Allergy EUROPEAN JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY

Allergy

ORIGINAL ARTICLE EPIDEMIOLOGY AND GENETICS

Chronic rhinosinusitis in Europe – an underestimated disease. A GA^{2}LEN study

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To cite this article: Hastan D, Fokkens WJ, Bachert C, Newson RB, Bislimovska J, Bockelbrink A, Bousquet PJ, Brozek G, Bruno A, Dahlén SE, Forsberg B, Gunnbjörnsdóttir M, Kasper L, Krämer U, Kowalski ML, Lange B, Lundbäck B, Salagean E, Todo-Bom A, Tomassen P, Toskala E, van Drunen CM, Bousquet J, Zuberbier T, Jarvis D, Burney P. Chronic rhinosinusitis in Europe – an underestimated disease. A GA^{2}LEN study. *Allergy* 2011; **66**: 1216–1223.

Keywords
allergic rhinitis; asthma; chronic rhinosinusitis; prevalence; sinusitis; smoking.

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Accepted for publication 19 April 2011

DOI:10.1111/j.1398-9995.2011.02646.x

Edited by: Marek Sanak

Abstract

Background: Chronic rhinosinusitis (CRS) is a common health problem, with significant medical costs and impact on general health. Even so, prevalence figures for Europe are unavailable. In this study, conducted by the GA^{2}LEN network of excellence, the European Position Paper on Rhinosinusitis and nasal Polyps (EP^{3}OS) diagnostic criteria are applied to estimate variation in the prevalence of Chronic rhinosinusitis (CRS) for Europe.

Method: A postal questionnaire was sent to a random sample of adults aged 15–75 years in 19 centres in Europe. Participants reported symptoms of CRS, and doctor diagnosed CRS, allergic rhinitis, age, gender and smoking history. Definition of CRS was based on the EP^{3}OS diagnostic criteria: the presence of more than two of the symptoms: (i) nasal blockage, (ii) nasal discharge, (iii) facial pain/pressure or (iv) reduction in sense of smell, for >12 weeks in the past year – with at least one symptom being nasal blockage or discharge.

Results: Information was obtained from 57 128 responders living in 19 centres in 12 countries. The overall prevalence of CRS by EP^{3}OS criteria was 10.9% (range 6.9–27.1). CRS was more common in smokers than in nonsmokers (OR 1.7: 95% CI 1.6–1.9). The prevalence of self-reported physician-diagnosed CRS within centres was highly correlated with the prevalence of EP^{3}OS-diagnosed CRS.

Conclusion: This is the first European international multicentre prevalence study of CRS. In this multicentre survey of adults in Europe, about one in ten participants had CRS with marked geographical variation. Smoking was associated with having CRS in all parts of Europe.

Chronic rhinosinusitis (CRS) is a common health problem with significant direct medical costs (1, 2). Its impact on quality of life (QoL) is comparable with other chronic diseases such as chronic obstructive pulmonary disease (COPD), asthma and diabetes (3, 4).

The prevalence of CRS is a matter of debate. A survey of 220 267 participants from the United States in 2007 showed that 14% had ever been told by a doctor or other health professional that they had sinusitis (5). In a Canadian national health survey of 73 364 participants, the prevalence of CRS, defined as an affirmative answer to 'Do you have sinusitis diagnosed by a health professional?' was 3.4% in men and 5.7% in women (6). However, in both studies, it is unclear whether the patients were asked about acute or chronic rhinosinusitis. In a Korean study, in which participants were specifically asked about chronic rhinosinusitis (defined as 'at least three nasal symptoms lasting more than 3 months plus endoscopic findings of nasal polyposis and/or mucopurulent discharge within the middle meatus'), the prevalence was 1.01% (7), with no difference between age groups or between men and women.

For Europe, the only estimation of CRS prevalence in the literature is from a study conducted on 99 Belgian patients with suspected intracranial disease who were undergoing MRI scan. Findings from the scan with information from a sinusitis questionnaire resulted in an estimate of nasal discharge at 6% and bilateral nasal obstruction at 19% (8).

Estimating the prevalence of CRS is difficult because of shortcomings in current epidemiological methodology, and no large study to estimate CRS prevalence has been conducted in Europe. Recently, a taskforce endorsed by the European Academy of Allergy and Clinical Immunology (EAACI) and the European Rhinologic Society (ERS) has agreed on a definition, 'the European Position Paper on Rhinosinusitis and nasal Polyps: EP^{3}OS criteria' for chronic rhinosinusitis, which can be used for epidemiological and clinical research (9). Based on this definition, the GA^{2}LEN network of excellence, funded by the European Union, conducted a European Survey to estimate the prevalence of CRS in Europe.

Material and methods

Postal survey

As part of The Global Allergy and Asthma European Network (GA^{2}LEN), a survey was conducted to collect information suitable for examining the epidemiology of asthma, allergy and upper airway disease in adults living in Europe. A questionnaire was prepared which included items previously used in the European Community Respiratory Health Survey (10) (ECRHS) and questions on rhinosinusitis consistent with the European Position Paper on Rhinosinusitis and Nasal Polyps 2007 (EP^{3}OS) criteria.

In each participating centre, the GA^{2}LEN questionnaire was translated into the local language, with independent back translations checked by the coordinating centre.

In 2008, a short postal questionnaire was sent to a random sample of people aged 15–75 years obtained from a suitable population-based sampling frame in each of the 25 sites. The questionnaire asked for symptoms of CRS (Appendix 1), age, gender and smoking history. If no response was obtained within 3 weeks, the questionnaire was sent again. This process was repeated one more time.

Outcome parameter

Rhinosinusitis was defined as suggested by the EP^{3}OS criteria 2007 which stated that the disease is an 'inflammation of the nose and the paranasal sinuses characterized by two or more symptoms, one of which should be either nasal blockage/obstruction/congestion or nasal discharge (anterior/posterior nasal drip):

1 Facial pain/pressure,
2 Reduction or loss of smell.

Chronic rhinosinusitis was said to be present if participants reported that the symptom complex had been present for more than 12 weeks during the last 12 months.

Self-reported physician-diagnosed CRS was considered to be present if the participant reported that they had 'ever been told by a doctor' that they had 'chronic sinusitis'.

Statistical analysis

Where information was available, the age and gender of responders and nonresponders were directly compared. To further assess the possible influence of response bias on calculated prevalence estimates, the time to return a completed questionnaire in those with CRS was compared with the time to return a completed questionnaire in those without CRS. The differences were compared using Somers D (11), a test statistic arising from a Mann–Whitney test of differences.

The prevalence of CRS in each centre, both in all subjects and in lifelong nonsmokers only, was standardized by gender and 5-year age groups to the European Standard Population for ages 15–74 years (12). Sampling-probability weights were applied, and confidence intervals were based on Huber variances. We also fitted, to the CRS data from each centre, a logistic regression model, containing odds ratios for 10-year age group (15–24, 25–34, 35–44, 45–54, 55–64 or 65–74), gender (male or female), smoking status (lifetime nonsmoker, ex-smoker, current smoker) and smoking exposure (pack years, modelled as a quadratic effect). The effects of 25 and 50 pack years of smoking, compared with zero pack years, were estimated, using the reference-spline method of Newson (13).

Within-centre effect estimates were combined between centres as geometric mean odds ratios weighted by centre sample size, with heterogeneity tested using the Wald chi-squared test, and measured using the I^2 statistic of Higgins and Thompson (14).

Excluded were cases with incomplete data concerning variables needed for statistical analysis.

Ethical approval

The study was approved by local ethics committees in all the study centres.

Results

Response

Twenty-five centres in 15 countries took part in the survey. Data collected from centres in Munich, Oslo and Athens were excluded from the main analyses as the age of the populations under study did not comply with the core protocol (20–30 years in Munich and 20–24 years in Oslo and Athens). Three centres in Russia were excluded as their sampling frame was not population based. One centre (Helsinki) carried out the survey as an administered questionnaire by phone, but results are still included (see Fig. 1).

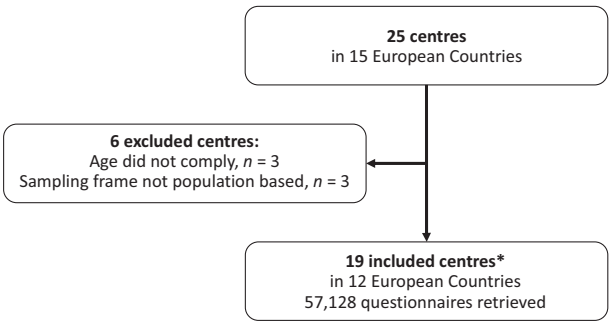

Figure 1 Selection of centre affiliated participants for statistical analysis. *One centre (Helsinki) carried out the survey as an administered questionnaire by phone but results are still included.

Therefore, this paper presents information from 19 centres in 12 countries. Table 1 shows the response rate for each centre, demographic information of the sample studied, and the age–sex standardized prevalence of CRS in each participating centre.

Response rates varied from a minimum of 23.2% in Duisburg, Germany to a maximum of 80.3% in Skopje Macedonia, and in all 57 128, questionnaires were returned with information on the presence of CRS. Some questionnaires were incomplete concerning variables for statistical analysis, and missing were 6.9% for smoking exposure (pack years), 1.5% for smoking status, 0.6–1% for rhinosinusitis symptoms, and 0.6% for self-reported physician-diagnosed CRS.

Limited information was available from eight centres on the age and gender of those who were sampled but did not return a completed questionnaire. In these eight centres, there

Table 1 Response rate and prevalence of chronic rhinosinusitis (CRS) defined by EP^{3}OS criteria in all participants and in lifetime nonsmokers (directly standardized to European population)

		Response*						Prevalence of self-reported CRS by EP^{3}OS criteria		
								All		Non smoker only
Country	Centre	*n/N*	RR†	Info on nonresponders*	Median age (IQR)	% male	% smoker	%	95%CI	%
Sweden	Gothenburg	8619/15 000	57.5	Age3, sex	42.9 (29.8–57.7)	44.9	16.1	8.3	7.7–8.9	7.0
	Stockholm	5887/10 000	58.1	YOB3, sex	43.1 (31.2–57.4)	45.8	16.7	9.6	8.9–10.4	8.1
	Umea	6055/10 000	60.6	YOB3, sex	42.6 (28.0–57.8)	46.0	9.8	8.1	7.4–8.8	7.0
	Uppsala	6114/10 000	61.1	YOB3, sex	43.2 (29.0–58.1)	45.0	13.0	8.6	7.9–9.4	7.3
Finland	Helsinki	1809/5510	32.8	–	41.0 (28.5–58.5)	47.3	26.4	6.9	5.7–8.2	4.3
Denmark	Odense	3340/5000	66.8	–	46.6 (34.0–59.2)	46.9	26.2	7.9	6.9–8.9	5.6
Poland	Katowice	2672/6000	44.5	Age, sex	44.8 (29.5–58.0)	45.9	30.8	17.3	15.9–18.9	14.2
	Krakow	1267/5000	25.3	–	44.9 (29.2–58.6)	41.4	23.5	19.7	17.5–22.1	18.6
	Lodz	1772/5000	35.4	–	48.8 (31.4–59.0)	44.6	27.6	14.4	12.7–16.2	10.2
UK	London	1825/5000	36.5	–	45.8 (35.3–57.7)	41.7	17.2	10.0	8.5–11.7	8.2
	Southampton	1191/5000	23.8	–	50.0 (37.1–61.3)	43.2	20.4	11.2	8.8–14.3	7.8
Netherlands	Amsterdam	3191/5000	63.8	–	48.8 (37.4–59.6)	45.3	20.7	14.3	12.9–15.8	12.1
Belgium	Ghent	1851/4921	37.6	Age, sex	44.9 (31.3–57.2)	45.9	23.9	18.8	17.0–20.8	14.4
Germany	Brandenburg	2252/5552	40.6	YOB sex	48.2 (37.6–61.2)	44.2	25.3	6.9	5.8–8.2	5.3
	Duisburg	1158/5000	23.2	Age, sex	47.6 (35.5–61.0)	45.7	28.7	14.1	12.0–16.6	11.9
France	Montpellier	1385/5000	27.7	–	47.9 (34.2–58.3)	41.3	22.8	13.3	11.5–15.3	11.2
Macedonia	Skopje	3613/4500	80.3	–	39.4 (25.7–52.9)	46.0	37.8	8.2	7.3–9.1	6.8
Italy	Palermo	965/2500	38.6	–	39.3 (27.9–51.8)	37.2	23.2	10.9	9.0–13.2	10.2
Portugal	Coimbra	2162/4877	44.3	–	43.0 (32.1–57.2)	40.1	14.6	27.1	25.0–29.3	27.3
	All centres	57 128/118 860	48.0		44.4 (30.6–57.9)	44.8	20.1	10.9	10.6–11.2	9.3

Countries are grouped geographically north to south, with all centres within that country ordered north to south.
*Eight centres provided information on age, 3-year age range within which an individuals true age existed, year of birth or 3 year range within which a potential participant was born and sex (Age3 = 3 year age range for participants age, YOB = year of birth, YOB3 = 3 year range in which individual was born).
†Response rate.

was evidence that response rates were higher in women than in men (OR 1.45, 95% CI 1.41–1.50) and in older subjects ($OR_{15–44\ years}$ 1.00; $OR_{45–64\ years}$ 1.63 95% CI 1.57–1.69; $OR_{65+\ years}$ 1.82, 95% CI 1.72–1.92).

There was no evidence that those with disease were more likely to respond to the survey earlier than those without disease. The within-centre Somers' D of response date with respect to disease status for all centres combined was 0.03 (95% CI 0.01–0.05), indicating that diseased subjects, if anything, tended to respond later than nondiseased subjects in the same centre. This tendency was strongest in Duisburg and Coimbra (centre-specific Somers' D respectively 0.16 and 0.09).

Prevalence of CRS

There was substantial variation in the prevalence of CRS. Of the centres studied, the median prevalence was found in London and was 10.0% (95% CI 8.5–11.7%). The highest prevalence was in Coimbra (27.1%; 95% CI 25.0–29.3%), with the lowest limit of the 95% confidence interval well exceeding all other centre estimates. The three centres in Poland, Amsterdam, Ghent, Duisburg and Montpellier had prevalence rates significantly higher than the median value (10.0%). All centres in Scandinavia, with the exception of Stockholm, and the centres in Brandenburg and Skopje had prevalence rates significantly below the median value. The most striking within-country variation was that observed in Germany where the prevalence was 6.9% in Brandenburg (95% CI 5.8–8.2%) and 14.1% in Duisburg (95% CI 12.0–16.6%).

Prevalence of component symptoms of CRS

There was no evidence that the high prevalence of CRS in Coimbra was related to over-reporting of one particular symptom, nor that the lower prevalence in Scandinavian centres was related to underreporting of one particular symptom. In general, the geographical variation seen for CRS was seen for each component (Table 2).

Prevalence of self-reported physician-diagnosed CRS

The prevalence of self-reported physician-diagnosed CRS within centres was highly correlated with the prevalence of EP^3OS-diagnosed CRS (Pearson rho = 0.76, $P < 0.01$, Fig. 2). Moreover, the prevalence of self-reported physician-diagnosed CRS was, for all centres, lower than the prevalence of EP^3OS-defined CRS (Table 2). The prevalence of self-reported physician-diagnosed CRS was higher in the older age groups than in the youngest age group ($OR_{15–34}$ 1.00,

Table 2 Prevalences of component symptoms, self-reported doctor-diagnosed chronic rhinosinusitis (CRS) and CRS defined by EP^3OS criteria

				CRS symptoms defined by EP^3OS criteria [1]As percentage of total sample [2]As percentage of EP^3OS CRS cases							
				Blocked nose		Discoloured nasal discharge		Pain or pressure		Reduced sense of smell	
Centre	*N*	Self-reported doctor-diagnosed CRS (%)	Self-reported CRS by EP^3OS criteria (%)	1	2	1	2	1	2	1	2
Gothenburg	8619	2.0	8.3	12.7	87.7	6.8	59.1	7.5	58.0	5.7	45.5
Stockholm	5887	2.1	9.6	13.7	87.5	8.5	65.4	8.8	60.0	6.2	41.4
Umea	6055	1.1	8.1	13.2	90.3	6.2	54.5	6.9	57.4	5.6	41.4
Uppsala	6114	1.8	8.6	14.2	88.7	6.6	57.0	7.1	55.2	6.0	48.5
Helsinki	1809	7.7	6.9	12.8	84.3	6.5	60.3	6.0	50.4	6.1	49.6
Odense	3340	1.8	7.9	9.3	74.5	8.4	68.7	7.4	61.4	6.5	49.4
Katowice	2672	11.3	17.3	21.2	89.0	9.5	47.2	19.7	79.0	11.5	50.6
Krakow	1267	12.4	19.7	25.1	92.4	9.2	40.4	19.4	72.4	14.2	56.8
Lodz	1772	10.5	14.4	18.2	84.4	8.9	50.4	15.9	73.1	12.1	53.9
London	1825	3.4	10.0	10.1	77.0	9.0	68.5	13.0	77.5	7.7	53.4
Southampton	1191	3.1	11.2	8.7	67.2	9.3	76.2	12.9	68.0	8.4	50.8
Amsterdam	3191	3.3	14.3	16.3	87.1	11.0	65.7	11.4	65.2	9.2	50.9
Ghent	1851	7.2	18.8	21.1	86.7	13.8	63.6	14.3	62.7	13.3	59.4
Brandenburg	2252	4.6	6.9	8.7	83.0	7.0	66.0	7.0	64.7	5.2	47.1
Duisburg	1158	8.4	14.1	13.0	79.2	11.7	71.5	10.5	68.1	8.0	50.0
Montpellier	1385	9.3	13.3	15.0	76.4	17.1	84.7	14.7	64.5	8.1	40.4
Skopje	3613	10.7	8.2	8.3	77.4	7.7	71.7	8.2	56.6	5.6	45.5
Palermo	965	6.9	10.9	14.8	83.0	8.2	56.6	11.9	62.3	6.9	45.3
Coimbra	2162	18.1	27.1	22.1	70.7	32.4	87.8	28.2	77.6	17.8	51.9
All centres	57 128	5.0	10.9	14.0	83.7	9.2	63.6	10.4	64.7	7.6	48.5

Countries are grouped geographically north to south, with all centres within that country ordered north to south.

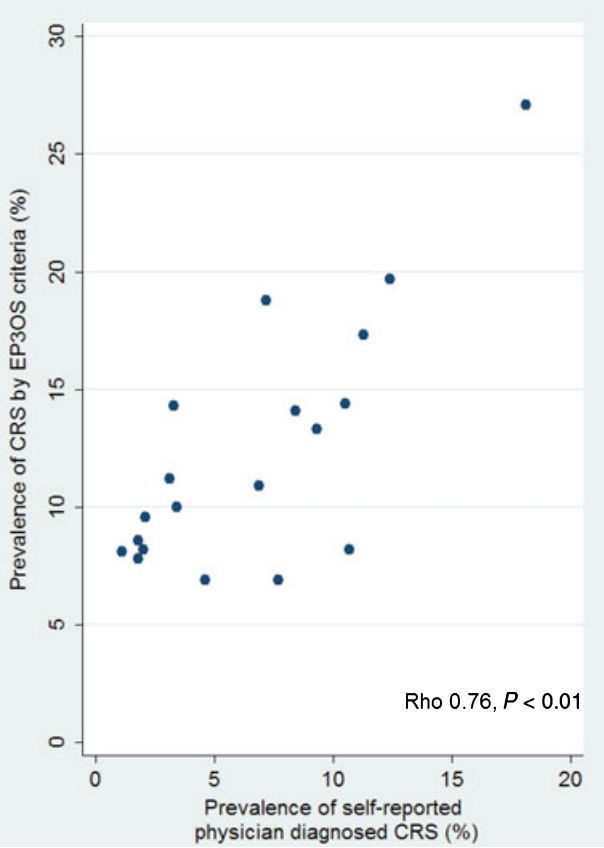

Figure 2 Correlation between prevalence of CRS as self-reported physician diagnosis and prevalence of CRS defined by EP^{3}OS criteria.

$OR_{35–54}$ 1.36 95% CI 1.24–1.50, $OR_{55–74}$ 1.37 95% CI 1.24–1.51, standardized for gender and smoking status.

Association of CRS with age and sex in lifetime nonsmokers

In lifetime nonsmokers, women were at a slightly greater risk of CRS than men (OR 1.20 95% CI 1.11–1.30), with some variation between centres (*P* for heterogeneity 0.05, I^2 38.3). This heterogeneity was largely because of a strong and highly significant association of CRS with being woman in Coimbra (OR 1.82 95% CI 1.39–2.37).

In lifetime nonsmokers, the prevalence of CRS was lower in participants above the age of 55 years compared with those below the age of 35 (OR 0.89 95% CI 0.81–0.98) with variation in the direction and strength of this association between centres (*P* for heterogeneity 0.004, I^2 52.2). No significant differences were observed between the age groups 35–54 and those below the age of 35 years.

When only lifetime nonsmokers were considered, the geographical variation in prevalence of CRS, reported earlier, was similar – that is, (i) Coimbra had the highest prevalence with the lower limit of the 95% confidence interval exceeding all other centres estimated prevalence, (ii) Scandinavian centres and centres in Brandenburg and Skopje had a low prevalence and (iii) all Polish centres and centres in Amsterdam, Ghent, Duisburg and Montpellier had a high prevalence of disease.

Association of CRS with age, sex and smoking in the entire sample

The prevalence of smoking varied from 9.8% in Umea Sweden to 30.8% in Katowice Poland (Table 1). When adjusted for age and sex (but not pack years of smoking), there was a small, but significant positive association of CRS with being an ex-smoker (1.28 95% CI 1.18–1.38) and a strong association with being a current smoker (1.91 95% CI 1.77–2.05). The strength of this latter association varied from centre to centre (*P* for heterogeneity $P < 0.0001$, I^2 79.2), but in all centres results were consistent with CRS being more common in smokers than in nonsmokers (Fig. 3). There was evidence that this relationship was dose-dependent, i.e., related to total number of pack years of smoking (Table 3). Participants who had 50 pack years of smoking were almost 50% more likely to report CRS than lifetime nonsmokers (OR 1.45 95% CI 1.23–1.70 *P* for heterogeneity 0.3 I^2 12.3).

Discussion

In this paper, we present for the first time results from a European multicentre study that has used a standardized definition of CRS to describe geographical variation in disease prevalence. Overall, about one in ten participants reported symptoms suggestive of the presence of CRS but there was

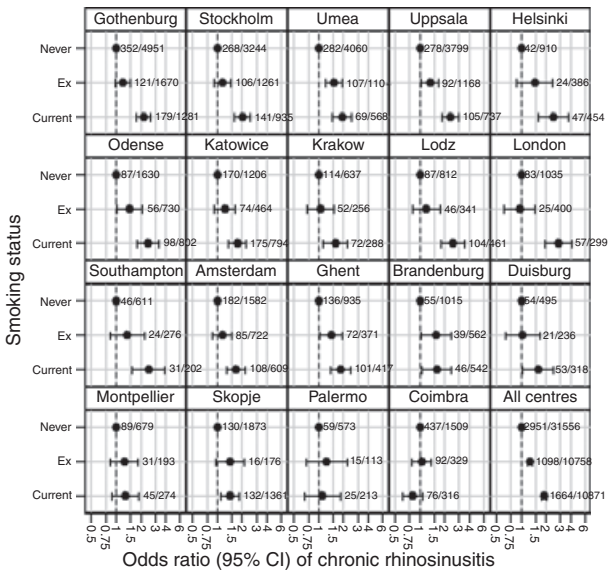

Figure 3 Adjusted odds of CRS with respect to smoking status in each centre and all centres. Smoking status (current, ex and never) was significantly related with CRS at the 0.05 level for all, except: Current *vs* never: Palermo, Montpellier, Coimbra. Ex *vs* current: Stockholm, Helsinki, Katowice, Krakow, Lodz, London, Southampton, Amsterdam, Duisburg, Montpellier, Palermo, Coimbra.

Table 3 Association of age, sex and smoking with prevalence of EP^{3}OS-defined Chronic rhinosinusitis in the entire sample

Risk factor	Cases/total			Tests for heterogeneity	
r	*I*	OR	95% CI	I^2	*P*
Gender					
Male	2457/23 701	1.00	Ref		
Female	3256/29 484	1.08	1.02, 1.15	24.6	0.16
10-year age group					
15–24	907/7910	1.00	Ref		
25–34	1164/10 161	0.93	0.84, 1.03	0.00	0.71
35–44	1062/9786	0.85	0.77, 0.94	11.5	0.31
45–54	1079/9604	0.81	0.73, 0.90	0.00	0.71
55–64	927/9509	0.65	0.58, 0.73	55.9	0.0016
65–74	574/6215	0.64	0.56, 0.73	28.5	0.12
Smoking status					
Never	2951/31 556	1.00	Ref		
Ex	1098/10 758	1.15	1.04, 1.28	33.9	0.075
Current	1664/10 871	1.70	1.55, 1.87	60.7	0.00031
Smoking exposure (pack years)					
25		1.19	1.07, 1.32	29.8	0.11
50		1.45	1.23, 1.70	12.7	0.3

substantial geographical variation with consistently low prevalence in the Scandinavian centres and Brandenburg, high in France and Poland and an isolated very high prevalence in Portugal. Disease was associated with smoking but smoking alone cannot explain the geographical variation of the disease.

To date, there have been few studies that have attempted to assess prevalence of CRS in population-based studies. CRS is difficult to study as the disease is difficult to define and diagnose. The EP^{3}OS group has proposed clear guidelines on the definition of rhinosinusitis that can be used for epidemiological and clinical research (9). The EP^{3}OS definition was the basis for the questions used in the GA^{2}LEN questionnaire. Previous work has shown this definition to have a reasonable reproducibility and correlation with endoscopic findings and should therefore be sufficiently reliable for use in epidemiological surveys (15). Furthermore, it has the advantage of not varying with local diagnostic practice and health service provision.

In large population-based surveys, prevalence estimates may be falsely high (or low) if those who take part in the survey differ substantially from those who do not take part. This is a particular problem if those with disease are more (or less) likely to respond than those without disease. Various methods have been used to assess responder bias but none are consistently better than any other (16). In some centres, data protection regulations and ethical permissions permit information on the age and gender of those who do not respond to be made directly available to researchers. In these centres, there was some evidence that response to the survey was higher amongst women and older participants, with the gender difference becoming less marked in the older age groups. Although such response bias is problematic, geographical comparisons between centres have been made following direct standardization to the European population, and therefore, such differences in response should have little direct influence on the conclusions drawn from our report. Knowing whether those with disease are more or less likely to respond is a more difficult problem, and the method we have used is to measure the tendency of diseased subjects to respond earlier (or later) than that of nondiseased subjects when mailed by the survey organizers. Within each centre, we found no clear tendency for diseased subjects to respond faster or slower than nondiseased subjects, suggesting that prevalence estimates are less likely to be biased by differential response between the two groups. Also, we did not translate the questionnaire in languages of ethnic minority groups, so these data are derived from subjects who are able to read the language spoken in the country.

The overall European CRS prevalence was estimated at 10.9%. The few studies available in the world show varying figures from 1% in Korea (based on symptoms and endoscopy) (7) to 14% in the USA (based on self-reported physician-diagnosed acute or chronic disease) (5). The only data available from Europe are from a very small sample of Belgian patients who were scanned for intracranial disease and of whom 6% complained of purulent discharge, 19% complained of nasal obstruction, and 40% had abnormalities on their MRI suggestive of CRS (8). That study was is in concordance with other MRI and CT studies, suggesting about 40% of those undergoing these investigations had abnormalities suggestive of CRS, showing a very poor correlation of symptoms with abnormalities on CT or MRI (17–19).

Differences were seen in the prevalence of CRS between countries, as well as between centres within the same country. Large differences were seen between North Europe and Central or South Europe, with on the whole, lower prevalence estimates in the Northern Scandinavian centres. This supports data from Canada and the USA where there is some evidence that CRS is more prevalent in the (warm) south than in the (colder) north (6).

The highest prevalence of CRS was seen in Coimbra-Portugal, 27.1%. At present, we have no explanation for this. As in other centres, participants were randomly selected from a population-based sampling frame. The response rate was lower than in Scandinavia but there is no information on the nonresponders. There was little evidence of response bias looking at the time taken to return completed questionnaires. The same area was investigated previously, and the prevalence of rhinitis was 26.1% based on the presence of at least two of the following symptoms: sneezing, itchy nose or blocked nose or runny nose without having a cold or the flu (20). More over, in a pan-European study, which examined outpatients attending allergy centres, participants in Coimbra had a relatively high prevalence of sensitization to both indoor and outdoor allergens, the latter being associated with a high prevalence of perennial allergies (21). In Coimbra, the prevalence of smoking was lower than in some other centres, and the overall association of CRS with smoking in this centre was not significant (although compatible with the overall association of CRS with smoking).

We have observed substantial within country differences of CRS prevalence (for example, in Germany, a prevalence of 14.1% in Duisburg compared with that of 6.9% in Brandenburg). The prevalence of smoking in both centres is similar, and the geographical differences are seen even amongst the nonsmokers, so other factors are likely to explain these differences. Brandenburg is a rural area just outside the city of Berlin. Many of the older participants were likely to have been brought up in the former East Germany (Germany Democratic Republic) and stark differences in disease prevalence have been described between children and adults from former East and West Germany (22). To date, no single factor has been identified to explain differing health status of the two populations although several have been proposed. We are aware also that air pollution levels [a potential risk factor for patients with nonallergic, noninfectious perennial rhinitis (23) and to a lesser extent to CRS(24)] are very different between the two sampled areas, Duisburg being a highly industrialized city with a sizeable steel industry and, in the past, coal industry.

The applied diagnosis for CRS in the survey was based on symptoms. Patients with allergic rhinitis may report similar symptoms, although facial pain/pressure is not generally considered a symptom of allergic rhinitis (AR) and was seen in 65% of CRS-EP^{3}OS positives. Accordingly, in a previous study, it was demonstrated that the correlation between symptomatic CRS diagnosis and self-reported doctors diagnosis remains significant in people with and without AR (15).

We have shown that CRS was more prevalent in women, confirming earlier data from the US National Health Interview Survey (NHIS) (5) and Canada (6). The prevalence of CRS was lower in older subjects than in younger subjects. This differs from an earlier report from Canada showing an increase from 20–60 years of age and a small decline afterwards. In the Canadian study, participants were asked 'Did your doctor ever tell you that you suffer from sinusitis?', and they may have answered positively if they only had 'acute rhinosinusitis'. Within our study, CRS was least prevalent in younger age groups. In cross-sectional studies, it is not possible to distinguish between the effects of ageing and factors that have different effects on people born at different times, so-called birth cohort effects. Birth-cohort effects have been demonstrated in atopic sensitization with those born later in the century having a higher risk of sensitization and in smoking-related diseases such as lung cancer. Either of these may explain the lower prevalence of disease in the older age groups.

The most striking observation within our data was the strong, and consistent association of CRS with smoking showing evidence of a dose–response relationship (increasing disease with increasing pack years smoked). Although there was striking variation in the prevalence of disease between countries, this was not explained by differences in reported smoking, as the geographical variation was seen amongst nonsmokers also. This is the first multicentre, European study to show that smokers have an increased risk of CRS. An association of CRS with smoking was seen in the Canadian study but not in another study in Korea. Our data strongly suggest that smoking cessation may be an important therapeutic option for those with CRS.

In conclusion, results from a European international multicentre study show that CRS is a prevalent disease in Europe with an overall prevalence of 10.9% and differences between countries ranging from 6.9 to 27.1%. Considering the significant direct medical costs and its impact on lower airway disease, there is an urgent need for further evaluation of different aspects of this disease.

Funding

This study was conducted as part of Workpackage 1.2.1 of the Global Allergy and Asthma European Network (GA^{2}LEN) funded through the Sixth European Union Framework program for research, contract no. FOOD-CT-2004-506378.

Conflict of interest

HD, FWJ, JD, NRB: data analysis, drafting of manuscript. FWJ, BP, JD: study conception, supervision. All authors: data acquisition, critical revision of manuscript.

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Appendix

Appendix 1. GA^{2}LEN Screening Survey.

	Yes	No
8. Has your nose been blocked for more than 12 weeks during the last 12 months?	☐	☐
9. Have you had pain or pressure around the forehead, nose or eyes for more than 12 weeks during the last 12 months?	☐	☐
10. Have you had discoloured nasal discharge (snot) or discoloured mucus in the throat for more than 12 weeks during the last 12 months?	☐	☐
11. Has your sense of smell been reduced or absent for more than 12 weeks during the last 12 months?	☐	☐
12. Has a doctor ever told you that you have chronic sinusitis?	☐	☐