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## Sino-nasal Outcome Test (SNOT-22): A predictor of post-surgical improvement in patients with chronic sinusitis

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### Introduction

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Chronic rhinosinusitis (CRS) is a common and debilitating condition with significant economic impact<sup>1</sup>. From 1995–2007, this disease accounted for 4.9 medical office visits out of every 100 people, approximately 1.5% of all office visits in the United States<sup>2</sup>. While estimates of cost vary, the 2007 Medical Expenditure Panel Survey, which analyzes expenditures and utilization in health care, suggests a national spending average on CRS approaching \$8.6 billion per year<sup>3</sup>.

First line therapy for treatment of CRS is aimed at reducing underlying inflammation and facilitating clearance of the paranasal sinuses. Antibiotics, topical steroids, systemic steroids, and nasal saline irrigation are mainstays of treatment<sup>4, 5</sup>. Also key to medical management is treatment of underlying disease processes, such as environmental allergies<sup>6</sup>. Unfortunately, many patients are refractory to this treatment and ultimately require functional endoscopic sinus surgery (FESS) to achieve improved symptom control and quality of life. It is estimated that approximately 500,000 surgeries are performed annually for treatment of CRS refractory to medical management alone.

Given the relevance and societal impact of this disease process, careful selection of patients for surgery is necessary to optimize outcomes and reduce unnecessary risk. To that end, prior studies have attempted to define patient characteristics predictive of surgical outcomes<sup>7–11</sup>. Unfortunately, there is conflicting information regarding which of these characteristics are important. For example, studies have contrastingly suggested increased rates of revision sinus surgery among smokers or that smoking had no influence on outcome<sup>12</sup>. Similarly, studies have variously shown positive and negative influences of polyps, aspirin sensitivity,

depression, female sex, and CT scores of disease severity<sup>11</sup>.

The goal of this study was to analyze outcomes of FESS using prospectively collected data in a single surgeon series obtained through a symptom-based rhinosinusitis outcome measure, the Sino-nasal Outcome Test-22 (SNOT-22). Additionally, demographic and baseline measures including asthma and smoking status, total IgE, absolute eosinophil counts (AEC), number of prior sinus surgeries, and Lund-Mackay CT scoring (LMS) were obtained for each subject and analyzed for correlation with surgical outcomes. Lastly, we wanted to define whether the additional two questions in the SNOT-22 as compared to the SNOT-20 (“nasal obstruction” and “loss of smell and taste”) added any predictive value to this patient-directed outcome measure. The predictive value of such correlations will be useful to the surgeon in patient selection and informative to the patient in consenting to operative intervention.

## Methods

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A retrospective analysis of prospectively collected patient data was performed utilizing a protocol approved by the Human Investigation Committee (HIC) at the University of Virginia (UVA), and informed consent was not required. Consecutive adult subjects presenting to the Otolaryngology Clinics at UVA with a diagnosis of CRS who remained refractory to at least 6 weeks of medical therapy were included ([Table 1](#)). In this context CRS was diagnosed if patients met criteria as previously described elsewhere<sup>13</sup> which requires that in addition to positive objective endoscopic or CT findings that the patients note at least two of the following four symptoms: nasal congestion, nasal drainage, facial pain/pressure, and/or diminished smell<sup>14</sup>. Prior to and after surgical intervention, these subjects were asked to maintain maximal medical therapy with medications directed towards the specific presumed underlying triggers, such as the presence of bacterial biofilms, allergies, eosinophilic inflammation, and aspirin sensitization as part of the standard of care for patients at UVA. At a minimum, pre-operative therapy included a 1–2 week course of oral corticosteroid, topically administered nasal steroid, isotonic saline nasal irrigations and culture-directed antibiotic if purulent or thickened mucous was noted on exam. Patients presenting with a history of prior surgery were also prescribed budesonide irrigations as reported by us previously<sup>4</sup>.

[Table 1](#)  
Patient Demographics and Characteristics.

Standard protocol for all patients presenting for evaluation also included completion of the SNOT-22 prior to and following surgical intervention. Each subject completed the SNOT-22 during a clinic visit by answering all questions based on a 0–5 scale, where 0 defines no problems with the given symptom and 5 defines maximal problems ([supplemental Figure S1](#)). This is a validated patient-reported measure of outcome established to delineate the presence and severity of sino-nasal disorders<sup>15</sup>. Patients were excluded if they had not completed both pre- and post-operative evaluations.

Perioperative demographic and medical histories were obtained from both the patient and the medical record. This included the presence of prior diagnosis by a physician of allergic rhinitis and/or asthma (this was not further evaluated with repeat pulmonary function or skin testing). Post-medical therapy acquired computed tomography (CT) scans performed preoperatively were evaluated using the Lund-MacKay CT scoring system<sup>16, 17</sup>. Lab values, specifically a complete blood count with differential to evaluate absolute eosinophil count and a total IgE, were obtained prior to surgery for those patients with nasal polyps. The post-operative SNOT-22 was completed between three and six months after the surgery.

## Statistical Methods

**Data Summarization** Categorical scaled patient demographic and patient characteristic data were summarized by frequencies and percentages, while total IgE concentration and total eosinophil count were summarized by the geometric mean, and the arithmetic mean of the measurement distribution, respectively.

**Univariate Analyses** Negative-binomial generalized estimating equation (GEE) regression models were utilized to estimate the mean pre-operative to post-operative percent change in the scores of each question of the SNOT-22 questionnaire, and to compare the mean pre-operative to post-operative percent change in the SNOT22 composite score (i.e total score) between patient groups with different underlying baseline characteristics. The GEE version of the Wald statistic was utilized as the test statistic in hypothesis testing and a two-sided  $p \leq 0.05$  decision rule was established *a priori* as the null hypothesis rejection rule for testing the null hypothesis that the mean preoperative to postoperative change in the SNOT-22 score was equal to zero.

**Multivariate Analyses** Multivariate Ordinary-Least-Squares (OLS) regression was utilized to determine which questions of the SNOT22 independently predicted the preoperative to postoperative change in the SNOT22 composite score. The type III, extra sum-of-squares F-test was utilized to determine the independent predictors of the pre-operative to post-operative change. The extra-sum-of-squares F-test also determined if specific *a priori* selected clusters of related questions of the SNOT-22 were *uniquely/independently* associated with the pre-operative to post-operative change in the SNOT22 composite score. A  $p \leq 0.05$  decision rule was established *a priori* as the null hypothesis rejection criterion for the statistical test of association.

**Statistical Software** The statistical software packages, SAS version 9.2.2 (SAS Institute Inc., Cary, NC), and Spotfire S-plus version 8.2 (TIBCO Inc, Palo Alto, CA), were used to conduct the statistical analyses.

## Results

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The data for a total of 104 subjects that met the defined criteria were included. The baseline characteristics for the subjects are summarized in [Table 1](#). Total IgE and absolute eosinophil counts were obtained on the subset of these patients with nasal polyps (n=51).

Our results indicated that all patients showed some level of improvement post-operatively, with an average improvement in the total symptom score (reduction in SNOT-22 composite score) of 51% (95% CI: [45, 57%]) of baseline, pre-operative values. However, when we examined the least severely symptomatic patients (those with the lowest quartile of SNOT-22 symptoms), there was a flooring effect with a reduction of only 35% (95% CI: [17, 49%]) ([Table 2](#)). Those patients who had never undergone functional endoscopic sinus surgery (FESS) prior to their presentation at the University of Virginia did significantly better than those who had previously undergone one or more surgeries (n=40 for 0 surgeries with 63.4% improvement (95% CI: [54.38, 70.63]), n=31 for one prior surgery with 48.4% improvement (95% CI: [33.74, 59.83]), and n=33 for greater than one prior surgeries with 54.5% improvement (95% CI: [42.27, 64.22]) ( $p=0.05$  (for no surgery v. one or more)) ([Table 3](#)).

Pre-operative Score	Number	Mean Post-operative Score	Percent Improvement
1-25	25	31.04	35%
26-33	33	33.74	48.4%
34-41	41	38.22	54.5%
42-51	51	45.38	63.4%

[Table 2](#)

Post-operative SNOT-22 improvement as a function of Pre-operative SNOT-22.

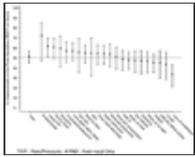
Prior Surgeries	Number	Mean Pre-operative Score	Mean Post-operative Score	Percent Improvement
0	40	45.38	33.74	25.3%
1	31	48.4	38.22	20.9%
>1	33	54.38	45.38	16.5%

[Table 3](#)

Comparison of prior surgeries and absolute improvement in SNOT-22 scores.

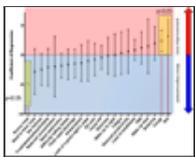
Each question from the SNOT-22 was initially evaluated utilizing univariate analysis. Individual questions improved significantly from the pre-operative scores with a range of 72% (95% CI: [47, 85%]) for “embarrassment” to 33% (95% CI: [21, 43%]) for “loss of smell/taste” ([Figure 1](#)). Because each parameter

improved, we evaluated which questions were uniquely and independently associated with post-operative improvement. For instance, because “embarrassment” improved, we posited whether this was simply an indicator that people reported that they were embarrassed because they had a “runny nose”, or whether this was uniquely associated with post-operative improvement. Utilizing multivariate regression analysis, we were able to establish which components of the SNOT-22 were “hinge-pin” questions that *independently* predicted post-operative improvement. “Runny nose” directly correlated with improved post-operative SNOT-22 scores ( $p < 0.01$ ). “Ear fullness” and “nasal obstruction” trended towards significance as well ( $p = 0.07$  and  $p = 0.09$ , respectively). In contrast, questions concerning “cough” and “sadness” independently had negative impacts on the degree of improvement ( $p < 0.05$  for both) ([Figure 2](#) and [supplemental Table S1](#)).



[Figure 1](#)

### Univariate Analysis of Post-operative Improvement in SNOT-22 Scores by Question



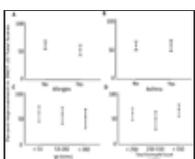
[Figure 2](#)

### Multivariate regression analysis comparing pre- and post-surgical SNOT-22 questions

Because many of the questions in the SNOT-22 cluster together, we conducted hypothesis tests related to determine which clusters of questions provided *uniquely/independently* predictive information about post-operative improvement. For these analyses, we grouped questions into 4 main categories: Nasal related (“need to blow nose”, “sneezing”, “runny nose”, “nasal obstruction”, “loss of smell/taste”, and “post-nasal drip” (PND), Ear and Facial Related (“ear fullness”, “dizziness”, “ear pain”, “facial pain and pressure”), Quality of Life related (“difficulty falling asleep”, “wake up at night”, “wake up tired”, “fatigue”, “reduced productivity”, “reduced concentration”), and Psychologically related (“frustrated/restless/irritable”, “sad”, “embarrassed”). Those clusters that related to nasal and to ear and facial symptoms were significantly associated with post-operative improvement ( $p < 0.001$ , and  $p = 0.015$ , respectively).

We next evaluated the question as to whether the additional questions in the SNOT-22 improve the ability of this test to predict post-surgical outcomes. Utilizing multivariate regression analyses, we determined that even though the question related to nasal obstruction trended toward significance, the two questions that make the SNOT-22 unique, i.e., “nasal obstruction” and “loss of smell and taste”, were not *independent* predictors of post-operative improvement when clustered together ( $p = 0.114$ ) nor did their removal from the “nasal related group” decrease its significance ( $p = 0.002$ ).

Finally, we evaluated whether the presence of asthma, allergy, smoking history, or aspirin sensitivity, as well as baseline total IgE, absolute eosinophil count, and Lund-MacKay scores predicted post-operative improvement. Neither patient-reported allergy nor asthma were associated with significant post-operative improvement in our cohort. Consistent with this, we were unable to show any predictive value of either total IgE or absolute eosinophil counts ([Figure 3A, B, C, D](#)). Surprisingly, aspirin sensitivity, smoking status, and Lund-MacKay scores were also *not* predictive of improvement in this patient population.



[Figure 3](#)

### Improvement in total SNOT-22 scores as a function of baseline measures

## Discussion

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In this study, we have provided further corroboration of previously identified prognostic factors and identified additional factors that inform the optimal selection of patients for FESS. The value of the overall SNOT-22 score was apparent with patients with the highest symptom scores experiencing the greatest degree of symptom improvement (Table II). This corresponds with previous studies, which have cited the relatively greater improvement among more severely affected patients<sup>9, 10</sup>. It is important to note that even the patients with the lowest pre-operative symptoms scores did experience improvement, although the magnitude of the change was limited by the associated flooring effect (Table II).

Via multivariate analysis it was revealed which individual components of the SNOT-22 provided unique information predictive of surgical outcomes. “Runny nose”, “cough”, and “sadness” each provided independent information, while “ear fullness” and “nasal obstruction” approached significance (Figure 2). Multiple regression analysis of the significant factors yielded the interesting observation that “runny nose” predicted *greater* improvement in symptoms, while “sadness” and “cough” were significantly predictive of *lesser* improvement.

There are conflicting reports on the effect of depression on quality of life and surgical outcomes in the CRS patient population<sup>7, 8, 10, 11, 18, 19</sup>. Depressed patients generally have greater subjective symptom scores than their non-depressed counterparts. Litvack and colleagues demonstrated that while patients with higher depression scores have worse disease-specific quality of life than non-depressed patients, they seem to experience comparable objective improvement with FESS. It is also interesting to note that in the Litvack study, depressed patients experienced a significant improvement in their depression<sup>8</sup>. Our study confirmed the ability of FESS to improve the overall symptom score in patients who identify “sadness” as a significant symptom. However, multiple regression analysis revealed that these scores correlated with *less* improvement in overall score after surgery. Given this finding in the greater context of the literature, it is advisable to address these considerations with the depressed patient.

“Cough” was associated with less improvement in total SNOT-22 scores. We hypothesized that this would be related to an underlying diagnosis of asthma, and, therefore, not amenable to improvement through FESS. However, upon further analysis, it was apparent that clinical diagnosis of asthma and “cough” scores on the survey were *not* associated. Furthermore, asthma was not predictive of outcomes (Figure 3B), as has also been noted in other studies<sup>10, 11</sup>. An alternative explanation may be that the presence of cough served as a surrogate marker of laryngopharyngeal reflux (LPR) in this subgroup of our population. Further study of this phenomenon is warranted.

Given the established negative impact of tobacco smoke on innate and humoral immunity<sup>20, 21</sup>, smoking is regarded as having a negative prognostic indicator in sinus disease. While smoking has previously been associated with the need for revision surgery and inferior surgical outcomes<sup>22, 23</sup>, more recent trials designed specifically to investigate the relationship of smoking with post operative outcomes, demonstrated *comparable* subjective outcomes to nonsmokers while endoscopy scores remain poor in both cohorts<sup>12</sup>. The present study revealed no significant relationship between smoking status and FESS outcomes. This finding lends further support to the mounting evidence that while smoking cessation should be encouraged, active smoking should not be regarded as a contraindication to FESS.

As noted, allergy status, eosinophilia, and IgE levels were not related to improvement in symptom scores on the SNOT-22, though these factors are limited in confirming the presence of allergic disease. We chose to include physician diagnosed allergy as recalled by the subjects primarily because of the high rate of false positive tests afforded to skin prick tests in this situation. The symptoms of sinus disease and allergy are similar, and history alone will not distinguish which disease is leading to the pathology, rendering positive skin tests difficult to interpret. We improved our diagnostic abilities by ensuring that those patients with physician diagnosed allergy

and asthma were on treatment at the time of enrollment.

Of all the evaluated demographic factors, only prior surgery was predictive of the magnitude of improvement, with the greatest absolute improvement seen in those with no prior surgery. This finding suggests that the first attempt at surgical intervention is extremely important. Alternatively, multiple revision surgeries may be a surrogate for the refractoriness of the disease process. Those requiring multiple surgeries likely had more complex disease that was difficult/impossible to treat with conventional therapies including surgical intervention. Importantly, FESS provides the opportunity to open windows into the sinuses that did not previously exist, thereby improving the application of post-operative medical treatments, including steroids<sup>27, 28</sup>. The addition of these windows might explain the differences in post-operative improvement in those patients with no prior surgeries, though, as was the practice of the surgeon in this study, only a small number of patients with prior surgery started budesonide rinses (for the first time) post-operatively.

In this large, single surgeon series, subjective symptom reporting through the SNOT-22 survey and demographic factors were evaluated for influence on post-surgical outcomes. While it is encouraging that all patients in the series noted improvement in symptoms, this universal improvement limits the power of the statistical model to identify patient features predictive of outcomes. Additionally, the aggressive medical management employed post-operatively may not reflect national practice trends, thereby potentially decreasing the general applicability of these findings. Lastly, outcomes were measured at six months in this study, and it is possible that the markers we found are not representative of longer-term outcomes after intervention. However, other studies in CRS have shown that 6-month outcomes are comparable to data at two-years post-intervention<sup>29</sup>.

In conclusion, our study showed that, with optimal surgical intervention (and post-operative medical management), FESS is an extremely effective treatment of CRS. Patient-based outcome measures, such as the SNOT-22, are helpful tools for quantifying changes in symptoms and, can be used to predict extent of post-operative improvement. While all of the components of the SNOT-22 significantly improved after surgery, only “runny nose” (associated with greater improvement), as well as “cough” and “sadness” (both associated with less improvement) were independent predictors of post-surgical SNOT-22 improvement. While further work is needed in this area, this study begins to define important questions, which must be asked prior to surgical intervention.

## Supplementary Material

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## Acknowledgments

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## Footnotes

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## Author Contributions:

Joshua L. Kennedy: Dr. Kennedy performed data analysis, patient enrollment, and drafted the manuscript with shared first author duties.

Matthew A. Hubbard: Dr. Hubbard performed data analysis, enrollment, and drafted the manuscript with shared first author duties.

Phil Huyett: Dr. Huyett performed data analysis and enrollment.

James T. Patrie: Mr. Patrie was involved in the statistical analysis and drafting of the manuscript.

Larry Borish: Dr. Borish helped to draft the manuscript.

Spencer C. Payne: Dr. Payne conceived the research, performed data analysis, patient enrollment, and drafted the manuscript.

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