

Hay fever, eczema, and wheeze: a nationwide UK study (ISAAC, international study of asthma and allergies in childhood)

Jane B Austin, Balvinder Kaur, H Ross Anderson, Michael Burr, Leigh S Harkins, David P Strachan, John O Warner

Abstract

Objectives—To describe the prevalence of atopic symptoms in children throughout the UK.

Method—A questionnaire survey of 12–14 year olds throughout England, Wales, Scotland, and the Scottish Islands using the international study of asthma and allergies in childhood (ISAAC) protocol.

Results—A total of 27 507 (86%) children took part. Recent rhinoconjunctivitis was reported by 18.2%, with 6.2% reporting symptoms between March and September; 16.4% reported itchy flexural rash in the past 12 months. The prevalence of atopic symptoms was higher in girls and subjects born within the UK. The prevalence of severe wheeze was highest in subjects reporting perennial rhinoconjunctivitis, as opposed to summertime only symptoms. Winter rhinoconjunctivitis was associated with severe wheeze and severe flexural rash. One or more current symptoms were reported by 47.6% of all children and 4% reported all three symptoms.

Conclusion—In general, geographical variations were small but the prevalence of symptoms was significantly higher in Scotland and northern England. The study demonstrates the importance of atopic diseases both in their own right and in association with asthma.

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Keywords: international study of asthma and allergies in childhood; hay fever; eczema; epidemiology; atopic disease

The prevalence of childhood hay fever shows wide variation throughout the world, ranging from 1.4% to 39.7%.¹ The literature suggests that the prevalence of atopy has increased throughout the UK over the past five decades. In terms of eczema, the national British birth cohort study showed a rise in prevalence from 5.1% in 6 year olds born in 1946 to 12.2% for children born in 1970 and assessed at 5 years of age,² whereas data from the Welsh study of 12 year olds by Burr *et al* showed a rise from 5% in 1973 to 16% in 1988.³ Similarly, the prevalence of hay fever in the same Welsh study rose from 9% to 15% over the 15 year period, whereas for Scottish children Russell reported a rise over a 25 year period from 3.2% in 1964 to 12.7% in 1994.^{4,5} Ross and Fleming

examined general practice data, which showed that the prevalence of hay fever was maximal in the age group 5–14 years and did not show any significant differences in geographical distribution throughout England or Wales.⁶

Prevalence studies in different geographical areas are often difficult to compare because of variations in methodology. In addition, the term atopy, meaning a predisposition to develop type I hypersensitivity demonstrated by skin prick testing and assay of IgE, is often used in relation to atopic diseases such as hay fever and eczema. Many of these difficulties have been overcome by the protocol developed for the international study of asthma and allergies in childhood (ISAAC), which standardises both methodology and terminology. The distribution of hay fever and eczema are of interest not only in their own right, but also as an indicator of the pattern of atopy, which contributes to the burden of asthma. The literature demonstrates a strong association between asthma, hay fever, and eczema⁷; however, the inter-relation between atopy, atopic disease, asthma, and wheeze is somewhat complex. The presence of atopy, particularly if early in onset, predicts the later development of asthma and bronchial hyper-responsiveness, which continues into late childhood.^{8,9} In addition, bronchial hyper-responsiveness and reduced lung function predict persistence of wheeze and level of bronchial responsiveness in adult life.¹⁰ Warner suggests a unifying hypothesis linking atopy, bronchial hyper-responsiveness, and airway inflammation, which together with genetic predisposition and environmental influences produce asthma.¹¹

Atopic diseases in childhood give rise to considerable morbidity and health care costs,^{12,13} with varying environmental influences being implicated in the rising prevalence. Studies have reported the association of hay fever and eczema with race, social class, and month of birth.^{14–16} The effect of outdoor or indoor air pollution on these disorders is inconsistent.^{17,18} The lower prevalence of allergic diseases in Leipzig compared with Munich suggests aetiological factors that are associated with Western lifestyle and living conditions.¹⁸

We report the regional variations in the prevalence and treatment of symptoms of hay fever and eczema throughout the UK and their association with sex, birthplace, wheeze, and asthma.

Department of Child Health, Highland Primary Care NHS Trust, Royal Northern Infirmary, Inverness IV3 5SF, UK
J B Austin

Department of Public Health Sciences, St George's Hospital Medical School, Cranmer Terrace, Tooting, London SW17 0RE, UK
B Kaur
H R Anderson
L S Harkins
D P Strachan

Centre for Applied Public Health Medicine, Temple of Peace and Health, Cathays Park, Cardiff CF1 3NW, UK
M Burr

Southampton General Hospital, Southampton SO16 6YD, UK
J O Warner

Correspondence to: Dr Austin.

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Table 1 Prevalence of reported current flexural rash symptoms, treatment, and lifetime eczema by geographical area in 12–14 year olds across the UK

	n	% With an intermittent, itchy flexural rash in the past 12 months	% With a severe flexural rash in the past 12 months	% Treating an itchy rash or eczema in the past 12 months	% Reporting ever having eczema
Great Britain	27507	16.4	2.2	22.7	22.5
Country			**		***
England	20712	16.5	2.1	22.8	23.1
Wales	2351	15.3	2.5	21.9	21.1
Scotland	4444	16.7	2.8	22.8	20.6
Area					***
Metropolitan	9902	16.9	2.3	22.6	21.1
Non-metropolitan	17605	16.2	2.1	22.7	23.3
Quadrant of England and Wales		*	***		
South west	5901	15.8	2.4	23.2	23.0
South east	7482	15.9	1.6	21.9	22.8
North east	5719	17.7	2.4	23.1	23.8
North west	3961	16.3	2.2	22.8	21.5
NHS region (1993)		**	***		***
South west	2707	15.1	1.6	22.4	24.6
North Thames	2220	16.0	1.6	22.7	23.1
South Thames	2297	16.6	1.6	21.2	20.9
East Anglia and Oxford	2324	15.6	1.7	22.6	24.6
West Midlands	2219	16.1	2.7	24.0	23.2
Trent	2207	15.9	1.5	21.7	23.2
North west	3029	17.0	2.5	23.1	20.7
North east and Yorkshire	3709	18.7	2.8	23.8	24.1
% Missing		1.6	1.4	3.1	3.4

* $p < 0.05$; ** $p < 0.01$; *** $p \leq 0.001$ (χ^2 test).

Methods

Subjects aged between 12 and 14 throughout England, Wales, and Scotland, including the Shetland Isles, Orkney, and the Western Isles, were invited to complete a questionnaire during the months of March and April in accordance with the ISAAC protocol.¹⁹ A sampling frame was prepared of mixed sex, state secondary schools with over 100 pupils in each school year for every county/region in the UK. In addition, randomly sampled districts from four of the six metropolitan counties were included, together with Glasgow, Edinburgh, and eight randomly selected London boroughs. One school was randomly selected from each sampling frame and all children in school years 8–9 (England and Wales) and S2–3 (Scotland), including those aged 12, were surveyed. Details of the method have been described previously,²⁰ and the core questions are presented in appendix 1. Results were analysed by cross tabulation, using SAS and Clinstat statistical packages.

Ethics approval was obtained from all the relevant local committees throughout the entire UK.

Results

The response rate to the self completed questionnaires was 85.9%. Replies were received from 27 507 subjects, attending 93 secondary schools throughout England, Wales, and Scotland; 49.2% were boys and 50.8% were girls. Subjects were aged between 12 and 14, with respondents being on average 6 months older in Scotland than in England and Wales, as a result of the different school entry system.

Missing values for any one question did not exceed 4%. Therefore, denominators for prevalence vary to a small degree between tables.

PREVALENCE OF LIFETIME ATOPY, REPORTED SYMPTOMS, AND TREATMENT

Eczema

The reported lifetime prevalence of eczema was 22.5% (6189 of 27 507). Of the 16.4% (4524 of 27 507) with an intermittent itchy flexural rash occurring in the past 12 months (answered yes to questions 27 and 28 in appendix 1), 49.7% (2248 of 4524) reported a previous label of eczema and 61.2% (2769 of 4524) reported treating the rash. Only 2.2% (606 of 27 507) reported a severe troublesome rash causing sleep disturbance for one night or more each week in the past 12 months, of which 56.3% (341 of 606) reported a label of eczema and 73.9% (448 of 606) had treatment.

Table 1 gives results by geographical area. The prevalence for reported symptoms was not significantly different in England compared with Wales or Scotland. However, within England there are significant differences between quadrants for the prevalence of intermittent and severe itchy flexural rash within the past 12 months ($p < 0.05$, χ^2 test of heterogeneity). In contrast, a label of eczema was reported more often in England than in Scotland (odds ratio (OR), 1.16; $p < 0.001$; 95% confidence interval (CI), 1.07 to 1.25) and in non-metropolitan compared with metropolitan areas (OR, 1.13; $p < 0.001$; 95% CI, 1.07 to 1.20).

Hay fever

Of the total study population, 34.9% (9610 of 27 507) reported hay fever at any time in their life and 37.9% reported rhinitis symptoms in the past 12 months.

The UK prevalence of rhinoconjunctivitis, as defined by nasal symptoms in the past 12 months accompanied by itchy watery eyes (answers yes to questions 20 and 21 in appendix 1), was 18.2% (5019 of 27 507). Of the 5019 with rhinoconjunctivitis, 100 (2.0%) omitted the question about which months their

Table 2 Prevalence of reported current rhinoconjunctivitis symptoms, treatment for rhinitis symptoms, and lifetime hay fever in 12–14 year olds across the UK

	n	% With rhinoconjunctivitis in the past 12 months	% Pupils with seasonal (Mar–Sept) rhinoconjunctivitis in the past 12 months	% Pupils using treatments for a runny/blocked nose or hay fever in the past 12 months	% Pupils reporting ever having hay fever
UK	27507	18.2	6.2	30.1	34.9
Country		***		**	***
England	20712	17.8	6.2	30.6	35.6
Wales	2351	18.5	5.9	29.2	32.6
Scotland	4444	20.3	6.5	28.1	33.2
Area			**		**
Metropolitan	9902	18.5	5.7	30.7	34.0
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Quadrant of England and Wales				***	***
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North west	3961	18.5	6.0	30.0	33.6
NHS Region (1993)		**		***	***
South west	2707	16.8	6.3	30.3	36.0
South Thames	2297	16.6	6.2	32.1	38.4
North Thames	2220	15.9	5.3	33.4	36.0
East Anglia and Oxford	2324	18.2	6.8	33.0	38.6
West Midlands	2219	19.0	5.9	30.7	35.9
Trent	2207	16.4	6.6	29.6	35.5
North west	3029	18.5	5.7	30.4	33.2
North east and Yorkshire	3709	19.4	6.6	27.3	33.1
% Missing		1.5	1.6	2.5	3.0

*p < 0.05; **p < 0.01; ***p ≤ 0.001 (χ² test).

symptoms occurred but over one third (37.8%; n = 1902) confirmed that it occurred perennially; a further third (34.1%; n = 1710) reported symptoms only from March to September and a quarter (26.0%; n = 1307) reported symptoms from October to February only.

Of the 18.2% (5019 of 27 507) of subjects with symptoms of rhinoconjunctivitis, 63.1% (3166 of 5019) reported hay fever and 54.2% (2720 of 5019) had received treatment. A total

of 21.6% (5943 of 27 507) reported that the rhinitis symptoms interfered with their daily activities only a little, but 1.5% (417 of 27 507) reported a lot of interference.

Table 2 shows the results by geographical area. The prevalence of rhinoconjunctivitis in the past 12 months was significantly higher in Scotland than in England (OR, 1.18; p < 0.001; 95% CI, 1.08 to 1.28). In contrast, subjects in England were more likely to report

Table 3 Prevalence of reported flexural rash symptoms and treatment in the past 12 months and lifetime eczema: impact of age, sex, birthplace, and wheeze in the past 12 months

	% With a flexural rash in the past 12 months	% With a severe flexural rash in the past 12 months	% Treating an itchy rash or eczema in the past 12 months	% Reporting ever having eczema
Overall (denominator excludes missing)	16.7	2.2	23.4	23.3
Age				***
12 years	17.5	2.3	23.3	25.3
13 years	16.6	2.2	23.4	23.1
14 years	16.4	2.2	23.0	22.6
Sex	***	***	***	***
Male	13.0	1.7	19.2	19.3
Female	20.6	2.8	27.5	27.7
Birthplace	*		***	***
Outside UK	14.1	2.1	15.2	17.9
Within UK	16.8	2.2	23.6	23.7
Wheeze in the past 12 months	***	***	***	***
No	12.2	1.4	19.2	19.3
Yes	25.5	3.8	31.5	31.4

*p < 0.05; **p < 0.01; ***p ≤ 0.001 (χ² test).

Table 4 Prevalence of reported rhinoconjunctivitis symptoms and treatment in the past 12 months and lifetime hay fever: impact of age, sex, birth in UK, and wheeze in the past 12 months

	% Pupils with rhinoconjunctivitis in the past 12 months	% Pupils with seasonal (Mar–Sept) rhinoconjunctivitis in the past 12 months	% Pupils using treatments for a runny/blocked nose or hay fever in the past 12 months	% Pupils reporting ever having hay fever
Overall (denominator excludes missing)	18.5	6.3	30.9	36.0
Age		**		
12 years	18.1	5.4	31.0	35.4
13 years	18.3	6.6	30.9	35.8
14 years	19.2	6.8	30.8	36.8
Sex	***	***	***	***
Male	16.0	5.4	29.9	33.7
Female	21.1	7.5	31.8	38.4
Birthplace	*	**		***
Outside UK	16.0	4.5	30.3	31.6
Within UK	18.6	6.5	30.9	36.2
Wheeze in the past 12 months	***	***	***	***
No	11.9	4.3	25.6	28.7
Yes	31.6	10.5	41.1	50.5

*p < 0.05; **p < 0.01; ***p ≤ 0.001 (χ² test).

Table 5 Symptoms of rhinoconjunctivitis in relation to wheeze attacks and itchy flexural rash (percentage of children)

	No rhinoconjunctivitis (n = 22488)	Winter only (Oct–Feb) (n = 1307)	Summer only (Mar–Sept) (n = 1710)	Perennial (n = 1902)
> 12 attacks of wheeze	2.0	4.0	6.4	10.5
< 12 attacks of wheeze	98	96	93.6	89.5
Severe rash	1.4	5.0	3.5	8.4
No severe rash	98.6	95	96.5	91.6

In perennial rhinoconjunctivitis, symptoms occurred in both summer and winter months, although not necessarily in every month.

Severe rash indicates that sleep was disturbed on more than one night each week.

One hundred children with rhinitis did not specify month of occurrence.

a previous label of hay fever than subjects in Scotland (OR, 1.11; $p < 0.003$; 95% CI, 1.03 to 1.19) and be taking treatment for their related rhinitis symptoms (OR, 1.13; $p < 0.001$; 95% CI, 1.05 to 1.21).

AGE, SEX, BIRTH PLACE, AND MONTH OF BIRTH
Symptom prevalences were not significantly different within the narrow age range studied (tables 3 and 4).

Girls reported symptoms more often than boys—for example, itchy flexural rash (OR, 1.74; $p < 0.001$; 95% CI, 1.63 to 1.86) and rhinoconjunctivitis (OR, 1.40; $p < 0.001$; 95% CI, 1.32 to 1.49). Children born within the UK also reported symptoms more often than children born abroad—for example, itchy flexural rash (OR, 1.23; $p = 0.023$; 95% CI, 1.02 to 1.48) and rhinoconjunctivitis (OR, 1.20; $p = 0.033$; 95% CI, 1.01 to 1.43). There was no significant difference in either condition in relation to month of birth ($p > 0.05$) (data not shown).

ASSOCIATION OF ATOPY WITH WHEEZE SYMPTOMS

Table 5 shows the results for the prevalence of allergic diseases in relation to the season of reporting rhinoconjunctivitis symptoms.

The prevalence of severe wheezing was higher in subjects reporting perennial rhinoconjunctivitis than in those with summer only symptoms (OR, 1.72; $p < 0.0001$; 95% CI, 1.34 to 2.21) and similarly for the prevalence of severe flexural rash (OR, 2.53; $p < 0.0001$; 95% CI, 1.84 to 3.48).

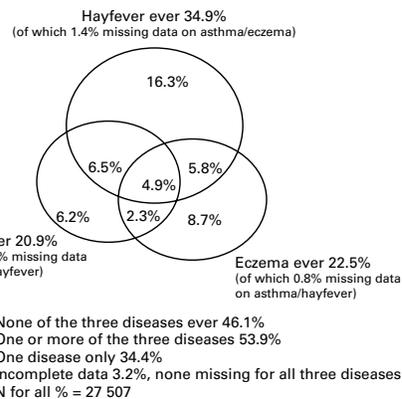
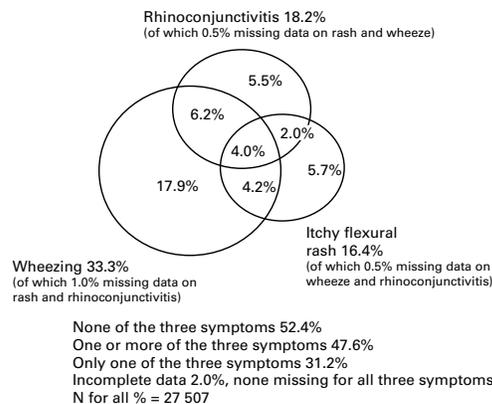


Figure 2 Lifetime prevalence of reported atopic diseases in 27 507 12–14 year old children across the UK in 1994–5. Overall, 53.96% of the children reported ever having one or more of the atopic diseases. Of these, 34.4%, 14.6%, and 4.9% report ever having one, two, or all three of the atopic diseases, respectively. In contrast to current symptoms, hay fever is the most common lifetime atopic disease in the UK, reported by 34.9%, followed by eczema (22.5%) and then asthma (20.9%).

In addition, winter rhinoconjunctivitis symptoms alone are predictive of other allergic diseases; that is, severe wheeze (OR, 2.05; $p < 0.0001$; 95% CI, 1.51 to 2.78) and severe flexural rash (OR, 3.63; $p < 0.0001$; 95% CI, 2.73 to 4.82).

Figure 1 illustrates the inter-relation between reported current symptoms of flexural rash, rhinoconjunctivitis, and wheeze. Of those reporting current wheezing, 43.3% (3965 of 9155) also had current symptoms of other atopic diseases, leaving 53.7% (4919 of 9155) reporting current wheeze alone. For the 18.2% with rhinoconjunctivitis and 16.4% with an itchy flexural rash, 66.5% (3338 of 5019) and 62.1% (2809 of 4524), respectively, reported symptoms of other atopic diseases.

Figure 2 shows the overlap between reported lifetime occurrence of eczema, hay fever, and asthma. In contrast with the symptom Venn diagram, 65.4% (3751 of 5736) of those with asthma reported having another atopic disease, 54.5% (3129 of 5736) reporting hay fever and 34.3% (1968 of 5736) reporting eczema. Of children with asthma, 29.8% (1709 of 5736) had no associated atopic diseases and 4.8% (276 of 5736) had incomplete data on eczema and hay fever.

Tables 4 and 5 illustrate the significantly higher reporting of symptoms and treatment of atopic disorders in wheezers compared with non-wheezers.

Discussion

LIFETIME PREVALENCE, SYMPTOMS, AND TREATMENT

Our results for reported eczema and hay fever are higher than previously reported studies in the UK, Wales, and Scotland,^{3 4 21} but interpretation should be cautious when comparing parent reported study results with pupil completed questionnaires. The general nature of the questions may also be a contributory factor, and objective testing was not included to differentiate between allergic and viral components of rhinitis. However, the questionnaire

has been validated previously, with the combination of itchy eyes in addition to nasal symptoms being found to be most closely related to objective indicators of allergic sensitisation.²² The UK prevalence of eczema and hay fever symptoms was less than the number reporting recent treatment, suggesting that, as expected, many children were receiving medication for non-eczematous rashes and non-allergic nasal symptoms, such as colds. Season of response has been shown to bias rhinitis but not eczema or most asthma symptom questions. Stewart *et al* reported the highest rhinitis prevalence in surveys carried out in the spring/early summer, with the lowest figures during winter surveys.²³ Our study was carried out in March/April, before the start of the pollen season, as recommended in the ISAAC protocol.

Oranje states that eczema is a term often used incorrectly.²⁴ Therefore, it is important in epidemiological studies to define the terminology used in questionnaires. Hence, we have described symptoms as well as reported diagnosis.

GEOGRAPHICAL VARIATIONS

The study by Åberg *et al* showed a higher prevalence of asthma in children living in the colder north of Sweden than in the rest of the country.²⁵ Our results showed a higher prevalence of symptoms in the north compared with the south of the UK, with the March temperatures for the study period in 1995 being 7.1°C in south west England, Torquay, compared with 4.3°C in Inverness and 2.9°C in Shetland.²⁶

Given the association between atopy and wheeze, our results are also consistent with the previous ISAAC UK paper that reported a higher prevalence of wheeze symptoms in Scotland than in England and Wales.²⁰

The reverse differences in figures between Scotland and England for reported symptoms of hay fever and recent treatment of nasal symptoms may be a reflection of socioeconomic factors and differing medical practices. We are not aware of how many children actually saw a doctor or who self diagnosed and treated themselves. Some differences may be the result of chance, in view of the number of parameters analysed.

SEX, AGE, PLACE OF BIRTH, SOCIAL CLASS, AND MONTH OF BIRTH

Although previous studies show a higher incidence of atopy in boys compared with girls aged 12, Anderson suggests that by 16 years the sex ratio reverses.²⁷ Our data suggest that this reverse ratio may be present as early as 12–14 years of age. The Swedish study of 14 year olds by Norrman *et al* showed that the most important risk factors for asthma were being a girl and having atopy,²⁸ a view supported by these data.

Morrison Smith's study of Birmingham schoolchildren showed that those born outside the UK had significantly lower prevalence of asthma and wheezing than those born in England, whereas Hurry *et al* found that children born in Australia had a higher prevalence of

atopy than foreign born children, suggesting that environmental factors in early life have an important role in understanding atopy.^{29–30} Our results are consistent with this view.

Morrison Smith and Springett showed no seasonal variation in the month of birth for pollen sensitive subjects although, as a group, children with asthma showed a difference in month of birth pattern from the general population.³¹ Anderson reviewed several population studies that examined the relation between respiratory symptoms, eczema, hay fever, and month of birth and concluded that the findings were inconsistent.³² Our results also showed no association between itchy rash, rhinoconjunctivitis, and month of birth.

ASSOCIATION OF ATOPIC DISEASES WITH WHEEZY SYMPTOMS AND ASTHMA

Our study clearly demonstrates the interrelation between wheeze and atopic disease. Remes reported rhinitis in 56% of children with asthma, and atopic dermatitis in 58% of children with asthma,³³ which is consistent with our results for reported diagnosis of hay fever, but higher than our results in other respects. The importance of this relation was demonstrated by Kokkonen and Linna, who showed that atopic dermatitis and frequent wheezing at school age were significant risk factors for severe asthma outcome as a young adult.³⁴ In a follow up study, Linna *et al* showed that asthma and wheeze developed more often in those with perennial rhinitis than in subjects with seasonal allergic symptoms,³⁵ which is consistent with our data. It is also interesting to note that we report an association between winter rhinoconjunctivitis symptoms and frequent wheeze or severe eczema, even among children with no summertime rhinoconjunctivitis. This suggests that the ISAAC questions relating to nose problems in the absence of a cold or influenza have some validity as indicators of allergic rhinitis, rather than infectious rhinitis, particularly when used (as in our study) in combination with reports of itchy eyes.

In view of the prognostic implications, the high percentage of adolescents reporting one or more atopic diseases, together with the high percentage of non-atopic wheezers, clearly demonstrates the importance of atopy both from an epidemiological and a clinical viewpoint. Further exploration is required to establish a possible clinical and aetiological differentiation between atopic and non-atopic wheezers and subjects with asthma.

CONCLUSION

The results demonstrate a high prevalence of atopic conditions throughout the UK. Nearly half the childhood population studied was affected by symptoms in some way and nearly one fifth reported more than one diagnosis. This highlights the importance of atopic diseases in children, both in their own right and in association with wheezy illness and asthma.

We thank the National Asthma Campaign for funding; the Departments of Education in England, Wales, and Scotland for providing data on schools; the directors of public health for confirming details of local ethics committees; ethics committees

for approving the study protocol; the field workers who assisted with data collection and coding; and the head teachers, teachers, and pupils at the 93 schools.

Appendix 1

NOSE

The following questions are about nose problems which occur when you DO NOT have a cold or the flu.

19. Have you *ever* had a problem with sneezing, or a runny, or blocked nose when you DID NOT have a cold or the flu? Yes/No

If you answered "No" please skip to question 24

20. *In the last 12 months*, have you had a problem with sneezing, or a runny, or blocked nose when you DID NOT have a cold or the flu? Yes/No

If you answered "No" please skip to question 24

21. *In the last 12 months*, has this nose problem been accompanied by itchy-watery eyes? Yes/No

22. In which of the *last 12 months* did this nose problem occur?

(Please tick any months which apply)

January; February; March; April; May; June; July; August; September; October; November; December

23. *In the last 12 months*, how much did this nose problem interfere with your daily activities? Not at all A little A moderate amount A lot

24. Have you *ever* had hay fever? Yes/No

25. *In the last 12 months*, have you taken any treatment (medicines or sprays) for a runny or blocked nose problem or hay fever? Yes/No

SKIN

These questions are about skin conditions:

26. Have you *ever* had an itchy rash which was coming and going for at least six months? Yes/No

If you have answered "No" please skip to question 31

27. Have you had *this* itchy rash at any time in the last 12 months? Yes/No

If you have answered "No" please skip to question 31

28. 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? Yes/No

29. Has *this* rash cleared completely at any time during the last 12 months? Yes/No

30. *In the last 12 months*, how often, on average, have you been kept awake at night by *this* itchy rash?

Never in the last 12 months; Less than one night per week; One or more nights per week

31. Have you *ever* had eczema? Yes/No

32. *In the past 12 months*, have you taken any treatment (medicines, creams, ointments) for an itchy rash or eczema? Yes/No

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