (%)	3.7	3.4	1.18 (0.95–1.48)	1.19 (0.94–1.51)

*Adjusted for centre, age and sex.

†Adjusted for centre and all other factors in table.

Bold indicate significant associations ($P > 0.05$).

OR, odds ratio; CI, confidence interval; ECRHS, European Community Respiratory Health Survey.

Table 2. Twelve-month period prevalence of eczema and atopic eczema, ranked by country and centre prevalence of eczema, as found in ECRHS II

Country	Centre	n	Twelve-month prevalence of eczema (% with 95% CI)	Twelve-month prevalence atopic eczema (% with 95% CI)*
Switzerland	Basel	446	2.2 (0.7–3.6)	0.3 (0.0–0.7)
Spain	Oviedo	241	2.2 (0.3–4.2)	
	Barcelona	272	2.4 (0.6–4.2)	
	Galdakao	360	3.3 (1.4–5.2)	
	Albacete	307	4.2 (2.1–6.3)	
	Huelva	204	10.1 (5.9–14.3)	
	Total	1384	4.2 (3.1–5.2)	0.8 (0.2–1.3)
Germany	Erfurt	287	3.9 (1.5–6.3)	
	Hamburg	303	6.5 (3.6–9.5)	
	Total	590	5.1 (3.2–7.1)	2.1 (0.77–33.4)
Belgium	South Antwerp	336	3.8 (1.67–35.9)	
	Antwerp City	291	8.5 (5.2–11.7)	
	Total	627	5.9 (4.0–7.7)	2.4 (0.9–3.9)
Italy	Turin	123	2.6 (0.0–5.5)	
	Verona	205	4.6 (2.0–7.2)	
	Pavia	192	10.7 (6.4–15.0)	
	Total	520	6.6 (4.5–8.8)	1.4 (0.3–2.6)
USA	Portland	197	7.4 (3.7–11.1)	2.4 (0.0–5.2)
France	Montpellier	200	4.4 (0.4–8.4)	
	Bordeaux	164	6.4 (2.8–10.0)	
	Grenoble	380	7.9 (4.7–11.1)	
	Paris	426	10.6 (7.5–13.8)	
	Total	1170	8.0 (6.3–9.7)	3.4 (2.1–4.7)
UK	Ipswich	295	6.7 (3.5–9.9)	
	Norwich	256	9.7 (5.8–13.7)	
	Total	551	8.1 (5.7–10.6)	4.9 (2.7–7.2)
Iceland	Reykjavik	455	8.1 (5.6–10.7)	1.4 (0.3–2.6)
Norway	Bergen	584	8.6 (6.3–10.9)	3.0 (1.5–4.6)
Sweden	Umea	421	8.2 (5.6–10.9)	
	Uppsala	511	8.8 (6.3–11.3)	
	Goteborg	491	9.7 (7.0–12.4)	
	Total	1423	9.0 (7.5–10.5)	3.3 (2.2–4.5)
Estonia	Tartu	259	17.6 (12.6–22.7)	6.2 (2.2–10.2)
Overall		8206	7.1 (6.6–7.7)	2.4 (2.1–2.9)

*Standardized prevalences for eczema and IgE sensitization ('atopic eczema') could not be calculated at a centre level due to limited sample size in some centres. IgE sensitization data was not available for all participants.

Bold indicate significant associations ($P > 0.05$).

OR, odds ratio; CI, confidence interval; ECRHS, European Community Respiratory Health Survey.

Smoking status was significantly ($P = 0.012$) associated with eczema overall, with eczema being more common in ex-smokers than lifetime non-smokers. Eczema was not significantly associated with sibship size (per sibling: OR 1.04; 95% CI 0.98–1.10) nor with number of older siblings (per older sibling: OR 1.03; 95% CI 0.97–1.11), although overall a higher prevalence of eczema was seen in those with any siblings compared with those with none. No association with occupational group was observed (data

Table 3. Association of eczema with suspected risk factors

Factor	Prevalence of eczema (%)	OR (95% CI) for eczema*	OR (95% CI) for eczema†
Gender			
Men	6.04	1.00	1.00
Women	8.01	1.33 (1.12–1.58)	1.25 (1.01–1.55)
Age group			
<35	8.77	1.00	1.00
35–40	6.99	0.80 (0.61–1.04)	0.88 (0.65–1.21)
40–45	7.04	0.81 (0.62–1.06)	0.85 (0.62–1.17)
45–50	7.15	0.81 (0.62–1.05)	0.83 (0.60–1.13)
>50	5.66	0.65 (0.49–0.86)	0.59 (0.42–0.84)
Smoking status			
Lifetime non-smoker	6.68	1.00	1.00
Ex-smoker	7.90	1.27 (1.03–1.56)	1.33 (1.04–1.70)
Current smoker	6.83	1.05 (0.85–1.30)	1.10 (0.86–1.41)
Number of siblings			
0	6.35	1.00	1.00
1	8.35	1.40 (1.02–1.92)	1.67 (1.11–2.51)
2	6.05	1.03 (0.73–1.44)	1.13 (0.73–1.74)
3 or more	6.88	1.24 (0.90–1.72)	1.48 (0.97–2.24)
Paternal history of atopic disease			
No	6.32	1.00	1.00
Yes	8.69	1.37 (1.10–1.70)	1.22 (0.96–1.55)
Maternal history of atopic disease			
No	5.97	1.00	1.00
Yes	10.06	1.64 (1.35–2.00)	1.60 (1.29–2.00)
Visible damp in last 12 months			
No	6.67	1.00	1.00
Yes	8.32	1.25 (1.01–1.54)	1.18 (0.90–1.55)
Visible mould in last 12 months			
No	6.44	1.00	1.00
Yes	9.10	1.35 (1.08–1.70)	1.18 (0.88–1.58)

*Adjusted for centre.

†Adjusted for centre, occupational group and all other factors in the table (Pavia and Turin considered as one centre, Portland dropped due to missing information on damp).

Bold indicate significant associations ($P > 0.05$).

OR, odds ratio; CI, confidence interval.

not shown). There was a non-significant ($P > 0.05$) positive association of eczema with visible mould (OR 1.26; 95% CI 0.98–1.65, adjusted for all factors except damp) and a significant association with visible damp (OR 1.28; 95% CI 1.00–1.60, adjusted for all factors except mould) but when both were considered simultaneously the effect estimates for both were diminished and neither were significant (see Table 3).

In the 6496 participants who had IgE measured, associations of eczema with risk factors were compatible with those described above. A positive association of eczema with sensitization to each of the allergens and with total IgE was observed (Table 4). There was a strong positive association with sensitization to *Cladosporium*, which was present following adjustment for sensitization to the other

Table 4. Association of eczema with serum-specific IgE

Factor	<i>n</i>	Prevalence of eczema (%)	OR (95% CI) for eczema*	OR (95% CI) for eczema†	OR (95% CI) for eczema‡
Mite IgE negative	5476	6.36	1.00	1.00	1.00
Mite IgE positive	1020	8.04	1.36 (1.05–1.76)	1.38 (1.04–1.84)	1.13 (0.83–1.54)
Cat IgE negative	5919	6.28	1.00	1.00	1.00
Cat IgE positive	577	10.05	1.64 (1.21–2.20)	1.60 (1.15–2.22)	1.23 (0.85–1.79)
Grass IgE negative	5420	6.27	1.00	1.00	1.00
Grass IgE positive	1075	8.27	1.46 (1.14–1.87)	1.48 (1.13–1.94)	1.25 (0.93–1.70)
<i>Cladosporium</i> IgE negative	6420	6.46	1.00	1.00	1.00
<i>Cladosporium</i> IgE positive	72	20.83	4.72 (2.57–8.67)	4.79 (2.46–9.31)	3.65 (1.81–7.37)
All specific IgE negative	4643	5.99	1.00	1.00	–
Any specific IgE positive	1849	8.22	1.46 (1.18–1.80)	1.50 (1.19–1.90)	–
Total IgE (kU/L)					
<15.3	1617	5.69	1.00	1.00	1.00
15.3 < 36.3	1632	5.64	1.02 (0.75–1.38)	1.15 (0.83–1.60)	1.17 (0.84–1.62)
36.3 < 91.1	1622	6.78	1.25 (0.94–1.68)	1.28 (0.92–1.77)	1.32 (0.95–1.82)
≥91.1	1622	8.32	1.56 (1.18–2.07)	1.50 (1.06–2.12)	1.47 (1.03–2.09)

*Adjusted for centre.

†Adjusted for centre, occupational group, gender, age group, smoking status, number of siblings, and family history of atopic disease.

‡Adjusted for centre, occupational group, gender, age group, smoking status, number of siblings, family history of atopic disease, and other serum specific IgE.

OR, odds ratio; CI, confidence interval.

three allergens or number (none, one, two or three) of other positive specific IgE (OR for *Cladosporium* 3.65; CI 1.81–7.37). There was a positive association with sensitization to 'any of the four allergens' but this was not due solely to IgE sensitization to *Cladosporium*, as there was increased risk associated with sensitization to 'any of HDM, cat or grass, but not *Cladosporium*', adjusted for IgE sensitization to *Cladosporium* (OR for sensitization to any of the three allergens 1.41; 95% CI 1.09–1.82; OR for sensitization to *Cladosporium* 5.22 95% CI 2.71–11.22). The number of participants with IgE sensitization to *Cladosporium* was small (72) but sensitized individuals were observed in every country except Iceland.

The addition of sensitization status to the models did not substantially alter the associations with gender, age, smoking and number of siblings. In this sub-group of participants who had IgE measures but without adjustment for sensitization, visible damp (adjusted OR 1.22; 95% CI 0.73–1.45) and visible mould (adjusted OR 1.03; 95% CI 0.73–1.45) were non-significantly associated with eczema. There was very little change in these associations following adjustment for sensitization to *Cladosporium*. After adjustment for visible damp and visible mould the association of eczema with IgE sensitization to *Cladosporium* persisted (OR for *Cladosporium* 3.77; 95% CI 1.79–7.91).

In participants with measures of mattress allergen, no association of eczema with mattress levels of Der f 1, Der p 1, total Der 1 or cat allergen was observed (Table 5). The risk of eczema with exposure to Fel d 1 appeared greater in those who were IgE sensitized to cat but there

was no statistically significant ($P > 0.05$) effect modification of allergen exposure by serum-specific IgE. In this group no association was observed with damp (OR 0.90; 95% CI 0.59–1.37) or with mould (OR 0.84; 95% CI 0.54–1.31). The effect estimate for the association of eczema with sensitization to *Cladosporium* remained high but the 95% CIs were wide and the association was not statistically significant (adjusted OR 2.07 95% CI 0.57–7.37). Adjustment for HDM allergen level did not substantially alter this estimate.

Eczema was negatively associated with IgG to mite and this was seen in both those who were and were not IgE sensitized to HDM (Table 6). Eczema was not associated with IgG4 to mite nor with IgG and IgG4 to cat (P for trend > 0.05). Although the data suggest that the association of eczema with cat IgG and IgG4 may differ by IgE sensitization status, formal testing of the interaction of IgE sensitization with IgG and IgG4 levels (expressed as linear variables) for eczema, suggested no interaction was present ($P > 0.05$). There were insufficient data to explore modification by mattress mite or cat allergen level fully. However in participants with the highest levels of mattress allergen exposure (as defined in Table 5), eczema was associated with increasing IgG4 to cat (P for trend across three tertiles of cat-specific IgG4 = 0.019) and a similar but non-significant trend for IgG4 to mite was observed (P for trend = 0.159). These associations were present in participants who were not IgE sensitized but there were too few participants to perform a separate adjusted analysis of this association in those who were IgE sensitized.

Table 5. Association of eczema with allergen exposure, and stratification by serum specific IgE

Factor	OR (95% CI) for eczema*	
	Specific IgE negative to house dust mite (HDM)	Specific IgE positive to HDM
Der f 1 level (µg/g)	<i>n</i> = 1985	<i>n</i> = 351
Not detected (<i>n</i> = 1447)	1.00	1.00
<0.39 (<i>n</i> = 358)	0.97 (0.51–1.86)	0.64 (0.14–2.82)
0.39 < 1.73 (<i>n</i> = 354)	1.22 (0.62–2.39)	1.09 (0.30–3.91)
1.73 < 8.78 (<i>n</i> = 356)	1.74 (0.94–3.21)	0.59 (0.12–2.82)
≥8.78 (<i>n</i> = 356)	1.45 (0.70–3.00)	0.30 (0.51–1.64)
	<i>P</i> for trend = 0.21	<i>P</i> for trend = 0.08
Der p 1 level (µg/g)		
Not detected (<i>n</i> = 1490)	1.00	1.00
<0.36 (<i>n</i> = 344)	1.19 (0.64–2.20)	0.53 (0.14–1.96)
0.36 < 1.82 (<i>n</i> = 347)	1.32 (0.72–2.42)	1.62 (0.47–5.58)
1.82 < 10.81 (<i>n</i> = 345)	0.77 (0.39–1.60)	1.16 (0.30–4.54)
≥10.81 (<i>n</i> = 345)	0.53 (0.21–1.35)	0.51 (0.08–3.31)
	<i>P</i> for trend = 0.31	<i>P</i> for trend = 0.95
Total Der 1 level (µg/g)		
Not detected (<i>n</i> = 919)	1.00	1.00
<0.78 (<i>n</i> = 493)	1.20 (0.65–2.19)	1.05 (0.26–4.14)
0.78 < 3.92 (<i>n</i> = 483)	1.26 (0.68–2.35)	1.93 (0.50–7.41)
3.92 < 15.99 (<i>n</i> = 488)	0.92 (0.45–1.87)	0.22 (0.04–1.36)
≥15.99 (<i>n</i> = 488)	1.12 (0.54–2.31)	0.73 (0.15–3.59)
	<i>P</i> for trend = 0.95	<i>P</i> for trend = 0.29
	Specific IgE negative to cat	Specific IgE positive to cat
Cat allergen level (µg/g)	<i>n</i> = 2101	<i>n</i> = 165
<0.18 (<i>n</i> = 964)	1.00	1.00
0.19–1.01 (<i>n</i> = 900)	1.36 (0.85–2.17)	1.74 (0.37–8.17)
>1.02 (<i>n</i> = 932)	1.03 (0.63–1.67)	1.38 (0.30–6.43)
	<i>P</i> for trend = 0.90	<i>P</i> for trend = 0.73

*Adjusted for country, occupational group, gender, age group, smoking status, number of siblings, and family history of atopic disease.
OR, odds ratio; CI, confidence interval.

No significant heterogeneity was observed in the associations reported, although this could not be fully tested for IgE sensitization to *Cladosporium* or for sibling groups due to low prevalences in some centres.

Discussion

In this international multi-centre study of eczema in adults we have shown geographical variation in disease prevalence, both between and within countries, and shown that disease is associated with IgE sensitization, particularly to *Cladosporium*, which was not explained by reported visible damp or mould. No association was found with mattress cat and dust mite allergen exposure.

Table 6. Association of eczema with serum-specific IgG and IgG4 stratified by specific-IgE status (house dust mite or cat as appropriate)

Factor	OR (95% CI) for eczema*	
	Specific IgE negative	Specific IgE positive
Mite IgG (mg/L)	<i>n</i> = 2121	<i>n</i> = 374
<21.8 (<i>n</i> = 692)	1.00	1.00
21.8 < 39.8 (<i>n</i> = 689)	0.81 (0.50–1.32)	0.69 (0.22–2.18)
39.8 < 68.2 (<i>n</i> = 694)	0.55 (0.32–0.93)	0.55 (0.17–1.76)
≥68.2 (<i>n</i> = 682)	0.66 (0.39–1.10)	0.71 (0.22–2.35)
	<i>P</i> for trend = 0.05	<i>P</i> for trend = 0.51
Mite IgG4 (µg/L)	<i>n</i> = 2121	<i>n</i> = 366
<253 (<i>n</i> = 693)	1.00	1.00
253–397 (<i>n</i> = 692)	0.84 (0.51–1.39)	0.80 (0.22–2.93)
397–616 (<i>n</i> = 691)	0.86 (0.52–1.43)	1.11 (0.31–3.98)
≥616 (<i>n</i> = 691)	1.05 (0.63–1.74)	0.83 (0.25–2.81)
	<i>P</i> for trend = 0.84	<i>P</i> for trend = 0.90
Cat IgG (mg/L)	<i>n</i> = 2302	<i>n</i> = 183
<40.8 (<i>n</i> = 924)	1.00	1.00
40.9–73.4 (<i>n</i> = 924)	0.88 (0.57–1.34)	0.26 (0.05–1.32)
>73.5 (<i>n</i> = 919)	1.00 (0.65–1.54)	0.29 (0.06–1.43)
	<i>P</i> for trend = 0.99	<i>P</i> for trend = 0.16
Cat IgG4 (µg/L)	<i>n</i> = 2302	<i>n</i> = 183
<3.92 (<i>n</i> = 926)	1.00	1.00
3.93–7.29 (<i>n</i> = 920)	1.10 (0.71–1.69)	0.45 (0.08–2.50)
>7.30 (<i>n</i> = 921)	1.32 (0.86–2.02)	0.45 (0.10–2.08)
	<i>P</i> for trend = 0.20	<i>P</i> for trend = 0.37

*Adjusted for country, gender, age group, smoking status, occupational group, number of siblings, and family history of atopic disease.
OR, odds ratio; CI, confidence interval.

Our analysis is based on self-reported disease and no objective assessment of disease status or severity was made. Eczema is likely to represent a group of diseases sharing several common clinical characteristics [1] and disease definition presents considerable difficulties due to the variability of clinical manifestations and lack of a laboratory reference test [4]. Similar questions to those used in our study had a sensitivity of 73.1% and a specificity of 87.3% for eczema when compared with controls suffering from other skin conditions, and a specificity of 97.1% when compared with controls not suffering from skin disease [15]. In the pilot phase of ISAAC the same questions had a sensitivity of 94% and specificity of 81% in the 5–19 age group (<http://isaac.auckland.ac.nz>). These questions performed well when validated in Romanian schoolchildren [19] but less well in Ethiopian children [20]. While this might be explained by the high prevalence of scabies and low prevalence of eczema in the latter population variation in performance of these questions between countries may occur.

The main strengths of our study are the use of a standardized methodology to enable direct comparison of disease prevalence between countries, and that we were able to compare non-responders with responders to a greater extent

than is normally possible. Although we cannot exclude response bias as an explanation for the observed variation, it is reassuring that responders were no more likely in any centre (with the exception of Barcelona) to have reported a history of 'eczema or skin allergy ever' in ECRHS I.

Most epidemiological studies on eczema have been carried out in children, while in adults data are sparse. Our estimated prevalences of eczema do not fully agree with previous reports [7, 9, 10, 21]. Differences in age groups studied and study methodologies, particularly in the definition and terminology of atopic dermatitis/eczema and the use of either self-reported symptoms or examination by trained observers, may explain some of the differences. Some may also be explained by changes in prevalence over time due to period or cohort effects. Comparison of our figures with data from ISAAC (which used the same questions) show some broad similarities, such as higher prevalences in Scandinavia and the United Kingdom and intermediate figures for western Europe. ISAAC reported low disease prevalence in former Socialist Europe but while we observed a low prevalence in Erfurt this was not so in Tartu, Estonia. Further studies in other parts of Estonia would be required to confirm that Estonian adults have a high prevalence of eczema. Not all participants suffering from eczema according to our questionnaire criteria, displayed IgE sensitivity to one of the studied allergens. This is consistent with previously reported results [22].

A population-based postal survey in Sweden has reported more eczema in women than men [9], but as the question asked only about the presence of eczema, and not its distribution on the body this may have been due to more 'hand only eczema' in women. Our definition of eczema would not include those with 'hand only eczema' and our results confirm a greater risk of eczema in women.

Our data show older people report less eczema. While this may be due to an ageing effect with a diminution of allergic responses with increasing age, it may also reflect a cohort effect with younger generations having a higher prevalence of eczema throughout their lives than those born earlier. Ageing and cohort effects cannot be distinguished using cross-sectional data and the relative importance of these effects will only be determined from longitudinal studies.

We have shown that a family history of atopic disease is associated with eczema in adults, as has been shown previously for children [4, 5]. We found no association overall with family size nor with birth order. A recent review identified several studies reporting a decreased risk of eczema in childhood with increasing family size [23].

We found an association between eczema and being an ex-smoker. No relation with personal current smoking was observed in Swedish [24] or Ethiopian [25] adults (ex-smokers were not reported separately in these studies)

or with former or current smoking in pregnant Japanese women [26].

As expected, eczema was associated with total IgE and with specific IgE sensitization. Associations between eczema and specific IgE to mite, cat, grass and *Cladosporium* have been shown in population-based studies of children [27, 28]. The strong association that we observed of eczema with specific IgE to *Cladosporium* was surprising and although it is possible that sensitivity to *Cladosporium* may be a marker for generalized disposition to produce IgE [29] this seemed unlikely as *Cladosporium* remained a significant risk factor following adjustment for 'atopy' in the form of number of other IgE sensitizations. Although the number of individuals sensitized to *Cladosporium* was small, they were spread geographically across the countries studied.

There was no evidence in our study for a relationship between current mattress dust mite allergen levels and eczema in adults. Some studies have suggested that mattress dust mite allergen levels may be higher in those with eczema but these studies were not conducted on community-based representative samples of the population, one including only mite-sensitized individuals [30], and another including as controls only non-mite sensitized patients with asthma [31]. One study of out-patients with eczema found a relation only with moderate to severe eczema [32], and another found no association [33]. Kramer *et al.* [34] have recently reported that eczema in children is associated with Der f 1 but not Der p 1 exposure but we saw no evidence to support this in our adult study. Our data shows no evidence for an association between eczema and mattress cat allergen levels but it was not possible to allow for the effect of bias due to cat avoidance by people who know they have cat allergy. The presence of animal fur in bedrooms has been shown to be a risk factor for eczema in children [35].

Our data suggest eczema is associated with visible damp and mould, although with adjustment for other factors the estimates lost their statistical significance. This is consistent with positive associations with mould reported in Finland for young adults [36] and with visible mould or damp in Sweden for children [37]. In Italy, eczema was associated with current and early life exposure to visible mould or damp in children, but not in adolescents [38].

The strong observed association of eczema with sensitization to *Cladosporium* was not explained by visible damp or mould in the home and, conversely, there was little evidence that the association of eczema with damp or mould could be explained by sensitization to *Cladosporium*. Other damp-related household variables may be of greater relevance to explain this association.

It has been shown previously that adult patients with eczema have higher levels of total [39] and serum-specific IgG4 to HDM [40] but the association with IgG is not clear [40, 41]. We found a negative association of eczema with

specific IgG to mite and no relationship overall with IgG4 to mite or IgG or IgG4 to cat, regardless of sensitization status. Although we observed an increased risk of eczema with increasing levels of specific IgG4 to cat, in those with high allergen exposure, our results should be interpreted with some caution. This may be a chance finding due to multiple hypothesis testing, although a similar trend (non-significant) was observed for mite IgG4 at high allergen exposure levels. In addition, we do not know whether disease severity varies by allergen exposure in this sample. If IgG and IgG4 are associated with eczema, it is unclear whether they play a functional role or are an epiphenomenon. Our data do not support the proposed protective role for specific IgG4 in eczema [42].

In conclusion, in this large international study of eczema in adults using a standardized methodology we have shown variation in the prevalence of eczema between and within countries in Europe, and have documented a strong association with IgE sensitization, in particular *Cladosporium*. We found an association with mite IgE but not with mattress mite or cat allergen levels. We found no clear evidence for a role for IgG and IgG4, and our data does not support a protective role for specific IgG4 in adult eczema.

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