



Social Factors in the Development of Chronic Rhinosinusitis: a Systematic Review

I. Geramas¹ · D. Terzakis¹ · E. Hatzimanolis² · C. Georgalas¹

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Abstract

Purpose of Review In an era where prevention is paramount, understanding social factors for chronic rhinosinusitis (CRS) may facilitate preventive interventions that mitigate risk factors associated with the initiation or progression of the disease.

Recent Findings Both passive and active smoking are clearly and unequivocally associated with both the incidence and the severity of rhinosinusitis, while there is an increasing body of evidence linking social deprivation and low socioeconomic status with rhinosinusitis and its complications. However, overall, only a handful of studies were longitudinal, while the available studies suffer from lack of standardized definitions of rhinosinusitis.

Summary In this systematic review, we assessed the available evidence linking CRS with social factors, such as socioeconomic status and class, educational status, family status, living and working location and conditions, and use of toxins or recreational drugs as well as exercise and diet. Thirty studies from 1995 onwards fulfilled our inclusion criteria and were used for this review. Social deprivation and low socioeconomic level seem to be directly associated with rhinosinusitis, as there are pollutants in living or working environment. A clear and direct association between smoking (both active and passive) and rhinosinusitis was also shown. However, the link between rhinosinusitis and education level, and exercise and diet, if any, seems to be more complex.

Keywords Chronic rhinosinusitis · Social factors · Social deprivation · Education level · Smoking · Pollutants · Occupational exposure · Exercise · Diet

Introduction

Chronic rhinosinusitis (CRS) is a common disease worldwide affecting persons of all age groups. CRS is estimated to affect about 13% of the population in the USA [1] and 10.9% of the population in Europe with an incidence of 1.13 per 100 person-years [2]. According to the European Position Paper on Rhinosinusitis and Nasal Polyps (EPOS), CRS is defined by using both subjective symptoms and objective evidence by endoscopy or sinus CT scan [3].

There are two subtypes in chronic rhinosinusitis, with (CRSwNP) and without (CRSSNP) nasal polyps, and its incidence and prevalence between countries differs [3]. This has been explained in terms of the different genetic makeup and different phenotypes of CRS while less emphasis has been placed on the role played by social and exposure factors [4]. However, in an era where prevention is paramount, a social health problem should also be analyzed in social health terms and we feel that not enough light has been shone on the ways that CRS could be potentially altered or prevented. Understanding social factors for CRS may facilitate preventive interventions that mitigate risk factors associated with the initiation or progression of the disease.

In this systematic review, we try to describe and assess the available evidence that links CRS with social factors, such as socioeconomic status and class, educational status, family status, living and working location and conditions, and use of toxins or recreational drugs (smoke, alcohol, or recreational drugs) as well as exercise and diet.

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✉ C. Georgalas
cgeorgalas@gmail.com

¹ Endoscopic Skull Base Centre Athens, Hygeia Hospital, 4 Erythrou Stavrou Str. & Kifisias Av., 151 23 Marousi, Athens, Greece

² Department of Head and Neck Surgery, Hygeia Hospital, 4 Erythrou Stavrou Str. & Kifisias Av., 151 23 Marousi, Athens, Greece

Methods

We searched PubMed of the U.S. National Library of Medicine using the following terms: socioeconomic status, class, education, family status, living and working location and conditions, use of toxins or recreational drugs (smoke, alcohol, or recreational drugs), exercise, and diet, including all possible combinations. We only analyzed studies from 1995 onwards.

We included articles if “sinusitis” or “rhinosinusitis” or “nasal polyps” and either one of the previous terms were mentioned in the title or abstract. We excluded single-case reports or small case series or publications that, following review of the full article, were deemed to not explicitly fulfill our criteria.

We abstracted information from the final set of articles across CRS definition, results, and the country in which the study took place. Then, we categorized the abstracts following the factors assessed (socioeconomic status and class, educational status, family status, living and working location and conditions, use of toxins or recreational drugs, exercise, and diet).

There was very little between-study consistency so we did not perform any meta-analysis of reported associations across studies. We also did not address publication bias using funnel plot as there were not enough studies with common methods to warrant the evaluation of publication bias.

Results

We found 30 studies of CRS prevalence/incidence which fulfilled our inclusion criteria, most of which assessed more than one factors. Eleven articles assessed socioeconomic, education, and marital status; 12 living/working environment conditions; 14 the use of toxins; 5 diet and exercise while only 1 assessed family/marital status.

The diagnosis of CRS was made by endoscopy in eight studies, by CT scan in three studies (two using Lund-Mackay scoring and one AFRS criteria), by Current Procedural Terminology (CPT) or International Classification of Diseases (ICD) codes in five studies, by “a certified otolaryngologist” in three studies, by questionnaire based on EPOS criteria in six studies, by the 2004 American Academy of Otolaryngology, Head and Neck Surgery guidelines in one study, by GA²LEN questionnaire in two studies, by the administration of a standardized questionnaire in one study, and by an affirmative answer to the question “Do you have sinusitis diagnosed by a health professional?” in one study. All the studies were published between 2008 and 2016. Fifteen of them were conducted in America, six in Europe, and nine in Asia.

Twelve studies were cross-sectional (including one stratified multistage clustered probability study), eight case-control, and eight cohort studies. We included one survey research and one comparative study.

Socioeconomic and Education Status

There is a significant association between lower income and/or lower socioeconomic status and CRS confirmed in four studies done in the USA, Canada, and South Korea including a total of 4866 patients and 77,564 controls [5•, 6–8]. The association was strong and was confirmed by the increase in disease severity with lower social and economic status [6, 8]. In one prospective case-control study done in the UK, a significant association between social class and CRS status was also shown, although the difference was no longer statistically significant ($p = 0.0684$) when it was adjusted for age and gender [9]. However, in two smaller studies, one in South Korea with 91 patients and one in the USA with 93 patients, the relation between CRS and socioeconomic conditions was not shown to be significant [10, 11]. In one cross-sectional questionnaire survey performed in the USA, findings suggest that children from socioeconomic minorities experience CRS less often but this result is related to significant disparity to access to appropriate diagnosis, subspecialty care, referral patterns, or perception of disease burden [12]. The same study showed increased prevalence of CRS in patients with less than median household income although the results did not reach statistical significance (Table 1).

Low educational level of the patients seems to be statistically significant factor for CRS in four studies [7, 8, 13, 17•]. More specifically, in the study by Kilty et al. [8], it was associated with increased symptom burden but not with higher CT Lund-Mackay scores; in the study by Kim et al. [7], it resulted in higher CRS prevalence (as diagnosed by the EPOS criteria including endoscopy) while in the study by Shi et al. [13], there seemed to be a U-shaped correlation, with increased prevalence both in the lowest and highest educational levels. However, this study was based exclusively on the self-reported symptoms, which could introduce reporting bias, similarly to another study where self-reported symptoms were used for the diagnosis where it was noted that CRS-associated impairment in general health increased with education level [16]. There was one study where no significant link between disease burden and highest educational qualification achieved was found [9] (Table 1).

Living and Working Environment

We subsequently assessed the relationship between living and working environment, location, conditions, and CRS. We found in four studies direct association of CRS and poor housing quality, dampness at home, living in crowded

Table 1 Characteristics of included socioeconomic, education, and family status studies

First author, year Country	Study design	Cases and controls	Diagnosis	Assessment	Data period	Sample size	Results
Kilty SJ, 2011 Canada [8]	Prospective cohort study	Patients of a tertiary rhinology clinic	Diagnosis was made by using the criteria of a published guideline [1]	CRS patients were assessed with SNAQ-11. In each patient, education level and family income were determined. A CT scan of the paranasal sinuses was completed as part of their evaluation and was scored using the Lund-Mackay system.	2010	Case <i>n</i> = 127	The educational level high school or less is significantly associated with self-reported sinus symptom score and it is nearly 7 points higher than for a person with post-secondary education (coef 6.89, <i>p</i> = 0.05). Also, lower family income is related to higher self-reported sinus disease symptom severity but has no effect on sinus disease.
Smith DF, 2013 USA [12]	Cohort study	Case: children with a primary diagnosis of CRS. Control: all new or consult patients seen in the same department over a 3-month period.	Diagnosis of CRS was made as classified through current procedural terminology codes.	Electronic medical records of children between ages 6 months and 18 years old with a primary diagnosis of CRS were used to evaluate differences in demographic distribution of race and socioeconomic status between children diagnosed with CRS and children within the representative comparison group.	2008–2011	Case <i>n</i> = 127 Control <i>n</i> = 430	Children with CRS were more likely to be white and/or more likely to have private insurance compared to the general population of patients seen in the same setting for all otolaryngologic conditions. These findings suggest either that children from socioeconomic minorities truly experience CRS less often or that there is a significant disparity related to access to appropriate diagnosis, subspectally care, referral patterns, or perception of disease burden. A significant association between CRS and marital status was also observed (<i>p</i> = 0.001). Among divorced people, CRS was approximately 1.75 times more prevalent than in married people (OR = 2.75, 95% CI 1.81–4.18), and the prevalence in unmarried people was also significantly higher than that in married people (OR = 1.21, 95% CI 1.03–1.43), while the difference between widowed people and married people was not statistically significant (OR = 1.20, 95% CI 0.85–1.68). Interestingly, we observed an inverted U-shaped relationship between CRS and education level. The prevalence among people with high school or college educations was higher than that among other groups (<i>p</i> = 0.023) There was a significant association between social class and CRS status
Shi JB, 2015 China [13]	Cross-sectional study	Case: patients with CRSwNP and CRSSNP Control: random sampling patients selected from 7 Chinese cities	Diagnosis was made by questions based on EPOS criteria [3].	CRS target subjects were all Chinese residents of chosen households who had lived in the local region for at least 1 year at the time the study was conducted.	2012	Case <i>n</i> = 851 Control <i>n</i> = 10,636	
Philpott C, 2016 UK [9]			The diagnosis of CRS was confirmed by an	The study commenced recruitment in ENT	2007–2013	Case <i>n</i> = 1249 Control <i>n</i> = 221	

Table 1 (continued)

First author, year Country	Study design	Cases and controls	Diagnosis	Assessment	Data period	Sample size	Results
	Prospective case-control study	Cases: patients with CRSwNP and CRSSNP Controls: patients with active sinonasal disease	ENT using the criteria laid out in EPOS 2012 [3]. Any patients with nasal polyps placed in the AFRS category met the Bent and Kuhn criteria [14] or the St Paul's Sinus Centre modification of this [15]. Patients and controls included were all adult.	departments of the East Anglia region (East of England Deanery) of the UK in 2007. Following elevation to the National Institute of Health Research Clinical Research Network Portfolio in 2012, a total of 30 sites from around the UK (including the devolved nations of Wales and Scotland). The study-specific questionnaire was anonymous and therefore, consent was implied through participation. Participant information leaflets were provided.			($p = 0.002$); however, when adjusted for age and sex, the difference was no longer statistically significant ($p = 0.0684$) and there was no specific direction of association. No significant differences were found on household income and the highest educational qualification achieved by the participant ($p = 0.599$).
Min YG, 1996 Korea [10]	Case-control study	Case: patients with CRSwNP and CRSSNP Control: Korean population	The diagnosis of CRS was confirmed by endoscopy.	The surveyed population was drawn from a panel that was considered representative of the Korean population. The sampling was done by a multistage clustered-stratified random method based on the Population and Housing Census Report of Korea (National Bureau of Statistics, 1990).	1991–1996	Case: 91 Control: 8978	The relation between CRS and low socioeconomic conditions was not significant in our study.
Kim YS, 2015 South Korea [7]	Cross-sectional study	Case: patients with CRSwNP and CRSSNP Control: Korean population	The diagnosis of CRS was confirmed by endoscopy.	The present analysis was based on the data of the Population and Housing Census Report of Korea (Statistics Korea, 2005). A multistage clustered-stratified random method was used to sample the surveyed population.	2008	Case: $n = 285$ Control: $n = 4098$	Among the sociodemographic factors, statistically significant factors for CRS are low education and low income.
Chen Y, 2003 Canada [5•]	Cross-sectional study	Case: patients with CRSwNP and CRSSNP Control: patients 12 years of age or older with chronic health problems that had lasted or were expected	Respondents who answered the following question affirmatively were considered to have rhinosinusitis: “Do you have sinusitis diagnosed by a health professional?” In the present analysis, we	The target population included household residents in all 10 provinces, excluding Indian reserves, Canadian military bases, and some remote areas of Quebec and Ontario. The NPHS used a multistage, stratified sampling design to draw a representative sample.	1996–1997	Case $n = 4488$ Control $n = 73,363$	Low income was associated with a higher prevalence of rhinosinusitis.

Table 1 (continued)

First author, year Country	Study design	Cases and controls	Diagnosis	Assessment	Data period	Sample size	Results
Miller JD, 2014 USA [6]	Retrospective cohort study	to last 6 months or longer Case: allergic fungal rhinosinusitis Control: AFRS patients who meet at least 3 out of 5 criteria for allergic fungal rhinosinusitis according to the Bent and Kuhn criteria	excluded subjects who did not answer this question. Preoperative definitive CT characteristics of AFRS	Patients after functional endoscopic sinus surgery whose preoperative CT scans were reviewed by the senior author and were determined to have definitive CT characteristics of AFRS	2000–2013	Case <i>n</i> = 93 Control <i>n</i> = 103	Disease severity was associated with lower income and less health care access. We also found disease severity to be associated with lower socioeconomic status by county level, suggesting that the disease's predisposition for a certain population may be secondary to healthcare accessibility or living conditions rather than race, as suggested previously.
Lu Myers Y, 2015 USA [11]	Retrospective cohort study	Case: CRS and AFRS patients	Patients with CRS were diagnosed preoperative by radiographic imaging and were graded by the senior authors using the Lund-Mackay scoring system. Patients with AFRS were diagnosed by previously documented Bent and Kuhn criteria.	Patients were extracted from the University of North Carolina Institutional Review Board using simple random sampling /Mth-name select.	2000–2013	Case <i>n</i> = 186 (CRS <i>n</i> = 93 AFRS <i>n</i> = 93)	When compared with AFRS patients, CRS patients are older, are mostly white as opposed to African American, have higher income, have more access to primary care, and have lower markers of disease severity. No associations between disease severity, socioeconomic status, and demographic factors were found within the CRS groups.
Fu QL, 2015 China [16]	Case-control study	Case: CRS Control: selected from clinical visits or inpatients without CRS	Symptom-based diagnosis of CRS based on EPOS criteria	The participants (above 15 years of age) were selected from the general population in Guangzhou using a four-stage random sampling method. The sampling method was described in details in Chinese multiplicity CRS investigation in which Guangzhou was involved as one of the seven cities under study [13].	2014	Case <i>n</i> = 118 Control <i>n</i> = 1411	In the present study, the CRS-associated impairment in general health was also observed to increase with education level, while the effects of CRS did not seem to differ with household per capita income in any of the domains.
Ahn JC, 2016 Korea [17]	Cross-sectional study	Case: adult CRS Control: random selected population	Diagnosis was based on otorhinolaryngologic interview and nasal endoscopy.	Korean National Health and Nutrition Examination Survey—KNHANES adopted a stratified cluster sampling method to select participants.	2008–2012	Case <i>n</i> = 2428 Control <i>n</i> = 28,912	An association was found between CRSwNP and age (odds ratio [OR], 1.03; 95% CI, 1.02–1.04; <i>p</i> < 0.001) and lower level of education (OR, 1.40; 95% CI, 1.02–1.92; <i>p</i> = 0.04)
Orb Q, 2016 USA [18]		Case: CRS	The current study utilized ICD-9-CM codes to	Patients 12 years of age or younger with a diagnosis of	1996–2011	Case <i>n</i> = 496	By analyzing extensive pedigrees in a unique population database, we

Table 1 (continued)

First author, year Country	Study design	Cases and controls	Diagnosis	Assessment	Data period	Sample size	Results
	Retrospective observational cohort study	Control: patients with no history of CRS were randomly selected from the Utah population.	identify patients with CRS with electronic records available in the Utah Population Database.	CRS and at least one previous CRS-related procedure		Control $n = 4959$	have established that there is a significant familial risk associated with CRS in pediatric patients. Parents of probands were also at increased risk, although it was much more likely for one parent to be affected than both, suggesting a genetic component of the disease.

CRS chronic rhinosinusitis, CRS_{NP} chronic rhinosinusitis without nasal polyps, CRS_{NP} chronic rhinosinusitis with nasal polyps, SNAQ-11 Sino Nasal Assessment Questionnaire, AFRS allergic fungal rhinosinusitis, EPOS European Position Paper on Rhinosinusitis and Nasal Polyps

environment, using air conditioning in the summer, or having a pet at home [6, 10, 19•, 20]. Also, in one study, a direct relationship was found between the prevalence of the disease and the pollutant levels of the cities (carbon monoxide, nitrous dioxide, sulfur dioxide, and particulate matter) [21••]. Two studies showed a substantial geographical variation of CRS. The one that took place in the USA revealed the highest incidence of allergic fungal rhinosinusitis (AFRS) along Mississippi and the Southern United States (including both the Southwest and Southeast) [22]. The other two which took place in EU showed a substantial geographical variation of CRS with consistently low prevalence in the Scandinavian centers and Brandenburg, high prevalence in France and Poland, and an isolated very high prevalence in Portugal [23••], although two studies have revealed CRS did not change substantially with living area [13, 24] (Table 2).

The occupational risk factors were assessed in six studies. Two of them described a significantly higher prevalence among blue-collar workers compared to white ones, who were exposed to gasses, fumes, dust, or smoke [20, 28•]. In two studies, there was a tendency towards increased CRS prevalence among individuals likely to be occupationally exposed to low molecular weight agents such as highly reactive chemicals and reactive cleaning disinfectants [26, 28•]. One study revealed that CRS prevalence was generally elevated in manual workers and was significantly elevated in plant or machine operators and assemblers, elementary occupations, and craft and related trades workers [25]. In another study, there was no significant difference in the proportion of health care-related jobs in subjects with and without CRS ($p = 0.509$ and $p = 0.559$ respectively) [19•] (Table 2).

Exposure to Smoke

In the third category of our study, seven papers (14 total number included) revealed a strong association between CRS and active smoking [5••, 13, 19•, 23••, 29••, 30, 31]. Furthermore, in two studies, there was also higher prevalence of CRS and secondhand tobacco exposure in a dose–response fashion, independently of environmental and occupational exposures [13, 32]. Also, the findings from a case–control study in children suggest that both childhood and current exposure to secondhand smoking (SHS) are risk factors for developing CRS and that current SHS exposure is related to more severe sinonasal symptoms in CRS patients [33]. Alcohol consumption was not related with CRS in one study [7]. There were no studies assessing the association between CRS and the use of recreational drugs (Table 3).

Diet and Exercise

In the fourth category of our study, there was an increased prevalence of obesity in the setting of CRS in four studies

Table 2 Living and working environment, location, and conditions

First author, year Country	Study design	Outcome measure	Diagnosis	Population	Data period	Sample size	Factors assessed
Bhattacharyya N, 2009 USA [21••]	Cross-sectional study	Case: CRSsNP and CRSsNP Control: patients with chronic health problems that had lasted 1 year	Extracting 1-year prevalence data for the disease condition sinusitis from a National Health Interview Survey	Adult sample of the National Health Interview Survey with chronic health problems that had lasted 1 year	1997–2006	Case $n = 47,725$ Control $n = 313,982$	A direct relationship was found between the prevalence of CRS and pollutant levels of carbon monoxide, nitrous dioxide, sulfur dioxide, and particulate matter
Absan SF, 2004 Aberdeen (UK) Trinidad (Spain) [24]	Comparative study	Case: CRS	By an experienced otolaryngologist of registrar or consultant grade	Outpatient otolaryngology clinic attendees at two hospitals providing secondary care to the 250,000 population of Aberdeen and tertiary care to a population of 700,000 in north-eastern Scotland were recorded prospectively.	1999	Case: $n = 561$ Aberdeen $n = 311$ Trinidad	Patients with CRS constitute a similar proportion of outpatient otolaryngology clinic attendees in the north of Scotland and the north of Trinidad. Rhinosinusitis sufferers with a history of allergic disease are more commonly seen in otolaryngology clinics in Trinidad
Ferguson BJ, 2000 USA [22]	Cohort study	Case: AFRS Control: sinus surgeries	By otolaryngologists who had histopathologic evidence of allergic mucin with presence of fungi, either histopathologically or on fungal culture	Forty-five otolaryngologists across the USA were contacted and asked to fill out a survey detailing the total number of sinus surgeries. The survey also requested the total number of cases diagnosed with AFRS over each of the two time periods.	1997–1999	Case $n = 188$ Control $n = 3855$	The highest incidence of AFRS exists along the Mississippi basin and the Southern United States, including both the Southwest and the Southeast
Koh DH, 2009 Korea [25]	Stratified multistage clustered probability study	Case: CRS Control: clerical workers	Trained interviewers visited subjects homes and administered a standardized questionnaire on diagnosed diseases	The major groups of KSCO using data from KNHANES	1998 (first) 2001 (sec) 2005 (third)	Case $n = 945$ Control $n = 59,563$	The prevalence ratio of chronic rhinosinusitis was generally elevated in manual workers and was significantly elevated in plant or machine operators and assemblers, elementary occupations, craft and related trade workers, and the unemployed.
Hox V 2012, EU [26]	Case-control study	Case: patients who had undergone one or more FESS procedures Control: subjects without a history of FESS	Endoscopy	Patients who underwent a FESS in the Department of Ear, Nose and Throat Diseases of the University Hospitals of Leuven were asked to answer an extensive questionnaire	2004–2008	Case $n = 890$ Control $n = 182$	Exposure at work appears to be a risk factor for the occurrence of CRS and for its recurrence or persistence, as evidenced by the need for revision surgery. Although HMW agents such as flour, latex, and laboratory

Table 2 (continued)

First author, year Country	Study design	Outcome measure	Diagnosis	Population	Data period	Sample size	Factors assessed
Gao WX, 2016 China [20]	Cross-sectional study	Case: CRS Control: population from 7 Chinese cities	The participants were interviewed face-to-face in their houses and were asked to complete a standardized questionnaire. The questionnaire was modified by GA ² LEN project and covered sociodemographic characteristics, CRS-related symptoms, and occupational and environmental exposures.	based on and modified from “the occupational history form” proposed by Bernstein et al. [27].	2016	Case <i>n</i> = 850 Control <i>n</i> = 10,633	animals are the best-known causal factors of occupational airway disease [2], we found here that exposure to such classical inducers of IgE-mediated allergic asthma and rhinitis was not so prevalent (< 5%) and the results were mainly driven by LMW agents, LMW sensitizers as well as irritants were frequently reported and often there was co exposure to both groups We found that having a clearance-related job (OR, 1.56; 95% CI 1.07–2.27), occupational exposure to dust (OR, 2.32; 95% CI 1.85–2.91), occupational exposure to poisonous gas (OR, 2.75; 95% CI 2.05–3.69), a pet at home (OR, 1.60; 95% CI 1.32–1.92), carpet at home (OR, 1.95; 95% CI 1.54–2.46) or at the workplace (OR, 6.55; 95% CI 4.60–9.32), and the method used to cook at home (electric or centralized heating, coal, firewood/charcoal) were significant risk factors for CRS. Furthermore, a trend test revealed a significant dose–response relationship with the risk of CRS increasing with the duration of time spent using air conditioning in summer and with the frequencies of exposure to moldy or damp environments (<i>p</i> = 0.016 and 0.001, respectively). However, there was no significant difference in the proportion of health

Table 2 (continued)

First author, year Country	Study design	Outcome measure	Diagnosis	Population	Data period	Sample size	Factors assessed
Ahroth Pind C, 2017 EU [19•]	Cross-sectional study	Case: CRS	Diagnosis of CRS was made according to the EPOS diagnostic criteria.	Subjects aged 16–75 years were randomly selected using civil registries of four cities in Sweden.	2008	Case <i>n</i> = 26,577	care-related jobs or the method used to cook at home in subjects with and without CRS (<i>p</i> = 0.509 and 0.559, respectively). In the present study, dampness at home is strongly related to CRS.
Thilising T, 2012 EU [28•]	Cross-sectional study	Case: CRS	Diagnosis was made by self-reported symptoms according to EPOS consensus report.	Random sample of subjects aged 15–75 years	2008	Case <i>n</i> = 243 Control <i>n</i> = 3099	The analyses on occupational risk factors in the present study revealed a significantly higher CRS prevalence among female blue-collar workers compared to female white-collar workers, among subjects occupationally exposed to gasses, fumes, dust, or smoke, and among subjects currently working in cleaning jobs. In addition, there was a tendency towards increased CRS prevalence among individuals likely to be occupationally exposed to low-molecular agents such as highly reactive chemicals and reactive cleaning disinfectants.
Shi JB, 2015 China [13]	Cross-sectional study	Case: patients with CRSwNP and CRSsNP Control: random sampling patients selected from 7 Chinese cities	Diagnosis was made by questions based on EPOS criteria.	CRS target subjects were all Chinese residents of chosen households who had lived in the local region for at least 1 year at the time the study was conducted.	2012	Case <i>n</i> = 851 Control <i>n</i> = 10,636	Chronic sinusitis did not change substantially with living area.
Min YG, 1996 Korea [10]	Case-control study	Case: patients with CRSwNP and CRSsNP Control: Korean population	The diagnosis of CRS was confirmed by endoscopy.	The surveyed population was drawn from a panel that was considered representative of the Korean population. The sampling was done by a multistage clustered-stratified random method based on the Population and Housing Census Report of Korea	1991–1996	Case: 91 Control: 8978	Risk factors for CRS included air pollution and crowded environment.

Table 2 (continued)

First author, year Country	Study design	Outcome measure	Diagnosis	Population	Data period	Sample size	Factors assessed
Miller JD, 2014 USA [6]	Retrospective cohort study	Case: AFRS Control: AFRS patients who meet at least 3 out of 5 criteria for allergic fungal rhinosinusitis according to the Bent and Kuhn criteria	Preoperative definitive CT characteristics of AFRS	(National Bureau of Statistics, 1990). Patients after functional endoscopic sinus surgery whose preoperative CT scans were reviewed by the senior author and were determined to have definitive CT characteristics of AFRS.	2000–2013	Case <i>n</i> = 93 Control <i>n</i> = 103	Disease severity was associated with poor housing quality and living in rural countries
Hastan D, 2011 EU [23••]	Survey research	Case: CRS Control: random sample of adults	GA ² LEN questionnaire	Random sample of people aged 15–75 years obtained from a suitable population-based sampling frame in each of the 25 sites	2008	Case <i>n</i> = 57,128 Control <i>n</i> = 118,860	The study showed a substantial geographical variation of CRS with consistently low prevalence in the Scandinavian centers and Brandenburg, high in France and Poland, and an isolated very high prevalence in Portugal.

CRS chronic rhinosinusitis, CRS_s/NP chronic rhinosinusitis without nasal polyps, CRS_w/NP chronic rhinosinusitis with nasal polyps, AFRS allergic fungal rhinosinusitis, EPOS European Position Paper on Rhinosinusitis and Nasal Polyps, KSCO Korean Standard Classification of Occupations, KNHANES Korea National Health and Nutrition Examination Survey, FESS functional endoscopic sinus surgery, HMMW height molecular weight, LMW low molecular weight, GA²LEN Global Allergy and Asthma European Network

Table 3 The use of toxins (smoke, alcohol, or recreational drugs)

First author, year, Country	Study design	Outcome measure	Diagnosis	Population	Data period	Sample size	Factors assessed
Reh DD, 2009 USA [33]	Case–control study	Case: CRS nonsmokers Control: cohort participants	Previous physician diagnosis of CRS by nasal endoscopy and CT scan	Population-based cohort of nonsmoking male and female residents in Washington County, MD, who have been followed for health status through yearly contact since 1996. They also met the criteria for CRS developed by the rhinosinusitis Task Force and endorsed by the American Academy of Otolaryngology.	2007–2008	Case <i>n</i> = 100 Control <i>n</i> = 2568	The findings from this community-based case–control study support that childhood and current exposure to secondhand smoking are risk factors for developing CRS and that current SHS exposure is related to more severe sinonasal symptoms in CRS patients.
Hastan D, 2011 EU [23••]	Survey research	Case: CRS Control: random sample of adults	GA ² LEN questionnaire	Random sample of people aged 15–75 years obtained from a suitable population-based sampling frame in each of the 25 sites	2008	Case <i>n</i> = 57,128 Control <i>n</i> = 118,860	Disease was associated with smoking. There was evidence that this relationship was dose-dependent, i.e., related to total number of pack years of smoking. 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; <i>p</i> for heterogeneity 0.3; <i>I</i> ² 12.3)
Berania I, 2013 Canada [29••]	Cohort study	Case: patients with CRS previously phenotyped for the purpose of a pGWAS	Diagnosis of CRS was according to the 2004 American Academy of Otolaryngology–Head and Neck Surgery guidelines	Our study population was composed of 2 existing populations. In the first population (GCRS1), 206 cases with severe CRS (with or without polyposis) were recruited according to the presence of sinus disease having been shown unresponsive to therapy. In the second population (GCRS2), 408 cases of CRS with nasal polyposis were recruited according to the presence of polyposis.	2013	Case <i>n</i> = 614	Active tobacco smoking in CRS patients is associated with increases in markers of systemic inflammation and may partially explain the tendency to refractory CRS seen in smokers. Nevertheless, these changes may be potentially reversible; thus, smoking cessation in CRS patients is strongly advised because it may have an impact on response of CRS to therapy.
Lee WH, 2015 Korea [30]	Case–control study	Case: CRS smokers Control: randomly selected participants	Endoscopy	Participants were randomly selected from a panel to represent the whole nation of South Korea. The panel was extracted using a multistage clustered and stratified random sampling method based on national census data.	2008–2011	Case <i>n</i> = 11,589 Control <i>n</i> = 37,753	The present nationwide survey and examination demonstrates association between smoking and rhinologic diseases. Our population-based study showed that 29.9% of Korean adults are active smokers. Among the rhinologic diseases examined, CRS is likely associated with active smoking in subjects over the age of 40 years. Passive smoking is not related to rhinologic diseases

Table 3 (continued)

First author, year, Country	Study design	Outcome measure	Diagnosis	Population	Data period	Sample size	Factors assessed
Houser SM, 2008 USA [31]	Retrospective cohort study	Case: CRSwNP	Nasal polyps were identified by visual inspection per endoscopy during surgery.	Patients who underwent sinus surgery were selected from the author's practice.	1999–2005	Case: 373	incidence. Interestingly, the total smoking period significantly influenced CRS prevalence but the number of cigarettes smoked did not.
Tammemagi CM, 2010 Canada [32]	Case-control study	Case: CRS patients Control: patients were randomly selected from the HFHS corporate database and had been free of CRS for 5 years before study entry. Controls were matched to case patients by age (plus or minus 5 years), sex, and race/ethnicity.	Diagnosis has been confirmed by computed tomography or nasal endoscopy.	Patients were identified through the HFHS corporate database and had been diagnosed as having CRS and treated in the HFHS Department of Otolaryngology.	2000–2004	Case <i>n</i> = 306 Control <i>n</i> = 306	Direct tobacco use and nasal polyposis were also strongly linked in our study. Exposure to secondhand smoking is associated with CRS in a dose-response fashion and independently of environmental and occupational exposures.
Wentzel JL, 2014 USA [34]	Case-control study	Case: CRS Control: patients who were undergoing surgery for cerebrospinal fluid leak repair, non-hormone-secreting pituitary tumors, or adenoidectomy	All patients with CRS met diagnostic criteria as defined by the EPOS criteria	Patients who underwent endoscopic sinus surgery at the Medical University of South Carolina	2007–2013	Case <i>n</i> = 404 Control <i>n</i> = 165	This study indicates that there was no clear pattern of passive smoke avoidance in CRS. Active smoking prevalence appeared to be decreased in polypoid disease compared with controls; however, an informal power analysis estimated an additional 117 AFRS and 280 control patients were needed to achieve significance at this ratio. With the apparent constancy of smoke exposure in CRS compared with controls, further studies are required to address the ramifications of exposure on disease pathology. Daily smokers have a self-reported score that is on average 8 points higher than what is the case for nonsmokers (coef 8.16, <i>p</i> = 0.06), but this was not statistically significant.
Kilty SJ, 2011 Canada [8]	Prospective cohort study	Patients of a tertiary rhinology clinic	Diagnosis was made by using the criteria of a published guideline [4]. A CT scan of the paranasal sinuses was completed as part of their evaluation and was scored using the Lund-Mackay system.	CRS patients were assessed for smoking behavior.	2010	Case <i>n</i> = 127	Among all of the subjects, there were 1680 (15.8%) current smokers. The smokers were approximately 50% more likely to have CRS than the never smokers (adjusted OR = 1.44, 95% CI 1.17–1.77), and the effect of tobacco smoke
Shi JB, 2015 China [13]	Cross-sectional study	Case: patients with CRSwNP and CRSsNP Control: random sampling patients selected from 7 Chinese cities	Diagnosis was made by questions based on the EPOS criteria.	CRS target subjects were all Chinese residents of chosen households who had lived in the local region for at least 1 year at the time the study was conducted.	2012	Case <i>n</i> = 851 Control <i>n</i> = 10,636	

Table 3 (continued)

First author, year, Country	Study design	Outcome measure	Diagnosis	Population	Data period	Sample size	Factors assessed
Philpott C, 2016 UK [9]	Prospective case-control study	Case: patients with CRSwNP and CRSsNP Control: patients with active sinonasal disease, e.g., acute or chronic forms of rhinitis/rhinosinusitis	The diagnosis of CRS was confirmed by an ENT using the criteria laid out in EPOS. Any patients with nasal polyps placed in the AFRS category met the Bent and Kuhn criteria [3] or the St Paul's Sinus Centre modification of this [4]. Patients and controls included were all adult.	The study commenced recruitment in ENT departments of the East Anglia region (East of England Deanery) of the UK in 2007. Following elevation to the National Institute of Health Research Clinical Research Network Portfolio in 2012, a total of 30 sites from around the UK (including the devolved nations of Wales and Scotland). The study-specific questionnaire was anonymous and therefore, consent was implied through participation. Participant information leaflets were provided.	2007–2013	Case <i>n</i> = 1249 Control <i>n</i> = 221	increased with the cumulative years of smoking ($p = 0.001$) and the number of cigarettes smoked per day ($p = 0.001$) with the exception of the smokers of 11–20 cigarettes per day. There was no clear evidence that former smokers were more susceptible to CRS (adjusted OR = 1.30, 95% CI 0.84–2.01). A greater prevalence was also observed among those who lived or worked with one smoker (adjusted OR = 1.21, 95% CI 1.03–1.43) compared to those who were not exposed to secondhand smoker. The effect of secondhand tobacco exposure tended to increase with the cumulative years ($p = 0.002$) and doses of exposure ($p = 0.003$). There were also no significant differences in smoking or alcohol consumption between controls and those with CRS.
Min YG, 1996 Korea [10]	Case-control study	Case: patients with CRSwNP and CRSsNP Control: Korean population	The diagnosis of CRS was confirmed by endoscopy.	The surveyed population was drawn from a panel that was considered representative of the Korean population. The sampling was done by a multistage clustered-stratified random method based on the Population and Housing Census Report of	1991–1996	Case: 91 Control: 8978	Smoking was no significant risk factor for CRS

Table 3 (continued)

First author, year	Study design	Outcome measure	Diagnosis	Population	Data period	Sample size	Factors assessed
Kim YS, 2015 Korea [7]	Cross-sectional study	Case: patients with CRSwNP and CRSsNP Control: Korean population	The diagnosis of CRS was confirmed by endoscopy.	Korea (National Bureau of Statistics, 1990). The present analysis was based on the data of the population and Housing Census Report of Korea (Statistics Korea, 2005). A multistage clustered-stratified random method was used to sample the surveyed population.	2008	Case: $n = 285$ Control: $n = 4098$	Alcohol consumption and smoking were not related with CRS.
Chen Y, 2003 Canada [5]	Cross-sectional study	Case: patients with CRSwNP and CRSsNP Control: patients 12 years of age or older with chronic health problems that had lasted or were expected to last 6 months or longer	Respondents who answered the following question affirmatively were considered to have rhinosinusitis: "Do you have sinusitis diagnosed by a health professional?" In the present analysis, we excluded subjects who did not answer this question.	The target population included household residents in all 10 provinces, excluding Indian reserves, Canadian military bases, and some remote areas of Quebec and Ontario. The NPHS used a multistage, stratified sampling design to draw a representative sample.	1996–1997	Case $n = 4488$ Control $n = 73,363$	Cigarette smoking was associated with a higher prevalence of rhinosinusitis.
Ahlroth Pind C, 2017 EU [19•]	Cross-sectional study	Case: CRS	Diagnosis of CRS was made according to the EPOS diagnostic criteria.	Subjects aged 16–75 years were randomly selected using civil registries of four cities in Sweden.	2008	Case $n = 26,577$	In the present study, there was a significant strong association between smoking and CRS.

CRS chronic rhinosinusitis, CRSwNP chronic rhinosinusitis without nasal polyps, CRSsNP chronic rhinosinusitis with nasal polyps, GA² LEN Global Allergy and Asthma European Network, EPOS European Position Paper on Rhinosinusitis and Nasal Polyps, pGWAS pooled based genome-wide association studies, GCRS1 genetics of chronic rhinosinusitis study 1, GCRS2 genetics of chronic rhinosinusitis study 2, HFFHS Henry Ford Health System, NPHS National Population Health Survey

Table 4 Diet and exercise

First author, year Country	Study design	Outcome measure	Diagnosis	Population	Data period	Sample size	Factors assessed
Ahn JC, 2016 Korea [17•]	Cross-sectional study	Case: adult CRS Control: random selected population	Diagnosis was based on otorhinolaryngologic interview and nasal endoscopy.	Korean National Health and Nutrition Examination Survey —KNHANES adopted a stratified cluster sampling method to select participants.	2008–2012	Case $n = 2428$ Control $n = 28,912$	An association was found between CRSwNP and obesity (OR, 1.46; 95% CI, 1.16–1.84; $p = 0.001$).
Bhattacharyya N, 2013 USA [36••]	Cross-sectional study	Case: CRS Control: representative national household sample of the American adult population	Patients were identified by examining the ICD-9-CM data field for each listed medical condition.	The data source for this study was MEPS consisting of the consolidated medical expenditure file and medical conditions file components, as administered by the Agency for Healthcare Research and Quality under the US Department of Health and Human Services. Data was restricted to adult patients (age > 18 years).	2008–2010	Case: $n = 13.0 \pm 0.5$ million Control $n = 229.3 \pm 4.6$ million	The current data demonstrate an increased prevalence of obesity in the setting of CRS. This association remained significant even when adjusting for multiple demographic variables and the Charlson Comorbidity Index.
Sidell D, 2013 USA [37]	Cross-sectional study	Case: CRS Control: school-aged children	ICD-9-CM data fields	Population collected from select US communities in household surveys (MEPS). Patients were then identified as suffering from CRS by examining the ICD-9-CM data fields, which come from analysis of health care provider data contained within the medical component file of the MEPS. Patients for whom the medical condition codes corresponded to each of the desired diagnoses were considered as having that diagnosis and the remaining patients were considered as not having the diagnosis.	2006–2008	Case: $n = 1.7$ million Control $n = 42.1$ million	In the present study, there does not appear to be an association between childhood obesity CRS at the population level.
Chung SD, 2014 Taiwan [35]	Cross-sectional study	Case: CRS	Patients were diagnosed by certified otolaryngologists.	This study used data from LHID2000, published by the Taiwan National Health Research Institute. The population was based from ICD-9.	2009	Case $n = 5734$	The results of our study further support the association between obesity in adults and CRS at the population level.
Kim YS, 2015 Korea [7]	Cross-sectional study	Case: patients with CRSwNP and CRSsNP Control: Korean population	The diagnosis of CRS was confirmed by endoscopy.	The present analysis was based on the data of the 2008 Population and Housing Census Report of Korea (Statistics Korea, 2005). A multistage clustered-stratified random method was used to sample the surveyed population.	2008	Case: $n = 285$ Control: $n = 4098$	Obesity and physical activity were not related with CRS.

CRS chronic rhinosinusitis; CRSwNP chronic rhinosinusitis without nasal polyps; CRSsNP chronic rhinosinusitis with nasal polyps; ICD9 - CMC International Statistical Classification of Diseases, 9th Revision, Clinical Modification Codes; MEPS Medical Expenditure Panel Survey; LHID2000 Taiwan's Longitudinal Health Insurance Database 2000

[17•, 21, 35, 36]. In two studies, however, there was no such association [7, 37] (Table 4).

Family Status

At the last category, we found, in two studies, an association between marital status and CRS that was observed in a cross-sectional study where divorced participants were approximately 1.75 times more likely to suffer from CRS compared with their married counterparts (OR = 2.75, 95% CI 1.81–4.18) [13]. In the same study, the prevalence in unmarried people was also significantly higher than that in married people (OR = 1.21, 95% CI 1.03–1.43), while the difference between widowed people and married people was not statistically significant (OR = 1.20, 95% CI 0.85–1.68) (Table 1).

Only one retrospective observational cohort study revealed a significant familial risk associated with CRS in pediatric patients [18•]. Parents of probands were also at increased risk, although it was much more likely for one parent to be affected than both, suggesting a genetic component of the disease (Table 1).

Discussion

There was significant heterogeneity in the studies studied, including the definition and diagnosis of sinusitis, the measures used to quantify socioeconomic level, and the study design itself. That precludes the performance of a statistical meta-analysis. However, a few conclusions can be made, relatively safely.

There seems to be a clear association between low socioeconomic level and the prevalence and incidence of rhinosinusitis. This is confirmed in a number of studies, and more importantly, it is clear in studies with significant numbers of participants (more powered) and when access to health care is (relatively) factored in. It seems to be the case that the more open and equitable and accessible the health care system is, the more prominent such discrepancies become. This is expected and follows the same pattern of a number of other respiratory diseases, namely COPD [38].

The same cannot be said regarding education level—although there is a clear association between education level and socioeconomic level, the link between education and CRS seems to be more convoluted: Studies where self-reported diagnosis of CRS was used showed that higher education was linked to CRS, although this could be a result of reporting bias and greater awareness of the condition.

The link between pollutants in the living or working environment and rhinosinusitis is also well defined and confirmed in our review: most studies confirmed poor, crowded housing conditions; dampness; and older housing to be associated with

increased CRS prevalence and severity, while occupational exposure to noxious factors was also linked to CRS.

Among recreational drugs, only smoking showed a consistent link with CRS, including both active smoking and secondhand smoke. This was, rather disturbingly, also shown for earlier-childhood exposure, suggesting a long-lasting effect. Marital status and exercise on the other hand did not show any clear link with the prevalence of CRS.

As we focus on the effects of genetic and medical factors (including the role of superantigens, biofilms, allergy, and cytokines) to the pathogenesis of CRS, we have perhaps neglected the important role played by external, preventable factors on CRS. Smoking is an activity where a lot of focus has been done over the last years, and with good reason—its cessation involves a lot of health benefits—however, a similar focus is needed to deal with the noxious health effects of poor housing, lack of access to health care, occupational or house exposure to noxious substances, and, of course, social deprivation that is very often linked with all of the above.

Compliance with Ethical Standards

Conflict of Interest The authors declare no conflicts of interest relevant to this manuscript.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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