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Original article

Geographical distribution of atopic rhinitis in the European Community Respiratory Health Survey I*

Background: No large studies in adults has examined geographical variation in the prevalence of nasal allergy/allergic rhinitis in adults or considered the proportion of reported nasal symptoms on exposure to allergen attributable to atopy. The aim of this report was to describe the geographic distribution of subjects with nasal symptoms who are sensitized as determined by skin prick tests, using data from the European Community Respiratory Health Survey I.
Methods: Information on the presence of nasal allergy, nasal symptoms on exposure to allergen and atopy using skin prick tests was collected from 15 394 adults aged 20–44 years living in 35 centres in 15 countries. Age sex standardized prevalence of symptoms and the attributable fraction of IgE sensitization for nasal symptoms on exposure to allergen were determined.
Results: The age-sex standardized prevalence of nasal allergy ranged from 11.8% in Oviedo (Spain) to 46.0% in Melbourne (Australia). The prevalence of atopic nasal allergy ranged from 4.6% in Oviedo to 31.8% in Melbourne (analysis limited on 12 566 subjects). The median attributable fraction for atopy on nasal symptoms on exposure ranged between 12.8% and 65.9% (median 27.2%).
Conclusion: In the general population there is a wide variation in the prevalence of nasal allergy in young adults. Many subjects complaining from nasal symptoms on exposure to allergen are not atopic.

P.-J. Bousquet[1,2], B. Leynaert[3], F. Neukirch[3], J. Sunyer[4], C. M. Janson[5], J. Anto[6], D. Jarvis[1], P. Burney[1]

[1]Imperial College, Emmanuel Kaye Building, London, UK; [2]Département de Biostatistique, Epidémiologie, Recherche Clinique, Santé Publique et Information Médicale, CHU Nîmes, Hôpital Carémeau, Nimes Cedex, France; [3]Institut National de la Santé et de la Recherche Médicale (INSERM), Epidemiologie, Faculté de Médecine Xavier Bichat, Paris, France; [4]Centre de Recerca en Epidemiologia Ambiental, Institut Municipal Investigacio Medica, Barcelona, Spain; [5]Department of Medical Science: Respiratory Medicine and Allergology, Uppsala University, Uppsala, Sweden; [6]Centre de Recerca en Epidemiologia Ambiental (CREAL), Institut Municipal d'Investigacio Medica (IMIM), Universitat Pompeu Fabra (UPF), Barcelona, Spain

Key words: attributable fraction; ECRHS; geographic variation; nasal allergy; rhinitis.

Philippe-Jean Bousquet
Imperial College
Emmanuel Kaye Building
Manresa Road
London SW3 6LR
UK

*List of prinipal participants of ECRHS is given in Appendix.

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Asthma and rhinitis are among the major chronic respiratory diseases (CRD). The WHO global alliance against chronic respiratory diseases (GARD), published in 2006 (1), was able to state the number of asthmatics obtained from the study of Masoli et al. (2) which derived its data from European Community Respiratory Health Study I (ECRHS-I) (3) and ISAAC (4). However, the number of subjects with atopic rhinitis was not officially defined in this WHO document because of the paucity of the published data (5, 6) and the lack of large international study differentiating atopic and nonatopic rhinitis. Finally, the effect of atopy on the prevalence of asthma varies wildly between centres, probably because variations in factors related to the expression of asthma and to the prevalence of sensitization (7).

The number of subjects with rhinitis symptoms can be estimated from large studies such as ECRHS-I (3) and ISAAC (8, 9), but, in the published studies, there is usually no differentiation between atopic and nonatopic rhinitis. However, the ECRHS-I study can differentiate rhinitis subjects with evidence of IgE sensitization from

Abbreviations: AF, attributable fraction; COPD, chronic obstructive pulmonary diseases; CRD, chronic respiratory diseases; ECRHS, European Community Respiratory Health Study; GARD, global alliance against chronic respiratory diseases; ISAAC, International Study on Asthma and Allergy in Children; OR, odds ratio; WHO, World Health Organization.

those who do not appear to be sensitized (10). A standardized protocol was developed for assessment of allergic sensitization by measurement of serum specific IgE to four allergens and by skin prick testing to nine allergens (10). Although skin prick tests and serum specific IgE do not have the same biological and clinical relevance and are not interchangeable (11) both can be used to assess the sensitization of subjects.

The aim of the study was to determine the geographic distribution of subjects with rhinitis/nasal allergy who are sensitized using skin prick tests, and to investigate whether these variations were explained by the prevalence of atopy at a population level. The attributable fraction (AF) for atopy in rhinitis was also determined, i.e. the impact of atopy in rhinitis, or, in the absolute, the proportion of rhinitis that could be avoid if atopy 'disappeared'.

Methods

The methods used in the ECRHS-I are described in detail elsewhere (10). Participating centres selected areas with populations of at least 150 000 people. In the first phase of the study, a random sample of at least 1500 people of each sex in each centre were sent the ECRHS screening questionnaire. In the second phase, a random sample of those responding to this postal questionnaire were invited to come for a more detailed interview, blood tests, skin tests, assessment of lung function and methacholine challenge.

Nasal allergy (as reported by participant)

'Nasal allergy' was considered to be present if a subject responded positively to the question 'Do you have hay fever or nasal allergies' in the ECRHS-I second phase.

'Atopic nasal allergy' was defined as giving a positive answer to this question and having a positive response to skin tests.

'Nasal symptoms on exposure' were considered to be present if a subject reported they experienced 'a runny or stuffy nose or start to sneeze' on exposure to indoor allergens ('animals, such as cats, dogs or horses, near feathers, including pillows, quilts or duvets, or in a dusty part of the house') or outdoor allergens ('trees, grass or flowers, or when there is a lot of pollen').

Skin tests and allergy

Skin testing was performed using Phazet® (Pharmacia Diagnostics, Uppsala, Sweden). The following panel of allergens was used: *Dermatophagoides pteronyssinus*, cat, *Cladosporium herbarium* timothy grass pollen, *Alternaria alternata*, birch, *Olea europea* (Olive), common ragweed, *Parietaria judaica* pollen, a positive control (histamine) and negative control (uncoated Phazet®). Skin testing was performed as previously described (10) and presented in the supplementary material. Allergens were divided into indoor (house dust mites, moulds and animals) and outdoor (or pollen) allergens (tree, weed and grass pollens).

A skin test was considered to be positive if the mean wheal diameter was greater than 0 mm (12, 13). Subjects were excluded if they had a positive negative control (405 subjects, 2.2%) or had a mean wheal diameter of over 30 mm for at least one allergen as this would lead to possible overlaps between two consecutive tests (two subjects, 0.01%). Atopy was defined as being positive to at least one of the nine skin tests (including indoor and outdoor allergens), and indoor and outdoor (or pollen) atopy as a positive response to indoor (house dust mites, moulds and animals) and outdoor (tree, weed and grass pollens) allergens respectively.

Statistical analysis

Age-sex standardized (direct standardization, 20% under 25 years old, 40% between 25 and 35, and 40% over 35; half male and female) prevalence of symptoms and prevalence of atopy in those with nasal symptoms on exposure were given for each centre and countries with 95% confidence intervals. Centres were then classified as having a high (95% confidence interval around centre age-sex standardized prevalence above and excluding study median value observed between all centres) or low (95% confidence interval around centre age-sex standardized prevalence below and excluding study median value) or average values for sensitization (95% confidence interval includes study median).

The AF of atopy for nasal symptoms on exposure was considered using a similar method to that used by Sunyer et al. for asthma (7). The association between skin prick tests and nasal symptoms on exposure to allergen at the individual level was estimated with odds ratio (OR) by using logistic regression and adjusting for age and sex. Similar analysis was performed for atopy to indoor allergens nasal symptoms on exposure to indoor allergens, and outdoor allergens symptoms on exposure to outdoor allergens.

At a population level (i.e. performing the analysis for the whole population, not for a single person), we estimated the AF for atopy in nasal symptoms on exposure. It was estimated by using maximum likelihood on the basis of logistic models as follow: $AF = Pc(RR-1)/RR$, were Pc is defined as the nonstandardized prevalence of atopy among the subjects with nasal symptoms on exposure and RR is defined as the adjusted OR (14). By considering the AF of atopy in subjects with nasal symptoms on exposure, it is therefore important to note that the AF is a function of the prevalence of the atopy in subjects with nasal symptoms on exposure and the relative risk (or the OR) previously calculated (14). In this way, it is possible to identify the impact of atopy in subjects with nasal symptoms on exposure, i.e. the proportion of subjects with nasal symptoms on exposure which in theory would not be present if atopy did not exist (15).

Finally, to understand the geographic heterogeneity in the AF, an ecologic analysis was performed with centre as the unit of observation, looking to the separate relationship between the AF and the two parameters of its function: the prevalence of atopy in subjects with nasal symptoms on exposure and the OR. For the later analysis, the two components of the OR (the prevalence of nasal symptoms on exposure in atopics and nonatopics) were studied.

All analyses were performed with Stata (StataCorp, College Station, TX, USA).

Results

Subject population

A total of 36 679 participants coming from 35 centres and 15 countries were selected for the second phase of the ECRHS survey. Among them, 18 102 (49.4%) attended to this phase, with a participation rate ranging from 12% in Montpellier, France to 90% in Umea, Sweden. 2708 were excluded mainly due to a lack of skin prick tests (2313) or lack of information on nasal allergies (306) (Fig. 1). The mean age of the 15 394 subjects (7634 – 49.6% of male and

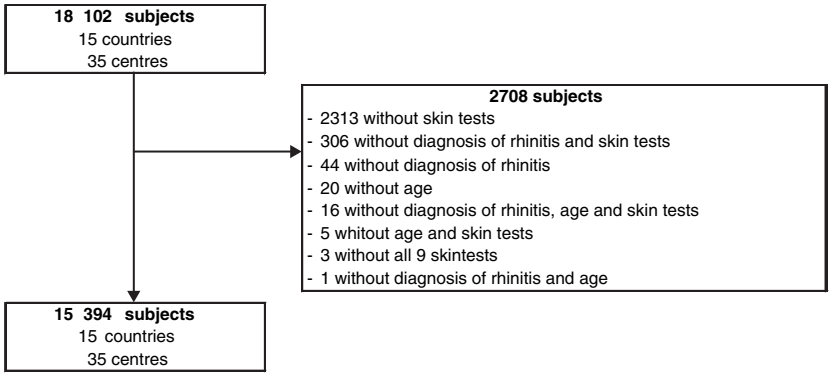

Figure 1. Flow chart.

7760 – 50.6% of female) was 33.7 ± 7.2 years old. In Germany (two centres – 1981 subjects) skin prick testing with timothy grass, olive, *Parietaria* and common ragweed pollens was not done. In Switzerland (847 subjects) ragweed was not tested. Atopy, indoor atopy and outdoor atopy were examined in 32 centres (12 566 subjects) (49.4% of male, mean age 33.8 ± 7.2 years old).

Prevalence of nasal allergy and nasal symptoms on exposure

Prevalence of nasal allergy. The age-sex standardized prevalence of nasal allergy ranged from 11.8% in Oviedo (Spain) to 46.0% in Melbourne (Australia) (Table 1). Low nasal allergy prevalence rates were found in Erfurt (Germany), Pavia (Italy), Norway, Barcelona, Galdakao and Oviedo (Spain) and Bergen-op-Zoom and Groningen (The Netherlands). On the other hand, high prevalence rates were found in Australia, most of the French centres (all centres except Grenoble), New Zealand, two centres in Sweden (Umeå and Uppsala), all centres except one (Caerphilly) in UK and in the USA.

Prevalence of atopic nasal allergy. The prevalence of atopic nasal allergy was low in South-Antwerp (Belgium), Iceland, Pavia (Italy), Norway, Spain, Bergen-op-Zoom and Groningen (The Netherlands) (Table 1). On the other hand, it was high in Australia, Bordeaux and Montpellier (France), Christchurch and Wellington (New Zealand), Norwich (UK) and USA.

Prevalence of nasal symptoms on exposure. Higher standardized (age and sex) prevalence was observed with nasal symptoms on exposure (Table 1). The prevalence ranged from 12.8% in Galdakao (Spain) to 67.7% in Wellington (New Zealand). A low prevalence of nasal symptoms on exposure was observed in Erfurt (Germany), Iceland, Pavia (Italy), Norway, Spain and The Netherlands (except Geleen). A high prevalence of nasal symptoms on exposure was observed in Australia, Belgium, France (except Montpellier), New Zealand, Switzerland, two centres in the United Kingdom (Cambridge and Norwich) and the USA.

Atopic prevalence in nasal allergy. The prevalence of skin test positivity to one of the nine allergens tested in those reporting nasal allergies varied from 38.5% in Albacete (Spain) to 81.8% in Verona (Italy) (median = 69.4%). It was significantly low in South-Antwerp (Belgium), in all French centres except one (Grenoble), in Iceland and in Spain. It was high in Verona (Italy) and Geleen (The Netherlands).

The prevalence of nasal allergy was higher in atopics than in non atopics. Thus, the prevalence in atopics ranged from 28.4% in Barcelona (Spain) to 75.9% in Montpellier (France) (median 49.9%); and in nonatopics from 5.1% in Verona (Italy) to 30.0% in Wellington (New Zealand) (median 15.8%).

Attributable fraction for atopy in subjects with nasal symptom on exposure

The median centre AF for skin test positivity for nasal symptoms on exposure (AF for atopy in nasal symptoms on exposure) adjusted for age and sex was 27.2% (range 12.8–65.9) (Table 2). Centres that were low were Belgium, USA, Paris (France) and Oviedo (Spain). On the other hand, some centres had a high rate: Sweden, Turin (Italy), Barcelona (Spain), Bergen-op-Zoom (The Netherlands) and Ipswich (UK).

The AF for indoor atopy and outdoor atopy (see section 'Skin tests and allergy' for definitions) in subjects with nasal symptoms on respectively indoor and outdoor exposure adjusted for age and sex was reported (Table 2). In most centres, AF was lower for indoor allergens than for outdoor allergens. This was not the case for Melbourne (Australia), Dublin (Ireland), Wellington (New Zealand), Huelva (Spain) and Portland (USA).

Relationship between the AF and the prevalence of atopy

At a centre level (i.e. performing the analysis for each centre), AF variations were well correlated with the prevalence of atopy among subjects with nasal allergies ($r = 0.82$, $P < 0.001$) and nasal symptoms on exposure subjects (Fig. 2, $r = 0.67$, $P < 0.001$). An increase of

Table 1. Standardized (age and sex) prevalence of nasal allergy and atopy in subjects with nasal allergy

			Prevalence of 'nasal allergy'			
	Prevalence of 'nasal allergy'	Prevalence of atopic 'nasal allergy'	In atopic	In nonatopic	Prevalence of atopy in 'nasal allergy'	Prevalence of indoor–outdoor 'nasal symptoms on exposure'
Australia						
Melbourne (549)	46 (41.7–50.4)	31.8 (27.8–35.9)	64.7 (58.8–70.6)	27.9 (22.4–33.5)	69 (63–74.9)	64.1 (0–42.6)
Belgium						
Antwerp-City (322)	28.2 (23.2–33.3)	19.8 (15.3–24.3)	49.2 (40.3–58)	14.3 (9.1–19.5)	69.3 (60–78.6)	52.3 (42.6–24.3)
South-Antwerp (357)	25.5 (21–29.9)	14.3 (10.7–18)	49.1 (39.9–58.2)	15.3 (10.9–19.6)	57.4 (48.1–66.7)	48.7 (52.3–42.6)
Overall	26.3 (23–29.6)	16.4 (13.6–19.2)	49.1 (42.6–55.6)	14.7 (11.4–17.9)	62.4 (55.3–69.5)	49.9 (46.2–53.7)
France						
Bordeaux (543)	41.6 (37.4–45.8)	25.4 (21.8–29)	61.6 (54.6–68.7)	25.6 (20.9–30.3)	61.9 (56–67.7)	53.7 (51.6–43.9)
Grenoble (466)	29.1 (24.4–33.8)	20.9 (16.7–25.1)	51.6 (43.7–59.4)	13.7 (8.9–18.5)	71.5 (63.3–79.7)	51.6 (43.9–47.4)
Montpellier (434)	40.1 (35.1–45.2)	24.8 (20.2–29.3)	75.9 (68.3–83.4)	22.7 (17.3–28.2)	61.1 (53.7–68.5)	43.9 (47.4–45.5)
Paris (609)	32.9 (28.4–37.3)	18.2 (14.4–21.9)	50.3 (42.8–57.8)	23.5 (17.8–29.1)	56.1 (47.3–64.8)	47.4 (45.5–26.9)
Overall	36 (33.8–38.2)	22.7 (20.8–24.7)	59.3 (55.8–62.9)	21 (18.7–23.4)	62.9 (59.5–66.3)	49.6 (47.4–51.9)
Germany						
Erfurt (729)	12.1 (9.7–14.5)					24.3 (12.9–12.8)
Hamburg (1252)	24.7 (22.3–27.2)					42.6 (24.3–12.9)
Overall	20 (18.2–21.8)					35.7 (33.6–37.9)
Iceland						
Reykjavik (513)	23.6 (19.9–27.4)	11.2 (8.4–14)	51.2 (41.5–60.8)	15.7 (12.1–19.3)	46.9 (38.3–55.5)	28.5 (32.7–39.2)
Italy						
Pavia (281)	14.6 (10.1–19.1)	9.2 (5.5–13)	43.7 (31.2–56.1)	6.8 (3.4–10.2)	61.3 (49–73.6)	26.9 (42.1–45.6)
Turin (202)	21 (15.1–26.9)	17 (11.7–22.4)	49.4 (37.3–61.4)	6.1 (1.6–10.6)	80.6 (68–93.1)	42.1 (45.6–35)
Verona (337)	20.7 (16.4–25.1)	17.2 (13.1–21.2)	53.3 (43.8–62.7)	5.1 (2.3–7.9)	81.8 (72.8–90.8)	45.6 (35–31.1)
Overall	18.6 (15.9–21.3)	14.4 (12–16.9)	49.4 (43–55.9)	5.8 (3.9–7.8)	76.3 (69.4–83.3)	38.4 (35–41.8)
Ireland						
Dublin (303)	23.6 (18.8–28.3)	14.3 (10.3–18.3)	35.3 (26.8–43.7)	15.5 (10.4–20.6)	61.6 (51.1–72.1)	45.5 (26.9–42.1)
New Zealand						
Christchurch (340)	34.8 (29.7–39.9)	24.3 (19.8–28.9)	53.1 (45.2–60.9)	18.6 (13.1–24.1)	70.3 (62.3–78.2)	56.7 (64.5–67)
Hawkes-Bay (195)	35.1 (28.2–42)	24 (17.6–30.5)	53 (42.6–63.4)	18.9 (12.4–25.4)	71.6 (62.5–80.8)	64.5 (67–64.1)
Wellington (338)	43.9 (38.3–49.4)	28.7 (23.5–33.8)	60.8 (53–68.6)	30 (22.7–37.2)	66.1 (58–74.2)	67.7 (56.7–64.5)
Overall	38.2 (34.9–41.5)	25.8 (22.8–28.8)	55.8 (50.8–60.8)	23 (19.1–26.9)	68.3 (63.2–73.4)	62.5 (59.2–65.8)
Norway						
Bergen (781)	16.8 (14.2–19.5)	11.6 (9.3–13.9)	39.6 (33.2–46.1)	7.4 (5.2–9.5)	69.5 (62.2–76.9)	32.7 (39.2–39.8)
Spain						
Albacete (421)	22.4 (18.4–26.4)	8.8 (6.2–11.5)	49 (37.3–60.8)	16.6 (12.7–20.6)	38.5 (28.6–48.4)	29 (21.7–27.1)
Barcelona (196)	17.3 (12–22.6)	9.3 (5.4–13.3)	28.4 (16.8–39.9)	12.2 (6.6–17.9)	50.6 (36.8–64.3)	12.9 (12.8–29)
Galdakao (395)	14.1 (10.7– 17.4)	6.9 (4.6– 9.2)	36.1 (22.9–49.2)	8.4 (5.4–11.3)	46.5 (32.7–60.4)	12.8 (29–21.7)
Huelva (249)	21.9 (16.7– 27.1)	10.9 (7–14.8)	43.7 (31.9–55.5)	15.3 (9.9–20.7)	50.7 (37.8–63.7)	27.1 (53.7–51.6)
Oviedo (252)	11.8 (7.8–15.8)	4.6 (1.9–7.4)	32.5 (17.6–47.3)	8.5 (4.8–12.3)	43.2 (27.6–58.8)	21.7 (27.1–53.7)
Overall	18.1 (16.1–20)	8.3 (6.9–9.7)	39.3 (33.9–44.7)	12.4 (10.5–14.3)	45.7 (40–51.5)	21.1 (19.1–23.1)
Sweden						
Göteborg (594)	24.8 (21.3–28.2)	18.3 (15.1–21.4)	47.4 (40.9–53.9)	10.4 (7.3–13.5)	74.4 (67.7–81.1)	39.2 (39.8–42.6)
Umeå (460)	29.6 (25.4–33.8)	21.2 (17.4–25)	58.2 (50.7–65.7)	13.4 (9.4–17.4)	72.4 (64.9–79.8)	39.8 (42.6–46.6)
Uppsala (539)	31.9 (28–35.9)	21.4 (18–24.9)	57.9 (51–64.9)	16.4 (12.4–20.3)	66.6 (59.6–73.6)	42.6 (46.6–67.7)
Overall	28.6 (26.4– 30.8)	20.2 (18.2–22.2)	53.9 (49.8–57.9)	13.4 (11.2–15.5)	70.6 (66.4–74.7)	40.5 (38.1–43)
Switzerland						
Basel (847)	25.7 (22.7–28.7)					46.6 (67.7–56.7)
The Netherlands						
Bergen-op-Zoom (431)	16.1 (12.6–19.7)	11.5 (8.5–14.6)	35.7 (27.7–43.7)	7.1 (4–10.2)	74.2 (63.9–84.6)	31.1 (37.1–55.8)
Geleen (324)	22.2 (17.4–27)	18.3 (13.9–22.8)	33.4 (26.3–40.5)	8.8 (3.6–14)	81 (71.2–90.8)	37.1 (55.8–45.3)
Groningen (367)	18.9 (14.8–22.9)	14.1 (10.5–17.7)	40.9 (32.5–49.2)	7.2 (4–10.4)	73.9 (63.5–84.3)	35 (31.1–37.1)
Overall	18.8 (16.5–21.2)	14.4 (12.3–16.5)	36.2 (31.7–40.7)	7.4 (5.3–9.4)	76.4 (70.5–82.2)	34.3 (31.5–37.1)
UK						
Caerphilly (356)	24 (19.2–28.8)	17.8 (13.4–22.1)	40.2 (32.1–48.2)	11 (5.3–16.6)	74 (64.2–83.8)	45.3 (42.2–56.6)
Cambridge (229)	32.6 (26.5–38.7)	23.7 (18.2–29.2)	54.7 (44.6–64.7)	15.3 (9–21.7)	71 (60.2–81.7)	55.8 (45.3–42.2)
Ipswich (407)	29.6 (25.1–34.1)	22.1 (18–26.2)	53.5 (45.8–61.3)	13.1 (8.4–17.7)	73.8 (66–81.7)	42.2 (56.6–28.5)
Norwich (402)	31.1 (26.5–35.8)	22.5 (18.3–26.6)	50.8 (43–58.7)	15.2 (10.2–20.2)	70.8 (62.9–78.7)	56.6 (28.5–32.7)
Overall	28.9 (26.5– 31.4)	21.3 (19.1–23.5)	49.7 (45.6–53.8)	13.3 (10.8–15.8)	72.7 (68.3–77.1)	49.6 (46.9–52.3)
USA						
Portland (374)	41.2 (35.4–47.1)	29.7 (24.2–35.3)	57.6 (49.6–65.5)	23.2 (17.1–29.3)	72.6 (65.6–79.6)	67 (64.1–0)
Median	24.8	18.2	49.9	15.8	69.4	42.6

Dark grey: centres with high prevalence; Light grey: centres with low prevalence. Figure are given with 95% confidence intervals. Prevalences are standardized on age and sex. Prevalences were based on 'nasal allergy', except for the last one (on the right of the table) which used nasal symptoms on exposure.

Table 2. Attributable fraction (AF) and odds ratio of nasal symptoms on exposure, indoor and outdoor nasal allergy, based on the basis of symptoms, caused by all allergens, indoor and outdoor allergens by centre

	Atopy in nasal symptoms (indoor–outdoor)		Indoor atopy in nasal symptoms (indoor allergens)		Outdoor atopy in nasal symptoms (outdoor allergens)	
	Odds ratio	AF	Odds ratio	AF	Odds ratio	AF
Australia						
Melbourne	4.9 (3.3–7.2)	26.2 (19.6–32.2)	4.6 (3.2–6.7)	30.2 (22.7–37.1)	6.4 (4.2–9.8)	27.9 (21.7–33.6)
Belgium						
Antwerp-City	2.6 (1.6–4.1)	17.2 (8.2–25.4)	2.2 (1.4–3.5)	14.4 (5.3–22.6)	6.6 (3.4–12.7)	27.1 (16–36.7)
South-Antwerp	3.2 (1.9–5.2)	16.4 (9.3–23)	3 (1.8–5.1)	13.7 (7–19.9)	7.4 (3.9–14.2)	28.3 (17.7–37.6)
Overall	2.9 (2–4)	17.1 (11.5–22.3)	2.6 (1.8–3.6)	14.4 (9–19.6)	7 (4.4–11.1)	27.8 (20.3–34.6)
France						
Bordeaux	4.4 (3–6.4)	26.6 (19.6–33)	3.5 (2.4–5.1)	23.9 (16.3–30.7)	5.7 (3.7–8.9)	26.1 (19.3–32.3)
Grenoble	3.8 (2.5–5.6)	23.9 (16.5–30.7)	3.1 (2–4.8)	17.5 (10.5–24)	9.9 (6.1–16.2)	39.8 (31–47.4)
Montpellier	5.2 (3.3–8.2)	27.7 (19.8–34.8)	4.2 (2.5–6.8)	22.6 (14.2–30.2)	10 (5.9–16.9)	37.4 (28.5–45.3)
Paris	2.1 (1.5–3)	12.8 (6.6–18.6)	2.5 (1.7–3.6)	15.4 (8.6–21.6)	4.1 (2.6–6.4)	20.9 (13.5–27.6)
Overall	3.5 (2.9–4.3)	22.3 (18.9–25.6)	3.2 (2.6–3.9)	20 (16.4–23.4)	6.7 (5.3–8.4)	30.2 (26.4–33.8)
Iceland						
Reykjavik	4.4 (2.8–6.9)	24.6 (16.3–32)	3.6 (2.1–6)	17.8 (9.1–25.6)	11.2 (6.1–20.6)	35.3 (24.3–44.7)
Italy						
Pavia	11.7 (5.9–23.4)	37.4 (26–47)	5.7 (2.5–12.9)	19.8 (8.1–30)	29.2 (12.1–70.6)	49.5 (34.8–60.9)
Turin	9.8 (4.9–19.5)	42.6 (29.3–53.5)	6.7 (3.2–14.3)	31.8 (17.9–43.4)	15 (6.9–32.6)	49.8 (34.6–61.5)
Verona	6 (3.6–10)	29.5 (20.9–37.1)	2 (1.1–3.5)	8.5 (1.1–15.3)	19.1 (10.1–36.4)	54.3 (41.8–64)
Overall	8.4 (5.9–11.9)	36.1 (30.2–41.5)	3.6 (2.5–5.3)	17.3 (11.6–22.6)	20.1 (13.1–30.9)	52.2 (44.5–58.7)
Ireland						
Dublin	2.6 (1.6–4.1)	20.3 (9.3–30)	2.6 (1.6–4.3)	22.3 (9.7–33.2)	7.7 (3.7–16.2)	21.3 (13.3–28.6)
New Zealand						
Christchurch	4.6 (2.9–7.3)	28 (19–36)	3.9 (2.4–6.3)	24.4 (15.6–32.4)	5 (3.1–8.2)	28 (19.2–35.9)
Hawkes-Bay	4.1 (2.1–8)	19.6 (9.8–28.4)	3.1 (1.6–5.8)	19.4 (8–29.4)	15.8 (5.3–47.1)	22.7 (15.5–29.3)
Wellington	5.9 (3.5–10.1)	24.7 (17.1–31.6)	5.2 (3.2–8.5)	27.4 (19–34.9)	4.6 (2.7–7.9)	20.7 (13.3–27.6)
Overall	4.9 (3.6–6.6)	25 (20.1–29.6)	4.2 (3.1–5.6)	24.9 (19.7–29.8)	5.5 (3.9–7.6)	23.9 (19.3–28.3)
Norway						
Bergen	5 (3.6–7)	32.3 (25.2–38.7)	3.2 (2.2–4.7)	19 (12–25.5)	13.9 (9.1–21.4)	45.3 (37.2–52.3)
Spain						
Albacete	4.8 (2.8–8.3)	22 (13.9–29.2)	4.5 (2.1–9.6)	11.6 (4.5–18.1)	8.6 (4.6–16)	36.7 (23.6–47.5)
Barcelona	9.7 (3.5–26.6)	65.9 (33.7–82.5)	5.4 (1.7–16.8)	52 (4.8–75.8)	25.5 (6.8–95.2)	68.3 (30.8–85.5)
Galdakao	6.9 (3.3–14.4)	36.3 (20–49.3)	3.1 (1.3–7.3)	20.4 (1–36.1)	26.8 (9.3–77.6)	36.7 (19.9–50)
Huelva	6.6 (3.2–13.7)	36.9 (22.5–48.6)	9 (3.9–20.4)	33 (19.6–44.1)	6.4 (2.6–15.7)	29.2 (11.2–43.5)
Oviedo	2.6 (1.2–5.6)	13.3 (0.8–24.2)	2.7 (1.2–6.2)	12.8 (0.4–23.7)	13.4 (3.1–57.1)	23.6 (1–41)
Overall	4.5 (3.4–6)	28.2 (22.3–33.7)	3.4 (2.4–4.8)	18.7 (12.6–24.4)	10.6 (7.2–15.6)	37.3 (29.4–44.3)
Sweden						
Göteborg	6 (4.1–8.6)	39.9 (31.6–47.3)	5.5 (3.7–8.1)	33.4 (25–40.9)	6.8 (4.5–10.2)	39 (30.2–46.6)
Umeå	7.3 (4.8–11.2)	41.5 (32.4–49.5)	7 (4.5–11)	38.7 (29.2–46.9)	11.8 (7–19.8)	49 (38.3–57.9)
Uppsala	6.3 (4.3–9.3)	37 (29–44.1)	3.9 (2.6–5.9)	24.6 (16.3–32)	10.2 (6.6–15.9)	45.3 (36.4–53)
Overall	6.4 (5.1–8)	39.4 (34.6–43.8)	5.3 (4.2–6.7)	32.1 (27.2–36.6)	9 (6.9–11.6)	43.9 (38.6–48.7)
The Netherlands						
Bergen-op-Zoom	6 (3.8–9.5)	40.1 (29.2–49.4)	4.1 (2.5–6.8)	28.4 (17–38.3)	9.5 (5.4–16.6)	42.3 (29.8–52.5)
Geleen	3.6 (2.2–5.9)	41.1 (24.4–54.1)	3.7 (2.2–6.2)	39.9 (23–53)	6.6 (3.6–12.3)	55 (35.8–68.4)
Groningen	4.8 (3–7.8)	33.7 (22.7–43.1)	4.8 (2.9–8.1)	31.5 (20.4–41)	13.6 (6.9–26.9)	46.8 (32.4–58.2)
Overall	4.6 (3.5–6)	38.4 (31.5–44.7)	4 (3–5.3)	32.6 (25.5–39.1)	8.6 (6.1–12)	47.5 (39.2–54.6)
UK						
Caerphilly	2.8 (1.8–4.3)	22.2 (11.8–31.4)	2.9 (1.8–4.7)	25.8 (12.6–37)	8.1 (4.5–14.8)	30.1 (21.1–38.2)
Cambridge	4.9 (2.7–8.9)	26.1 (15.8–35.2)	5.4 (2.9–10.2)	29.1 (17.9–38.8)	7.2 (3.8–13.9)	31.7 (20.9–41)
Ipswich	8.2 (5.2–13.1)	45.1 (35–53.6)	4.8 (3–7.8)	38.3 (25.9–48.6)	16 (9.1–28.2)	44.8 (35.5–52.9)
Norwich	3.3 (2.1–5)	21.1 (13.2–28.2)	2.5 (1.6–3.8)	19.3 (10–27.6)	5.3 (3.2–8.7)	24.4 (17–31.1)
Overall	4.3 (3.4–5.4)	28.7 (24–33)	3.4 (2.7–4.4)	27.6 (22.1–32.7)	8.4 (6.3–11.1)	32.6 (28.3–36.7)
USA						
Portland	3.3 (2.1–5.3)	19.2 (11.5–26.2)	2.8 (1.8–4.2)	21.3 (11.9–29.6)	5.2 (3.1– 8.7)	21.1 (14.8– 27)
Median	4.9	27.2	3.8	23.2	9.0	36.0

Dark grey: centres with high prevalence; Light grey: centres with low prevalence. Figure are given with 95% confidence intervals. Odds ratios and attributable fraction adjusting for age and sex. Attributable fraction is expressed in percentage.

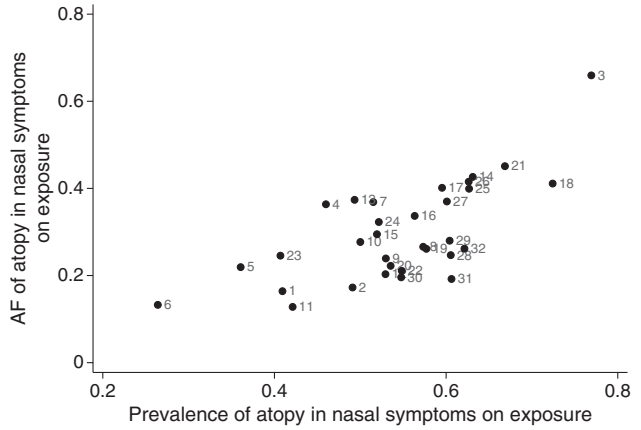

Figure 2. Distribution of centres according to the prevalence of atopy in 'nasal symptoms on exposure' subjects and the attributable fraction for atopy, based on skin prick tests. 1 – South-Antwerp, 2 – Antwerp-City, 3 – Barcelona, 4 – Galdakao, 5 – Albacete, 6 – Oviedo, 7 – Huelva, 8 – Bordeaux, 9 – Grenoble, 10 – Montpellier, 11 – Paris, 12 – Dublin, 13 – Pavia, 14 – Turin, 15 – Verona, 16 – Groningen, 17 – Bergen-op-Zoom, 18 – Geleen, 19 – Cambridge, 20 – Caerphilly, 21 – Ipswich, 22 – Norwich, 23 – Reykjavik, 24 – Bergen, 25 – Goteborg, 26 – UmeÂ, 27 – Uppsala, 28 – Wellington, 29 – Christchurch, 30 – Hawkes-Bay, 31 – Portland, 32 – Melbourne.

atopy in subjects with nasal symptoms on exposure was associated with an increase in AF. When indoor and outdoor nasal symptoms on exposure were considered separately, similar findings were observed for atopy to indoor and atopy to outdoor allergens ($r = 0.74$, $P < 0.001$ and 0.77, $P < 0.001$ respectively) (See Supporting information Figures).

Relationship between the AF and the odds ratio

The relationship between the AF and the two components of the OR (the prevalence of nasal symptoms on exposure among atopic and non atopic) was studied. The AF was negatively correlated with one component of the OR, the prevalence of nasal symptoms on exposure in nonatopic subjects ($r = -0.57$, $P < 0.001$) showing that an increase in the prevalence of reported nasal symptoms in nonatopic subjects was associated with a decrease in AF for atopy (Fig. 3). Similar findings were observed for indoor ($r = -0.46$, $P < 0.001$) and outdoor rhinitis ($r = -0.65$, $P < 0.001$) in nonatopic subjects to indoor and outdoor allergens respectively.

Discussion

The present study shows large geographical variations in the reporting of nasal allergies across 35 centres in 15 countries taking part in the ECRHS-I. About one in four cases of reported nasal allergies among adult between 20 and 44 years old in the general population could be attributed to sensitization to common allergen as judged by positive skin prick tests. However, wide variations of AF of atopy in nasal symptoms on exposure were also observed.

In the present study, the prevalence of rhinitis may differ from previous ECRHS-I studies since the populations studied are not entirely similar due to the methods used (16). The characterization of IgE-mediated allergy may be done using skin prick tests or serum specific IgE. Since nine allergens were used in skin tests and only four in IgE measurements we decided to use skin tests. This is of particular interest for *Parietaria*, birch and ragweed pollen which are important local allergens and were not tested using IgE. Skin tests are more variable than IgE measurements in a single laboratory. However, Phazet® is of interest in multicentre studies as precoating of the lancet with allergen allows for the control of the amount of allergen delivered to the skin and it is highly reproducible (17). One possibly controversial part of the

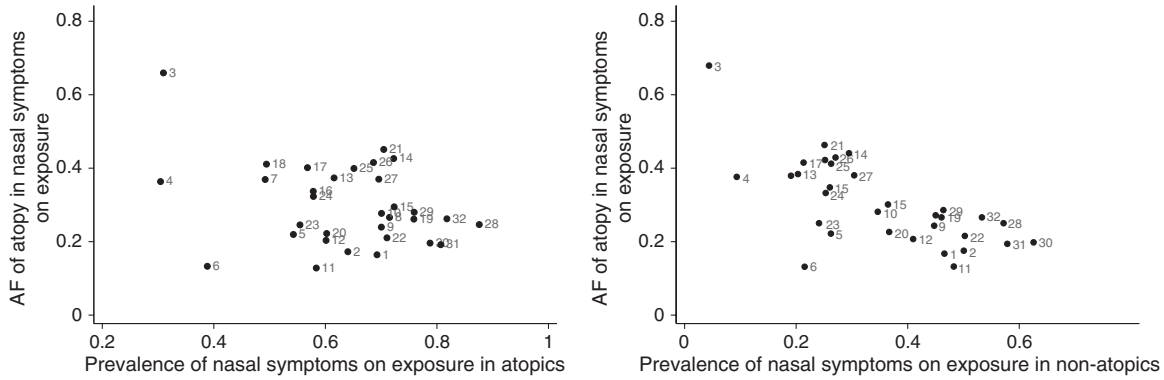

Figure 3. Distribution of centres according to the attributable fraction among the prevalence of 'nasal symptoms on exposure' in atopic subjects and non atopic subjects. 1 – South-Antwerp, 2 – Antwerp-City, 3 – Barcelona,4 – Galdakao, 5 – Albacete, 6 – Oviedo, 7 – Huelva, 8 – Bordeaux, 9 – Grenoble, 10 – Montpellier, 11 – Paris, 12 – Dublin, 13 – Pavia, 14 – Turin, 15 – Verona, 16 – Groningen, 17 – Bergen-op-Zoom, 18 – Geleen, 19 – Cambridge, 20 – Caerphilly, 21 – Ipswich, 22 – Norwich, 23 – Reykjavik, 24 – Bergen, 25– Goteborg, 26 – UmeÂ 27 – Uppsala, 28 – Wellington, 29 – Christchurch, 30 – Hawkes-Bay, 31 – Portland, 32 – Melbourne.

present analysis was to consider a skin test positive if the wheal was greater than 0 mm. Most allergists use a cut off of 3 mm (18). For this epidemiological study we wanted to identify a measurable skin test response indicative of an immunological reaction and therefore a lower cut off was used. In addition, it was shown that a 0 mm cut off was the most relevant for epidemiologic studies (12, 13). Finally, conducting the analysis with a 3 mm cut-off did not change markedly the results.

The prevalence of nasal allergy was standardized on age and sex, but not on family size even though there is a negative relationship between atopic rhinitis (nasal allergy) and family size (19). When we standardized the prevalence of nasal allergy on family size, age and sex there was little change to our results (data not shown, the average change of AF between centres being 0.4%).

Although it was shown that seven allergens could identify nearly all atopic subjects in an epidemiologic study (13), some important allergens have not been tested and our estimation of prevalence of atopy may be underestimated. For some Southern centres, *Cupressus sempervirens* (cypress) would have been of interest but it was not standardized and available with Phazet®, skin prick tests are not always positive and the epidemic of cypress pollen allergy has only been recognized in recent years (20). Moreover, the study was carried out in the early 1990s and the prevalence of allergy has likely increased in most centres, albeit not in all. In the ECRHS-II survey, carried out 9 years after the ECRHS-I in the same subjects, there was evidence that sensitization to at least one allergen was higher in more recent cohorts, and this was largely explained by a higher prevalence of sensitization to grass (21). Taking these considerations into account and, even if we used a low skin test cut-off (0 mm), we may have underestimated the prevalence of atopic rhinitis in the population tested.

Some patients with a local allergic reaction may not have been characterized since allergen-specific IgE can only be detected in nasal secretions, but it is likely that this group of patients will not account for a large proportion of patients (22).

We based the prevalence of rhinitis on reported 'nasal allergy'. The prevalence was lower than that based on nasal symptoms on exposure to allergens. It is possible that the 'true' prevalence in this study is between both definitions. As expected, the prevalence of nasal allergies observed in atopic subjects was higher than in nonatopic subjects.

The AF is the proportion of the case of nasal allergy that is attributable to the exposure assuming there is a causal relationship. It is based on the difference between the number of cases in a population that occur when the population is subject to a given exposure, and the number that would occur in the same population if that exposure was changed (i.e. if exposure was reduced or eliminated by an intervention). The prevalence of the exposure (i.e. the fact to be atopic) and the relative risk (or the OR), i.e. the impact at the individual level, composed the AF of atopy in nasal symptoms on exposure. The choice of the skin test threshold of positivity should not affect the AF, since a well-balanced bias of classification has little effect (23). Even if the observed AF might be low, results on AF were similar to those observed for asthma (7). This suggests that nonallergic rhinitis is a common disease. Moreover, the AF was computed for the atopy as a whole (sensitization to at least one allergen) and not for each allergen. The calculation of an AF for each allergen was not possible, the sum of these various AFs being higher than 1.

Overall, around 30% of the subjects who answered positively to the question 'Do you have nasal symptoms' had negative skin tests. Similarly, the AF of atopy for nasal symptoms on exposure was not close to 1, even though the question asked specifically about allergies (in presence of indoor or outdoor allergens 'do you ever get a runny or stuffy nose or start to sneeze'). We would expect most of those answering positively to such questions to have evidence of IgE sensitization, especially when a low skin test cut-off (0 mm) was used. Similar findings were observed when the AF of atopy for 'nasal allergy' ('Do you have any nasal allergies, including hay fever') was computed (data not shown). A few epidemiologic studies have assessed the AF of allergic sensitization in rhinitis. A review of 22 papers found that the overall proportion of rhinitis cases that were atopic was 61%, the proportion of noncases that were atopic was 20%, and the proportion of rhinitis cases that were attributable to atopy was 53% (5). In the ECRHS-I, the AF for atopy in asthmatic subjects was around 30% (7). The present study shows similar figures for nasal symptoms since the median proportion of nasal symptoms on exposure attributable to atopy ranges from 23.2% (indoor allergens) to 36.0% (outdoor allergens). Zacharasiewicz et al. found a higher rate (65.6%) for the ECRHS using data published by Leynaert et al. (24), differences mainly due to the subject's selection. It is important to observe that a significant proportion of subjects reporting nasal symptoms are not atopic, which confirms the importance of this type of rhinitis even if differentiation is not always easy (24, 25). More epidemiologic studies are needed to fully appreciate the prevalence of nonatopic rhinitis.

This study suggests that symptoms of atopic and nonatopic rhinitis cannot be distinguished easily (26). Recent study (6) found a slightly higher prevalence of atopic rhinitis in adults in Europe [17% (Italy) to 29% (Belgium)]. Differences may be explained by methods used in the two studies, choice of the sample, and in the study of Bachau et al. (6), only around 85% subjects had a demonstrated allergy.

In conclusion, this study in the general population shows that atopic rhinitis as well as nonatopic rhinitis are a common disease. It makes it possible to appreciate the prevalence of both atopic and nonatopic rhinitis in a large number of centres and suggests that factors other than

allergy are involved in nasal symptoms that the general population report as nasal allergies or as symptoms that develop on exposure to allergens.

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Supporting Information

Additional Supporting Information may be found in the online version of this article.

Figure S1. Distribution of centres according to the attributable fraction for atopy in 'nasal symptoms on exposure' and the prevalence of atopy in 'nasal symptoms on exposure' based on skin prick tests. Analysis done for indoor (left graphs) and outdoor (right graphs) allergens.
Figure S2. Distribution of centres according to the attributable fraction for atopy in 'nasal symptoms on exposure' and the prevalence of 'nasal symptoms on exposure' in atopic. Analysis done for indoor (left graphs) and outdoor (right graphs) allergens.
Figure S3. Distribution of centres according to the attributable fraction for atopy in 'nasal symptoms on exposure' and the prevalence of 'nasal symptoms on exposure' in non atopic subjects (C). Analysis done for indoor (left graphs) and outdoor (right graphs) allergens.
Skin testing techniques. Relation between AF using 'nasal symptoms on exposure' and 'nasal allergy'.

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Appendix

List of principal participants

Co-ordinating centre (London). Peter Burney, MD, Susan Chinn, DSc, Christina Luczynska, PhD, Deborah Jarvis, MFPHM, Eric Lai, BSc

Project management group. Peter Burney, MD (project leader), Susan Chinn, DSc, Christina Luezynska, PhD, Deborah Jarvis, MFPHM, (London); Paul Vermeire, MD, (Antwerp); Hugo Kesteloot, MD, PhD, (Leuven); Jean Bousquet, MD, (Montpellier); Dennis Nowak, MD, (Hamburg); the late John Prichard, PhD, FRCPI, (Dublin); Roberto de Marco, MD, (Verona); Bert Rijcken, MD, PhD, (Groningen) Josep M. Anto, MD, (Barcelona); Jose Aires, MD, (Oporto); Gunnar Boman, MD, (Uppsala)

Participating centres providing samples for assays of IgE. Australia: Michael Abramson, MB, BS, PhD, Jozica Kutin, BA, MPsych, (Melbourne); *Belgium:* Paul Vermeire, MD, Frank van Bastelaer, MD, (Antwerp South, Antwerp Central); *France:* Jean Bousquet, MD, (Montpellier); Françoise Neukirch, MD, Renata Liard, PhD, (Paris); Isabelle Pin, MD, Christophe Pison, MD, (Grenoble); André Taytard, MD, (Bordeaux); *Germany:* Helgo Magnussen, MD, Dennis Nowak, MD, (Hamburg); H-Erich Wichmann, MD, Joachim Heinrich, MD (Erfurt); *Iceland.*:Thorarinn Gislason, MD, PhD, H. David Gislason, MD, (Reykjavik); *Ireland:* the late John Prichard, D Phil, FRCPI, Shane Allwright, PhD, Dominic MacLeod, MB, BSc, (Dublin); *Italy:* Massimiliano Bugiani, MD, Caterina Bucca, MD, Canzio Romano, MD, (Turin); Roberto de Marco, MD, Vincenzo Lo Cascio, MD, Cesare Campello, MD, (Verona); Alessandra Marinoni, MD, Isa Cerveri, MD, Lucio Casali, MD, (Pavia); *Netherlands:* Bert Rijcken, MD, PhD, Anja M. Kremer, MD, PhD, (Groningen, Bergen-op-Zoom, Geleen); *New Zealand:* Julian Crane, FRACP, Simon Lewis, BSc, (Wellington, Christchurch, Hawkes Bay); *Norway:* Around Gulsvik, MD, PhD, Ernst Omenaas, MD, PhD, (Bergen); *Spain:* Josep M. Anto, MD, Jordi Sunyer, MD, Felip Burgos, Resp Tech, Jordi Castellsague, MD, Josep Roca, MD, Joan Soriano, MD, Aureli Tobias, BSc, Dip Stat, (Barcelona); Nerea Muniozguren, MD, Jacinto Ramos-Gonzalez, MD, Alberto Capelastegui, MD, (Galdakao); Jose Castillo, MD, Jose Rodriguez-Portal, MD, (Seville); Jesus Martinez-Moratalla, MD, Enrique Almar-Marqnes, MD, (Albacete); Jose Maldonado-Pérez, MD, Antonio Pereira, MD, Jose Sfinchez-Ramos, MD (Huelva); Roman Quiros, MD, Ismael Huerta, MD, Felix Payo-Losa, MD (Oviedo); *Sweden:* Gunnar Boman, MD, PhD, Christer Janson, MD, PhD, Eythor Björnsson, MD, PbD, (Uppsala); Leif Rosenhall, MD, PhD, Eva Norrman, MD, Bo Lundbgck, MD, PhD (Umefi), Nalle Lindholm, MD, PhD, Peter Plaschke, MD (Goteborg); *Switzerland:* Ursula Ackermann-Liebrich, MD, Nino Kfinzli, MD, André Perruchoud, MD (Basel); *United Kingdom:* Michael Burr, MD, Jane Layzell, MRCGP, (Caerphilly); B. Russell Hall, MD, (Ipswich); Brian Harrison, FRCP, (Norwich); John Stark, MD, (Cambridge); *United States:* A. Sonia Buist, MD, William M. Vollmer, PhD, Molly L. Osborne, MD, PhD, (Portland).

