Twenty-two–item Sino-Nasal Outcome Test in a control population: a cross-sectional study and systematic review

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Background: **The 22-item Sino-Nasal Outcome Test (SNOT-22) is a commonly utilized outcome measure for chronic rhinosinusitis (CRS). However, what constitutes a normal score remains poorly defined. The goal of this study was to evaluate SNOT-22 scores in a control population without CRS and perform a systematic review and meta-analysis of "normal" values.**

Methods: **Ninety-nine subjects without CRS were enrolled, with 95 fully completing the SNOT-22 questionnaire. Multivariable linear regression was used to determine whether demographic factors or medical comorbidities influence SNOT-22 scores in a population without CRS. A systematic literature search was performed, identifying studies that evaluated the SNOT-22 in a non-CRS population and estimates for SNOT-22 values were pooled.**

Results: **Thirty-six males and 59 females were included in the primary analysis with a mean age of 53.4 ± 17.3 years (range, 18–88 years). The mean SNOT-22 score was 16.4 ± 15.2. Asthma ($p = 0.003$) and depression ($p = 0.002$) were found to be independent predictors of higher SNOT-22 scores. Thirteen articles were identified in the literature search and 1 was provided via author correspondence, with 10 reporting sufficient data to be included in the meta-analysis. Weighted mean SNOT-22 score was 11 ± 9.4 (n = 1517). Our data differed significantly from published data (mean difference = 5.4; 95% confidence interval [CI], 3.4 to 7.5; $p < 0.0001$) likely owing to differences in comorbidities.**

Conclusion: **SNOT-22 scores vary in non-CRS populations depending upon the group queried. Asthma and depression are associated with higher SNOT-22 scores and should be considered when determining what constitutes a normal value.** © 2015 ARS-AAOA, LLC.

Key Words:
sinusitis; quality-of-life; validation studies; meta-analysis; healthy volunteers

***How to Cite this Article*:**
Farhood Z, Schlosser RJ, Pearse ME, et al. Twenty-two–item Sino-Nasal Outcome Test in a control population: a cross-sectional study and systematic review. *Int Forum Allergy Rhinol*. 2015;XX:1–10.

Chronic rhinosinusitis (CRS) is one of the most common conditions in the United States, with a population prevalence of up to 12.5%.[1] Symptoms related to CRS include cardinal sinonasal complaints and extrarhinologic impacts such as fatigue and cognitive dysfunction, resulting in significant overall quality of life (QOL) declines.[2] The goal of most CRS treatments is to improve patient-reported symptoms and thus an emphasis has been placed on sinus-specific QOL as a metric to assess outcomes after both medical and surgical treatments.[3,4] The 22-item Sino-Nasal Outcome Test (SNOT-22) is a sinus-specific QOL questionnaire designed to quantitatively rate the severity of sinonasal disease. This questionnaire has been shown to be valid and reliable among patient populations with CRS and in recent years has become the most commonly used QOL instrument worldwide.[5]

A primary goal of CRS treatment is to improve sinus-specific QOL, ideally restoring it to a prediseased or "normal" level. With this goal in mind, it is imperative to have an estimate of what constitutes a normal SNOT-22 score. To date, a number of studies have examined SNOT-22 scores in various control populations without CRS. However, these studies vary in size and subjects often differ from typical patients with CRS with regard to age and common

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Potential conflict of interest: None provided.
Presented at the Annual ARS Meeting at the American Academy of Otolaryngology–Head and Neck Surgery (AAO-HNS) meeting, September 26, 2015, in Dallas, TX.
Supported by a grant from the Flight Attendant Medical Research Institute (ID#113042_CIA)

Received: 10 August 2015; Revised: 14 September 2015; Accepted: 18 September 2015
DOI: 10.1002/alr.21668
View this article online at wileyonlinelibrary.com.

CRS-associated comorbidities that might influence QOL scores. Additionally, most of these studies include patients from outside of North America. As a result it is difficult to establish expectations regarding what SNOT-22 score truly represents "normal" QOL. The first objective of this study was to prospectively evaluate SNOT-22 scores in a control population without CRS, exploring which factors might influence responses. The second objective was to perform a systematic review and meta-analysis of "normal" values across all published control populations.

Patients and methods

Cross-sectional study design

Adults accompanying patients during visits to the Otolaryngology–Head and Neck Surgery clinic at the Medical University of South Carolina (MUSC) were recruited to complete the SNOT-22 QOL questionnaire. The SNOT-22 contains 22 questions (total score range, 0–110), with higher scores representing more severe QOL impact. Information regarding demographics and medical comorbidities was also gathered by a trained study coordinator. Demographic information pertained to age, sex, gender, race, ethnicity, and level of education. Medical comorbidities included aspirin sensitivity, asthma, depression, chronic obstructive pulmonary disease (COPD), obstructive sleep apnea (OSA), and allergies. All comorbidities required a prior physician-given diagnosis or prior objective testing such as pulmonary function testing, polysomnography, or allergy skin testing where appropriate. Patients were excluded if they thought they had CRS, had a prior physician-given diagnosis of CRS, or a symptom profile that met criteria for CRS (2 or more cardinal symptoms for a minimum duration of 12 weeks) based on guidelines proposed by the American Academy of Otolaryngology–Head and Neck Surgery (AAO-HNS)[6] and European Position Paper on Rhinosinusitis and Nasal Polyps.[7] Active smokers were also excluded from the study. Institutional review board (IRB) approval was obtained at MUSC under protocol #16334.

Cross-sectional study data analysis

All data analyses were performed with SPSS 22.0 (IBM Corporation, Armonk, NY), SigmaPlot 12.5 (Systat Software, Inc., San Jose, CA), and MedCal 12.0.2.0 (MedCalc Software, Belgium). From the cross-sectional study data, patient information and demographic variables, such as age, gender, and medical conditions, were described with summary statistics. All continuous variables were assessed for normality by the Shapiro-Wilk test. Comparisons of outcomes for categorical variables were performed using the chi square or Fisher's exact test. For comparison of continuous variables between 2 groups, an independent t test or a Mann-Whitney test was used for the comparison of SNOT-22 scores between those patients with and without medical conditions like asthma and depression. In addition, Pearson's and Spearman correlations were employed to test for associations between SNOT-22 and age, gender, race, ethnicity, years of education, asthma, allergy, depression, OSA, and diabetes. If a significant correlation was observed among multiple variables and SNOT-22, then a regression model was used to determine whether any variables were independent predictors of SNOT-22 scores. A p value of <0.05 was considered statistically significant for all statistical tests.

Systematic review

A comprehensive literature search of the PubMed, Scopus, and EMBASE databases was performed on July, 8 2015 using the search terms "sino-nasal outcome test," "SNOT-22," and "validation" with an English language filter. Medline filters were applied to Scopus [AND NOT DBCOLL(medl*)] and EMBASE (NOT su = medline) to assist in removing duplicates. To be included, studies must have reported SNOT-22 scores from a control population without CRS. Studies that reported only statistical reliability/reproducibility without mean total scores were excluded. The search was performed by 2 authors (Z.F. and M.E.P.) and there were no date restrictions. Results were first reviewed by title and abstract before a full-text review was performed. References from all fully-reviewed texts were also screened for additional articles. Figure 1 shows a flowchart of the studies included.

Each included study was evaluated by using the Oxford Center for Evidence-Based Medicine (OCEBM) criteria.[8] Mean SNOT-22 scores along with standard deviations were extracted from each article by 2 authors (Z.F. and Z.M.S.), as well as demographic and comorbidity data when reported. The corresponding authors of the included studies were also contacted to solicit additional information when necessary. An overall weighted mean SNOT-22 score and standard deviation from all reported studies were calculated, including data from the current study. Additionally, the mean difference was determined between the pooled data from all studies (minus the MUSC data) and means scores from the MUSC cohort.

Results

Cross-sectional study

Of the 99 patients without CRS recruited for the study, 95 had fully-completed patient questionnaires, including 36 males and 59 females. Mean SNOT-22 score was 16.4 $\pm$ 15.2. The average age of patients was 53.4 $\pm$ 17.3 years (range, 18–88 years). No patients reported aspirin sensitivity or COPD. One patient had Crohn's disease. A summary of patient demographics can be found in Table 1.

Bivariate analysis revealed significant differences in SNOT-22 scores among patients with and without asthma (34.8 $\pm$ 16.2 and 15.1 $\pm$ 14.4, respectively; $p = 0.002$). A similar finding was seen with depression vs no depression (34.1 $\pm$ 17.2 and 15.0 $\pm$ 14.2, respectively; $p = 0.001$). Multiple linear regression was then performed using depression and asthma as independent variables of SNOT-22.

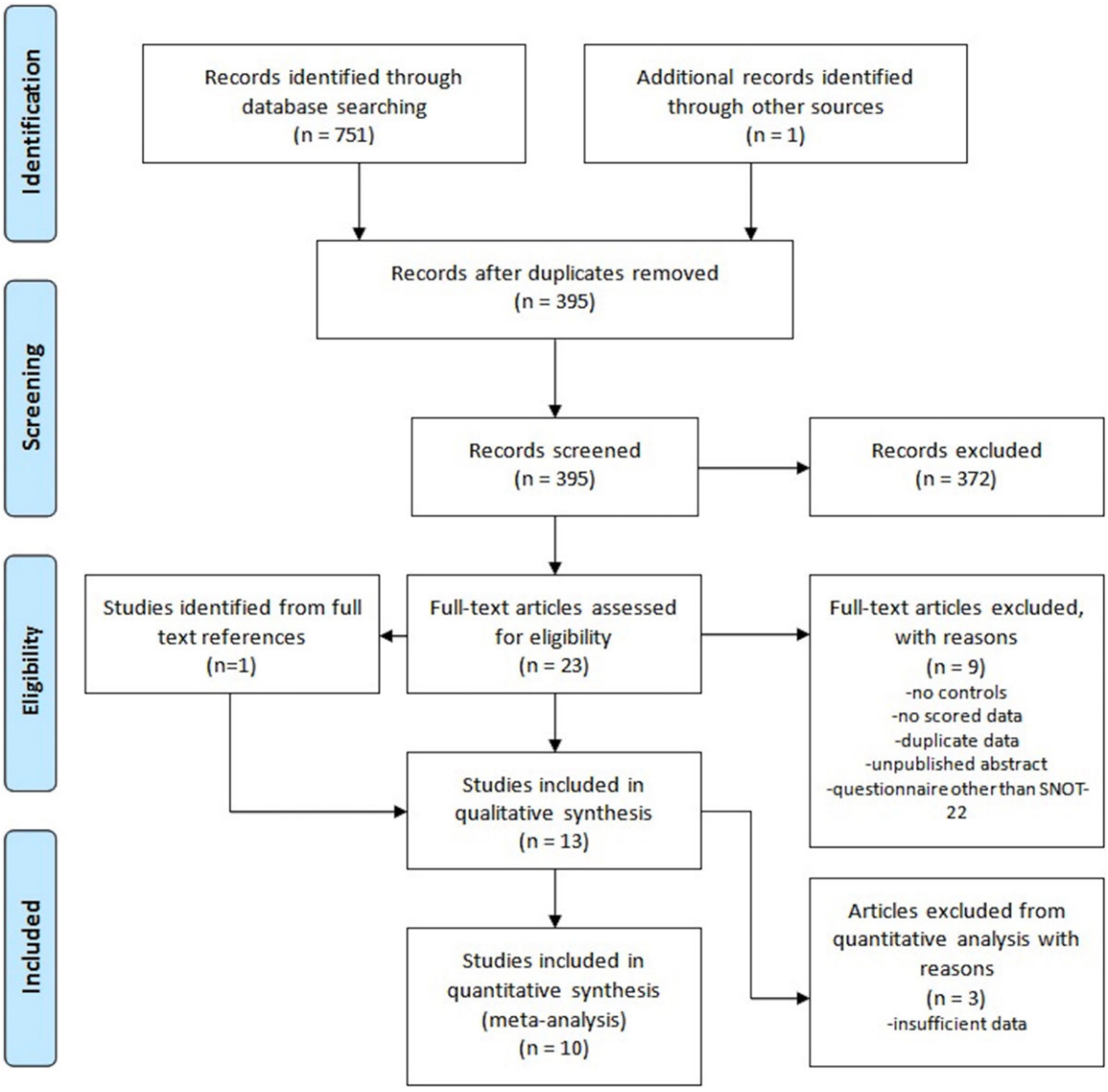

FIGURE 1. Literature search results. SNOT-22 = 22-item Sino-Nasal Outcome Test.

Both depression ($p = 0.002$) and asthma ($p = 0.003$) were significantly associated with SNOT-22, even after adjusting for each other. Those with asthma had an average SNOT-22 score that was 17.9 points higher than those without asthma, and those with depression had an average SNOT-22 score that was 17.6 points higher than those without depression.

Systematic review

A total of 395 articles were identified. Of these, 29 were selected based on title or abstract. After full-text screening, 13 articles[9–22] were selected for inclusion in the systematic review and 10 articles[9,10,12–18,21] were pooled for meta-analysis. One of the 10 articles was obtained by author correspondence[16,17] and another was retrieved from the references of 1 of the fully screened texts.[22] A summary of all articles can be found in Table 2. All were cross-sectional or prospective studies (level of evidence: 3).

The 10 articles were combined for a total number of 1517 patients with SNOT-22 data and 1417 patients for age data. Weighted mean SNOT-22 score was 11 ± 9.4. When the MUSC cohort was included, the mean score was 11.3 ± 9.8. MUSC on average had a higher SNOT-22 with a mean difference of 5.4 (95% confidence interval [CI], 3.4 to 7.5; $p < 0.0001$). Weighted mean age of published studies was 42.1 ± 13 years. When the MUSC cohort was included, the mean age was 42.8 ± 13.3 years. Comparison of means *t* test found a difference of 11.3 years between our population and the overall populations in the literature (95% CI, 8.5 to 14.1; $p < .0001$). These results are summarized in Table 3.

Discussion

In this prospective investigation of SNOT-22 scores in a non-CRS population, we found overall worse scores than

TABLE 1. Patient demographic and clinical data of cross-sectional study*

Variable	Mean ± SD	n	Association with SNOT-22 (*p*)
SNOT-22	16.4 ± 15.2	95	–
Age (years)	53.4 ± 17.3	95	0.921
Gender			0.754
Male		36	
Female		59	
Race			0.568
African American		26	
White		69	
Ethnicity			0.269
Hispanic/Latino		2	
Non-Hispanic/Latino		93	
Years of education	14.5 ± 2.6	95	0.778
Asthma		6	**0.002**
Allergy (by testing)		13	0.739
Depression		7	**0.001**
OSA		6	0.259
Diabetes		7	0.674

*Bold values are significant.
OSA = obstructive sleep apnea; SD = standard deviation; SNOT-22 = 22-item Sino-Nasal Outcome Test.

had previously been reported in the literature, with asthma and depression having a significant influence on the severity of scores. The average SNOT-22 score in our population was higher than all other studies with the exception of the study by Vaitkus et al.[21] There are several possible explanations for this finding. Prior studies recruited patients from populations that may not be entirely representative of a population with CRS; ie, from local tennis and sports clubs, medical students, and hospital staff and personnel. These patients would likely be younger with fewer medical comorbidities to potentially affect their scores. The optimal control population is one derived from the same theoretical source population as the disease of interest. Additionally, most other studies did not focus on the impact of other comorbidities and thus may have had a lower proportion of asthmatics and depressed patients. It is certainly possible that other comorbidities, not specifically recorded, also contributed to the higher scores in our population. Other explanations to account for differences in results could include seasonal variation, geographical location (urban vs rural),[23] and cultural variances.

The finding that asthma and depression might impact SNOT-22 scores is not entirely unexpected. The relationship between lower airway disease (ie, asthma) and the upper airway has previously been proposed through the unified airway theory.[24,25] Studies have shown that 70% of asthmatics have self-reported rhinosinusitis and that the odds of asthmatics having CRS is 3.5 times larger than nonasthmatics.[26,27] Thus it is possible that subclinical CRS contributed to higher SNOT-22 scores in our asthmatic cohort. Asthma and CRS are both chronic inflammatory diseases that exhibit "shared inflammation," and effective management of one disease can have a positive influence on the outcomes of the other.[25] A study by Zhang et al.[28] demonstrated that patients with asthma have been shown to exhibit a higher degree of improvement in SNOT-22 scores following surgical intervention; however comorbid-free CRS patients in their cohort still boasted a higher mean QOL. Similarly, Hopkins et al.[29] were able to discriminate between CRS patients with asthma and those without asthma based on SNOT-22 scores.

Regarding asthma in control populations, 2 studies in our systematic review noted a higher prevalence of asthma in their CRS populations than in their controls, although de Dorlodot et al.[9] were unable to find an interaction with asthma and SNOT-22 in their cohort.[19] Lange et al.[18] noted a significant difference in SNOT-22 scores in patients with allergic rhinitis, but not those with asthma, despite a higher prevalence of asthma patients in their control cohort. It is not entirely clear why this discrepancy in findings exists.

Similarly, psychiatric illness has been associated with worse QOL in the CRS population.[30] In their prospective study, Mace et al.[31] demonstrated that those with depression and CRS report worse QOL scores both preoperatively and postoperatively when compared to a euthymic cohort, but still showed a benefit from functional endoscopic sinus surgery (FESS). Litvack et al.[32] revealed similar findings (worse QOL baseline; clear benefit from operative intervention) and demonstrated a significant improvement in depression severity. Anxiety, which was not examined in this study, is also associated with a worse baseline SNOT-22 and less improvement in CRS patients following FESS.[33] We believe that ours is the first study to examine the effect of depression on SNOT-22 scores in a control population. This potential relationship is likely due to the overlap of QOL symptomatology between depression and specific SNOT-22 domains (ie, questions regarding energy level, sleep, ability to concentrate, and emotional state).

Our study excluded smokers, but previous studies have examined this phenomenon in CRS and control populations and found it to be an influential factor on QOL.[16,17,29,34,35] Lachanas et al.[16,17] showed that control smokers had a significantly higher SNOT-22 score across 5 of the 6 subscales proposed by Lange et al.[36] when compared to nonsmoking controls and that active smoking, but neither pack-years nor packs per day, had a positive influence on the SNOT-22. European and Asian populations tend to have a higher prevalence of smokers compared to the Americas and so results of future studies should be interpreted with geographic consideration.[37]

TABLE 2. Summary of studies in systematic review

Sources	Subjects	Exclusion criteria[a]	Sample size (n)	Age (years) (mean ± SD)	Males; females (n)	SNOT-22 score (mean ± SD)
de Dorlodot et al.[9] (2015)	Medical staff and sports clubs	Under 18 years; pregnant	46	45.2 ± 13.5	25; 21	8.3 ± 8.7
de los Santos et al.[10] (2015)	Patients and their relatives, physicians and their relatives, neighbors		59	41	25; 34	4.49 ± 7.35
Gillett et al.[11] (2009)	Hospital staff and local tennis club	Under 16 years; rhinosinusitis medication use	40	40	54; 62	9.3
Gregorio et al.[12] (2015)	Patient relatives and companions	Rhinosinusitis medication use	539	43.91 ± 16.36	253; 286	9.83 ± 8.16
Jalessi et al.[13] (2013)	Patient family members and medical personnel	Under 18 years; rhinosinusitis medication use	30	33 ± 6.7	11; 19	7.6 ± 9.1
Kosugi et al.[14] (2011)	Medical university staff and patient companions	Under 18 years	113	23.35 ± 8.13	49; 64	11.42 ± 9.46
Lachanas et al.[15] (2014)	Medical staff and patient companions	Under 18 years; pregnant	120	40.5 ± 9.97	65; 55	13 ± 11.68
Lachanas et al.[16,17] (2015)	Smokers	Under 18 years; pregnant, URI in last month	52	40.51 ± 1.19	27; 25	17.59 ± 1.79
	Nonsmokers		75	40.88 ± 1.34	42; 33	9.76 ± 1.06
Lange et al.[18] (in press)	Respondents to postal questionnaire		268	47.1 ± 14.6	126; 142	10.5 ± 11.6
Marambaia et al.[19] (2013)		Illiterate; smokers	98	37.8 ± 12.9	40; 58	8[b]
Schalek et al.[20] (2010)	Admitted patients		50	44.9	24; 26	13.68 ± 11.74
	Students		50	24.1	22; 28	10.22 ± 11.59
Vaitkus et al.[21] (2013)	Medical staff and otology in-patients	Under 18 years; pregnant	115	45.58 ± 14.96	37; 78	16.78 ± 16.1
Yeolekar et al.[22] (2013)	Medical students	Rhinosinusitis medication use	230	21	97; 133	8.07
MUSC + Literature			1512	42.8 ± 13	704; 808	11.3 ± 9.8
			1612		750; 862	

[a]All patients with CRS excluded.
[b]Median.
CRS = chronic rhinosinusitis; MUSC = Medical University of South Carolina; SD = standard deviation; SNOT-22 = 22-item Sino-Nasal Outcome Test; URI = upper respiratory infection.

Strengths of the cohort study in this article include relativity large sample size and inclusion of medical comorbidities. Additionally, patients were recruited from the same source population as patients with CRS seeking medical treatment, helping to minimize ascertainment bias. Given that the patients in our cohort were not subject to prospective independent confirmation of their medical comorbidities, there remains the possibility of misclassification bias for some comorbidities. Because we did not use objective criteria to rule out a diagnosis of CRS (ie, computed tomography [CT] or nasal endoscopy), it is also possible that unobserved sinonasal inflammation contributed to the higher scores in our cohort, especially given that asthma severity is correlated with abnormal CT scan findings.[38]

Determination of a "normal" SNOT-22 score has incredibly useful clinical implications. In CRS patients with preoperative scores <20, it has been shown that FESS is unlikely to yield clinical improvement.[39,40] Pretreatment SNOT-22 scores across multiple studies have been between 40 and 60, and following intervention have shown notable improvement.[9,19,29,41–43] A recent study examining the 4 CRS subtypes found no difference between groups for

TABLE 3. Comparison of mean SNOT-22 scores and ages between literature and study cohort

Variable	Literature	MUSC	Mean difference	95% CI	*p*
SNOT-22, mean ± SD	11 ± 9.4[a]	16.4 ± 15.2	5.4	3.4–7.5	<0.0001
Age (years), mean ± SD	42.1 ± 13[b]	53.4 ± 17.3	11.3	8.5–14.1	<0.0001

[a]10 studies, 1517 patients, 12 populations.
[b]9 studies, 1417 patients, 10 populations.
CI = confidence interval; MUSC = Medical University of South Carolina; SD = standard deviation; SNOT-22 = 22-item Sino-Nasal Outcome Test.

preoperative SNOT-22 scores, and all groups showed significant improvement following surgery, with mean postoperative scores ranging between approximately 10 and 25.[44] This can certainly help in counseling patients regarding disease management strategies and outcome expectations, especially because it has been shown that those with worse SNOT-22 scores are more likely to elect FESS.[45] Considering the results of our current study, it would seem reasonable for clinicians to aim for similar scores when managing CRS. For patients with low preoperative scores, the risks and benefits of surgery should be carefully weighed.

To date this is the first study in North America that examines SNOT-22 scores in a disease-free population and findings were notably different from the majority of prior publications. Having reliable normative data for the SNOT-22 instrument is critical for future clinical research, both in setting patient expectations and judging success of various treatments. Future studies are needed utilizing even larger sample sizes and recruiting from diverse geographic regions, with information gathered on factors such as depression, asthma, and smoking status. This would allow more precise estimates to be developed for any given patient or population of patients, based on their individual comorbidities.

Conclusion

SNOT-22 scores vary in non-CRS populations depending on the group queried. Asthma and depression are associated with SNOT-22 scores up to 17 to 18 points higher than those without either comorbidity and should be considered when determining what constitutes a normal value.

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