

Letter to the Editor

Chronic rhinosinusitis is rare but bothersome in adolescents from a Swedish population-based cohort

To the Editor:

Chronic rhinosinusitis (CRS) is common (around 10%) in adults¹ and has been shown to be associated with reduced quality of life.² No study has focused on adolescents specifically. Therefore we wanted to estimate the prevalence of CRS in adolescence and evaluate the burden of symptoms.

The Swedish population-based birth cohort Barn (Children), Allergy, Milieu, Stockholm Epidemiological Study (BAMSE) consists of 4089 children recruited at a mean age of 2 months, as previously described in detail.³ This study is based on 3112 children (76% from baseline) who participated at the 16-year follow-up (November 2010 to May 2013) and had completed the questions on CRS (see Table E1 in this article's Online Repository at www.jacionline.org). Everyone who fulfilled the criteria for CRS according to the European Position Paper on Rhinosinusitis 2007 (EP3OS)⁴ was contacted by telephone, and symptoms were affirmed by a structured interview (n = 48). The median time between questionnaire and telephone interview was 16 months.

Adolescents with ongoing symptoms (n = 27) were asked to participate in a clinical follow-up with nasal endoscopy,⁵ an olfactory threshold test (Sniffin' Sticks; Burghart Messtechnik GmbH, Wedel, Germany),⁶ and the Sino-Nasal Outcome Test 22 (SNOT-22), a disease-specific quality-of-life questionnaire.⁷ To compare their health-related quality-of-life (HRQoL) with that of the remaining participants of the BAMSE 16-year follow-up, the generic EQ-5D visual analog scale (VAS) was used.⁸ A flow chart of the study (see Fig E1 in this article's Online Repository at www.jacionline.org), a table of outcome definitions (see Table E2 in this article's Online Repository at www.jacionline.org), and descriptions of Sniffin' Sticks, SNOT-22, and the EQ-VAS are presented in the Methods section in this article's Online Repository at www.jacionline.org.

Nasal endoscopy was performed by 2 specialists in ear, nose, and throat diseases (M.W. and M.H.). Before application of topical anesthesia (naphazoline-lidocaine spray), inspection by means of anterior nasoscopy was performed, and afterward, endoscopy with a 0° rigid endoscope and, in some cases, fiberoptic endoscopy was performed. The estimate of the prevalence of CRS is presented in the Methods section in this article's Online Repository.

The χ^2 test of independence was used for comparison of dichotomous variables. A *P* value of less than .050 was considered statistically significant. EQ-VAS scores are presented as median values and 25th and 75th percentiles, and median values were compared with quantile regression. All analyses were conducted with STATA Statistical Software, version 13.1 (StataCorp, College Station, Tex).

Among the 3112 16-year-olds from the BAMSE birth cohort, 43.5% reported symptoms from the upper airways during the last 12 months, but only 1.5% (n = 48) reported symptoms of CRS (see Fig E2 in this article's Online Repository at www.jacionline.org). When the children's criteria from EPOS 2012 were used, the prevalence was 2.0% (n = 62). Forty-two (87.5%) of the 48 adolescents fulfilled both the adult's and children's criteria. At the time of the telephone interview, 27 of the 48 adolescents still

TABLE I. Adolescents with symptoms of CRS compared with those without symptoms of CRS regarding cofactors and HRQoL

	CRS symptoms (n = 22)		Without CRS symptoms (n = 3090)		<i>P</i> value
	No.	Percent	No.	Percent	
Cofactors					
Allergic rhinitis symptoms	12	57.1	815	28.1	.003
Asthma	5	25.0	332	11.0	.047
Cough ≥12 wk	3	13.6	103	3.4	.008
Eczema	3	14.3	250	8.3	.324
Sensitization*	9	50.0	1093	43.5	.577
Current smoking	2	9.1	371	12.0	.673
Current passive smoking	3	13.6	358	12.1	.830
Girls†	15	68.2	1565	50.7	.101
Low socioeconomic status‡	2	9.5	487	15.8	.431
HRQoL	Mean	Median	Mean	Median	
EQ-VAS	77	80	85	90	.024

*Among the 2547 adolescents with results from Phadiatop (Pharmacia, Uppsala, Sweden).

†Prevalence of CRS among girls versus boys was 1.0% versus 0.5% (*P* = .101).

‡For the household according to dominance (blue collar worker).

had ongoing symptoms of CRS (see Fig E1). After the clinical examination of 23 of these 27 adolescents, 22 still fulfilled the symptom criteria of CRS, corresponding to a prevalence of 0.8% (Table I). At clinical examination, endoscopic signs of CRS were found in 9 of the 23 adolescents, corresponding to a prevalence of 0.3%. None of the subjects had nasal polyps or enlarged adenoids or had undergone sinus surgery.

The 22 adolescents with CRS more often had allergic rhinitis symptoms (57.1% vs 28.1%, *P* = .003), asthma (25.0% vs 11.0%, *P* = .047), and cough for 3 months or longer (13.6% vs 3.4%, *P* = .008) compared with those without CRS (Table I). The median EQ-VAS score was lower compared with the rest of the population (80 vs 90, *P* = .024 and *P* = .052 after adjustment for sex; Table I and see Fig E3 in this article's Online Repository at www.jacionline.org). The mean SNOT-22 score was 38.2 among the 22 adolescents with symptoms of CRS and 44.2 among the 9 adolescents with endoscopic signs of CRS (Table II). The corresponding mean values for the olfactory threshold were 6.08 and 6.33, respectively.

In this Swedish population-based study of 3112 adolescents, we estimated the 12-month prevalence of CRS based on questionnaire to be 1.5% and that after clinical follow-up to be 0.3% to 0.8%. The adolescents with CRS more often had allergic rhinitis, asthma, chronic cough, and impaired HRQoL compared with those without CRS.

The estimation of prevalence leaves a window of interpretation. At the telephone interview, 13 subjects did not fulfill the criteria for CRS currently or at the time of the questionnaire. Thus the questionnaire-based definition is probably an overestimation. We did not interview control adolescents (ie, subjects whose results were negative according to the questionnaire), but because the prevalence was low, we would probably not have missed more than a few. Moreover, the median delay of 16 months needs to be considered. Eight children who fulfilled the criteria at the time of the questionnaire had remitted and were excluded from clinical

TABLE II. Prevalence, symptoms, SNOT-22 scores, olfactory thresholds, and EQ-VAS scores for the 22 adolescents with CRS verified by means of telephone and clinical interview ($n = 22$) and the subgroup of children who also had endoscopic signs of CRS ($n = 9$)

CRS symptoms (n = 22)			CRS endoscopic signs (n = 9)			
Prevalence	0.8%		0.3%			
Symptoms ≥ 12 wk	No.	Percent	No.	Percent		
Nasal blockage/congestion	20	90.9	8	88.9		
Runny nose/postnasal discharge	13	59.1	5	55.6		
Facial pain/pressure	3	13.6	2	22.2		
Loss of smell	12	54.6	5	55.6		
	Mean	Median	IQR	Mean	Median	IQR
SNOT-22 total score	38.2	39.5	25-47	44.2	47	42-56
Olfactory threshold test	6.08	6.00	4.75-7.5	6.33	6.25	5.75-7.25
EQ-VAS score	77	80	70-85	77.5	77.5	72.5-85

IQR, Interquartile range.

examination, which might have led to an underestimation of the prevalence of CRS after clinical follow-up. For ethical reasons, because the subjects were growing children participating in a population-based cohort, we did not perform computed tomographic scans. The use of computed tomographic scans might have increased the proportion of clinically defined CRS among those with symptoms.

The prevalence of CRS is probably more than 0.3% but less than 1.5% in adolescence, which is similar to what was found in a Korean study in which the prevalence in the age group 15 to 19 years was 1.1% based on symptoms and nasal endoscopy.⁹ This is much lower than what was seen in a European population-based survey in which the prevalence of reported symptoms according to the EPOS criteria was 11.5% in the age group 15 to 24 years.¹ Possible explanations for differences in prevalence might be geographic differences,^{1,9} differences in response rate between studies, or age differences.

Adolescents with CRS in this study seemed to have a reduced HRQoL measured with both disease-specific and generic instruments. Their mean SNOT-22 score (38.2-44.2) was in level with what was found in a validation study among patients with CRS aged 16 years or more undergoing sinonasal surgery and might be compared with a mean value for healthy patients of 9.3 (7.1-11.1).⁷ Their median EQ-VAS score was lower than scores among those without CRS. Furthermore, the mean value for olfactory threshold (6.08) was in the level of hyposmia (6.25) and lower than that reported for the age group of 16 to 35 years (9.32) in a multicenter study of more than 3000 healthy subjects.⁶ When the 4 dropouts from the clinical examination were included in the analyses of EQ-VAS scores and current cofactors, there was no effect on the results.

The strength of this study is the population-based design, with a 76% response rate from baseline in combination with clinical examination. The number of patients with CRS confirmed after clinical follow-up was low, which was why the possibility of statistical analyses was limited. However, to summarize, CRS exists at adolescence, even though the prevalence is low. Those affected have a significantly reduced quality of life.

Marit Westman, MD, PhD^{a,b}
 Pär Stjärne, MD, PhD^{a,b}
 Anna Bergström, PhD^c

Inger Kull, PhD^{c,d,e}
 Elina Toskala, MD, PhD^f
 Lars Olaf Cardell, MD, PhD^{a,b}
 Magnus Wickman, MD, PhD^{c,d}
 Mats Holmström, MD, PhD^{a,b}

From ^athe Department of Clinical Science, Intervention and Technology, Division of Ear, Nose and Throat Diseases, ^cthe Institute of Environmental Medicine, and ^dthe Department of Clinical Science and Education, Karolinska Institutet, Stockholm, Sweden; ^bthe Department of Ear, Nose and Throat Diseases, Karolinska University Hospital, Stockholm, Sweden; ^eSachs' Children's Hospital, Södersjukhuset, Stockholm, Sweden; and ^fthe Department of Otolaryngology-Head and Neck Surgery, Temple University, Philadelphia, Pa. E-mail: marit.westman@ki.se.

Supported by the Swedish Asthma and Allergy Research Foundation (F2013-0012); the Frimurare Barnhuset Foundation; the Acta Oto-Laryngologica Foundation; the Stockholm County Council (20100169); the Swedish Research Council of Health, Working Life and Welfare (2010-0451); and the Swedish Research Council (2008-5928).

Disclosure of potential conflict of interest: E. Toskala has consultant arrangements with Merck. The rest of the authors declare that they have no relevant conflicts of interest.

REFERENCES

- Hastan D, Fokkens WJ, Bachert C, Newson RB, Bislimovska J, Bockelbrink A, et al. Chronic rhinosinusitis in Europe—an underestimated disease. A GA(2) LEN study. *Allergy* 2011;66:1216-23.
- Fokkens WJ, Lund VJ, Mullol J, Bachert C, Alobid I, Baroody F, et al. European position paper on rhinosinusitis and nasal polyps 2012. *Rhinol Suppl* 2012;(23): 1-298, 3 p preceding table of contents.
- Wickman M, Kull I, Pershagen G, Nordvall SL. The BAMSE project: presentation of a prospective longitudinal birth cohort study. *Pediatr Allergy Immunol* 2002; 13(suppl 15):11-3.
- Fokkens WJ, Lund V, Mullol J. European Position Paper on Rhinosinusitis and Nasal Polyps Group. European position paper on rhinosinusitis and nasal polyps 2007. *Rhinol Suppl* 2007;(20):1-136.
- Tomassen P, Newson RB, Hoffmans R, Lotvall J, Cardell LO, Gunnbjörnsdóttir M, et al. Reliability of EP30S symptom criteria and nasal endoscopy in the assessment of chronic rhinosinusitis—a GA(2) LEN study. *Allergy* 2011;66:556-61.
- Hummel T, Kobal G, Gudziol H, Mackay-Sim A. Normative data for the "Sniffin' Sticks" including tests of odor identification, odor discrimination, and olfactory thresholds: an upgrade based on a group of more than 3,000 subjects. *Eur Arch Otorhinolaryngol* 2007;264:237-43.
- Hopkins C, Gillett S, Slack R, Lund VJ, Browne JP. Psychometric validity of the 12-item Sinonasal Outcome Test. *Clin Otolaryngol* 2009;34:447-54.
- Remensneider AK, D'Amico L, Gray ST, Holbrook EH, Gliklich RE, Metson R. The EQ-5D: a new tool for studying clinical outcomes in chronic rhinosinusitis. *Laryngoscope* 2015;125:7-15.
- Min YG, Jung HW, Kim HS, Park SK, Yoo KY. Prevalence and risk factors of chronic sinusitis in Korea: results of a nationwide survey. *Eur Arch Otorhinolaryngol* 1996;253:435-9.

<http://dx.doi.org/10.1016/j.jaci.2015.02.019>

METHODS

Sniffin' Sticks

Sniffin' Sticks is a validated test of nasal chemosensory function that is based on pen-like odor-dispensing devices. It consists of tests for olfactory threshold, odor discrimination, and odor identification. Test results are age dependent. The highest-scoring age group is 16 to 35 years and is listed as the reference group. Odor detection decreases with age but is also lower than in the reference group in subjects aged 5 to 15 years. In this study the test for olfactory threshold was used. The test was performed by a nurse with a long experience of using this test.

SNOT-22

SNOT-22 is a validated disease-specific questionnaire consisting of 22 parameters on symptoms and disease-related quality of life with scores ranging from 0 to 5. The total score can be between 0 (no symptoms) and 110 (maximum symptoms). The questionnaire was filled out at the time of the clinical examination.

EQ-VAS

EQ-5D is a well-established and widely used generic instrument for assessment of HRQoL. It has previously been widely used for assessment of general self-reported health in patients with different chronic conditions and recently also in patients with CRS. It consists of 2 parts. The first part collects

information from 5 separate domains. In the second part, called EQ-VAS, the respondent evaluates his or her state of health by indicating a position on a VAS from 0 (worst health state imaginable) to 100 (best health state imaginable). EQ-VAS was used at the time of the BAMSE 16-year follow-up.

Statistics

Prevalence. The prevalence of endoscopy-determined CRS was calculated as the proportion of children with positive endoscopic results times the number of children with ongoing symptoms divided by the total number of children who answered the EP3OS questions in the BAMSE questionnaire: $([\text{Proportion positive endoscopic results}] \times [\text{Number of children with ongoing symptoms}]) / 3112$.

Venn diagram. For drawing of proportional Venn diagrams, eulerAPE was used (<http://www.eulardiagrams.org/eulerAPE>).^{E1}

REFERENCES

- E1. Micallef L, Rodgers P. eulerAPE: drawing area-proportional 3-Venn diagrams using ellipses. *PLoS One* 2014;9:e101717.
- E2. Asher MI, Keil U, Anderson HR, Beasley R, Crane J, Martinez F, et al. International Study of Asthma and Allergies in Childhood (ISAAC): rationale and methods. *Eur Respir J* 1995;8:483-91.
- E3. Haland G, Carlsen KC, Sandvik L, Devulapalli CS, Munthe-Kaas MC, Pettersen M, et al. Reduced lung function at birth and the risk of asthma at 10 years of age. *N Engl J Med* 2006;355:1682-9.

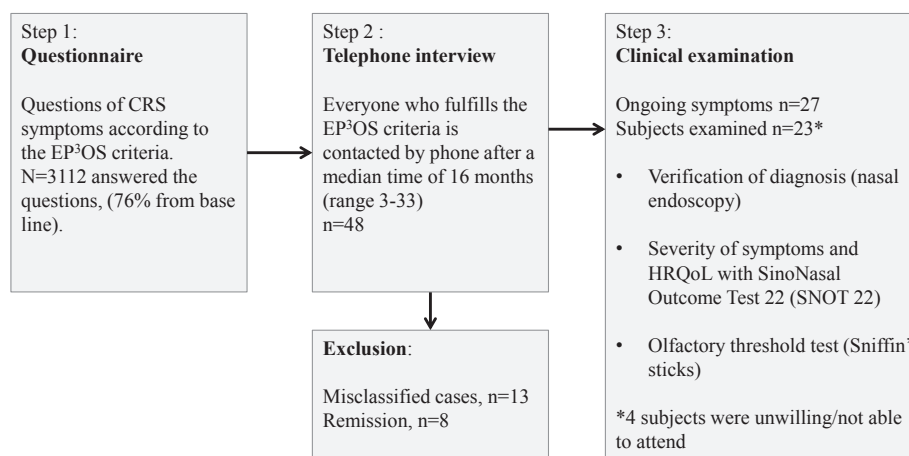


FIG E1. Flow chart of the study.

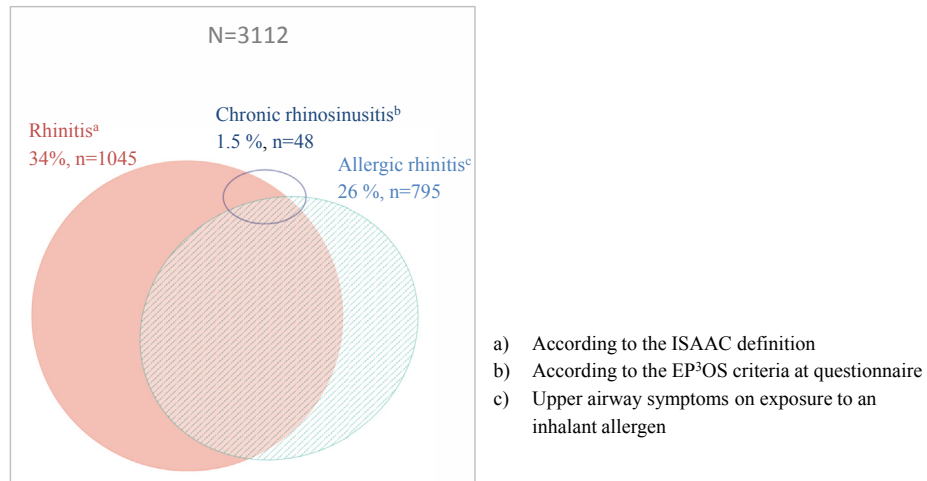


FIG E2. Proportional Venn diagram of upper airway symptoms among 3112 16-year-olds from the BAMSE birth cohort, Stockholm, Sweden. *ISAAC*, International Study of Asthma and Allergies in Childhood.

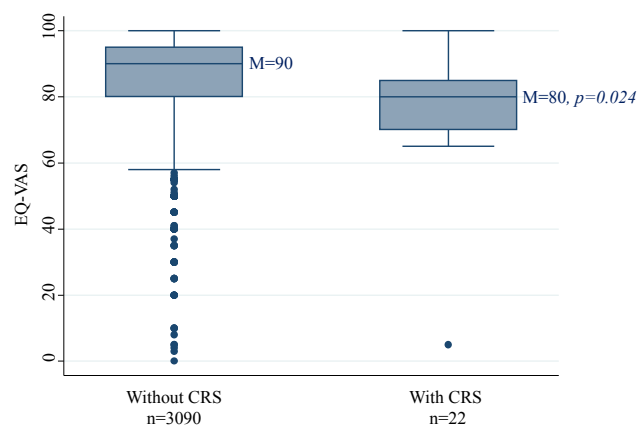


FIG E3. EQ-VAS scores for overall perceived health among adolescents with and without CRS. Boxes show median values and 25th and 75th percentiles.

TABLE E1. Baseline characteristics of participants in the BAMSE birth cohort, Stockholm, Sweden, compared with the study population

	Study population (n = 3112)			BAMSE cohort (n = 4089)		
	No.	Percent	95% CI	No.	Percent	95% CI
Sex						
Male	1532	49.2	47.5-51.0	2065	50.5	49.0-52.0
Heredity for allergic disease						
Yes	946	30.7	29.1-32.3	1200	29.7	28.3-31.1
Low socioeconomic status						
Yes	489	15.8	14.5-17.1	695	17.1	15.9-18.2
Mother's age						
<26 y	229	7.4	6.4-8.3	319	7.8	7.0-8.6
Parent born outside Scandinavia						
Yes	602	20.5	19.0-21.9	707	20.8	19.4-22.2
Older siblings						
Yes	1471	47.3	45.5-49.0	1980	48.4	46.9-50.0
Breast-feeding exclusively ≥ 4 mo						
Yes	2443	80.3	78.9-81.7	3116	79.5	78.2-80.8
Mother smoking during and/or after pregnancy						
Yes	407	13.1	11.9-14.3	563	13.8	12.7-14.8
Smell of mildew in home						
Yes	235	7.6	6.6-8.5	324	7.9	7.1-8.8
Moisture damage in home						
Yes	611	19.6	18.2-21.0	812	19.9	18.6-21.1

TABLE E2. Definitions of outcomes

Variables	Definitions
CRS	
Symptom definition*	At least 2 symptoms of the following for ≥ 12 wk: (1) blockage/congestion of the nose, (2) runny nose/postnasal discharge, (3) facial pain/pressure, or (4) loss of smell, where 1 symptom had to be number 1 or 2 (according to the EP3OS criteria)
Endoscopic signs	Nasal polyps, mucopurulent secretion, or edema/mucosal obstruction mainly in the middle meatus (according to the EP3OS criteria)
Rhinitis	Sneezing, runny, or blocked nose without common cold or flu during the last 12 mo (according to the International Study of Asthma and Allergy in Childhood) ^{E2}
Allergic rhinitis	Sneezing, runny, blocked, or itchy nose or itchy eyes at exposure to an inhalant allergen during the last 12 mo
Asthma	At least 2 of the following: wheeze during the last 12 mo, doctor's diagnosis of asthma ever, or asthma medication (according to GA ² LEN) ^{E3}
Sensitization	Positive Phadiatop test result (≥ 0.35 kU/L), including the inhalant allergens birch, timothy, mugwort, cat, dog, horse, <i>Cladosporium herbarum</i> , and <i>Dermatophagoides pteronyssinus</i>

*The EPOS symptom criteria were used in the questionnaire, as well as in the telephone interview.