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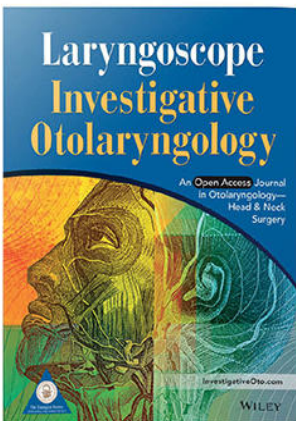


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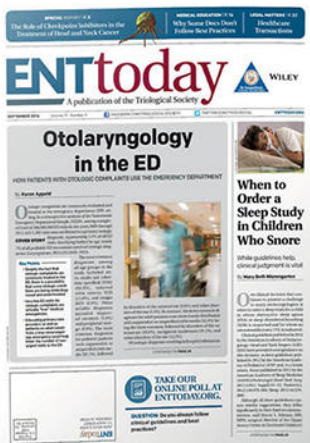
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
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WILEY

## Socioeconomic, comorbidity, lifestyle, and quality of life comparisons between chronic rhinosinusitis phenotypes

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**Background:** Chronic rhinosinusitis (CRS) is a heterogeneous group of inflammatory sinonasal disorders with key defining symptoms, but traditionally separated into phenotypes by clinical/endoscopic findings. It is not known whether the two phenotypes have differing socioeconomic, comorbidity, and lifestyle differences. This analysis of the Chronic Rhinosinusitis Epidemiology Study (CRES) database sought to analyze any key differences in the socioeconomic variables between those with CRS with nasal polyps (CRSwNPs) and those without nasal polyps (CRSSNPs). We also sought to analyze differences in comorbidities, lifestyle, and quality of life.

**Methods:** Patients with a confirmed diagnosis of CRS in secondary and tertiary care outpatient settings in the UK were invited to participate in a questionnaire-based case-control study. Variables included demographics, socioeconomic factors, comorbidities, lifestyle factors, and health-related quality of life (HRQoL) (level 3 evidence).

**Results:** A total of 1204 patients' data were analyzed: 553 CRSSNP and 651 CRSwNP participants. The key socioeconomic variables did not demonstrate any notable differences, nor did lifestyle variables other than alcohol consumption being higher in those with CRSwNP ( $P = .032$ ), but the latter was not significant after adjusting for age and sex. Aside from confirmation of asthma being more common in CRSwNP, it was notable that this group complained less of upper respiratory tract infections (URTIs), and CRSSNP participants showed evidence of worse HRQoL scores in respect of body pain ( $P = .001$ ).

**Conclusions:** Patients with CRSwNP experience higher rates of asthma and lower rates of URTIs; patients with CRSSNP have worse body pain scores. Otherwise, there are no demonstrable significant socioeconomic, comorbidity, lifestyle, or quality of life differences between the two phenotypes.

**Level of evidence:** 3

**Key Words:** Rhinosinusitis, socioeconomic, quality of life, comorbidity, lifestyle.

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Additional supporting information may be found in the online version of this article.

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This study has been reported in accordance with the STROBE statement guidelines for the reporting of observational studies.

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According to the ICMJE authorship criteria: substantial contributions to conception and design of, or acquisition of data or analysis and interpretation of data (A.C., C.P.); drafting the article or revising it critically for important intellectual content (A.C., C.P., N.T.); final approval of the version to be published (A.C., C.P., N.T.). All the remaining authors are included in substantial contributions to conception and design of, or acquisition of, data or analysis and interpretation of data, and final approval of the version to be published.

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## INTRODUCTION

### Background

Chronic rhinosinusitis (CRS) is a common condition of the upper respiratory tract<sup>1</sup> with poor quality of life and known associations with the lower respiratory tract.<sup>2</sup> It is known that socioeconomic deprivation can be associated with a higher prevalence of asthma and poorer lung function.<sup>3,4</sup> The Chronic Rhinosinusitis Epidemiology Study (CRES) was designed to distinguish differences in socioeconomic status, geography, medical/psychiatric comorbidity, lifestyle, and overall quality of life between patients with CRS and healthy controls. Our previous analysis of the CRES data set did not show evidence of any socioeconomic disparity between CRS cases and controls,<sup>5</sup> and this was corroborated by a recent systematic review that found smoking was the only key association.<sup>6</sup> However, given the differing rates of asthma in the two main phenotypes of CRS,<sup>2</sup> it is possible that disparities between these two phenotypes exist and this had not been explored in the original analyses.<sup>5</sup> Smoking does not appear to differ between phenotypes in our both recent analysis and a larger data set.<sup>7,8</sup> Other studies have considered socioeconomic variables but have not usually compared the two main phenotypes.<sup>6,9</sup> The latter review by Geramas et al.<sup>6</sup> showed an association in some studies between CRS and low socioeconomic status but not all studies relied on clinicians confirming the diagnosis of CRS, as is the case in the CRES.<sup>5</sup> As we had already contrasted controls and CRS participants, it was determined that a separate comparative analysis of the two main phenotypes was needed.

### Aims and Objectives

Previous analyses of the CRES data set have considered quality of life, mood disturbances, rates of surgery and revision surgery, use of medication, rates of allergy, asthma, aspirin sensitivity and Eustachian tube dysfunction, and the role of dietary salicylates and smoking, as well as qualitative analyses.<sup>2,7,10–18</sup> The aim of the analysis of the CRES database presented here was to specifically compare these variables between the two phenotypes of CRS, as this was not a feature of our original analysis,<sup>5</sup> and for any variables not examined in any of the subsequent analyses that appeared worthy of closer examination including comorbidities.

## MATERIALS AND METHODS

This study has been reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement guidelines for the reporting of observational studies. STROBE guidelines were developed following an initiative of epidemiologists, methodologists, statisticians, researchers, and journal editors in 2004 to ensure rigorous reporting and assessment of data.<sup>19</sup> The study was sponsored by the University of East Anglia (UEA) and funded by the Anthony Long and Bernice Bibby Trusts. Ethical approval was granted by the Oxford C Research Ethics Committee (Ref: 07/H0606/100).

### Study Design

The CRES was a prospective, questionnaire-based, case-control study conducted between October 2007 and September 2013 at 30 tertiary/secondary care sites across the United Kingdom. Patients with diagnosed CRS alongside healthy control subjects were asked to complete a single, study-specific questionnaire, capturing a variety of demographic and socioeconomic variables, environmental exposures, and medical comorbidities (see Supporting Information, Appendix 1, in the online version of this article). As the healthy control participants are not part of this analysis, the details of their involvement are not considered further here.

### Participants and Data Sources

Prospective participants were identified for recruitment at ENT outpatient clinics at 30 participating centers. Patients with CRS were examined by an ENT clinician and classified into CRS phenotypes (CRSwNPs, CRSsNPs, or allergic fungal rhinosinusitis (AFRS)) as per European Position Paper on Sinusitis and Nasal Polyps (EPOS) 2012 criteria<sup>20</sup> (see Section 2.2.1). Questionnaires were completed during the clinic visit or taken home to be completed and returned by prepaid post. No participant identifiable data were captured, therefore consent was not required although it was implied through return of the questionnaire. Returned questionnaires were scanned and the data were imported into an electronic database in Microsoft Excel. Records in the database were compared to physical copies of the questionnaires by two members of the research team to ensure accuracy and consistency between the two.

All CRS participants were required to meet the inclusion/exclusion criteria outlined later.

#### CRS participants

**Inclusion criteria.** Criteria for diagnosis of CRS with or without polyps (EPOS 2012 guidelines—*as were relevant at the time of study*).<sup>20</sup>

At least two symptoms must be present for at least 12 weeks and include the following:

- One of either nasal blockage/obstruction/congestion and/or nasal discharge (anterior/posterior nasal drip)
- Either facial pain/pressure and/or reduction or loss of sense of smell

and in addition:

- Endoscopic signs: polyps and/or mucopurulent discharge primarily from middle meatus and/or edema/mucosal obstruction primarily in middle meatus
- CT changes: mucosal changes within the ostiomeatal complex and/or sinuses

Patients were then classified as having CRS without polyps (CRSsNPs), CRS with nasal polyps (CRSwNPs), or AFRS; patients with the latter were not included in this analysis.

#### Exclusion criteria

- Patients/controls unable to comprehend written English.
- Patients/controls under the age of 18 years.

### Quantitative Variables and Bias

The detailed questionnaire can be seen in Supporting Information, Appendix 1, in the online version of this article). The variables considered here in this updated analysis include the following:

1. The presence of comorbidities including asthma, chronic obstructive pulmonary disease (COPD), bronchiectasis,

diabetes, hypothyroidism, autoimmune diseases, immunodeficiency and ciliary dysmotility; data on the frequency of URTIs were also collected using the question: “How often do you get a cold or sore throat in the space of 1 year?”

2. Quality of life as recorded by the domains of the SF-36.
3. Socioeconomic variables including mean index of multiple deprivation (IMD), mean household income, household occupancy, and education level.
4. Lifestyle factors including smoking and alcohol.
5. Environmental factors including urban or nonurban domestic home location and occupational setting (indoor/outdoor/unclear). For the latter, the research team reviewed the list of occupations and classified them as either “indoor” (where the setting would be predominately indoors, e.g., secretary), outdoor (where the setting would be predominantly outdoors, e.g., tree surgeon), or unclear where a judgment could not easily be made.

### Sample Size Calculation

The sample size calculation was based on the original primary outcome of the study, which was to look for common associations between socioeconomic factors between CRS participants and controls.<sup>5</sup> In order for the study to have 80% power to detect a difference of 10% in “low social class” between controls and CRS participants, assuming a 30% rate in the CRS participants, with approximately 5 CRS participants to 1 control patient, 965 CRS participants and 193 controls were required. The context of this can be found in our previous publication.<sup>5</sup>

### Statistical Methods

Patient demographics were summarized by CRS phenotype status using mean and SD for continuous variables and the number and percentage for categorical variables. For the comparisons between the two phenotypes, we planned the following analyses:

1. Comorbidities—comparisons using logistic regression and adjusting for age and sex of the rate of:

- asthma
- COPD
- bronchiectasis
- URTIs per year
- diabetes
- hypothyroidism
- immunodeficiency
- autoimmune diseases
- ciliary dysmotility

Note that psychiatric comorbidity has already been considered previously.<sup>15</sup>

2. Quality of life: Comparing the mean SF-36 score, its subscales (vitality, physical function, bodily pain, general health perceptions, physical role functioning, emotional role functioning, social role functioning, and mental health) and its summary score (physical health and mental health) between the two groups using regression, adjusting for age and sex.

3. Socio-economic status:

- Mean index of multiple deprivation (IMD) using regression, adjusting for age and sex
- Mean household income using regression, adjusting for age and sex
- Median household occupancy using a Mann–Whitney test
- Highest education level achieved using a chi-squared test for individual levels and an odds ratio for grouped levels

of GSCE/A-level (secondary school level qualifications) and degree/higher degree (higher education level qualifications).

4. Lifestyle factors were compared using multinomial logistic regression adjusting for age and sex

- Comparison of alcohol consumption
- Comparison of smoking rates

5. Environmental exposure was compared using a chi-squared test

- Comparison of the percentage of people who live in a village (as a proxy for being less exposed to environmental pollution)
- Comparison of the percentage of people who work outdoors (as judged by occupation)

All analyses were conducted using Stata MP 16.0.

## RESULTS

### Study Participants

A total of 1535 questionnaires were returned with 1470 considered eligible for inclusion after removal of duplicates and questionnaires with missing data; only CRSwNP and CRSsNP cases were included in this analysis (see Fig. 1). This analysis is therefore based on the 1204 CRS participants who completed the relevant parts of the questionnaire. The overall response rate of those identified to take part in the study was 66% of those distributed.

### Descriptive Data

For the purpose of this analysis, participants with AFRS were not analyzed due to smaller numbers of cases in the database. As such, there were 553 participants with CRSsNPs and 651 participants with CRSwNPs. The mean age of CRSsNP participants was 52 years (range 18–84 years) and of CRSwNP participants was 56 years (range 18–102 years). CRSsNP and CRSwNP participants were 53% and 31% females, respectively; 65 and 77 participants in those two phenotypes, respectively, did not

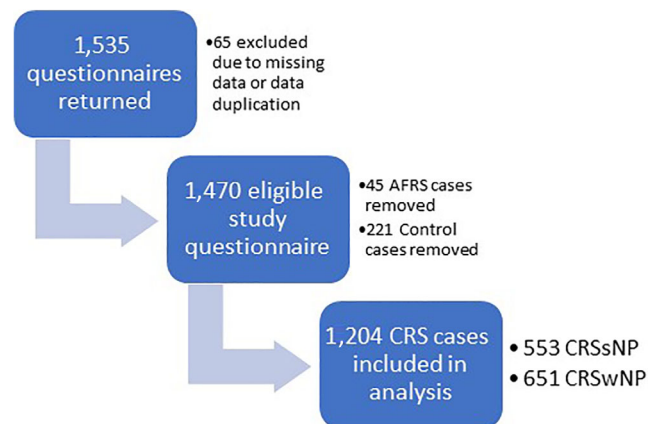


Fig. 1. Participant flow diagram. [Color figure can be viewed in the online issue, which is available at [www.laryngoscope.com](http://www.laryngoscope.com).]

TABLE I.  
Comparison of Comorbidities Between CRSsNP and CRSwNP.

Comorbidity	CRSsNP (n = 553) N (%)	CRSwNPs (n = 651) N (%)	Unadjusted		Adjusted	
			OR (95% CI)	P-value	OR (95% CI) <sup>†</sup>	P-value
Asthma	117 (21.2%)	303 (46.9%)	3.29 (2.55, 4.25)	<.001	3.67 (2.70, 4.98)	<b>&lt;.001</b>
COPD	19 (3.4%)	35 (5.4%)	1.61 (0.91, 2.52)	.102	1.26 (0.64, 2.47)	.500
Bronchiectasis	30 (5.4%)	43 (6.7%)	1.24 (0.77, 2.02)	.375	0.94 (0.55, 1.61)	.826
Diabetes	31 (5.6%)	34 (5.3%)	0.94 (0.57, 1.54)	.794	0.66 (0.38, 1.16)	.147
Hypothyroidism	30 (5.4%)	32 (5.0%)	0.91 (0.55, 1.52)	.718	1.30 (0.74, 2.28)	.370
Immunodeficiency	14 (2.5%)	15 (2.3%)	0.92 (0.44, 1.92)	.817	1.16 (0.50, 2.70)	.728
Autoimmune disorder	37 (6.7%)	25 (3.9%)	0.56 (0.33, 0.95)	.030	0.51 (0.28, 0.93)	<b>.029</b>
Ciliary dysmotility	4 (0.7%)	0 (0.0%)		.045 <sup>‡</sup>		
Number of colds per year						
Never	14 (2.5%)	23 (3.6%)		<b>&lt;.001</b>		
Seldom	216 (39.2%)	309 (48.4%)				
Often	196 (35.6%)	201 (31.5%)				
Frequent	125 (22.7%)	106 (16.6%)				

Bold values indicates significant *p*-value (<0.05).

<sup>†</sup>Adjusted for age, sex, asthma, and aspirin sensitivity.

<sup>‡</sup>Fisher's exact test.

declare their sex. There were 80 (7%) of participants identifying aspirin sensitivity.

### Primary Outcome Data and Main Results

**Comorbidities.** There were significant differences in asthma, with those with CRSwNPs having more than three times the odds of having asthma compared to those with CRSsNPs (Table I).<sup>2</sup> Other statistically significant differences included autoimmune disorders being more common in CRSsNP and with CRSwNP patients more likely to say they “never” or “seldom” suffered an URTI (autoimmune disorders reported are listed in Table II).

Table II.

Autoimmune disorders by phenotype when details reported (numbers represent frequency of the disorders not the number of participants as some participants reported more than 1 disorder); not all participants specified details in the free text.

Autoimmune disorder specified in free text	Frequency in CRSsNP (n = 37)	Frequency in CRSwNP (n = 25)
Coeliac disease		1
Crohn's disease		1
Polymyalgia	3	
Pancreatitis	1	
Pemphigus		1
Psoriasis		1
Pulmonary fibrosis	2	
Rheumatoid arthritis	4	4
Sarcoidosis	2	
Sjogren's syndrome	2	1
Ulcerative colitis		1
Vasculitis (ANCA +ve)	1	1
Vitiligo	1	

### Quality of Life

Most of the domains showed a statistically significant difference in the unadjusted analysis; however, only a difference in body pain (*P* = .001) between those with polyps and those without remained between the groups after adjusting for age and sex (Table III). Therefore, worse scores were observed in those with CRSsNP for body pain only.

### Socioeconomic Status

There was no evidence of a difference in deprivation (*P* = .787), income (*P* = .424), household occupancy (*P* = .43), or educational qualification (*P* = .251) between those with polyps and those without (Table IV). Figure 2 demonstrates the distribution of household income across both groups.

### Lifestyle Variables

The comparison of the two phenotypes showed no evidence of a difference in smoking (*P* = .25) or home location (*P* = .12), but did show a difference in alcohol consumption, with CRSwNP participants likely to drink more alcohol than those with CRSsNP (*P* = .032) (Table V).

## DISCUSSION

### Key Results

No demonstrable differences were found for the key socioeconomic variables between the two groups, nor were there any differences in lifestyle variables other than alcohol consumption being higher in those with CRSwNP. Aside from confirmation of asthma being more common in CRSwNP, it was notable that this group complained less of

Table III.  
Comparison of quality of life between CRSSsNP and CRSwNP.

Comorbidity	CRSSsNP (n = 553) N (%)	CRSwNPs (n = 651) N (%)	Unadjusted		Adjusted <sup>†</sup>	
			Mean difference (95% CI)	P-value	Mean difference (95% CI)	P-value
Vitality, mean (SD)	50.97 (23.35)	54.81 (22.98)	3.84 (1.17, 6.51)	<b>.005</b>	1.64 (-1.29, 4.57)	.273
Physical function, mean (SD)	71.07 (28.26)	72.76 (26.31)	1.70 (-1.44, 4.84)	.289	2.30 (-1.12, 4.84)	.187
Body pain, mean (SD)	63.34 (27.14)	70.66 (25.89)	7.32 (4.26, 10.37)	<b>&lt;.001</b>	5.77 (2.40, 9.13)	<b>.001</b>
General health, mean (SD)	53.13 (22.97)	53.45 (23.16)	0.31 (-2.35, 2.97)	.818	-0.77 (-3.71, 2.17)	.607
Role physical, mean (SD)	67.48 (40.86)	71.19 (39.61)	3.71 (-0.92, 8.35)	<b>.0016</b>	2.47 (-2.68, 7.62)	.347
Role emotional, mean (SD)	78.13 (37.05)	82.87 (33.51)	4.74 (0.68, 8.79)	<b>.022</b>	2.71 (-1.76, 7.18)	.234
Social functioning, mean (SD)	73.47 (27.76)	78.19 (25.18)	4.72 (1.68, 7.77)	<b>.002</b>	2.96 (-0.38, 6.30)	.083
Mental health, mean (SD)	69.58 (19.82)	72.72 (18.23)	3.14 (0.95, 5.33)	<b>.005</b>	0.81 (-1.52, 3.15)	.495
Physical health, mean (SD)	61.14 (22.40)	64.47 (21.05)	3.33 (0.83, 5.83)	<b>.009</b>	2.23 (-0.52, 4.97)	.112
Mental health, mean (SD)	65.07 (20.81)	68.40 (19.47)	3.33 (1.01, 5.65)	<b>.005</b>	1.46 (-1.05, 3.96)	.254
TOTAL SF36 Score, mean (SD)	65.92 (21.41)	69.61 (19.63)	3.70 (1.34, 6.06)	<b>.002</b>	2.24 (-0.33, 4.81)	.088

Bold values indicates significant *p*-value (<0.05).

<sup>†</sup>Adjusted for age and sex.

URTIs. CRSSsNP participants showed evidence of worse (lower) health-related quality of life (HRQoL) scores in respect of body pain. The difference in alcohol consumption may be explained by the gender differences. In the United Kingdom, men consume more alcohol than women. The 2018 Health Survey for England showed that the mean male weekly alcohol consumption in units was 15.5 while for females it was 9.<sup>21</sup> The same survey also found that 14% of male responders were teetotal compared to 21% of female responders. Our data show that males are significantly more likely to suffer from CRSwNP than females.

### Interpretation

CRES is the largest epidemiological study of CRS and the first study since the 2001 Sinonasal Audit<sup>22</sup> to

collect detailed information on socioeconomic variables in the United Kingdom. As mentioned earlier, a systematic review in 2018 concluded that smoking, social deprivation, and low socioeconomic level appear to have a direct correlation with rhinosinusitis.<sup>6</sup> They also concluded that education level, and exercise and diet appear to have a more complex relationship with CRS. In the Korean KNHANES study, CRSwNP was more prevalent in rural areas and with a lower level of education, obesity, increased amounts of smoking and alcohol consumption, and comorbid asthma.<sup>8</sup> It is possible that some of these differences are accounted for by ethnic differences in the underlying pathophysiology.<sup>23</sup>

A small study (*n* = 186) comparing patients with AFRS and CRS found that the CRS cases were predominantly white and older at the time of diagnosis with

Table IV.  
Comparison of socio-economic status between CRSSsNP and CRSwNP.

Variable	CRSSsNP (n = 553) N (%)	CRSwNPs (n = 651) N (%)	Unadjusted		Adjusted <sup>†</sup>	
			Mean difference (95% CI)	P-value	Mean difference (95% CI)	P-value
IMD score	16.49 (10.60)	16.66 (9.88)	0.17 (-1.06, 1.40)	.787	0.18 (-1.20, 1.56)	.795
Income	39426.13 (30567.75)	41203.37 (30478.51)	1777.23 (-2580.13, 6134.59)	.4241	2467.90 (-2277.50, 7213.29)	.3081
Qualifications						
GCSE	108 (27.6%)	125 (26.6%)		.2512		
A-level	36 (9.2%)	51 (10.9%)				
NVQ	65 (16.6%)	78 (16.6%)				
Degree	135 (34.5%)	138 (29.4%)				
Higher degree	46 (11.8%)	76 (16.2%)				
Qualification (grouped)						
GCSE/A-level	144 (36.9%)	176 (37.6%)	1		1	
NVQ/degree/higher degree	246 (63.1%)	292 (62.4%)	0.97 (0.74, 1.28) <sup>‡</sup>	.837	1.01 (0.74, 1.38) <sup>‡</sup>	.946

Based on a chi-squared test.

<sup>†</sup>Adjusted for age and gender based on a nonparametric bootstrap with 10,000 replications.

<sup>‡</sup>Odds ratio (95% CI).

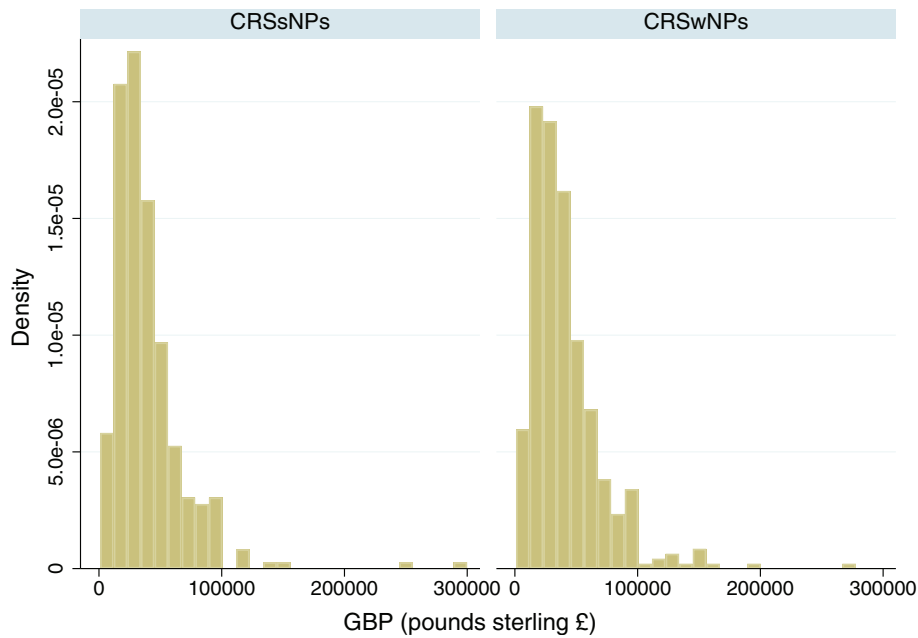


Fig. 2. A histogram of household income by group. [Color figure can be viewed in the online issue, which is available at [www.laryngoscope.com](http://www.laryngoscope.com).]

higher income levels. They found no associations between disease severity, socioeconomic status, and demographic factors within the CRS groups.<sup>24</sup> In a North American study published in 2019, Beswick et al. reported that their analysis of 392 patients showed that medical insurance status and male gender were significantly associated with worse smell test scores, and also that higher household income and lower age led to better outcomes on HRQoL scores (SNOT-22) following sinus surgery.<sup>25</sup> In this study, 36% of the cases were CRS with nasal polyps

(CRSwNP) and 37% reported asthma. Differing findings and differing diagnostic and sampling methods across various studies and healthcare systems suggest that the true picture has yet to be clarified.

Although our CRES study has not demonstrated any evidence that socioeconomic deprivation is a risk factor for CRS or either of the two main phenotypes, other related work on the cost of managing CRS has shown higher out-of-pocket expenditure, primary care and secondary care utilization, and time lost from work compared to those

Table V.  
Comparison of life-style variables between CRSSsNP and CRSwNP.

Variable		CRSsNP (n = 553) N (%)	CRSwNPs (n = 651) N (%)	P-value <sup>†</sup>	RR (95% CI)	P-value <sup>‡</sup>	RR (95% CI)	P-value <sup>§</sup>
Alcohol (units/wk)	None	196 (35.8%)	180 (28.1%)	.032	1			
	1 to 10	269 (49.1%)	342 (53.4%)		1.38 (1.07, 1.79)	.013	1.23 (0.92, 1.66)	.155
	11 to 20	73 (13.3%)	107 (16.7%)		1.60 (1.11, 2.29)	.011	1.13 (0.75, 1.69)	.567
	>20	10 (1.8%)	11 (1.7%)		1.20 (0.50, 2.89)	.688	0.69 (0.25, 1.88)	.468
Smoke (cigarettes/d)	None	470 (86.1%)	574 (89.7%)	.25	1		1	
	1 to 10	46 (8.4%)	41 (6.4%)		0.73 (0.47, 1.13)	.159	0.96 (0.58, 1.59)	.883
	11 to 20	25 (4.6%)	19 (3.0%)		0.62 (0.34, 1.14)	.127	0.58 (0.29, 1.18)	.134
	>20	5 (0.9%)	6 (0.9%)		0.98 (0.30, 3.24)	.977	1.16 (0.31, 4.28)	.827
Living location	Village	195 (37.9%)	222 (35.7%)	.12				
	Suburbs	160 (31.1%)	229 (36.9%)					
	Urban	159 (30.9%)	170 (27.4%)					
Occupation	Indoor	354 (70.2%)	422 (70.9%)	.96				
	Outdoor	20 (4.0%)	24 (4.0%)					
	Unclear	130 (25.8%)	149 (25.0%)					

<sup>†</sup>Based on a chi-squared test.

<sup>‡</sup>Unadjusted.

<sup>§</sup>Adjusted for age and sex.

without CRS.<sup>26</sup> This study estimated an annual average out of pocket expenses of £304.84 secondary to CRS over 3 months, with a 5.3-fold greater spending on over-the-counter medication when compared to the general population and an association with an average 18.7 missed workdays per year. For those in lower socioeconomic groups, they are more likely to be disadvantaged by this implication. This effect appears to have been more pronounced in a private healthcare system<sup>25</sup> but may be less apparent in the National Health Service where direct health care is free at the point of service, excluding prescription costs (England not Scotland).

Although the initial analysis showed that CRSwNP participants overall reported higher rates of alcohol consumption than those with CRSsNP, when stratified by level of alcohol consumption (mild and moderate consumption), this significance did not persist after adjusting for age and sex. This association requires further investigation to better understand any link that might be present and may perhaps be more discernible when future studies compare endotypes instead of phenotypes.

In terms of the differences in reporting URTIs, Wu et al. elucidated the difficulties in defining acute exacerbations of CRS<sup>27</sup> and highlighted that others had used various metrics to measure this including the number of patient-reported “sinus infections,” CRS-related antibiotic courses, and CRS-related oral corticosteroid courses.<sup>28–30</sup> These are of course subjective metrics on the part of the patient and clinician, and in practice, it will be difficult to separate viral URTIs from bacterial episodes. Evidence from a large data set shows that in a primary care setting in the United Kingdom, 46% of CRS patients had received an antibiotic prescription within 5 days of their diagnosis, with 9% are estimated to have had 5 or more antibiotics over 5 years.<sup>31</sup> It is possible that the CRSsNP groups tend to report an exacerbation of their CRS as an URTI more often than the CRSwNP group, but it is not clear why that might be.

With respect to the worse body pain scores, these data are perhaps not surprising given that a previous analysis of the CRES data showed higher scores in the facial domain of the SNOT-22 in CRSsNP, particularly with respect to facial pain that is less prominent in CRSwNP cases.<sup>15</sup> It is likely that this correlates with the higher rates of depression and anxiety that were evident in the CRSsNP participants. Talat et al. found similar comparisons between the two phenotypes but noted that CRSwNP patients had lower levels of symptom control for every incremental increase in symptom burden and suggested that this was due to greater sensitivity or intolerance to CRS symptoms.<sup>32</sup>

### Limitations

The CRES study design has certain limitations, although the diagnosis was made by a clinician, the remaining data were self-reported and may therefore predispose to recall bias. Second, although we collected information on household occupancy, we did not collect information on the number of bedrooms and the potential for overcrowding. In asthma, overcrowding has been shown to have a positive<sup>33</sup> correlation and a negative<sup>34</sup> correlation with respiratory symptoms with no clear

relationship in other studies,<sup>35</sup> so there is no clear relationship in the lower respiratory tract. Our study has also sampled a mainly British White ethnic demographic and may not fully reflect the wider population in the United Kingdom today, but our data do represent a good spread of the socioeconomic spectrum.<sup>5</sup>

### Generalizability

CRES is a cross-sectional UK-based study incorporating a variety of the CRS population from across the country presenting to secondary care. The CRES study does not necessarily capture the whole CRS spectrum as mild sufferers may be managed by primary care alone and may therefore be underrepresented. In contrast to other studies, CRS was diagnosed by ENT specialists according to accepted diagnostic guidelines (EPOS 2012) (16); other existing studies have relied on self-diagnosis and/or used different criteria making direct comparisons with the existing literature more complicated. Although we realize EPOS2020<sup>1</sup> has now superseded EPOS2012, the former was relevant at the time of the study being conducted. In the current era making comparisons between endotypes such as those with or without type 2 mediated inflammation may provide further clinical relevance, but for now these are perhaps not adequately defined.

### CONCLUSION

British patients with CRSwNP experience higher self-reported rates of asthma and lower rates of URTIs; patients with CRSsNP have worse body pain scores. Other comparisons for comorbidity, lifestyle, and environmental factors did not show any significant differences. In the future, as endotyping replaces the current phenotypes and means of sampling larger sections of the populations become easier, it will be useful to revisit these findings through further epidemiological study.

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