SNOT-20 Questionnaire as Predictor of Chronic Rhinosinusitis or Non-sinusitis Facial Pain Disorders

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GLOSSARY

AAO-HNS:	American Academy of Otolaryngology – Head and Neck Surgery
CI:	confidence interval
CRS:	chronic rhinosinusitis
CT:	computed tomography
LM:	Lund-Mackay sinusitis-specific computed tomography grading system
OR:	odds ratio
ROC:	receiver operator characteristic
RSTF:	the American Academy of Otolaryngology – Head and Neck Surgery Rhinosinusitis Task Force
SD:	standard deviation
SNOT-20:	Sino-Nasal Outcomes Test
TFR:	the American Academy of Otolaryngology – Head and Neck Surgery Task Force on Rhinosinusitis
TMJ:	temporomandibular joint dysfunction/pain
UW:	University of Washington, Seattle WA
UWMC:	University of Washington Medical Center, Seattle WA

INTRODUCTION

Chronic rhinosinusitis (CRS) is one of the most common chronic diseases in the United States, affecting more than 11 million adult Americans, or approximately five percent of the population each year[1]. This condition has a significant impact on the patient's quality of life and on the healthcare system overall. The costs for treating patients' sinus complaints equal more than $8.6 billion annually[1] with an estimated 11.5 million workdays lost[2]. Common symptoms of CRS include nasal drainage, nasal obstruction, decreased sense of smell, facial pain or pressure, headache, and fatigue.

Several non-sinusitis headache and facial pain disorders may present with symptoms similar to those of CRS, thus complicating the accurate diagnosis of both disease categories. These disorders represent greater than 60 separate disease entities that cause pain and other symptoms related to the head[3]. Migraine headaches, cluster headaches, tension-type headaches, rebound headaches, chronic daily headaches, persistent idiopathic facial pain and temporomandibular joint dysfunction (TMJ) are among several included disorders with symptoms ranging from dull facial pressure to intense stabbing or throbbing pain. This combination of headache and facial pain symptom disorders will be referred to as "facial pain disorders" from here on. Facial pain disorders are commonly categorized into three distinct groups based on underlying etiology: musculoligamentous/soft tissue, dentoalveolar, neurological/vascular[4] (Table 1).

Treatment guidelines for CRS vary, but may include a stepwise combination of nasal saline lavage, nasal corticosteroids, antibiotics, oral corticosteroids and eventually surgery[5]. Treatments for facial pain disorders may differ greatly depending on the specific diagnosis, but range from medications such as antidepressants, gabapentin, oral corticosteroids and antivirals to alternative therapies such as biofeedback and hypnosis, as well as treatments including

injections of botulinum toxin and surgery[6]. The currently accepted method for differentiating between CRS and facial pain disorders requires a computed tomography (CT) scan or nasal endoscopy. Though CT scans are relatively safe, they do expose patients to radiation. Nasal endoscopy is another method used by otolaryngologists to help diagnose CRS, however this procedure also leads to increased patient time invested and health care dollars spent.

Given that there is considerable overlap in symptoms related to CRS and facial pain disorders, the ability to more easily and accurately determine whether a patient suffers from one or the other could significantly affect treatment recommendations and lead to more cost effective treatment. Historically the diagnosis of CRS was made predominantly by patients' report of symptoms[7]. However, in 2007 the American Academy of Otolaryngology – Head and Neck Surgery (AAO-HNS) Rhinosinusitis Task Force (RSTF)[*] recommended establishing nasal endoscopic evidence of CRS and/or CT evidence to make the diagnosis in addition to the previously noted symptom requirements[8]. A subjective screening or diagnostic tool to differentiate CRS from other non-sinusitis facial pain disorders, and particularly an instrument that is already widely utilized in the clinical setting, would be of great benefit[9].

Previous studies have investigated the association between facial pain symptom severity and the Lund-Mackay (LM) CT staging score[10], which is a grading scale used to objectively quantify radiographic evidence of sinus mucosal inflammation[11] (Appendix A). Other studies have investigated the relationship between CRS and LM CT score[12,13], and between various CRS symptom based scores and CT findings[14-16]. As such, the 20 question Sino-Nasal Outcomes Test (SNOT-20)[17] (Appendix B) is a well validated questionnaire that is used extensively in

[*] The Rhinosinusitis Task Force (RSTF) is also commonly cited in the literature as the Task force on Rhinosinusitis (TFR).

rhinology clinics across the US and the world to assess for subjective rhinosinusitis disease-specific quality of life response to treatment.

We sought to determine if the SNOT-20 instrument has value as a non-invasive and inexpensive tool to help improve providers' diagnostic accuracy between CRS and facial pain disorders. Such an instrument could be used widely in the primary care setting as well as the rhinology clinic to help streamline patients with facial pain disorders into a speedier course of action. These patients could potentially be spared from taking up to several courses of antibiotics that would otherwise be used to treat their subjective symptoms consistent with CRS until they undergo CT scan that demonstrates normal mucosa of the paranasal sinuses, thus ruling out CRS. Helping providers decide which patients might have non-sinusitis related facial pain would mean that patients would undergo CT sooner than if waiting for standard response to medical therapies. The sooner these patients are able to be appropriately CT scanned, the sooner other potential sinister pathologies can be caught or ruled out, and the sooner the patient can be diagnosed and treated appropriately for their disease. We also investigated whether individual questions of the SNOT-20 could distinguish between CRS and facial pain disorders.

METHODS

Study design: This was a cross sectional study where the primary exposure of interest was the SNOT-20 score and the primary outcome of interest was disease status (CRS or facial pain disorder). For patients included in our main analyses, the SNOT-20 score for each of the 20 questions was collected and the total score calculated. CRS was defined according to the 2007 RSTF criteria which include: two or more symptoms of purulent nasal drainage, nasal obstruction, facial pain/pressure/fullness, and/or decreased sense of smell in addition to evidence of inflammation (including purulent mucus or edema of the middle meatus or ethmoid region, nasal polyps, and/or radiographic imaging confirming paranasal sinus inflammation persisting for more than 12 weeks)[7] (Table 2). The diagnosis of facial pain disorder was assigned to symptomatic patients that did not have objective signs to meet RSTF criteria for CRS, for whom a specific facial pain disorder etiology was suspected (Table 3).

Study setting: The study consisted of patients who presented to the senior author's (G.E.D) rhinology clinic at the University of Washington Medical Center (UWMC) for the first time between 06/30/2008 and 09/30/2010 for evaluation of symptoms consistent with CRS. The UWMC is a tertiary care center, which has a referral area that includes the states of Washington, Wyoming, Alaska, Montana and Idaho.

Study subjects: We screened for inclusion all subjects with specific diagnostic codes for either CRS or a facial pain disorder. Those subjects who were included in main analyses had been further screened for accuracy of diagnosis per 2007 RSTF criteria and other inclusion criteria such as presence of CT scan in the UWMC system available for review, and availability of a completed SNOT-20 instrument prior to maximal medical therapy intervention[†]. However, not all

[†] Maximal medical therapy included nasal saline irrigation, nasal corticosteroids and a course of antibiotics.

CRS patients who were identified by diagnostic code and confirmed by chart review were included in our main analyses, as inclusion of all such patients was deemed unnecessary. We calculated that with 33 subjects in each group we would be able to provide 85% power to detect a mean difference equal to the minimally reported clinical difference (0.8) in total SNOT-20 scores[17]. A convenience sample of CRS subjects chosen for inclusion in SNOT-20 analyses consisted of patients selected in alphabetical order from the list of those with confirmed diagnoses who met inclusion criteria. All facial pain disorder subjects with available CT scan and presence of SNOT-20 prior to maximal medial therapy who did not have concomitant CRS were included in our primary analyses.

Data collection: This protocol was approved by the Institutional Review Board for Protection of Human Subjects at UWMC prior to conducting this study. All data were abstracted from subjects' UWMC medical record. Relevant data included age, sex, SNOT-20 questionnaires and CT images from which LM CT scores were calculated. Prior relevant medication and surgical histories, and specific facial pain disorder diagnoses were not recorded. All data were de-identified and stored on a secure online server.

Data analysis: For our primary goal of determining if the total SNOT-20 score was different between patients with CRS and patients with facial pain disorders we first performed multiple imputation of all missing values using STATA 11 (College Station, TX) to assist in estimating average SNOT-20 scores. Multiple imputation is a method for handling missing data values. In this method, ten versions of the dataset were created using the available data to predict the missing values. Stata's user written "ice" package was implemented for this purpose; to predict the missing scores of individual questions on the SNOT-20. Imputation was not utilized for values of age or sex, as this information was successfully ascertained from all patients' records. The ice procedure uses a regression switching or "chained equations" approach to imputation

for multiple variables with missing values. Once the ten data sets have been created, they are used to conduct ten regression analyses, each with its own coefficient estimates and standard errors. These analyses are then combined into one inferential analysis using Rubin's combining rules[18,19]. From these values we generated simple and multiple linear regression models to test for evidence of statistically meaningful differences in SNOT-20 total scores between the two disease populations before and after adjustment for potential confounding factors.

In order to further determine if the individual questions of the SNOT-20 instrument differed significantly between patients with CRS and facial pain disorders we performed a non-parametric test of equality of distribution, the Wilcoxon rank sum test. This was performed on the pre-imputed SNOT-20 data as the Wilcoxon rank sum test is not compatible with multiple imputation. This test generated estimates regarding the null hypothesis that there was no difference between groups, and was performed for each question of the SNOT-20 by diagnosis. Additional variables comprising specific combinations of questions of the SNOT-20 were also generated and analyzed.

Subsequently, logistic regression of the imputed datasets provided ORs with 95% confidence intervals (CIs) for each question & combination of questions of the SNOT-20 instrument and their association with diagnosis of CRS. Additionally, receiver operator characteristic (ROC) curve analysis was performed for each individual question and combination of questions. The area under the curve (AUC), sensitivity and specificity for diagnosis of CRS were calculated for various cutoff points for each question to determine if meaningful predictive value could be generated. These analyses were directed to predict diagnosis of CRS, such that a test with relatively high sensitivity would effectively rule out the diagnosis of CRS with a negative result. Data from all subjects meeting complete diagnostic criteria, though not necessarily all inclusion criteria for either CRS or a facial pain disorder were then used to generate summary statistics,

such as proportion of patients with facial pain disorders in this clinic population.

RESULTS

We screened for inclusion 397 patients who presented to the UW Rhinology Clinic for evaluation of facial pain and other symptoms consistent with CRS between 6/2008 and 9/2010, via specific diagnostic codes for either CRS or a facial pain disorder. Two hundred and eighteen of these new patients were diagnosed with CRS without concomitant facial pain disorder. We found 49 facial pain disorder patients, and nine patients who met criteria for both disease entities. Accordingly, we determined the proportion of facial pain disorders relative to diagnoses of CRS in this group of patients referred to an urban tertiary care rhinology clinic with a presumed diagnosis of CRS to be 18% (95% CI 0.14 – 0.24) (Table 4). On average, patients with facial pain disorders in this overall sample were slightly younger than patients with CRS (42.9 years vs. 48.2 years), and were more likely to be female (75.5% vs. 56.4%).

Our main analyses involving the SNOT-20 included 73 subjects with CRS and 34 with facial pain disorders who met complete inclusion criteria for analysis of the primary study aims (Table 5). These analyses did not include 169 patients from the overall sample who, apart from those simply left out of the convenience sample were most commonly excluded due to lack of SNOT-20 available for review from prior to initiation of maximal medical therapy, or due to lack of CT scan available for review within the UWMC system. The distributions of both age and sex among patients in this study sample were very similar to those among the overall sample. Lund-Mackay CT scores differed significantly with a mean of 10.4 for patients with CRS and 1.2 for patients with facial pain disorders. Total SNOT-20 scores were normally distributed across diagnoses in our study population (Figure 1). Consistent with prior literature, we found that total SNOT-20 scores did not correlate significantly with LM CT score[20,21] (Figure 2). Mean total SNOT-20 score for patients with CRS was 41.5 (95% CI 37.0 - 46.1). Patients with facial pain disorders had mean total score of 43.7 (95% CI 37.0 – 50.4). There was no statistical evidence

that the mean SNOT-20 total scores were different for patients who have CRS from patients who have facial pain disorders (p=0.42).

Even after adjusting for sex and age the association between mean SNOT-20 score and diagnosis was not statistically significant (Table 6). Upon graphical analysis there appeared to be no association with SNOT-20 total score between the ages of roughly 35 and 65, whereas there appeared to be a positive association prior to 35 and a negative association after 65 (Figure 3). Using a change in the OR of ≥ 10% from crude to adjusted as an indicator of a confounder *a priori*, sex and age appeared to confound the relationship between diagnosis and SNOT-20 total score. However they both demonstrated wide CIs, which included the crude OR. The same was true for the interaction of age and sex on the relationship between diagnosis and SNOT-20 total score. Additionally the p-value (0.68) did not reach our predetermined significance level (0.05).

According to the Wilcoxon rank-sum test for individual SNOT-20 questions 1-5, 7,8 and 11-20, there was no statistical evidence of a true difference between median SNOT-20 scores for patients with CRS and those with facial pain disorders (Table 7). However, for individual SNOT-20 questions 6, 9 & 10 (thick nasal discharge, ear pain, facial pain/pressure), there was statistical evidence that a difference existed between median scores of each of these questions for patients with CRS and facial pain disorders (p=0.044, p=0.003, p=0.002 respectively). When the scores from questions 9 & 10 were combined, there was a corresponding increase in the strength of the evidence for a difference between median scores for patients with CRS and facial pain disorders (p<0.0001). As shown in Table 5, a high score on question 6 corresponded to diagnosis of CRS, whereas high values for questions 9 &10 were negatively associated with CRS and positively associated with diagnosis of a facial pain disorder. The values for these three questions were combined to jointly predict diagnosis of CRS using a simple equation.

Since each question was scored 0-5, values were combined to predict CRS by adding the score of question six to the inverse scores of questions 9 & 10 i.e., 10 – q9+q10. Accordingly, for the combination of questions 6, 9 & 10 we found statistically significant evidence of a difference between median scores for patients with CRS and facial pain disorders ($p<0.0001$).

Using logistic regression models we calculated ORs for each individual question or combination of selected questions' utility as a successful predictor of CRS (Table 8). Potentially meaningful ORs were found for question 6 (OR = 1.33, 95% CI 1.03 – 1.70), question 9 (OR = 0.60, 95% CI 0.44 – 0.83), and question 10 (OR = 0.63, 95% CI 0.46 – 0.86). The ORs for questions 7 & 20 (ear fullness & embarrassed) also stood out, however, their confidence intervals both included one. Other statistically meaningful ORs were calculated for the combination of 9 + 10 (OR = 0.71, 95% CI 1.15 – 1.73), and the combination of 6, 9, & 10 (OR = 1.67, 95% CI 1.32 – 2.12).

ROC curve analysis performed for each individual question and combination of questions identified several meaningful relationships with diagnosis of CRS (Figure 4). Most notably, the AUC for the combination of values from questions 6, 9 & 10 was 0.79 (95% CI 0.70, 0.87) (Table 9). The sensitivity and specificity were calculated for various cutoff points for questions and combinations of questions to determine if valuable predictive statistics could be generated (Table 10). For the combined test of questions 6, 9, & 10 a total score of ≥ seven was found to be highly sensitive for diagnosis of CRS (94.0% sensitivity). The specificity at that cutoff was 46.7%.

DISCUSSION

The primary aim of this study was to determine if the total SNOT-20 scores were significantly different between patients with CRS and patients with facial pain disorders, such as to improve the diagnosis and care for both of these groups of patients. Secondary goals included analyses of individual questions and combinations of questions of the SNOT-20 for the ability to differentiate these two disease entities for the same overall purpose of improving diagnosis and care. Novel findings included that combinations of individual questions of the SNOT-20, but not the SNOT-20 total score, were highly sensitive in differentiating between CRS and facial pain disorders. We were also interested in determining the ratio of patients with facial pain disorders to patients with CRS in the setting of an urban tertiary care rhinology clinic as this had not been previously reported in the US. Such clinics likely represent a substantial proportion of providers who utilize the SNOT-20.

One motivation for this study was a concern that some clinicians may be interpreting the SNOT-20 scores of their patients incorrectly. Specifically, some clinicians may hold the implicit or explicit belief that since the SNOT-20 is described as a sinusitis disease specific instrument, higher total SNOT-20 scores are more likely to indicate a diagnosis of CRS**.** We have shown this to be false. Total SNOT-20 scores were not significantly different between patients with CRS or facial pain disorders.

The SNOT-20 was designed for the purpose of evaluating subjective sinonasal symptom response to treatment of rhinosinusitis. However, it was previously unknown if certain subsets of its questions could help to differentiate patients suffering from symptoms consistent with CRS into diagnostic categories of facial pain disorder or CRS. Although we found that the total SNOT-20 score was not associated with either disease, our subsequent analyses demonstrated three individual questions (6 = thick nasal discharge, 9 = ear pain, 10 = facial pain/pressure)

that showed statistically significant different values between CRS and facial pain disorder patients. When the three significant questions were combined together their predictive value increased.

Interestingly, question 9 (ear pain) represents a symptom that was included in previous versions of diagnostic criteria for CRS[22], but was removed prior to the 2007 RSTF report. A prior report by Hessler[23] et al. also found that of the individual questions in the SNOT-20, ear pain showed the least amount of overall change in score in response to medical therapy, indicating that it either might not be a symptom of CRS or that it may respond to medical therapy differently. The finding that ear pain was not associated with CRS in our study population is consistent with such prior literature.

In designing the analyses for our study, we considered the implications of prioritizing sensitivity, specificity, or overall % classified correctly for the purpose of achieving meaningful conclusions. At the risk of incorrectly predicting that some patients with facial pain disorders might have had CRS, it was more important in our interpretation to accurately predict a diagnosis of CRS for all patients that had the disease, than it was to predict all diagnoses of facial pain disorders. As such, our analyses were performed to investigate variables from the SNOT-20 instrument that predicted diagnosis of CRS at various cutoff values. The high sensitivity and relatively low specificity of the combination of questions 6, 9 and 10 for several cutoff values indicated that we were able to correctly predict diagnosis for nearly all of the patients with CRS, while correctly classifying close to half of the facial pain disorder patients.

For the combination of questions 6, 9, & 10, a cutoff score ≥ seven, as calculated by the equation ({question 6} + 10 – {question 9 + question 10}), attained 94% sensitivity for diagnosis of CRS. This meant that only six percent of CRS patients were misclassified by these criteria.

Thus for a patient with undifferentiated symptoms of CRS and a combined score less than seven, antibiotic therapy might not be necessary as part of the workup of disease classification prior to the patient receiving a CT. In the setting of the rhinologist's office implementation of these screening criteria would have effectively eliminated nearly half of all unnecessary courses of antibiotics for patients with facial pain disorders who were presumed to have CRS prior to CT scan-confirmed absence of CRS. In the primary care setting, however, the magnitude of the effect could be even greater. Most patients with sinonasal or facial pain symptoms consistent with CRS are referred to a rhinologist often only after several unsuccessful treatments with antibiotics and other appropriate treatment modalities for symptoms of CRS[24]. Such therapeutic trials that eventually lead to consultation by a rhinologist and subsequent diagnosis of CRS or a facial pain disorder can substantially delay correct diagnosis of facial pain disorders that masquerade as CRS, or equivalently delay the diagnosis of other potentially more dangerous pathologies. These results represent significant potential financial benefit to the patient and healthcare system, and overall decreased risk from unnecessary antibiotic treatments.

Previous estimates of the prevalence of non-sinusitis based facial pain disorders in the otolaryngology literature were calculated prior to the currently accepted diagnostic criteria for CRS, and additionally, they were generated from a specific subset of the population in the UK[25,26]. Obtaining an accurate estimate of this prevalence is important for our ability to better understand the magnitude of the problem of non-sinusitis facial pain in the outpatient rhinology setting. Our study design allowed us to calculate a ratio of these diagnoses. If this ratio is interpreted as prevalence, however, this may lead to overestimation, as our calculations were not based off of the total population of patients seeking evaluation for CRS, but rather only from patients who were diagnosed with CRS or a facial pain disorder. Hence, we cannot extrapolate the true prevalence of facial pain disorders among all patients with symptoms consistent with CRS. Nonetheless, the relatively high estimate found in this study does provide insight into this

patient population. For every 4.5 patients diagnosed with CRS from 6/2008 – 9/2010, one was diagnosed with a facial pain disorder.

In 2002, Macfarlane et al[27]. reported the overall prevalence of orofacial pain in a particular UK community to be 26%. This figure cannot be compared to our calculated proportion (18%) given that they estimated the population prevalence of overall orofacial pain symptoms in an English community, and that their disease definition was distinct from that utilized in our investigation. Nonetheless, the relatively high ratio of patients with facial pain disorders to patients with CRS found in our population is evidence that facial pain disorders may represent a clinically meaningful fraction of this patient population. These findings should provide even further impetus to develop improved screening or diagnostic methods that can differentiate patients with facial pain disorders from those with CRS.

Limitations: A potentially meaningful limitation to our study was that we did not have a large enough sample of men and women to conduct analyses by sex. Given our data it was difficult to predict whether or not either sex would have been a significant confounder or effect modifier in our analyses, although it appears to not have been a confounder with regards to the SNOT-20 total score (Figure 5). Another potential limitation was that numerous patients included in this study had been previously diagnosed with CRS by other providers and many had undergone previous sinus surgery. Though these patients were new to the senior author, they did not truly represent new diagnoses of CRS and their inclusion in the study may have led to potential bias such that patients with numerous prior sinus surgeries may represent a fundamentally different population, who may also respond to the SNOT-20 instrument differently. Alternatively, it is also possible that the inclusion of these patients led to a more realistic summary statistic of the population because of the complex histories of many rhinology patients regularly seen in any clinic setting. There is concern, however, that the urban tertiary care rhinology population from

which our study subjects were chosen might not be representative of patients in the greater community of patients with these conditions, due to the fact that tertiary care centers more commonly treat severe, recalcitrant, or diagnostically challenging diseases. Thus the generalizability of our findings may be limited to similar health care settings.

Furthermore, there is potential for bias incurred by the fact that some of the patients included in the study were already receiving some form of medical therapy for treatment of their rhinosinusitis symptoms at the time of SNOT-20 questionnaire. This was unavoidable as patients with CRS symptoms were often referred from other providers after repeated failure to respond and were expediently seen in clinic while still being treated, or having just recently finished medical therapy. Previous studies have shown that medical therapy is associated with modest improvement in SNOT-20 scores[23], so it is possible that a slight differential response was present for these individuals compared to others who were not taking medications to the same degree. However, since we did not actively measure these data we do not know whether or not facial pain disorder and CRS patients differentially received prior treatments for CRS-like symptoms.

Future studies: We would like to suggest that further investigations into the relationship between CRS, facial pain and methods to distinguish the two via subjective questionnaires be performed prospectively, and include a larger, more diverse overall patient population with patients recruited from multiple hospital sources to improve generalizability. It would also be beneficial for analyses to utilize in the specific type and duration of prior medical treatment for symptoms as well as to obtain the specific type of facial pain disorders affecting each patient. This would permit further stratification of data, potentially yielding different sensitivities and specificities for prediction of individual facial pain disorders. Other information, which may be of interest for future investigations includes race/ethnicity, socioeconomic status, smoking status, presence of

nasal polyps, prior sinus surgery, history of specific facial pain disorder diagnoses, and other medical comorbidities.

Table 1.
Common classification schemes of facial pain, adopted from Zakrzewska, 2002[28].

Musculoligamentous/soft tissue	Dentoalveolar	Neurological/vascular
Temporomandibular joint (TMJ) pain	Dentinal	Trigeminal neuralgia
Facial arthromyalgia, myofascial pain	Periodontal	Glossopharyngeal neuralgia
Atypical facial pain/idiopathic orofacial pain	Pulpal	Nerve compression
Salivary gland disease	Cracked tooth syndrome	Cluster headache
Optic neuritis	Maxillary sinusitis	Post-herpetic neuralgia
Internal derangements TMJ	Thermal sensitivities	Cranial arteritis
Burning mouth	Atypical odontalgia	Pre-trigeminal neuralgia
Candidiasis		SUNCT*
Cancer, sinuses, nasopharynx, brain		Ramsay Hunt
		Tolosa Hunt syndrome
		Migraine headaches

*SUNCT, short lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing.

Table 2.
Diagnostic criteria for chronic rhinosinusitis

Diagnostic criteria: CRS

Twelve (12) weeks or longer of two or more of the following signs and symptoms:

- Mucopurulent drainage (anterior, posterior, or both)
- Nasal obstruction (congestion)
- Facial pain-pressure-fullness, or
- Decreased sense of smell

AND inflammation is documented by one or more of the following findings:

- Purulent (not clear) mucus or edema in the idle meatus or ethmoid region,
- Polyps in the nasal cavity or middle meatus, and/or
- Radiographic imaging showing inflammation of the paranasal sinuses

Table 3.
Diagnostic criteria for facial pain disorders

Table 4.
Proportion and characteristics of CRS, facial pain disorder, and concomitant CRS & facial pain disorder patients included in proportion calculation, UW Rhinology Clinic, 2008 – 2010

	CRS	**Facial pain disorder**	**Concomitant CRS & facial pain disorder**
N	218	49	9
Sex (% female)	56.4	75.5	44.4
Age in years	48.2 (15.3)	42.9 (9.7)	47.1 (8.8)
Proportion (95% CI)	0.82 (0.76, 0.86)	0.18 (0.14, 0.24)	*

* Patients with concomitant CRS and facial pain disorders were excluded from proportion and all other calculations

Table 5.
Characteristics of chronic rhinosinusitis and facial pain disorder patients, UW Rhinology Clinic, 2008 – 2010

	CRS (n=73)		**Facial pain disorder (n=34)**	
	Mean (sd)	% missing	Mean (sd)	% missing
Age (years)	49.6 (15.9)	0	43.4 (9.9)	0
Sex (% female)	56 (50)	0	79 (41)	0
LM CT score	10.4 (4.8)	0	1.2 (1.1)	0
SNOT-20 Questions				
1. Need to blow nose	2.69 (1.5)	2.7	2.39 (1.3)	2.9
2. Sneezing	1.52 (1.4)	2.7	1.47 (1.2)	5.9
3. Runny nose	2.28 (1.4)	4.1	1.97 (1.4)	5.9
4. Cough	1.87 (1.6)	2.7	1.55 (1.2)	2.9
5. Post-nasal discharge	2.84 (1.5)	2.7	2.45 (1.3)	8.8
6. Thick nasal discharge	2.78 (1.7)	4.1	2.00 (1.6)	8.8
7. Ear fullness	1.65 (1.5)	5.5	2.21 (1.3)	2.9
8. Dizziness	1.32 (1.5)	4.1	1.69 (1.5)	5.9
9. Ear pain	0.88 (1.2)	4.1	1.73 (1.5)	2.9
10. Facial pain/pressure	2.58 (1.6)	1.4	3.59 (1.3)	0
11. Difficulty falling asleep	1.96 (1.8)	4.1	2.00 (1.6)	2.9
12. Wake up at night	2.44 (1.7)	2.7	2.09 (1.7)	2.9
13. Lack of a good night's sleep	2.76 (1.7)	4.1	2.52 (1.7)	2.9
14. Wake up tired	2.65 (1.6)	1.4	3.06 (1.6)	5.9
15. Fatigue	2.66 (1.7)	0	3.13 (1.4)	5.9
16. Reduced productivity	2.37 (1.7)	2.7	2.73 (1.6)	2.9
17. Reduced concentration	2.21 (1.7)	1.4	2.58 (1.5)	8.8
18. Frustrated/restless/irritable	2.03 (1.7)	2.7	2.48 (1.6)	2.9
19. Sad	1.31 (1.6)	1.4	1.59 (1.6)	5.9
20. Embarrassed	0.83 (1.4)	4.1	0.41 (0.9)	5.9
SNOT-20 total*	41.51 (20.9)	2.5	43.54 (15.6)	3.2

* SNOT-20 total scores calculated using imputed data

Table 6.
Association between SNOT-20 total score and diagnosis, and between combined questions 6, 9 & 10 (ear pressure, ear pain & facial pain/pressure) and diagnosis after adjustment for potential confounding factors, UW Rhinology Clinic 2008-2010

SNOT-20 total			
Model adjusted for:	**OR**	**P value**	**95% CI**
Crude	0.12	0.60	0.00, 379.9
Sex	0.46	0.85	0.00, 1472.7
Age	0.04	0.45	0.00, 162.2
Sex, age	0.17	0.67	0.00, 709.8
Sex, age, sex*age	0.18	0.68	0.00, 778.9
Combined questions 6, 9 & 10[#]*			
Model adjusted for:	**OR**	**P value**	**95% CI**
Crude	16.0	< 0.01	6.0, 42.6
Sex	11.9	< 0.01	4.5, 31.6
Age	15.1	< 0.01	5.5, 41.5
Sex, age	11.5	< 0.01	4.2, 31.3
Sex, age, sex*age	11.1	< 0.01	4.2, 29.7

[#]*Questions are combined using the formula: {(question 6) + 10 – (question 9 + question 10)}

Table 7.
P-values for the Wilcoxon rank-sum test of difference between individual SNOT-20 item scores for patients with CRS and patients with facial pain disorders, UW Rhinology Clinic 2008-2010

SNOT-20 Questions	P value
1. Need to blow nose	0.279
2. Sneezing	0.956
3. Runny nose	0.342
4. Cough	0.387
5. Post-nasal discharge	0.119
6. Thick nasal discharge	0.044
7. Ear fullness	0.074
8. Dizziness	0.171
9. Ear pain	0.003
10. Facial pain/pressure	0.002
11. Difficulty falling asleep	0.791
12. Wake up at night	0.352
13. Lack of a good night's sleep	0.505
14. Wake up tired	0.223
15. Fatigue	0.245
16. Reduced productivity	0.300
17. Reduced concentration	0.424
18. Frustrated/restless/irritable	0.164
19. Sad	0.294
20. Embarrassed	0.160
Combination: 9 + 10* (ear pain + facial pain/pressure)	< 0.0001
Combination: 6, 9 & 10** (ear pressure, ear pain & facial pain/pressure)	< 0.0001

*Questions were combined using the formula: question 9 + question 10
**Questions were combined using the formula: {(question 6) + 10 – (question 9 + question 10)}

Table 8.
Odds ratios for diagnosis of CRS for each question & combination of questions of the SNOT-20 instrument, UW Rhinology Clinic, 2008-2010

SNOT-20 Question	Coefficient	OR	95% CI
1. Need to blow nose	0.14	1.15	0.87, 1.55
2. Sneezing	0.01	1.01	0.73, 1.39
3. Runny nose	0.13	1.14	0.84, 1.55
4. Cough	0.15	1.16	0.87, 1.54
5. Post-nasal discharge	0.19	1.21	0.91, 1.60
6. Thick nasal discharge	0.28	1.33	1.03, 1.70
7. Ear fullness	-0.26	0.77	0.58, 1.02
8. Dizziness	-0.15	0.86	0.65, 1.14
9. Ear pain	-0.50	0.60	0.44, 0.83
10. Facial pain/pressure	-0.46	0.63	0.46, 0.86
11. Difficulty falling asleep	-0.03	0.97	0.77, 1.24
12. Wake up at night	0.11	1.11	0.87, 1.41
13. Lack of a good night's sleep	0.08	1.08	0.85, 1.38
14. Wake up tired	-0.17	0.84	0.65, 1.10
15. Fatigue	-0.17	0.85	0.65, 1.10
16. Reduced productivity	-0.12	0.89	0.69, 1.15
17. Reduced concentration	-0.14	0.87	0.66, 1.13
18. Frustrated/restless/irritable	-0.16	0.85	0.66, 1.09
19. Sad	-0.13	0.87	0.68, 1.13
20. Embarrassed	0.33	1.39	0.92, 2.11
SNOT-20 Total	-0.01	0.99	0.97, 1.02
Combination 9 + 10* (ear pain + facial pain/pressure)	-0.34	0.71	1.15, 1.73
Combination 6, 9 & 10** (ear pressure, ear pain & facial pain/pressure)	0.51	1.67	1.32, 2.12

*Questions were combined using the formula: question 9 + question 10
**Questions were combined using the formula: {(question 6) + 10 – (question 9 + question 10)}

Table 9.
Area under the curve (AUC) for select questions & combinations of questions in the ROC model for diagnosis of CRS, UW Rhinology Clinic, 2008-2010

SNOT-20 questions	AUC	95% CI
6. Thick nasal discharge	0.62	0.52, 0.72
9. Ear pain	0.33	0.24, 0.43
10. Facial pain/pressure	0.31	0.22, 0.41
9 + 10.* Ear pain & facial pain/pressure	0.72	0.62, 0.80
6, 9 & 10.** Thick nasal discharge, ear pain & facial pain/pressure	0.79	0.70, 0.87

*Questions were combined using the formula: question 9 + question 10
**Questions were combined using the formula: {(question 6) + 10 – (question 9 + question 10)}

Table 10.
Cutpoints with corresponding sensitivity and specificity for combination of questions 6, 9 & 10* (thick nasal discharge, ear pain & facial pain/pressure), UW Rhinology Clinic 2008-2010

Cutpoint	Sensitivity (%)	Specificity (%)
≥ 3	100.0	6.7
≥ 4	98.5	10.0
≥ 5	98.5	13.3
≥ 6	94.0	33.3
≥ 7	94.0	46.7
≥ 8	79.1	60.0
≥ 9	64.2	73.3
≥ 10	53.7	83.3
≥ 11	28.4	100.0

*Questions were combined using the formula: {(question 6) + 10 – (question 9 + question 10)}

Appendix A:

Lund-Mackay staging system to assess severity of chronic rhinosinusitis from computed tomographic images of the paranasal sinuses.

Paranasal sinuses	Possible values	Right	Left	Total
Maxillary	0, 1, 2			
Anterior ethmoid	0, 1, 2			
Posterior ethmoid	0, 1, 2			
Sphenoid	0, 1, 2			
Frontal	0, 1, 2			
Osteomeatal complex	0* or 2*			
Total points		/12	/12	/24
0 = no abnormalities; 1= partial opacification; 2 = total opacification 0* = non-occlusion; 2* = occlusion				

Appendix B:

SNOT-20 questionnaire

I.D.:_____ **SINO-NASAL OUTCOME TEST (SNOT-20)** DATE:_____

Below you will find a list of symptoms and social/emotional consequences of your rhinosinusitis. We would like to know more about these problems and would appreciate your answering the following questions to the best of your ability. There are no right or wrong answers, and only you can provide us with this information. Please rate your problems as they have been over the past two weeks. Thank you for your participation. Do not hesitate to ask for assistance if necessary.

1. Considering how severe the problem is when you experience it and how frequently it happens, please rate each item below on how "bad" it is by circling the number that corresponds with how you feel using this scale: →	No problem	Very mild problem	Mild or slight problem	Moderate Problem	Severe Problem	Problem as bad as it can be	5 Most Important Items
1. Need to blow nose	0	1	2	3	4	5	O
2. Sneezing	0	1	2	3	4	5	O
3. Runny nose	0	1	2	3	4	5	O
4. Cough	0	1	2	3	4	5	O
5. Post-nasal discharge	0	1	2	3	4	5	O
6. Thick nasal discharge	0	1	2	3	4	5	O
7. Ear fullness	0	1	2	3	4	5	O
8. Dizziness	0	1	2	3	4	5	O
9. Ear pain	0	1	2	3	4	5	O
10. Facial pain/pressure	0	1	2	3	4	5	O
11. Difficulty falling asleep	0	1	2	3	4	5	O
12. Wake up at night	0	1	2	3	4	5	O
13. Lack of a good night's sleep	0	1	2	3	4	5	O
14. Wake up tired	0	1	2	3	4	5	O
15. Fatigue	0	1	2	3	4	5	O
16. Reduced productivity	0	1	2	3	4	5	O
17. Reduced concentration	0	1	2	3	4	5	O
18. Frustrated/restless/irritable	0	1	2	3	4	5	O
19. Sad	0	1	2	3	4	5	O
20. Embarrassed	0	1	2	3	4	5	O

2. Please mark the most important items affecting your health (maximum of 5 items)_____ ↑

Appendix C:

Data Figures

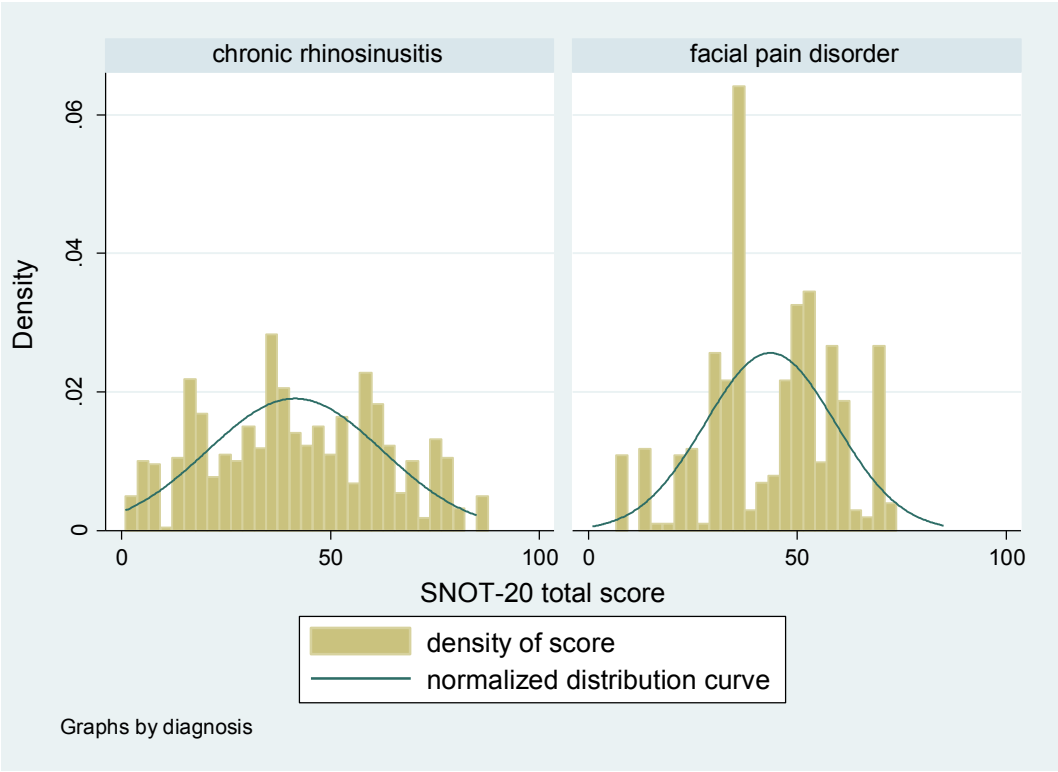


Figure 1.
SNOT-20 total scores by diagnosis of CRS or facial pain disorder, compared to normalized curve, UW Rhinology Clinic 2008-2010

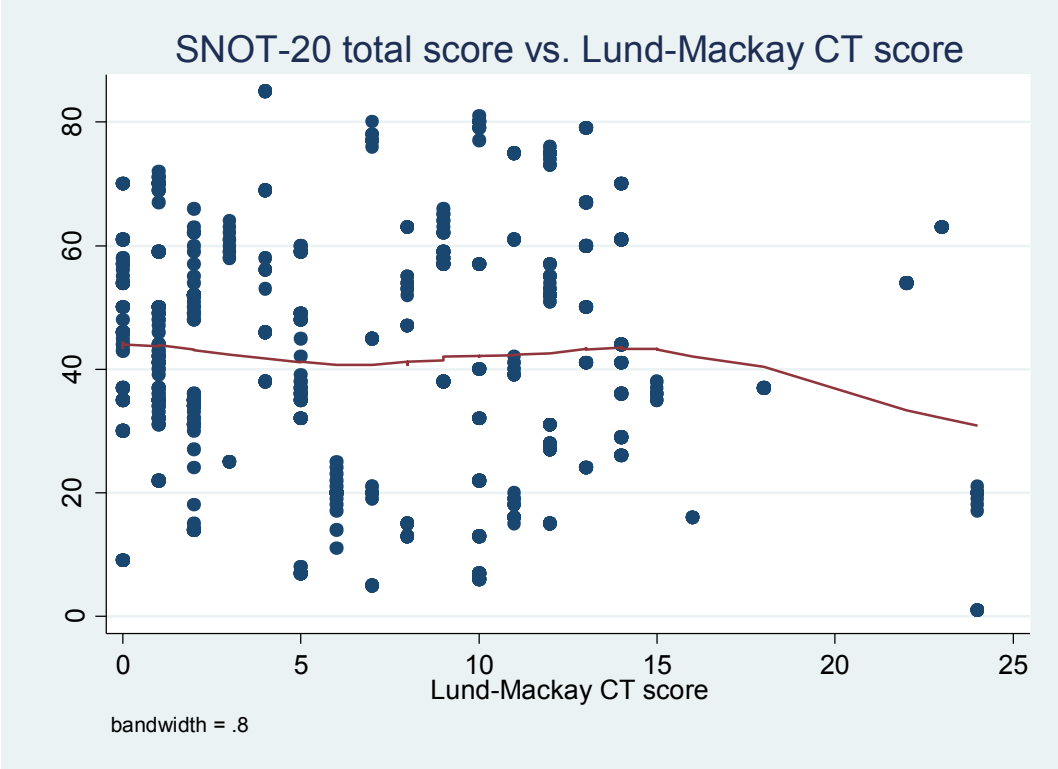


Figure 2.
Relationship between SNOT-20 total score and Lund-Mackay CT score, UW Rhinology Clinic 2008-2010. The red line represents the "lowess" curve, which represents the smoothed "logically weighted" regression of SNOT-20 total score on LM CT score obtained using Stata 11

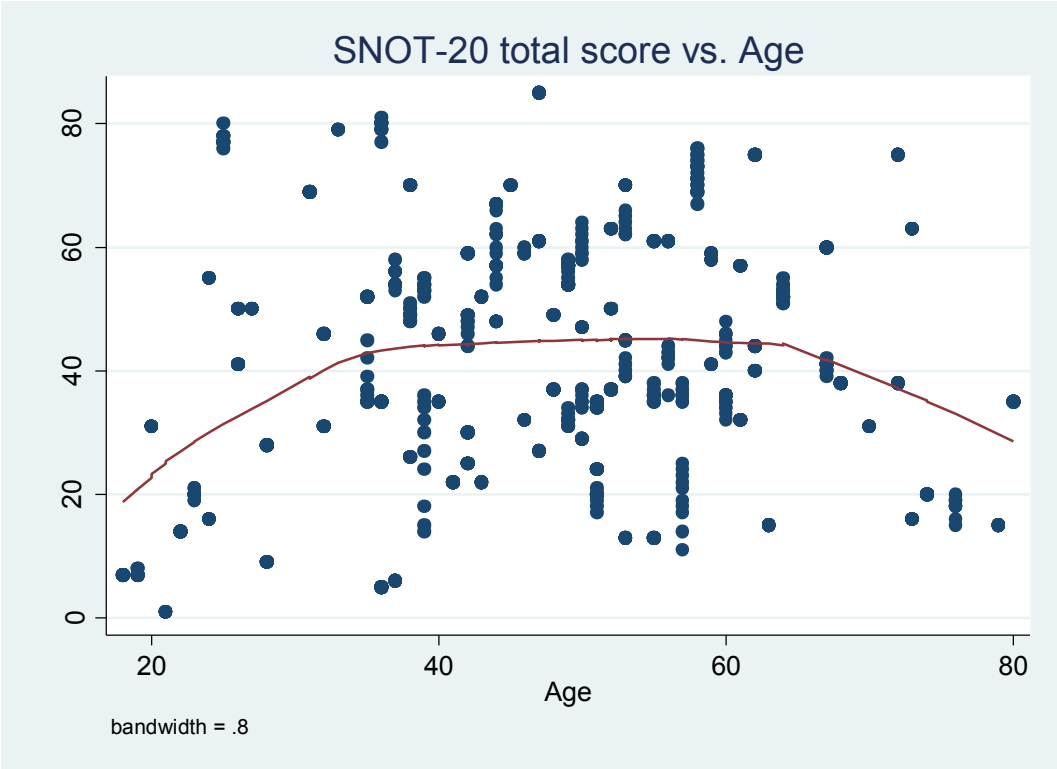
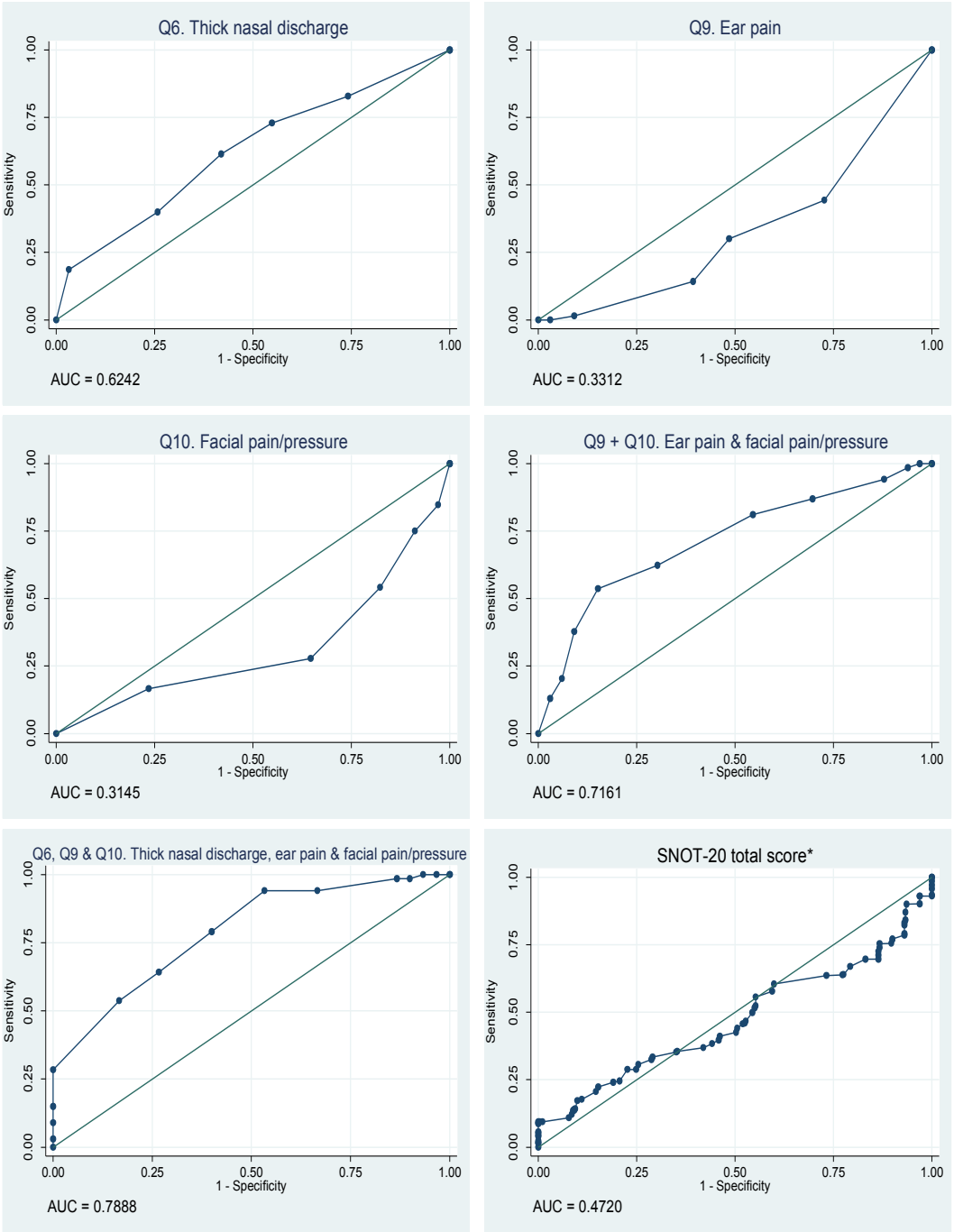


Figure 3.
Relationship between SNOT-20 total score and age, UW Rhinology Clinic 2008-2010. The red line represents the “lowess” curve, which represents the smoothed “logically weighted” regression of SNOT-20 total score on age obtained using Stata 11



*SNOT-20 total score ROC curve analysis was performed with imputed data, whereas all other ROC curve analysis was performed with pre-imputed data.

Figure 4.
ROC curves for individual and combinations of questions of the SNOT-20, UW Rhinology Clinic 2008-2010

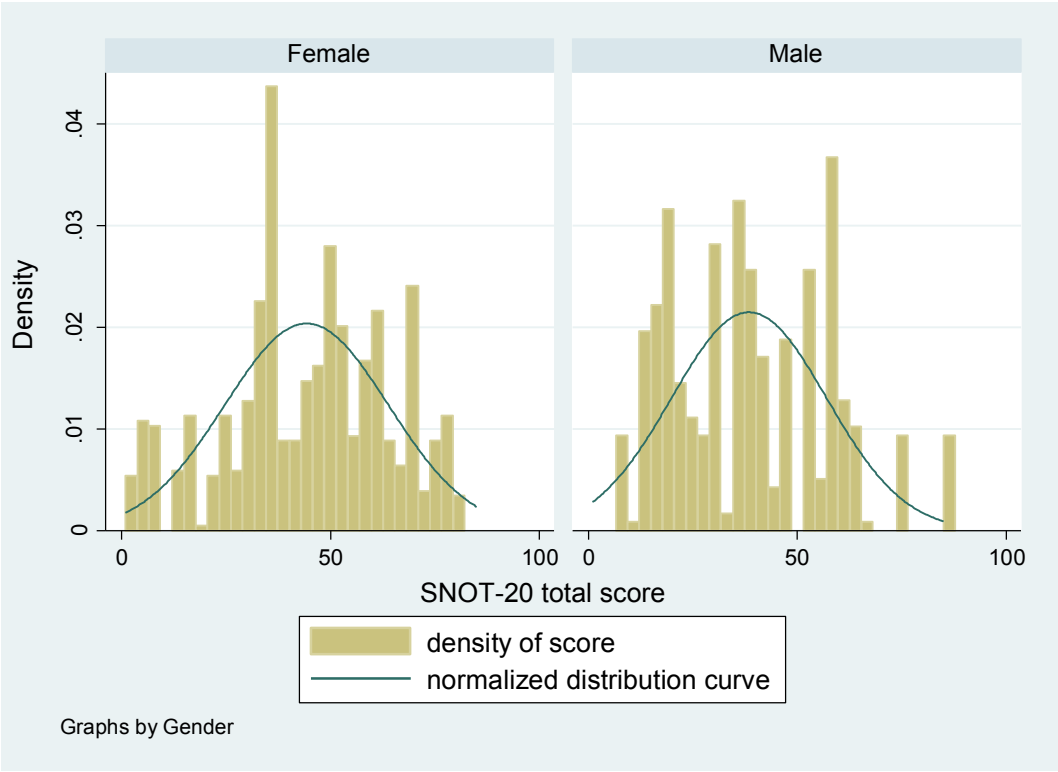


Figure 5.
SNOT-20 total scores by sex, compared to normalized curve, UW Rhinology Clinic 2008-2010

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