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ORIGINAL RESEARCH

Clinical Remission of Asthma and Allergic Rhinitis - in a Longitudinal Population Study

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Background: Although asthma and allergic rhinitis are chronic diseases, some patients experience periods of remission. Information on prognostic factors associated with the remission of asthma and allergic rhinitis is valuable in resource prioritization. This study investigated factors associated with the clinical remission of asthma and allergic rhinitis.

Methods: In the Respiratory Health In Northern Europe (RHINE) study, data was collected with questionnaires in stage one (RHINE I, 1989–1992) and two follow-ups (RHINE II, 1999–2001 and RHINE III, 2010–2012) from Sweden, Norway, Denmark, Iceland and Estonia. Clinical remission was defined as having reported asthma or allergic rhinitis in RHINE I or RHINE II but not in RHINE III.

Results: Of 13,052 participants, 975 (7.5%) reported asthma in RHINE I or RHINE II, and 3379 (25.9%) allergic rhinitis. Clinical remission of asthma and allergic rhinitis was found in 46.4% and 31.8%, respectively. Living in Estonia (OR (95% CI) 2.44 (1.22–4.85)) and living in an apartment (1.45 (1.06–1.98)) were related to remission of asthma, while subjects reporting allergic rhinitis (0.68 (0.51–0.90)), asthma onset ≤ 12 years of age (0.49 (0.35–0.68)), receiving treatment with antibiotics for respiratory illness (0.64 (0.47–0.87)) were less likely to have asthma remission. Factors related to a higher likelihood of remission of allergic rhinitis were no asthma at baseline, age ≥ 58 years in RHINE III, allergic rhinitis onset after 12 years of age, living in rural areas as a child, having only a primary school education and not being pregnant.

Conclusion: Clinical remission was found in almost one-half of those with asthma and one-third of persons with allergic rhinitis. Coexisting allergic symptoms were associated with less clinical asthma remission. Age, asthma symptoms and environmental factors in childhood, such as living in a rural area, were found to influence the clinical remission of allergic rhinitis.

Keywords: asthma, allergic rhinitis, remission, epidemiology

Introduction

The prevalence of asthma and allergic rhinitis in adults ranges between 4–9%[1–4] and 20–30%, respectively.[2,3] Asthma and allergic rhinitis significantly impact public health since they are common diseases closely associated with decreased quality of life[1,2] and impaired sleep.[3,4] Both disorders are often associated with IgE sensitization and type-2 inflammation.[5]

Although asthma and allergic rhinitis are chronic diseases, some patients experience periods of remission. Clinical remission of asthma occurred in 20–43% of patients followed during 10–30 years,[6–9] while remission of allergic rhinitis

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has occurred in up to 25% of the patients in previous studies.[6,7] Factors associated with a higher possibility of remission of asthma are younger age,[8] milder disease,[8,10,11] smoking cessation,[10,12] shorter time since onset of asthma, and not having allergic rhinitis.[13] Remission of allergic rhinitis has been associated with the absence of IgE sensitization,[14] older age, and not having asthma symptoms at baseline.[7] Most studies have not shown any significant difference by sex regarding remission of asthma or allergic rhinitis. However, one recent study indicated that women were less likely to have an asthma remission.[15]

Information on prognostic factors associated with remission of asthma and allergic rhinitis is valuable in resource prioritization in the early stages of medical care. Few studies focus on adult patients with clinical remission of asthma and allergic rhinitis. The current study aimed to investigate factors related to clinical remission of asthma and allergic rhinitis using data from a large general population sample in Northern Europe.

Methods

Population

This study population is from the Respiratory Health In Northern Europe (RHINE) study, a longitudinal survey with randomly selected subjects from Sweden (Uppsala, Umea, Gothenburg), Norway (Bergen), Iceland (Reykjavik), Estonia (Tartu) and Denmark (Aarhus). The population participated in stage one of the European Respiratory Health Survey (ECRHS) (1989–1992, also called RHINE I for the Northern European study centers) and the two follow-up questionnaire studies in 1999–2001 (RHINE II) and 2010–2012 (RHINE III).[16,17] The participants were 20–44 years old in RHINE I, 30–54 years old in RHINE II and 38–66 years old in RHINE III.[16,17] Of the 21,595 that participated in the first survey 16,049 (74.3%) participated in RHINE II and 13,093 (60.6%) in RHINE III.[17] The present analyses included 13,053 participants where information on remission on asthma and allergic rhinitis was available (Figure 1).

Ethics

The study complies with the declaration of Helsinki. Informed consent was obtained from each participant. The study was approved by The Regional Committees for Medical and Health Research Ethics West in Norway (2010/759), the National Bioethics Committee in Iceland (VSN-11-121), the Research Ethics Committee of the University of Tartu in Estonia (209T-17 and 225/M-24), The Regional Ethical Review Board in Uppsala, Sweden (1990/257, 1998/495 and 2010/068) and the Scientific Committees for Central Jutland in Denmark (M20110106).

Questionnaires

In RHINE I, subjects answered questions about asthma symptoms in the past 12 months; wheezing, nocturnal asthma symptoms, asthma attacks, current asthma medication, and allergic rhinitis.

The questionnaire in the first follow-up in 1999–2001 (RHINE II) consisted of the same questions as given in RHINE I with the addition of questions such as weight, height, smoking history, age of asthma onset, seasonal rhinitis,

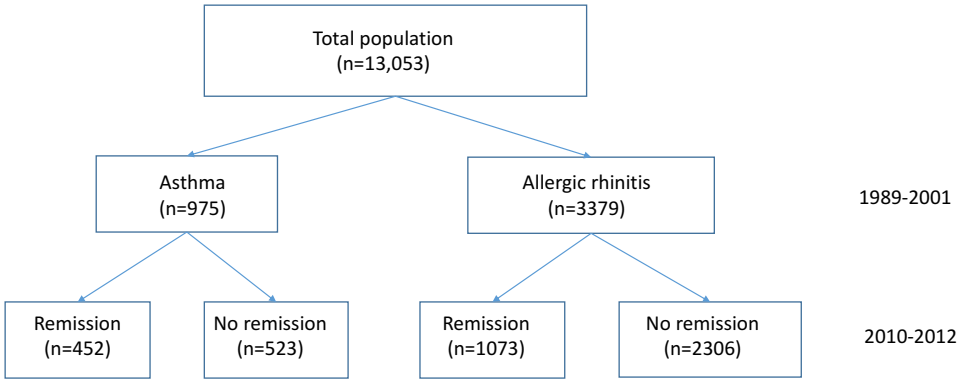

Figure 1 Study flow and number of participants with and without a clinical remission of asthma and allergic rhinitis.

age of allergic rhinitis onset, accommodation, employment, diet, infections, antibiotics, childhood and family history, parents' educational level, sleep and daytime symptoms, comorbidity, and women-specific questions (pregnancy, periods, contraception methods, menopause).

The questionnaire used in the second follow-up in 2010–2012 (RHINE III) were almost identical to the one used in RHINE II. It included additional questions regarding smoking habits, asthma history and chronic obstructive pulmonary disease, sinusitis, indoor and outdoor environment, marital status, participants' educational level, work, childhood and family, comorbidity, sleep and daytime symptoms, and general symptoms of health and exercise.

Definitions

Asthma was defined as an affirmative answer to either "Have you had an attack of asthma in the last 12 months?" or "Are you currently taking any medicine (including inhalers, aerosols or tablets) for asthma?". Allergic rhinitis was defined as an affirmative answer to "Do you have any nasal allergies, including hay fever?".[18]

Clinical remission of asthma was defined as an affirmative answer to having an asthma attack in the last 12 months or taking asthma medication in either RHINE I or RHINE II and a negating answer to both questions in RHINE III. Clinical remission of allergic rhinitis was defined as an affirmative answer to having allergic rhinitis in either RHINE I or RHINE II and a negating answer to having allergic rhinitis in RHINE III.

Persistent rhinitis was defined as an affirmative answer to the question "Have you ever experienced nasal symptoms such as nasal congestion, rhinorrhea (runny nose) and sneezing attacks without having a cold?" and answering "always" to "At which time of the year are your nasal symptoms worst?". Subjects that reported nasal symptoms that were worst during spring or summer were defined as having seasonal rhinitis.

Asthma symptoms over the past 12 months included an affirmative answer to either of the following questions "Have you had wheezing or whistling in your chest at any time in the last 12 months?"; "Have you woken up with a feeling of tightness in your chest at any time in the last 12 months?"; "Have you been woken by an attack of shortness of breath at any time in the last 12 months?" and "Have you been woken by an attack of coughing at any time in the last 12 months?".

Smoking status was defined based on the smoking history (never, ex-, and current smoker), cigarettes/week, years of smoking, and a change in smoking habits between RHINE II and III. Environmental tobacco smoke was defined as tobacco smoke taking place in the present home (RHINE II) and if any parent or others were smoking regularly during the participants' childhood (RHINE III).

Educational levels ranged from primary school to lower or upper secondary school to technical school to college or university.

Variables Included in the Analysis

Remission of asthma and allergic rhinitis were analyzed in relation to the following data from 1999–2001 (RHINE II): age, asthma symptoms the past 12 months, asthma and age of onset, allergic rhinitis and age of onset, persistent rhinitis, body mass index (BMI), hypertension, cardiac disease, diabetes, snoring, gastroesophageal reflux, tobacco smoke in present home, smoking history, number of respiratory infections the past 12 months, hospitalization due to airway/respiratory illness after the age of 2 years, treatment with antibiotics the past 12 months, parents' educational level, mothers age at the subject's birth, childhood infections such as repeated otitis, pets at home as a newborn or child, and for women remission were also analyzed regarding pregnancy, contraception methods, and menopause. Following additional data were collected and analyzed from 2010-to 2012 (RHINE III): living in towns or rural areas at age under five years, subjects' educational level, sleep apnea, ulcerative colitis, Crohn's disease, occupation as painter or cleaner, smoking habits, tobacco smoke by anyone at home during the subject's childhood, biological parents with asthma, exercise, and any serious respiratory infection before the age of five. All the variables were analyzed, and those shown significant were presented in the tables. Each variable found significant was separately adjusted for age, sex and centre.

Statistical Methods

The analyses included all participants who answered affirmative to asthma and allergic rhinitis questions in RHINE I or II and answered the same questions in RHINE III. The statistical software used was STATA version 13.1 (Stata Corp,

College Texas, US). Chi-squared test was used for bivariable analyses of categorical variables and *t*-test for continuous variables. Binomial logistic regression was used to calculate the adjusted odds ratio (aOR). Centre, age and sex were obligatory in the logistic regression models. A p-value <0.05 was considered statistically significant. Apart from centre, age and sex, the tables only include the variables significantly associated with remission of asthma and allergic rhinitis.

Results

A total number of 13,053 subjects, 975 (7.5%) with asthma and 3379 (25.9%) with allergic rhinitis, 5% with both, in either RHINE I or II formed the study population (Figure 1). In total, 452 (46.4%) and 1073 (31.8%) had clinical remission of asthma and allergic rhinitis in RHINE III, respectively (Figure 1). Of those with remission of asthma 168 had asthma only in RHINE I, 207 only in RHINE II and 77 in both, the corresponding figures for remission of rhinitis were 437, 384 and 252, respectively.

Geographical Differences

The highest proportion of participants with clinical remission of allergic rhinitis was found in Tartu (42.7%) and Reykjavik (40.6%). Tartu also had the highest percentage of clinical asthma remissions (67.5) (Table 1).

Age and Sex

The highest proportion of participants with clinical remission of allergic rhinitis was found in the oldest age group (≥58 years) (36.3%), whereas no statistically significant age-related differences were found for asthma remission (Table 2). There were no statistically significant differences by sex for clinical remission of asthma or allergic rhinitis.

Multivariable Analysis of Asthma Remission

In the multiple variable analyses, living in Tartu, Estonia was independently associated with a higher likelihood of asthma remission than participants living in Sweden (aOR (95% CI) 2.60 (1.28–5.28) (Figure 2). Participants residing in an apartment were also more likely to have a clinical asthma remission.

Decreased likelihood of clinical remission was found at the occurrence of asthma symptoms at any time in the past 12 months, allergic rhinitis in RHINE I or II, the onset of rhinitis ≤ 12 years of age, the onset of asthma ≤ 12 years of age, heredity for asthma, and receiving treatment with antibiotics for respiratory illness the past 12 months (RHINE II) (Table 3). There was no significant association between asthma remission and smoking, environmental tobacco smoke in the present home (RHINE II) or during childhood, BMI, comorbidities, environmental factors in childhood or hormonal status in women (data not shown).

Table 1 Numbers and Proportion of Participants That Had Clinical Remission in the Different Centres in 2010–2012

		Participants with Remission Asthma (%)	p-value	Participants with Remission Allergic Rhinitis (%)	p-value
Centre	Aarhus	67 (46.2)	0.055	131 (25.7)	<0.0001
	Reykjavik	62 (49.2)		196 (40.6)	
	Bergen	64 (43.8)		140 (27.0)	
	Gothenburg	70 (51.9)		142 (30.9)	
	Umea	89 (41.4)		161 (30.9)	
	Uppsala	95 (43.5)		158 (28.8)	
	Tartu	13 (67.5)		145 (42.7)	
Whole population		452 (46.4)		1073 (31.8)	

Table 2 Numbers and Proportion of Participants That Had Clinical Remission in Relations to Age

		Participants with Remission Asthma (%)	p-value	Participants with Remission Allergic Rhinitis (%)	p-value
Age 2010–2012 (all)	<45	102 (50.0)	0.41	177 (26.0)	<0.0001
	45–51	116 (45.7)		231 (27.0)	
	52–57	93 (43.3)		234 (32.5)	
	≥58	102 (42.7)		263 (36.3)	
Age 2010–2012 (women)	<45	59 (50.9)	0.37	106 (28.1)	0.009
	45–51	61 (41.5)		128 (27.8)	
	52–57	51 (41.1)		130 (34.6)	
	≥58	58 (42.3)		155 (36.6)	
Age 2010–2012 (men)	<45	43 (48.9)	0.67	71 (23.4)	0.003
	45–51	55 (51.4)		103 (26.0)	
	52–57	42 (46.2)		104 (30.2)	
	≥58	44 (43.1)		108 (36.0)	

Multivariable Analysis of Allergic Rhinitis

Participants living in Tartu and Reykjavik had a higher likelihood of allergic rhinitis remission than those living in the Swedish centres (aOR (95% CI) 1.78 (1.40–2.27) and 1.56 (1.26–1.93), respectively (Figure 2). Other factors related to a higher likelihood of clinical remission of allergic rhinitis were age ≥ 58 years in RHINE III, persistent and ex smoking, allergic rhinitis onset after 12 years of age, diabetes mellitus, having a cat at home as a newborn, living on a farm or in rural areas as a child and having no more than primary school education. Factors related to a lower likelihood of clinical remission of allergic rhinitis were coexisting asthma in RHINE I or RHINE II, pregnancy and having woken up with a feeling of tightness in the chest (RHINE II) (Table 4). There was no significant association between clinical allergic rhinitis remission and BMI, type of dwelling or hereditary asthma factors (data not shown).

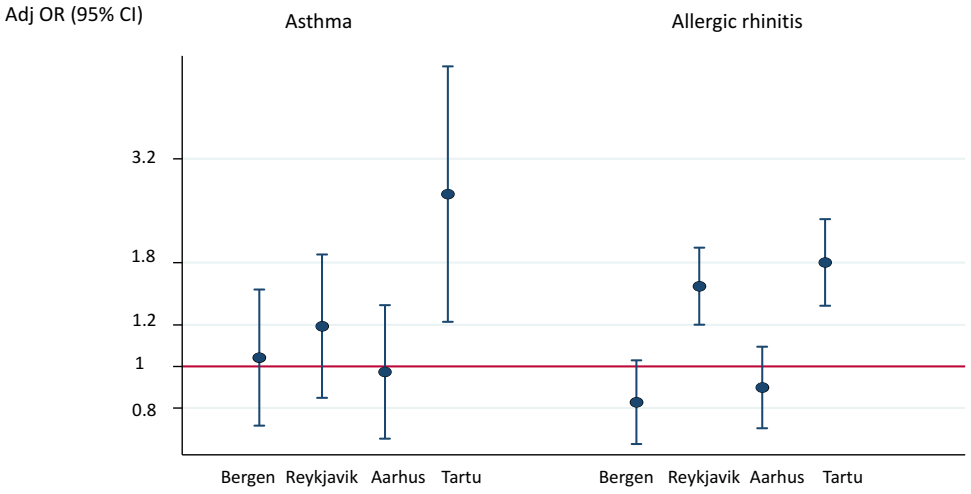

Figure 2 The difference in remission of asthma and allergic rhinitis was expressed as an adjusted odds ratio with a 95% confidence interval with the three Swedish centres as reference.

Table 3 Factors Related to Remission of Asthma (% and Adjusted Odds Ratios (aOR))

		Remission Asthma			aOR (95% CI)[¶]
		Yes	No	p-value	
Sex	Female	54.7	59.3	0.145	–
Rhinitis	Allergic rhinitis 1990 or 2000	65.1	73.0	0.008	0.68 (0.51–0.90)
	No rhinitis	34.9	27.0	0.027	1
	Persistent rhinitis	13.8	12.4		0.86 (0.57–1.32)
	Seasonal rhinitis	25.8	31.8		0.63 (0.45–0.88)
Onset	Rhinitis onset age ≤12 years	27.0	34.0	0.049	0.67 (0.47–0.95)
	Asthma onset age ≤12 years	15.3	26.2	<0.0001	0.49 (0.35–0.68)
Have or ever had	Ulcerative colitis	1.1	3.2	0.034	0.39 (0.14–1.07)
Symptoms at any time the last 12 months	Wheezing or whistling in the chest	60.4	82.2	<0.0001	0.32 (0.24–0.44)
	Woken up with a feeling of tightness in the chest	30.1	47.1	<0.0001	0.48 (0.36–0.63)
	Woken by an attack of shortness of breath	13.4	23.1	<0.0001	0.51 (0.35–0.73)
	Woken by an attack of coughing	41.6	50.1	0.010	0.74 (0.56–0.97)
Antibiotics	Treatment with antibiotics last 12 months for respiratory illness	25.3	33.0	0.012	0.64 (0.47–0.87)
Heredity	None of biological parents with asthma	77.3	69.3	0.003	1
	One biological parent with asthma	22.5	28.5		0.71 (0.51–0.97)
	Both biological parents with asthma	0.3	2.3		0.10 (0.01–0.80)
Dwelling	Detached house	39.2	46.0	0.048	1
	Semidetached or terrace house	16.3	17.5		1.08 (0.74–1.59)
	Apartment	41.4	32.5		1.45 (1.06–1.98)
	Other	3.1	4.0		0.75 (0.35–1.64)

Abbreviation: [¶]aOR, adjusted for centre, age and sex.

Discussion

The study's main finding is that almost half of the participants that reported having asthma and a third of those reporting allergic rhinitis did not do so in 2010–2012. We found that participants living in Tartu, Estonia, were more likely to have clinical remission of asthma and allergic rhinitis than participants from other countries in Northern Europe. In addition, a higher likelihood of asthma remission was also related to living in apartments. Factors related to a lower likelihood of asthma remission were early onset of asthma, allergic rhinitis in RHINE I or II, treatment with antibiotics for respiratory disease, and heredity of asthma. As for allergic rhinitis, factors associated with a higher likelihood of remission were older age, smoking, having a cat at home as a newborn, allergic rhinitis onset after 12 years of age, and living on a farm or a rural area as a child. Nocturnal asthma symptoms, asthma in RHINE I and/or II, higher educational level, and pregnancy-related factors related to a lower likelihood of allergic rhinitis remission.

Asthma and Rhinitis

In our study, participants with allergic rhinitis in RHINE I or II were found to have less clinical remission of asthma in RHINE III; this is in accordance with the results of several previous studies.[13,19] We also found that having fewer asthma

Table 4 Factors Related to Remission of Allergic Rhinitis (% and Adjusted Odds Ratios (aOR))

		Remission Allergic Rhinitis (%)			aOR (95% CI)[¶]
		Yes	No	P-value	
Sex	Female	57.1	54.9	0.234	–
Asthma	Asthma 1990 or 2000	14.1	22.2	<0.0001	0.60 (0.49–0.73)
Onset	Rhinitis onset >12 years of age	94.2	74.2	<0.0001	5.31 (4.03–7.00)
Smoking history and change in habit between RHINE II & III	Never smoked	43.4	52.8	<0.0001	1
	Ex-smoker	25.7	22.9		1.25 (1.02–1.53)
	Quit smoking	12.6	10.4		1.42 (1.09–1.84)
	Persistent smoker	12.4	8.9		1.62 (1.23–2.13)
	Started smoking	6.0	5.0		1.29 (0.90–1.87)
Comorbidity	Hypertension	9.6	6.3	0.001	1.33 (1.00–1.76)
	Diabetes	2.2	1.0	0.006	2.06 (1.12–3.79)
Symptoms at any time the last 12 months	Woken up with feeling of tightness in the chest	13.5	19.5	<0.0001	0.61 (0.49–0.75)
Educational level patient	Primary school	12.6	8.1	<0.0001	1.63 (1.26–2.11)
	Lower or upper secondary school, or technical school	41.8	37.6		1.28 (1.09–1.50)
	College or university	45.6	54.2		1
Pet at home newborn	Cat	19.8	15.5	0.004	1.37 (1.10–1.70)
Place lived in most of the time when age under 5 years	Farm/Rural area	31.0	25.9	0.002	1.28 (1.07–1.52)
	Town/city	69.0	74.1		1
Specific for women	Pregnancy	1.5	3.6	0.014	0.46 (0.21–1.00)
	Menopause	14.9	11.0	0.024	1.18 (0.83–1.68)

Abbreviation: [¶]aOR, adjusted for centre, age and sex.

symptoms and not being treated with antibiotics for respiratory illness (RHINE II) were associated with a higher likelihood of having a clinical asthma remission in RHINE III. These results are in accordance with studies finding a correlation between milder diseases and a higher rate of clinical remission of asthma.[8,10,11]

Participants that reported waking up with a feeling of tightness in the chest in RHINE II did not have clinical remission of allergic rhinitis in RHINE III as often as those who did not have the same symptoms. This is in accordance with a study by Nihlen et al reporting that those with asthma symptoms in the past 12 months did not go into clinical remission of allergic rhinitis as often as those who did not have these symptoms.[7]

That we find that allergic rhinitis decrease the possibility of remission of asthma and that asthma symptoms decrease the chance of a remission of rhinitis is not surprising. Asthma and allergic rhinitis are often referred to as united airway diseases since inflammation in the upper respiratory tract usually coexists with inflammation in the lower respiratory tract. The upper and lower respiratory tract symptoms are also closely coupled.[20]

Heredity

Participants with parental asthma had a lower frequency of clinical remission. It is known that children with parental asthma have a higher risk of developing asthma.[21] Several genes have also been implicated in asthma heredity.[22] However, genetic findings explain only a minor part of the prevalence of asthma.[23,24]

Smoking

In the present study, those that continued to smoke between RHINE II and III and ex-smokers were more likely to show clinical remission of allergic rhinitis than those who never had smoked, ex-smokers, and those who quit smoking between the surveys showed a higher likelihood. This is partly in accordance with the results from two previous studies.[14,25] Our results might be explained by definition "healthy smokers", suggesting that the subjects' smoking habits might reflect other factors such as symptoms and other health issues.[25,26]

Allergy, Childhood Environment and Geographical Location

Previous studies show that atopic subjects are less likely to have a remission of asthma than non-atopic.[25] In line with this, we found that having seasonal rhinitis was associated with a lower chance of asthma remission. This role of atopy is supported by our findings that participants who grew up on farms or rural areas were more likely to have a clinical remission of allergic rhinitis than those living in towns and that clinical remission of asthma was higher in Estonia than in Sweden. Several studies have shown that children living on a farm have a lower risk of atopy[27,28] and that the prevalence of atopy is lower in Estonia than in Sweden.[29] A combination of environmental and genetic factors could also explain why a higher clinical remission rate of allergic rhinitis was found in Estonia and Iceland than in the other Nordic countries.

Strengths and Limitations

The strengths of our study include its longitudinal design and the high number of participants. Another advantage is that we have multi centers data from different countries. Also, clinical asthma remission was defined as other authors have done.[9] A limitation of our study is that it is based on self-reported information and because we have had no access to medical records we have not been able to confirm the diagnoses and we also lack information about specific treatment for asthma and allergic rhinitis. Another limitation is that every variable is adjusted for only age, sex and centre, and other factors may correlate to the associations. In addition to this, we do not have data on lung function and inflammation, which is generally considered important in defining asthma remission. We also have a loss of subjects in the follow-ups, but a previous analysis indicates that this probable has not influenced our result greatly.[16]

Clinical Implications and Conclusion

The clinical implications of our study are that clinical remission of both asthma and allergic rhinitis are relatively common. This may have particular relevance when meeting patients with mild symptoms and suggest that down titration of treatment or even stopping treatment may be indicated in some patients.

In conclusion, many participants were found to have clinical remission of asthma and allergic rhinitis after 10–20 years. The severity of asthma and coexisting allergic symptoms decreased the likelihood of a clinical asthma remission. As for allergic rhinitis, environmental factors in childhood, age and asthma symptoms influenced the likelihood of clinical remission.

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Disclosure

The authors report no conflicts of interest in this work.

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