Radiologic sinus inflammation and symptoms of chronic rhinosinusitis in a population-based sample

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Abstract

Background—Chronic rhinosinusitis (CRS) epidemiology has been largely studied using symptom-based case definitions, without assessment of objective sinus findings.

Objective—To describe radiologic sinus opacification and the prevalence of CRS, defined by the co-occurrence of symptoms and sinus opacification, in a general population-based sample.

Methods—We collected questionnaires and sinus CT scans from 646 participants selected from a source population of 200,769 primary care patients. Symptom status (CRS_S) was based on guideline criteria and objective radiologic inflammation (CRS_O) was based on the Lund-Mackay (L-M) score using multiple L-M thresholds for positivity. Participants with symptoms and radiologic inflammation were classified as CRS_{S+O}. We performed negative binomial regression to assess factors associated with L-M score and logistic regression to evaluate factors associated with CRS_{S+O}. Using weighted analysis, we calculated estimates for the source population.

Results—The proportion of women with L-M scores greater than or equal to three, four, or six (CRS_O) was 11.1%, 9.9%, and 5.7%, respectively, and 16.1%, 14.6%, and 8.7% among men. The respective proportion with CRS_{S+O} was 1.7%, 1.6%, and 0.45% among women and 8.8%, 7.5%, and 3.6% among men. Men had higher odds of CRS_{S+O} compared to women. A greater proportion of men (vs. women) had any opacification in the frontal, anterior ethmoid, and sphenoid sinuses.

Conclusion—In a general population-based sample in Pennsylvania, sinus opacification was more common among men than in women and opacification occurred in different locations by sex. Male sex, migraine headache, and prior sinus surgery were associated with higher odds of CRS_{S+O}.

Graphical Abstract
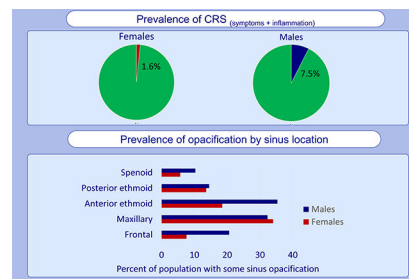
Keywords

Chronic rhinosinusitis; CT scan; Epidemiology; Sex; Sinus

Chronic rhinosinusitis (CRS) has been referred to as "the unrecognized epidemic" because of reports of its high prevalence and burden, coupled with a limited understanding of its epidemiology.[1] CRS is defined by the presence of nasal and sinus symptoms for at least three months, accompanied by sinus inflammation, documented by either sinus computed tomography (CT) scan or endoscopy.[2,3] However, most of the knowledge of the epidemiology of CRS has been derived from studies that defined CRS based on symptoms alone, despite discordance between symptoms and CT evidence of disease.[4,5] Such case definitions, while informative about sinus symptom epidemiology, may not accurately identify persons with sinus inflammation. This could potentially result in incorrect assumptions about the pathophysiology of CRS.

CRS epidemiologic studies generally depend on symptoms due to the logistical challenges of obtaining endoscopy or CTs. The Lund-Mackay (L-M) scoring system, the opacification staging system recommended by the Task Force on Rhinosinusitis,[6] was developed for

patients undergoing sinus surgery. Studies that have incorporated this measure have largely been confined to patients seeking care for sinus disease in tertiary care settings, representing the severe end of the disease spectrum.[4,6,7,8] These studies tell us little about the full spectrum of CRS in the general population. In 2018, the GA2LEN study attempted to address this limitation in a study of CRS prevalence in Europe. This study was confined to patients in a non-rhinologic population undergoing CT for clinical indications other than sinus disease.[9] Excluding patients undergoing sinus CT scans may have resulted in an underestimate of CRS prevalence and a patient population having a sinus CT scan may not be representative of the full spectrum of disease in the general population. No study to date has evaluated the prevalence of CRS, based on sinus CT and appropriate symptoms, in the general population.

We report on a cross-sectional study of nasal and sinus symptoms and sinus CT opacification among a general population sample. The goals of the analysis were to describe radiologic sinus inflammation patterns by sex; estimate the prevalence of CRS, defined by the co-occurrence of symptoms and sinus inflammation; and evaluate risk factors for these outcomes in a general population-representative sample in the U.S.

METHODS

Study population

We conducted sinus CT scans on 646 subjects from a previously-reported cohort,[10] the 7847 baseline questionnaire respondents in the Chronic Rhinosinusitis Integrative Study Program's (CRISP) study. Briefly, 23,700 individuals were selected from 200,769 Geisinger adult primary care patients to receive questionnaires regarding nasal and sinus symptoms. Stratified random sampling was used to over-sample those with sinus symptoms and racial/ethnic minorities to ensure adequate sample sizes. Geisinger is a health system serving more than 40 counties in Pennsylvania. Geisinger's primary care population is representative of the general population in the region.[11] This study was approved by Geisinger's Institutional Review Board.

Participant selection and recruitment

Stratified random sampling was used to over-sample those with nasal and sinus symptoms based on previously completed questionnaires. We sent letters to eligible participants asking them to return a signed consent form if they were interested in participating. We scheduled a sinus CT examination with consented participants and mailed them a sinus symptom questionnaire to be returned prior to the CT visit. Individuals who were pregnant were excluded. CT visits were postponed for individuals reporting a cold or upper respiratory infection. Patients received a $60 gift card for participating. A total of 3269 subjects were invited to participate.

CT imaging and scoring

Non-contrast sinus CT scans (coronal 3 mm slices) were obtained with a low radiation dose research protocol approved by Geisinger's Radiation Safety Committee. All CT images were de-identified and then independently read by two otorhinolaryngologists who were blinded

to subject data, using a modified L-M protocol that scored each of five sinus locations (maxillary, anterior ethmoid, posterior ethmoid, sphenoid, frontal sinus) on the left and right side for degree of opacification on a scale of 0 to 4 (0 = 0% opacification, 1 = 1–33%, 2 = 34–66%, 3 = 67–99%, or 4 = 100%). Reviewers scored the osteomeatal complex from 0 to 2 (0 = not occluded, 1 = partially occluded, or 2 = occluded); and the degree of nasal cavity opacification from 0 to 4 (0 = none, 1 = above middle turbinate, 2 = above inferior turbinate, 3 = at or below inferior turbinate, or 4 = total opacification). When reviewer scores on a sinus location differed by two or more points, reviewers were asked to reconcile scores. Average scores were used when scores differed by one point. Finally, reviewers were asked to indicate if there was evidence on the CT images of prior sinus surgery. Reviewer scores were converted to the standard L-M scoring for sinuses (0 = no opacification, 1 = partial, or 2 = complete) and osteomeatal complex (0 = not occluded or 2 = occluded). Converted scores were then summed to generate a total L-M score,[4] ranging from 0 to 24. Objective evidence of CRS (CRS_O, o for objective) was evaluated using multiple thresholds for L-M score positivity.

Clinical and demographic characteristics

CRS symptom status (CRS_S) was determined based on responses to a questionnaire sent at time of CT study recruitment. As previously reported,[10] participants were categorized into one of three CRS_S categories based on the European Position Paper on Rhinosinusitis (EPOS) symptom criteria: "current" if participants met EPOS criteria at the time of the questionnaire, "past" if they reported EPOS symptoms in the past, and "never" if they did not meet EPOS criteria in their lifetime.[10] Subjects were defined as meeting the CRS clinical criteria if they had both CRS_S current and CRS_O (CRS_{S+O}).

Demographic data were obtained from electronic health records. Migraine headache, asthma, and anxiety sensitivity index (ASI) data were collected via CRISP questionnaires.[12,13] Migraine headache status was based on the ID Migraine questionnaire[12] and asthma was based on self-report of a doctor diagnosis. Anxiety sensitivity refers to the fear of anxiety-related physical sensations resulting from the belief that these sensations may have potentially harmful consequences.[13,14] The ASI is a validated instrument with total scores ranging from 0 to 64; higher scores indicate higher anxiety sensitivity.[14] We hypothesized that ASI scores could be used as an indicator of the propensity to overreport symptoms. Sinus surgery history (yes vs. no) was based on evidence of surgery on the sinus CT scan.

Statistical analysis

The goal of the analysis was to describe the prevalence of CRS_O and CRS_{S+O} in the general population in our study region and to evaluate associations between demographic and clinical factors with CRS_{S+O}. We first estimated the prevalence of CRS_O and CRS_{S+O} in the source population, the original 200,769 primary care patients from whom participants were selected, using three different L-M thresholds for positivity (3, 4, 6). Analysis was weighted using native weights for sampling and participation by symptom status and race/ethnicity for the baseline questionnaire and CT portions of the study, enabling the calculation of these estimates for the source population (Online Repository).

We used chi-square tests to compare the proportion of individuals with CRS_O by sex; race/ethnicity (white, non-white); age (years); migraine headache status (yes/no); CRS_S (current, past, never); ASI score (below median vs. at or above median); self-reported physician-diagnosed asthma status (yes/no); and prior sinus surgery (yes/no). We then compared the proportions of subjects who had any opacification (L-M score > 0) by sinus location using chi-square tests by the previously described subject characteristics. Next, we determined the proportion of subjects with CRS_{S+O} by these characteristics.

To assess what factors were associated with L-M score, we conducted negative binomial regression with integer L-M score as the outcome. We developed a model that included demographic (sex, age, race/ethnicity) characteristics and CRS_S, parameterized as described above. We then added the following variables one at a time: migraine headache, asthma, surgery history, ASI, and smoking status from the electronic health record (current, past, never). Variables were retained if they were associated with L-M score. Next, we evaluated whether sex, migraine headache, or ASI score modified associations between CRS_S and L-M score, by adding interaction terms to the previously described model. Finally, we used logistic regression to evaluate associations between this same set of covariates and CRS_{S+O} status (yes/no).

For all models, we conducted analysis using unweighted, native weighting, and truncated weighting. For weighted analysis using native weights, we applied the weighting methods described above to balance bias with precision in association estimates; bias is reduced with weighted analysis but precision is also reduced.[15,16] Using this weighting approach inflated standard errors, a known consequence of large sampling weights,[15,16] so we truncated our native weights to a maximum relative weight of 30 times the smallest weight, a standard method for dealing with larger weights (Online Repository). Interpretation of models using native weights are presented in the online repository. When evaluating associations with CRS_O and CRS_{S+O}, we conducted sensitivity analysis, excluding individuals with evidence of prior sinus surgery on the CT images, as sinus surgery has the potential to cause changes to the sinuses that change L-M scores.[17]

RESULTS

Study population

Of the 3269 subjects invited to participate in the sinus CT study, 646 (19.8%) completed the scan. In the study sample, two-thirds were women and the mean age was 58 years, similar to the CRISP cohort from which individuals were recruited.[10] (Table I).

Prevalence of CRS_S, CRS_O and $CRSS_{S+O}$

Reviewers agreed, within one point, on 95 to 98% of the scores for the five sinus locations. In the source population analysis (native weights), 16.1% of individuals had current CRS_S (Table II). An estimated 50% had an L-M score of 0, 38.6% had an L-M score of 1 – 3, and 11.2% had an L-M 4. CRS_O estimates in the source population ranged from 6.6% for L-M 6 to 12.4% for L-M 3. Opacification (any versus none) was most common in the

maxillary (28.6%) and anterior ethmoid (21.7%) sinuses and least common in the sphenoid (5.1%) and frontal sinuses (8.3%).

Among those with evidence of radiologic inflammation, the prevalence of CRS symptoms varied by L-M score threshold (Table III). In the source population, we estimated that 28.3% of individuals with an L-M score ≥ 4 had current CRS_S, 30.1% had CRS_S in the past, and 41.6% had no history of CRS_S. An estimated 20% of the source population with current CRS_S had an L-M score ≥ 4.

CRS_O by demographic and clinical characteristics

Prior sinus surgery was associated with more sinus opacification. As estimated in the source population, the prevalence of CRS_O among those with sinus surgery was over 50% (using L-M score ≥ 3 or 4), more than five times the prevalence of those without evidence of sinus surgery (Table IV). In the 646 study participants, the prevalence of CRS_O in men was nearly double that of women, depending on the L-M score threshold. This trend was present in source population estimates as well, though the magnitude of the differences were attenuated. In the source population 14.6% of men and 9.9% of women were estimated to have a L-M score ≥ 4. These sex differences remained when the analysis was restricted to participants with no evidence of sinus surgery (n = 526) (Online Repository Table E2).

In unadjusted analysis migraine headache was negatively associated with CRS_O. The presence of asthma, current CRS_S, and high ASI were positively associated with CRS_O in the source population in unadjusted analysis (Table IV). Among participants with no prior sinus surgery, similar trends were observed for migraine headache and asthma, but not for CRS_S and ASI (Online Repository Table E2).

CRS_{S+O} by demographic and clinical characteristics

Similar to CRS_O, in unadjusted analysis the proportion with CRS_{S+O} differed by sex and sinus surgery history. In the source population, 7.5% of men and 1.6% of women met CRS_{S+O} criteria (using L-M ≥ 4). More than one-third of those with a prior sinus surgery in the source population (34.5%) met CRS_{S+O} (using L-M ≥ 4), compared to 1.6% among those without evidence of surgery. A similar trend for sex was observed among participants with no prior sinus surgery (Online Repository Table E3).

Opacification of sinus location by demographic and clinical characteristics

In the source population, in unadjusted analysis a greater proportion of men compared to women had evidence of opacification (any) in the frontal, anterior ethmoid, and sphenoid sinuses (Table V). Opacification was more common among those who did not meet (vs. met) the criteria for migraine headache, in all sinus locations except the posterior ethmoid. Prior sinus surgery (vs. none) was associated with opacification in all sinus locations. In the subgroup of non-surgical participants, men (vs. women) were more likely to have at least some opacification in all locations and those with no (vs. yes) migraine headache were more likely to have opacification in a subset of sinus locations (Online Repository Tables E4 and E5).

Factors associated with integer Lund-Mackay score

In adjusted models reflected to the source population (truncated weighting), sex and sinus surgery were associated with L-M scores. Women had an average L-M score 31% lower than men (incident rate ratio, 95% confidence interval (IRR, CI): 0.69, 0.48 – 0.98) and those with prior sinus surgery had two times the average L-M score of those without (IRR, CI: 2.06, 1.28 – 3.30). Similar sex differences were observed among participants without sinus surgery (Online Repository Table E6). There was no evidence of effect modification of the association between CRS_S and L-M score by sex, migraine headache status, or ASI score in the source population or when analysis was restricted to participants without prior sinus surgery (results not shown).

Factors associated with CRS_{S+O} status

Sex, migraine headache, and sinus surgery history were associated with CRS_{S+O} status in the source population (truncated weighting), adjusting for age and ASI (Figure I). Men had three to nearly five times the odds of CRS_{S+O} compared to women, depending on the L-M score criterion. Subjects with prior sinus surgery had five to more than eight times the odds of CRS_{S+O} compared to subjects with no prior sinus surgery. Those with migraine headache had 2.8 times the odds of CRS_{S+O} compared to those without migraine headache ($p < 0.05$) when L-M 3 was used as the threshold for positivity. Thus, while migraine headache was not associated with radiologic inflammation in adjusted models, it was associated with the co-occurrence of inflammation and CRS symptoms. This trend was also observed at other L-M thresholds. Similar, but attenuated, sex and migraine associations were observed in analysis restricted to participants without evidence of prior sinus surgery (Figure I).

DISCUSSION

Prior reports on the epidemiology of CRS are largely based on studies that used symptoms alone to identify persons with CRS. To our knowledge, this is the first U.S. population-based study to investigate the epidemiology of CRS_{S+O}, based on the co-occurrence of radiologic sinus inflammation and nasal and sinus symptoms. In contrast to symptom-based studies, our study found that CRS_{S+O} is more common in men than in women. Male sex, migraine headache, and prior sinus surgery were positively associated with CRS_{S+O}.

Prior to this study, radiologic sinus inflammation was generally studied in patients being evaluated for sinus surgery or other clinical indications. The L-M cut-off of four as the criterion for sinus surgery was originally based on the observation that the mean "normal" score in patients who undergo imaging for non-rhinologic symptoms was 4.3.[4,18] In the general population, we found that 14.6% of men and 9.9% of women had an L-M score 4 (CRS_O).

The prevalence of CRS_{S+O} using an L-M score positivity criterion 4 was 7.5% for men and 1.6% for women, a large enough difference to suggest that an overall prevalence would be dependent on the proportion of men and women in the study. Two other studies, outside the U.S., have evaluated the prevalence of CRS_{S+O}. A study in Korea used symptoms and endoscopy and reported a CRS_{S+O} prevalence of 9.6% in men and 7.1% in women.[19] The

European GA2LEN study used CT images from patients who underwent CT imaging for non-rhinologic indications to estimate CRS_{S+O} prevalence.[9] Similar to our overall prevalence, the GA2LEN study had an overall prevalence of 3.0%, and a population that was over two-thirds women. Prevalence by sex was not reported. Given the overrepresentation of women and the exclusion of rhinologic patients, a prevalence of 3.0% may be an underestimate of CRS in Europe.

Prior studies reported that CRS symptoms did not differ by sex or were more prevalent in women.[20–22] One hypothesis is that women, in whom migraine headache is more prevalent, may be more often misclassified as CRS_S. While prior studies did not formally test this hypothesis, we accounted for sex and migraine headache status, and the odds of CRS_{S+O} was higher in both persons with migraine headache and in males. Potential mechanisms for the migraine association are the crossover interactions of neurogenic and immunogenic inflammation or the association could be due to the overlapping symptoms of these conditions.[10,23] Sex differences in CRS_{S+O} could be due to different CRS endotypes by sex with different clinical presentations.[24] Endotypes may vary in their tendency to cause radiologic opacification, a measure of inflammation observable from sinus CT scan.[25,26] Future studies should explore alternative methods of measuring inflammation.[27]

In our study, persons with radiologic inflammation had a range of symptoms. An estimated 28% of the source population with an L-M score ≥ 4 had current CRS_S, while more than 40% had no history of CRS_S. Thus, radiologic inflammation does not necessarily lead to symptoms. Similarly, symptoms cannot always be attributed to sinus inflammation. An estimated 20% of the source population with current CRS_S had an L-M score ≥ 4. Consistent with our findings, 23% of those with CRS symptoms in the GA2LEN study had radiologic evidence of inflammation.[9] Prior studies have hypothesized that symptom overreporting may explain why many persons who meet CRSs do not have CRSo;[24] such overreporting may differ by sex. However, we found no evidence that ASI (a surrogate measure for symptom over-reporting), sex, or migraine headache modified associations between CRS_O and CRS_S. It may also be that current approaches to measuring CRS symptoms identify other diseases that are unrelated to sinus inflammation and, thus, do not align with objective evidence of disease. Alternative approaches to symptom measurement may identify symptom subgroups differentially associated with sinus inflammation; findings that would have potential relevance to targeted disease management strategies.[28]

Prior sinus surgery was associated with both higher L-M scores and higher odds of CRS_{S+O}. Sinus surgery can cause sinus changes that would be scored as opacification using L-M criteria and recurrent sinus inflammation is common after surgery.[29,30] Sinus surgery may also be a surrogate for disease severity, such that individuals with the most severe disease burden are more likely to seek surgical intervention. Thus, excluding patients with prior sinus surgery or seeking sinus surgery from epidemiologic studies might fail to capture the severe end of the disease spectrum.

This is the first study, to our knowledge, to assess and report differences in the prevalence of opacification by sinus location in a population-based sample. Associations of sex and migraine with opacification differed by sinus location. Location of sinus opacification may

be indicative of the pathophysiology of a CRS subtype.[31] Future studies should assess how specific patterns of radiologic opacification relate to CRS phenotypes and endotypes.

This study had a number of strengths. First, we prospectively collected sinus CT scans from the general population. Prior studies have depended upon existing sinus CT scans obtained from patients in tertiary care settings who may not be representative of the full spectrum of disease. Second, we were able to account for sampling and participation rates using weighting methods. This strategy enabled us to account for potential selection and participation bias by CRS symptom status and demographic characteristics. This study had the following limitations. First, while our weighting strategy largely mitigated participation bias by symptom status assessed prior to selection into the CT study, we were unable to account for symptoms that were present at time of recruitment. If individuals with new sinus symptoms were more likely to participate, prevalence estimates may be slightly inflated. Participation rates did not differ by sex or sinus surgery history. Differences in participation by unmeasured factors were likely non-differential and would not have impacted our observed associations. Second, the findings of our study may not be generalizable to populations with different sociodemographic characteristics or from different regions of the U.S. However, our findings provide a valid estimate of the prevalence of CRS in the region studied. Finally, we measured inflammation using sinus CT, a surrogate measure. Future studies should incorporate alternative measures of inflammation.

Conclusion

Radiologic sinus inflammation was prevalent in the general population in central and northeastern Pennsylvania, and more common among men than in women. The odds of CRS meeting symptom and objective criteria was higher in men and persons with migraine headache and prior sinus surgery. There were sex differences in the sinus locations with opacification. Differences observed across sinus locations may reflect different disease endotypes that should be further explored.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements:

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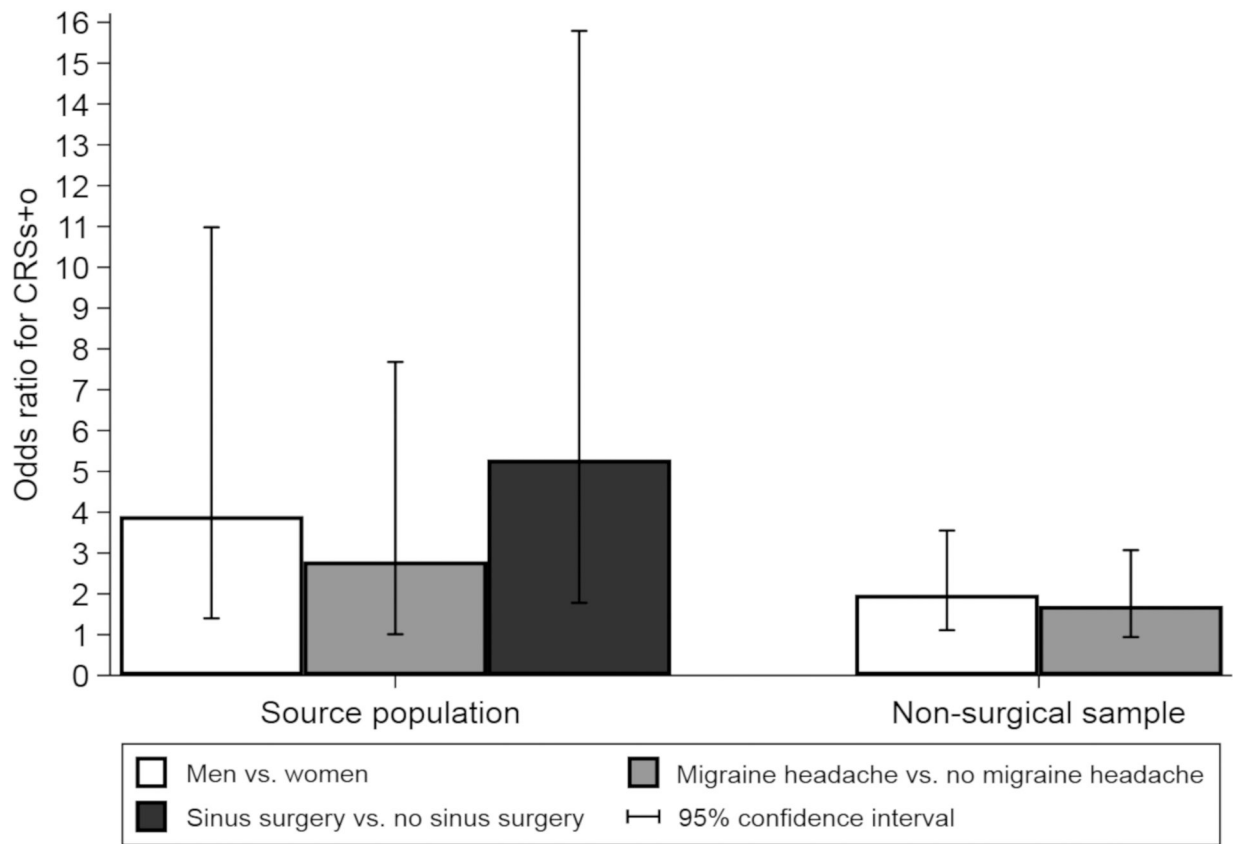
Figure I.

Associations (odds ratios) of sex, migraine headache, and prior sinus surgery with CRS_{S+O} (CRS symptoms with Lund-Mackay ≥ 3) in the source population (646 sinus CT participants weighted for sampling and participation using truncated weights) and among participants with no evidence of prior sinus surgery on sinus CT (n = 526). Adjusted for age (centered), sex, anxiety sensitivity index, and patient-reported asthma diagnosis.

Table I.

Characteristics of participants with completed sinus CT scans (n = 646)

Characteristic	N (%)
Sex	
Female	431 (66.7)
Male	215 (33.3)
Age, years	
18–39	57 (8.8)
40–49	111 (17.2)
50–59	184 (28.5)
60–69	190 (29.4)
70+	104 (16.1)
Race/ethnicity	
Non- Hispanic white	620 (96.0)
Other	26 (4.0)
Migraine headache [†]	
Yes	229 (35.4)
No	417 (64.6)
Anxiety sensitivity index [‡]	
High	309 (47.8)
Low	337 (52.2)
Asthma, self-reported physician diagnosis, ever	
Yes	197 (30.5)
No	449 (69.5)
Prior sinus surgery [§]	
Yes	120 (18.6)
No	526 (81.4)
TOTAL	646 (100.0)

[†] Based on questions from the ID Migraine Questionnaire

[‡] Divided at the median: high = at/above median; low = less than the median.

[§] Evidence of sinus surgery on sinus CT.

Table II.

Proportion of study participants meeting various CRS symptom and radiologic opacification definitions in study sample (unweighted) and as estimated prevalence in source population (native weights)

Characteristic	Study Sample (n = 646) Unweighted Percent (SE)	Source Population Weighted[†] Percent (SE)
CRS_S status[‡]		
Current (n = 324)	50.2 (2.0)	16.1 (1.9)
Past (n = 249)	38.5 (1.9)	24.5 (1.8)
Never (n = 73)	11.3 (1.2)	59.5 (2.0)
CRS_O status[§]		
Lund-Mackay 3 (n = 168)	26.0 (1.7)	12.4 (2.3)
Lund-Mackay 4 (n = 137)	21.2 (1.6)	11.2 (2.3)
Lund-Mackay 6 (n = 89)	13.8 (1.4)	6.6 (1.9)
CRS_{S-O} status[¶]		
Lund-Mackay 3 (n = 89)	13.8 (1.4)	3.6 (0.80)
Lund-Mackay 4 (n = 73)	11.3 (1.2)	3.2 (0.79)
Lund-Mackay 6 (n = 41)	6.3 (0.96)	1.3 (0.67)
Frontal sinus opacification[¥]	13.0 (1.3)	8.3 (2.5)
Maxillary sinus opacification[¥]	42.6 (1.9)	28.6 (7.1)
Anterior ethmoid opacitication[¥]	28.8 (1.8)	21.7 (7.1)
Posterior ethmoid opacification[¥]	19.4 (1.6)	14.7 (6.7)
Sphenoid opacification[¥]	9.9 (1.2)	5.1 (1.7)
Ostiomeatal complex opacification[¥]	12.9 (1.3)	8.1 (2.2)
Nasal cavity opacification[¥]	5.3 (0.88)	1.6 (0.48)

[†]
Weighted for sampling and participation rates to estimate prevalence in source population.

[‡]
Never: did not report European Position Paper on Rhinosinusitis (EPOS) CRS symptoms in lifetime; past: met EPOS CRS symptoms in lifetime but not currently; current: met EPOS CRS symptoms in the last 3 months.

[§]
Lund-Mackay score based on CT scoring by two otolaryngologists blinded to CRS_S status.

[¶]
Met criteria for current CRS_S and CRS_O criteria at different Lund-Mackay cut-points.

[¥]
Any opacification/occlusion score >0.

Table III.

Proportion with CRS_S[†] at different Lund-Mackay thresholds for positivity of radiologic inflammation in study sample (unweighted) and as estimated in source population (native weights)

	Study Sample (n = 646) Unweighted			Source Population Weighted[‡]		
Lund-Mackay score	CRS_S Current	CRS_S Past	CRS_S Never	CRS_S Current	CRS_S Past	CRS_S Never
3 (%)	53.0	37.5	9.5	29.2	31.9	39.0
4 (%)	53.3	37.2	9.5	28.3	30.1	41.6
6 (%)	46.1	41.6	12.4	19.7	32.4	48.0

[†]Never: did not report European Position Paper on Rhinosinusitis (EPOS) CRS symptoms in lifetime; past: met EPOS CRS symptoms in lifetime but not currently; current: met EPOS CRS symptoms in the last 3 months.

[‡]Weighted for sampling and participation rates back to source population

Table IV.

Proportion of study participants meeting various criteria for Lund-Mackay (L-M) scores by subject characteristics, in study sample (unweighted) and estimated in source population (native weights)

Characteristic	N (%)	Study Sample (n = 646) Unweighted Percent (SE)			Source Population Weighted[†] Percent (SE)		
		L-M ≥3	L-M ≥4	L-M ≥6	L-M ≥3	L-M ≥4	L-M ≥6
Sex							
Female	431 (66.7)	20.7 (2.0)*	15.7 (1.8)*	10.7 (1.5)**	11.1 (3.0)	9.9 (3.0)	5.7 (2.3)
Male	215 (33.3)	36.7 (3.3)	32.1 (3.2)	20.0 (2.7)	16.1 (5.0)	14.6 (4.7)	8.7 (3.6)
Age, years							
18–39	57 (8.8)	26.3 (5.8)	21.1 (5.4)	19.3 (5.2)	25.5 (9.9)	22.0 (9.5)	21.8 (9.4)**
40–49	111 (17.2)	19.8 (3.8)	15.3 (3.4)	9.9 (2.8)	2.3 (1.2)	2.1 (1.1)	1.5 (0.9)
50–59	184 (28.5)	27.7 (3.3)	22.3 (3.1)	12.0 (2.4)	17.2 (7.8)	15.7 (7.6)	3.9 (2.0)
60–69	190 (29.4)	24.7 (3.1)	21.6 (3.0)	14.2 (2.5)	14.7 (6.0)	14.4 (6.0)	11.5 (5.5)
70+	104 (16.1)	31.7 (4.6)	25.0 (4.2)	17.3 (3.7)	10.2 (4.6)	6.8 (3.0)	2.6 (1.4)
Race/ethnicity							
Non-Hispanic white	620 (96.0)	26.3 (1.8)	21.3 (1.6)	13.7 (1.4)	11.8 (2.3)	10.5 (2.2)	5.7 (1.7)
Non-white	26 (4.0)	19.2 (7.7)	19.2 (7.7)	15.4 (7.1)	28.6 (21.5)	28.6 (21.5)	27.8 (21.5)
Migraine headache[‡]							
Yes	229 (35.4)	22.3 (2.8)	15.7 (2.4)*	9.2 (1.9)**	9.6 (4.0)	8.0 (3.5)	4.3 (2.3)
No	417 (64.6)	28.1 (2.2)	24.2 (2.1)	16.3 (1.8)	13.2 (3.0)	12.0 (3.0)	7.2 (2.4)
CRS$_S$ status[§]							
Current	324 (50.2)	27.5 (2.5)	22.5 (2.3)	12.7 (1.8)	22.5 (4.7)**	19.7 (4.6)	8.0 (4.1)
Past	249 (38.5)	25.3 (2.8)	20.5 (2.6)	14.9 (2.3)	16.2 (3.2)	13.8 (2.9)	8.7 (2.5)
Never	73 (11.3)	21.9 (4.8)	17.8 (4.5)	15.1 (4.2)	8.1 (3.4)	7.8 (3.4)	5.3 (2.7)
Anxiety sensitivity index[¶]							
High	309 (47.8)	27.5 (2.5)	19.6 (2.2)	14.6 (2.0)	21.1 (7.3)[3]	19.7 (7.1)*	11.3 (5.4)
Low	337 (52.2)	24.6 (2.3)	23.0 (2.4)	13.1 (1.8)	8.5 (1.7)	7.4 (1.6)	4.4 (1.4)
Asthma, self-reported physician diagnosis, ever							
Yes	197 (30.5)	33.0 (3.4)**	27.4 (3.2)**	19.8 (2.8)**	28.1 (8.8)**	22.8 (8.5)**	11.2 (3.5)
No	449 (69.5)	22.9 (2.0)	18.5 (1.8)	11.1 (1.5)	9.6 (2.2)	9.1 (2.2)	5.7 (2.1)
Prior sinus surgery[¥]							
Yes	120 (18.6)	50.8 (4.6)*	41.7 (4.5)*	29.2 (4.2)*	56.0 (7.4)*	53.2 (7.7)*	31.3 (12.6)*
No	526 (81.4	20.3 (1.8)	16.5 (1.6)	10.3 (1.3)	10.1 (2.3)	9.1 (2.3)	5.3 (1.8)
TOTAL	646 (100.0)	26.01 (1.7)	21.2 (1.6)	13.8 (1.4)	12.4 (2.3)	11.2 (2.3)	6.6 (1.9)

[†]Weighted for sampling and participation rates back to source population.

*p < 0.0001

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**

p < 0.05

†
Based on questions from the ID Migraine Questionnaire.

§
Never: did not report European Position Paper on Rhinosinusitis (EPOS) CRS symptoms in lifetime; past: met EPOS CRS symptoms in lifetime but not currently; current: met EPOS CRS symptoms in the last 3 months.

¶
Divided at the median: high = at/above median; low = less than the median.

¥
Evidence of sinus surgery on sinus CT.

Table V.

Opacification of nasal or sinus location for selected participant characteristics, native weights (n = 646) [†]

Characteristic	Estimated percent in source population with any opacification (SE) [‡]						
	Frontal	Maxillary	Anterior Ethmoid	Posterior Ethmoid	Sphenoid	Osteomeatal Complex	Nasal cavity opacification
Sex							
Female	7.6 (3.4) [*]	34.0 (6.4)	18.5 (4.9)	13.6 (4.8)	5.7 (3.0)	12.4 (4.2)	2.6 (1.0)
Male	20.6 (7.2)	32.3 (7.6)	35.3 (8.7)	14.5 (4.3)	10.3 (3.7)	9.5 (2.6)	1.5 (0.70)
Migraine headache [§]							
Yes	4.5 (2.4) [*]	30.7 (5.9)	12.1 (3.2) [*]	14.6 (9.0)	5.6 (2.7)	9.0 (3.4)	3.8 (2.4)
No	13.7 (4.4)	34.3 (6.1)	27.2 (5.8)	13.6 (3.4)	7.6 (2.9)	12.2 (3.4)	1.9 (0.5)
CRS$_S$ [¶]							
Current	13.8 (4.1)	45.3 (6.5)	23.1 (4.5)	12.1 (4.4)	10.1 (4.1)	9.1 (2.8)	1.4 (0.66)
Past	12.4 (7.1)	34.1 (8.0)	31.4 (8.4)	12.2 (2.9)	5.5 (2.2)	9.3 (2.8)	3.8 (1.7)
Never	9.9 (5.3)	26.8 (8.8)	18.0 (7.6)	16.2 (7.6)	6.9 (4.6)	14.5 (6.6)	1.6 (0.8)
Anxiety sensitivity index [¥]							
High	18.2 (7.9)	37.2 (7.6)	26.5 (7.8)	14.5 (5.8)	10.5 (5.1)	20.9 (6.9) [**]	1.3 (0.5)
Low	7.8 (2.0)	31.4 (5.6)	22.1 (5.4)	13.5 (4.3)	5.1 (1.9)	6.0 (1.6)	2.9 (1.1)
Asthma, self-reported physician diagnosis, ever							
Yes	9.2 (3.2)	41.5 (10.2)	20.4 (5.1)	12.2 (3.2)	7.9 (3.0)	22.5 (8.7)	6.8 (3.0)
No	12.3 (4.3)	31.3 (5.1)	24.7 (5.7)	14.3 (4.5)	6.9 (2.9)	8.4 (3.1)	1.1 (0.4)
Prior sinus surgery [£]							
Yes	47.7 (8.3) [**]	61.6 (6.8) [**]	56.0 (7.4) [**]	39.9 (12.6) [**]	24.8 (12.6) [**]	15.1 (4.7)	12.1 (3.8) [**]
No	9.0 (3.6)	31.5 (5.2)	21.4 (4.9)	12.0 (3.7)	5.8 (2.3)	11.2 (3.3)	1.6 (0.70)
TOTAL	8.3 (2.5)	28.6 (7.1)	21.7 (7.1)	13.8 (1.4)	5.1 (1.7)	8.1 (2.2)	1.6 (0.48)

[†] Weighted for sampling and participation rates, weights of 6 participants at the highest weight were truncated to next highest weight for these bivariate comparisons because of large influence on estimates.

[‡] Score on Lund-Mackay > 0

[*] p ≤ 0.05

[**] p < 0.01

[§] Based on questions from the ID Migraine questionnaire.

[¶] Never: did not report European Position Paper on Rhinosinusitis (EPOS) CRS symptoms in lifetime; past: met EPOS CRS symptoms in lifetime but not currently; current: met EPOS CRS symptoms in the last 3 months.

[¥] Divided at the median: high = at/above median; low = less than the median.

[£] Evidence of sinus surgery on sinus CT.