Published in final edited form as:

Int Forum Allergy Rhinol. 2017 July ; 7(7): 734–740. doi:10.1002/alr.21940.

Understanding the Relationship Between Olfactory-Specific Quality of Life, Objective Olfactory Loss, and Patient Factors in Chronic Rhinosinusitis

Jose L. Mattos, MD, MPH¹, Rodney J. Schlosser, MD^{1,2}, Kristina A. Storck, MSPH¹, and Zachary M. Soler, MD, MSc¹

¹Division of Rhinology and Sinus Surgery, Department of Otolaryngology – Head and Neck Surgery, Medical University of South Carolina, 135 Rutledge Ave, MSC 550, Charleston, SC 29425, USA

²Department of Surgery, Ralph H. Johnson VA Medical Center, 109 Bee St, Charleston, SC, 29401, USA

Abstract

Background—Chronic rhinosinusitis (CRS) significantly impacts olfaction. However, the relationship between objective olfaction and patient-reported olfactory-specific quality of life (QOL) is not well understood. Furthermore, objective olfactory testing can be time consuming, so we sought to determine if patient-reported olfactory QOL can be used as screening tool for olfactory dysfunction.

Methods—Olfactory dysfunction was evaluated in 109 patients with CRS using the Questionnaire of Olfactory Disorders-Negative Statements (QOD-NS) and the Sniffin' Sticks Test, assessing for olfactory threshold, discrimination, identification, and overall composite scores (TDI). Regression analysis was performed to correlate olfactory metrics and patient and disease-specific factors with QOD-NS scores. Optimal QOD-NS scores to classify patients based upon objective olfactory function were established.

Results—Bivariate and multivariate regression analyses of QOD-NS and CRS-associated comorbidities, objective measures of disease, demographics, and CRS-specific QOL were performed. Non-white race, depression, and worse SNOT-22 scores correlated with worse QOD-NS scores ($p<0.005$). Worse TDI scores correlated with worse QOD-NS scores, and discrimination had the strongest correlation ($p<0.001$). Mean (SD) QOD-NS scores for normosmia, hyposmia, and anosmia were 44 (7.2), 35.7 (12.8), and 31.6 (10.7) respectively. Receiver operating characteristics analysis revealed an area under the curve of 0.770 ($p<0.001$), and a QOD-NS cut off of 38.5 to have maximal Youden's Index to define normal versus abnormal TDI score.

Correspondence to be sent to: Zachary M. Soler, MD, MSc, Department of Otolaryngology – Head and Neck Surgery, Medical University of South Carolina, 135 Rutledge Ave, MSC 550, Charleston, SC 29425, USA. solerz@usc.edu.

Conflict of Interest: There are no disclosures for Jose L. Mattos or Kristina A. Storck.

Conclusions—In CRS, QOD-NS correlates with non-white race, depression, SNOT-22, and TDI score, with discrimination having the strongest correlation. QOD-NS also appears to be a feasible tool for olfaction screening.

Keywords

sinusitis; Sniffin'; Sticks; olfaction; quality of life

Introduction

The association between chronic rhinosinusitis (CRS) and olfactory dysfunction (OD) is well established.^{1,2} Patients who suffer from CRS frequently have decreased smell capability, and OD is considered one of the cardinal symptoms of CRS.^{1,2} The incidence of OD in CRS has been reported to range between 40 and 80%, and patients with CRS have significant decreases in olfactory specific quality of life (QOL).³

There remain, however, important unanswered questions on the exact nature of the relationship between OD and olfactory-specific QOL.³ For example, OD in CRS has been associated with decreased economic productivity, but worse olfactory QOL is more closely associated with economic metrics than psychophysical measures of smell identification.⁴ Identification of odorants is not the only method for detecting OD. A comprehensive olfactory evaluation also measures a patient's olfactory threshold as well the ability to discriminate between different odors. We have previously reported olfactory findings in this CRS patient cohort using Sniffin' Sticks to provide comprehensive psychophysical olfactory information.⁵

The current study has two primary objectives. First, to define the relationship between olfactory-specific QOL and objective olfactory information provided by Sniffin' Stick testing in patients with CRS. While the information provided by psychophysical olfactory testing is valuable, it can be time-consuming and cumbersome for clinical practice or efficient screening methods. As such, our second goal was to explore the feasibility of developing QOD-NS cut-off scores for screening and identifying patients with objective olfactory dysfunction.

Methods

Enrollment

Adult patients (≥ 18 years) who satisfied diagnostic criteria for CRS according to the European Position Paper on Rhinosinusitis (EPOS12)¹ were enrolled from Rhinology clinics at the Medical University of South Carolina in a prospective, cross-sectional fashion. Each patient was required to have at least 2 cardinal symptoms for greater than 3 months and objective evidence of inflammation on both sinonasal endoscopy and computed tomography (CT) scan. Patients were enrolled irrespective of perceived olfactory ability. Patients were excluded if they had been prescribed short-term oral corticosteroids within the last month, had sinonasal surgery within the last 6 months, or had any existing condition known to induce systemic inflammation. Participants were able to complete all study questions in

English. The MUSC Institutional Review Board approved this study (Pro 28632), and all subjects provided written, informed consent.

Demographics and comorbidities

Demographic information and medical comorbidities were specifically collected from the patients and included age, gender, race/ethnicity, smoking status (yes/no), and prior sinus surgery (yes/no). For the race variable, the Asian and Black race groups were combined into a non-white category. The presence of medical comorbidities (i.e. depression, asthma, etc.) was determined by patient-report of a prior, existing physician diagnosis for all conditions except allergic rhinitis, which required prior positive objective testing (skin prick or in vitro testing).

Chronic rhinosinusitis disease severity

Sinusitis-specific disease severity was assessed based on endoscopy, imaging, and patient-reported QOL. Sinonasal endoscopy was performed on each patient and scored according to the Lund-Kennedy algorithm (range 0–20; higher scores indicate greater disease) by their treating physician, who was blinded to other study data.⁶ Patients were further categorized as those without polyps (CRSsNP) and those with visible polyps (CRSwNP). CT scans performed during the course of clinical care were graded by the physician according to the Lund-Mackay scoring system (range 0–24; higher scores indicate greater disease).⁷ Sinus-specific QOL was assessed using the 22-item Sino-Nasal Outcome Test (SNOT-22) (Hopkins et al. 2009). The SNOT-22 contains 22 questions (total score range, 0–110), with higher scores representing more severe QOL impact.

Olfactory Outcome Metrics

Our primary outcome of interest was olfactory-specific QOL that was assessed using the previously validated, short modified version of the Questionnaire of Olfactory Disorders (QOD-NS).⁸ This instrument consists of 17 negative statements that are graded on a scale from 0 to 3, for a total score ranging from 0 to 51, with higher scores reflecting better QOL.

Quantitative olfactory testing was performed using the “Sniffin’ Sticks” test (Burghardt, Wedel, Germany).⁹ All tests were performed by the same clinical research coordinator who was blinded to all other study responses. The test battery included odor threshold, odor discrimination, and odor identification. The threshold test was performed using dilutions of n-butanol in a single-staircase, triple-forced choice procedure. The discrimination test used triplets of pens presented in random order with two containing the same odorant and the third a different odorant. The identification test utilized 16 odorants presented at supra-threshold intensity using multiple-choice procedure. All subjects were blindfolded to avoid visual identification of odorant-containing pens. The 3 test scores were reported independently. Discrimination and identification were scored from 0–16, and threshold was scored from 1–16. The overall results were also combined for an overall score called the “composite threshold-discrimination-identification score” (TDI), which ranged from 1–48 with higher scores indicating superior olfactory performance.

Prevalence based on ideal olfaction—The prevalence of olfactory loss was determined for the overall cohort using “ideal” cut-offs, rather than age-specific cutoffs. Ideal cut-offs were defined as the scores that would be expected for normal subjects aged 16–35 years, using expected TDI values for normosmic, hyposmic, and anosmic categories.¹⁰ For individual olfactory domains (threshold, discrimination, identification), subjects were classified as having impaired olfaction if their individual scores was 10th percentile based on the 16–35 year age group.¹⁰ Ideal olfaction cut-offs were chosen because these represent unencumbered olfaction, and the 16–35 range is based on published normative data. Age-specific cut-offs take into account expected age-related decline in olfaction. As such, age-specific cut-offs might classify older patients with impaired olfaction as normal for their age group. The goal of this study is to analyze the relationship of any decline in olfaction, whether it is age-appropriate or not, on olfactory-specific QOL.

Statistical Analysis

Regression analysis—In order to understand the correlates that might be associated with QOD-NS, a regression modeling approach was used. First, bivariate testing of patient factors, disease-specific factors, and olfactory testing metrics was performed. The variables that were ≥ 0.200 on bivariate testing were incorporated into a multi-variable model. A step-wise backward elimination technique was performed until only significant correlates were left. Two different multi-variable models were built. The first utilized the composite TDI score, and the second one used threshold, discrimination, and identification as separate, independent correlates.

Establishing QOD-NS cut-offs—Cut-off scores for QOD-NS were developed in order to provide values of the QOD-NS that might predict a patient’s olfactory status on objective, psychophysical testing. To determine these cut-off scores three analyses were performed. First, mean QOD-NS scores were calculated for the normosmia, hyposmia, and anosmia groups, as established by the composite TDI score. This provides an overall picture of the range QOD-NS for differing olfaction status.

Patients were then organized into two groups; those with normal olfaction, as defined by normosmia, and those with any olfactory dysfunction (OD) as defined by either hyposmia or anosmia. In order to understand the range of mean QOD-NS scores for patients with normal olfaction vs. OD, comparison tables were developed between threshold and discrimination, threshold and identification, and discrimination and identification; comparing QOD-NS scores when olfaction was normal or abnormal for each of the separate components. Finally, receiver-operator curve (ROC) analyses using the two-group olfaction categorization were performed. ROC testing was chosen in order to understand the sensitivity and specificity of different QOD-NS values in identifying patients with normal olfaction vs. OD as defined by TDI composite scores. Youden’s index was calculated for each of the values of the ROC analysis. The Youden’s index allows the identification of the cut-off score that provides the highest combination of sensitivity and specificity. However, the exact value used will depend on the desire to maximize sensitivity, specificity, or both.

Results

Baseline Characteristics

Baseline patient characteristics are detailed in Table 1. A total of 109 patients with CRS were enrolled of which 40.4% were CRSsNP and 59.6% were CRSwNP. The average age of the cohort was 52.7 years (SD=16.14), with just over half female (56%). Asthma and allergic rhinitis were present in 48.6% and 56% of the cohort respectively, with greater prevalence seen in the CRSwNP subgroup. Overall, the cohort had a high degree of disease severity with mean CT score of 12.2 (SD=6.8), endoscopy score of 6.3 (SD=3.8), and average SNOT-22 of 46.5 (SD=21.1). As expected, the CRSwNP subgroup had worse CT and endoscopy scores ($P<0.020$ for both). The overall mean TDI score for the cohort was 20.98 (SD=9.0), with lower scores seen in the CRSwNP cohort as compared to CRSsNP (18.3 ± 7.9 vs 25.0 ± 9.1 ; $p<0.001$). The overall mean QOD-NS score was 35.78 ± 11.88 .

Regression Analysis

Multivariate regression revealed that non-white race, presence of depression, and worse SNOT-22 scores were all independent correlates of worse QOD-NS scores. Additionally, poorer scores in composite olfactory testing (TDI) were associated with worse QOD-NS scores. When testing threshold, discrimination, and identification independently, rather than as a composite TDI score, two important observations were noted. First, the relationship between discrimination and QOD-NS in our data is not linear, but rather it is quadratic, while threshold and identification have a linear relationship with QOD-NS. Second, to account for this non-linear relationship, a discrimination-squared term was introduced into the regression model. When this quadratic pattern was taken into account, discrimination had the strongest correlation to QOD-NS as compared to threshold or identification. Tables 2 and 3 provide details of these models.

QOD-NS Cut-off Values

The mean (SD) QOD-NS scores for normosmia, hyposmia, and anosmia were 44 (7.2), 35.7 (12.8), and 31.6 (10.7) respectively. When comparing the 4×4 table values of the normal olfaction vs. OD groups, mean QOD-NS can range between 43 and 45 for patients with normal scores in all TDI components, and 31 to 32.5 for those with abnormal values in any of the three components (Table 4). As seen in table 4.1, it can be seen that in patients with normal discrimination, QOD-NS does not vary significantly with olfactory threshold dysfunction (44 vs 42). Significant decline in QOD-NS requires both threshold and discrimination dysfunction. When examining the relationship between threshold and identification, once threshold dysfunction occurs, QOD-NS declines even when identification is normal (45 vs 39). QOD-NS declines even further once dysfunction of both threshold and identification occurs to 32.5. When examining the relationships between discrimination and identification, patients with normal discrimination have similar QOD-NS regardless of identification (43 vs 42), but once discrimination dysfunction occurs, QOD-NS declines to 34 and 31, regardless of identification function.

As expected, worse olfactory status was associated with a negative impact on QOD-NS. ROC analysis revealed an area under the curve of 0.77, and the QOD-NS score with the

maximal Youden's Index was 38.5. This score gives a sensitivity of 60.9% and specificity of 81.8% of detecting patients with OD (see Figure 1 and Table 5).

Discussion

The high prevalence and nature of OD, as detailed by TDI scores obtained during Sniffin' Sticks testing, in this patient cohort has been previously studied and reported.⁵ The current analysis aimed to further elucidate the relationship between objective OD and olfactory-specific QOL as measured by the QOD-NS questionnaire. Multi-variate regression revealed that non-white race, the presence of depression, worse disease-specific patient reported symptoms as measured by SNOT-22 score, and decreased objective olfaction are all associated with QOD-NS. In regard to the olfaction metrics, the composite TDI score is associated with QOD-NS, and when the individual components of the TDI were analyzed, it appears that odorant discrimination correlates most strongly. The relationship of discrimination to QOD-NS is non-linear but rather quadratic in nature. While the interpretation of a quadratic association is more challenging, we can say that in these data as discrimination scores worsen, so does olfactory-specific QOL.

While olfactory dysfunction is usually defined by comparing patient performance on objective testing to normative data, perhaps this may not best reflect the degree to which patients are affected by olfaction in their daily life. Olfactory-specific QOL, as measured by the QOD-NS, directly deals with the real world impact of smell loss in CRS patients. In CRS as a whole, there seems to be a disconnect between objective findings and the subjective experience of the disease.¹¹ Olfactory dysfunction in CRS is apparently not different. Most strikingly, many patients with normosmia on TDI testing have non-perfect olfactory-specific QOL. The opposite is also likely true, that patients with impaired olfaction on objective psychophysical testing may not experience an impact on their QOL. This may be related to patients' professional and/or lifestyle choices. For example, food and wine aficionados might be more negatively impacted by olfactory dysfunction, compared to those with different interests that rely less on olfaction.

At a minimum, objective psychophysical testing and olfactory-specific QOL are complimentary evaluations of olfaction in CRS that provide unique and insights into the patient experience of smell loss. While certainly TDI and QOD-NS are correlated, the relationship is not perfect, and there are other related factors. In our data, CRS-specific QOL and depression impact QOD-NS, which is expected since these likely impact QOL as a whole. The strong relationship of discrimination to QOD-NS is somewhat surprising. Discrimination is a supra-threshold measure of the ability to determine whether two odorants are different. Perhaps, CRS patients might have changes in odorant threshold detection that do not necessarily impact daily life until the ability to distinguish between different odors is affected. Our data show that essentially no patients have normal threshold with abnormal discrimination, further supporting the idea that threshold detection levels might be the first to be affected, and once discrimination ability becomes impacted then olfactory-specific QOL decreases.

It should be noted that discrimination and identification are highly correlated.^{5,9} This is likely due to the fact that both tests involve supra-threshold stimulation. However identification did not remain a significant correlate in our multivariate model. The reason for this is unclear. One possibility is that not all patients were familiar with the odorants presented as part of identification testing, which would introduce unnecessary variation. Perhaps identification is more affected by higher level cognitive processing since it requires the precise naming of an odorant, whereas discrimination simply requires the understanding that odorants are different. However, a recent report by Hummel's group suggests that patients with cognitive or neurodegenerative disease perform poorly in both discrimination and identification, while sinonasal disease patients perform poorly in threshold testing.¹² This report supports the theory that threshold is affected first in sino-nasal disease, and that perhaps once discrimination is affected olfactory-specific QOL begins to decline more severely. It does not, however, explain the exclusion of identification from our model. This may be due to the nature of our data, and further study is warranted to understand the complex interplay between these different psychophysical olfactory tests.

The relationship between worse QOD scores and non-white race is also surprising. One possible explanation for this is that, in our population, African American individuals (which are the majority of our "non-white" group) have a higher incidence of allergic fungal rhinosinusitis with a larger polyp burden, which might impact olfaction. However, in our model-building process nasal polyposis, CT scores, and endoscopy scores did not remain significant. Perhaps these indicators of polyp burden are explained by the race variable in our model, but further study is required to answer this question as there may be other contributing factors to this relationship.

Given the high incidence of olfactory dysfunction in CRS,³ the ability to perform efficient screening in this population might prove useful in clinical practice and research. Unfortunately, the majority of objective smell screening tools require a significant amount of time or administration by a trained provider. We strove to establish cut-off scores of QOD-NS scores that would allow for classification of a patient's olfaction based on objective testing. The QOD-NS can be completed by patients while awaiting evaluation and is relatively short to complete. Interestingly, this analysis discovered that even patients with normal olfaction as measured by TDI can have QOD-NS scores that are not perfect. Given our findings that QOD-NS is affected by factors other than purely objective olfaction, it makes sense that perfect QOD-NS scores should not be the cut-off to detect olfactory dysfunction. It appears that varying scores of QOD-NS can be used to establish different olfaction classifications (see Tables 4 and 5). The exact sensitivity and specificity of this type of screening can be adjusted according to the clinicians or investigators needs or desires. Further prospective studies to validate QOD-NS as olfaction screening tool are needed.

While this study is a cross-sectional study that recorded demographics, comorbidities, CRS-specific disease severity measures, and several objective olfactory tests, it does have several limitations. This is a small cohort, recruited from a tertiary rhinology practice with a high burden of disease and large incidence of prior sinus surgery, and so the results may not be broadly applicable. The cross-sectional nature does not allow insights into mechanisms of

disease. We assumed that the olfactory dysfunction in this cohort relates to their underlying CRS. Olfactory loss in CRS is not well understood, and there are different factors like diminished airflow into the olfactory cleft, and inflammation or damage of the olfactory epithelium which might impact olfaction in these patients to varying degrees.

Conclusion

The relationship between objective olfactory dysfunction and olfactory-specific QOL, as measured by QOD-NS, in patients with CRS is complex. In these data, non-white race, depression, and worse SNOT-22 scores were associated with worse QOD-NS results. Also, worse TDI scores were associated with decreased QOD-NS. Of the three TDI components, our study suggests that odorant discrimination may be the most important predictor of QOD-NS scores. QOD-NS scores are not perfect in normosmic CRS patients, supporting our findings that factors beyond objective olfaction impact olfactory-specific QOL. Finally, the use of QOD-NS cut-off scores to screen for olfactory dysfunction appears feasible and deserves further investigation.

Acknowledgments

Funding: This work was supported by grants from the National Institute on Deafness and Other Communication Disorders (NIDCD), one of the National Institutes of Health, Bethesda, MD (R03 DC013651-01; PI: ZM Soler).

Zachary M. Soler is supported by grants from Entellus, Intersect, and Optinose, none of which are affiliated with this manuscript. Dr. Soler is a consultant for Olympus, which is not affiliated with this manuscript. Rodney J. Schlosser is supported by grants from OptiNose, Entellus and IntersectENT, none of which are associated with this manuscript. Dr. Schlosser is also a consultant for Olympus, Medtronic and Arrinex, which are not affiliated with this study.

References

1. Fokkens WJ, Lund VJ, Mullol J, et al. European position paper on rhinosinusitis and nasal polyps 2012. *Rhinology*. 2012; 50(SUPPL. 23):4–305. DOI: 10.4193/Rhino12.000
2. Rosenfeld RM, Piccirillo JF, Chandrasekhar SS, et al. Clinical Practice Guideline (Update): Adult Sinusitis Executive Summary. *Otolaryngol -- Head Neck Surg*. 2015; 152(4):598–609. DOI: 10.1177/0194599815574247 [PubMed: 25833927]
3. Soler ZM, Smith TL, Alt JA, Ramakrishnan VR, Mace JC, Schlosser RJ. Olfactory-specific quality of life outcomes after endoscopic sinus surgery. *Int Forum Allergy Rhinol*. 2015; 6(4)doi: 10.1002/alr.21679
4. Schlosser RJ, Storck Ka, Rudmik L, et al. Association of olfactory dysfunction in chronic rhinosinusitis with economic productivity and medication usage. *Int Forum Allergy Rhinol*. 2016
5. Soler ZM, Kohli P, Storck KA, Schlosser RJ. Olfactory Impairment in Chronic Rhinosinusitis Using Threshold, Discrimination, and Identification Scores. *Chem Senses*. Jul.2016 doi: 10.1093/chemse/bjw080
6. Lund VJ, Kennedy DW. Staging for rhinosinusitis. *Otolaryngol - Head Neck Surg*. 1997; 117(3):S35–40. [PubMed: 9334786]
7. Lund VJ, Mackay IS. Staging in rhinosinusitis. *Rhinology*. 1993; 31(4):183–184. <http://www.ncbi.nlm.nih.gov/pubmed/8140385>. [PubMed: 8140385]
8. Simopoulos E, Katotomichelakis M, Gouveris H, Tripsianis G, Livaditis M, Danielides V. Olfaction-associated quality of life in chronic rhinosinusitis: adaptation and validation of an olfaction-specific questionnaire. *Laryngoscope*. 2012; 122(7):1450–1454. DOI: 10.1002/lary.23349 [PubMed: 22566102]

9. Hummel T, Sekinger B, Wolf SR, Pauli E, Kobal G. "Sniffin" sticks': olfactory performance assessed by the combined testing of odor identification, odor discrimination and olfactory threshold. *Chem Senses*. 1997; 22(1):39–52. <http://www.ncbi.nlm.nih.gov/pubmed/9056084>. [PubMed: 9056084]
10. Hummel T, Kobal G, Gudziol H, Mackay-Sim A. Normative data for the "Sniffin' Sticks" including tests of odor identification, odor discrimination, and olfactory thresholds: an upgrade based on a group of more than 3,000 subjects. *Eur Arch Otorhinolaryngol*. 2007; 264(3):237–243. DOI: 10.1007/s00405-006-0173-0 [PubMed: 17021776]
11. Soler ZM, Hyer JM, Ramakrishnan V. Identification of chronic rhinosinusitis phenotypes using cluster analysis. 2015; 5(5):399–407. DOI: 10.1002/alr.21496
12. Whitcroft KL, Cuevas M, Haehner A, Hummel T. Patterns of olfactory impairment reflect underlying disease etiology. *Laryngoscope*. Aug.2016 doi: 10.1002/lary.26229

Figure 1. ROC Curve of QOD-NS Ability to Detect Olfactory Dysfunction

ROC: Receiver Operating Characteristics; QOD-NS: Questionnaire of Olfactory Disorders
Negative Statements

Table 1

Demographics, Comorbidities, CRS Characteristics and Olfactory Metrics

Demographic/QOL Measure	All CRS Mean (SD) Count (%)	CRSsNP Mean (SD) Count (%)	CRSwNP Mean (SD) Count (%)	P-Value Differences between CRSwNP & CRSsNP
Demographics and comorbidities				
Age	52.70 (16.14)	53.72 (16.48)	52.01 (16.00)	0.591
Sex	Male	15 (34.09)	33 (50.77)	0.085
	Female	29 (65.91)	32 (49.23)	
Race	White	37 (84.09)	40 (61.54)	0.025
	Asian	0 (0)	2 (3.08)	
	African American	7 (15.91)	23 (35.38)	
Ethnicity	Hispanic	1 (2.27)	1 (1.54)	1.000
	Non-Hispanic	43 (97.73)	64 (98.46)	
Asthma	53 (48.62)	10 (22.73)	43 (66.15)	<0.001
AERD	10 (9.17)	2 (4.55)	8 (12.31)	0.198
Allergy by Testing	61 (55.96)	20 (45.45)	41 (63.08)	0.069
COPD	8 (7.34)	3 (6.82)	5 (7.69)	1.000
Depression	20 (18.35)	10 (22.73)	10 (15.38)	0.331
Fibromyalgia	6 (5.50)	5 (11.36)	1 (1.54)	0.038
Immunodeficiency	2 (1.85)	1 (2.33)	1 (1.54)	1.000
Autoimmune disease	3 (2.75)	1 (2.27)	2 (3.08)	1.000
Steroid Dependent	3 (2.80)	1 (2.33)	2 (3.13)	1.000
Diabetes	18 (16.51)	8 (18.18)	10 (15.38)	0.887
Smoker	4 (3.67)	2 (4.55)	2 (3.08)	1.000
Alcohol (drinks/week)	1.80 (3.49)	1.1 (2.47)	2.27 (3.99)	0.208
CRS factors				
Prior sinus surgery	80 (73.39)	31 (70.45)	49 (75.38)	0.568
Endoscopy Score	6.33 (3.79)	5.36 (3.24)	6.98 (4.02)	0.022
CT Score	12.22 (6.77)	8.65 (5.80)	15.58 (5.89)	<0.001

Demographic/QOL Measure	All CRS Mean (SD) Count (%)	CRSsNP Mean (SD) Count (%)	CRSwNP Mean (SD) Count (%)	P-Value Differences between CRSwNP& CRSsNP
SNOT-22 Score	46.46 (21.11)	49.70 (17.27)	44.32 (23.18)	0.171
Olfactory factors				
TDI	20.98 (9.01)	25.01 (9.12)	18.26 (7.90)	<0.001
Threshold	2.93 (2.42)	3.85 (2.74)	2.30 (1.96)	0.002
Discrimination	8.69 (3.31)	10.09 (3.35)	7.74 (2.95)	<0.001
Identification	9.37 (4.42)	11.07 (4.20)	8.22 (4.23)	0.001
QOD	35.78 (11.88)	38.32 (11.30)	34.06 (12.03)	0.066

COPD: Chronic Obstructive Pulmonary Disease; CT: Computer Tomography; SNOT-22: 22-item Sino-nasal Outcomes Test; TDI: Composite score of threshold, discrimination, and identification; QOD-NS: Questionnaire of Olfactory Disorders Negative Statements. AERD: Aspiring Exacerbated Respiratory Disease.

Table 2

Factors Associated with QOD-NS on Multivariate Modelling using TDI Composite Score

	B	SE	t-statistic	P-value
Race (non-white)	-7.25	2.02	-3.59	0.001
Depression	-7.59	2.39	3.18	0.002
SNOT-22	-0.19	0.44	-4.21	<0.001
TDI	0.42	0.10	4.11	<0.001

QOD-NS: Questionnaire of Olfactory Disorders Negative Statements; TDI: Composite score of threshold, discrimination, and identification; SNOT-22: 22-item Sino-nasal Outcomes Test.

Table 3

Factors Associated with QOD-NS on Multivariate Modelling Using Separate T, D, I Components

	B	SE	t-statistic	P-value
Race (non-white)	−6.57	2.03	−3.25	0.002
Depression	−7.63	2.37	3.22	0.002
SNOT-22	−0.18	0.04	−4.16	<0.001
D	0.73	0.28	3.27	0.10
D-Squared	0.28	0.09	3.27	0.001

QOD-NS: Questionnaire of Olfactory Disorders Negative Statements; SNOT-22: 22-item Sino-nasal Outcomes Test; T: Threshold; D: Discrimination; I: Identification.

Table 4

Mean QOD-NS Overlap Between Individual Components of TDI Score

		D		P-Value
		Normal	Abnormal	
T	Normal	n=9 mean (SD) = 44.7 (4.9)	n= 1 mean (SD) = 48.0	
	Abnormal	n=30 mean (SD) = 42.5 (8.8)	n=69 mean (SD) = 31.5 (11.7)	<0.001
P-Value		0.481		

		I		P-Value
		Normal	Abnormal	
T	Normal	n= 10 mean (SD)= 45.0 (4.8)	n=0	
	Abnormal	n=33 mean (SD) = 39.6 (11.2)	n=66 mean (SD) = 32.5 (11.8)	0.005
P-Value		0.034		

		I		P-Value
		Normal	Abnormal	
D	Normal	n=31 Mean (SD) = 43.1 (8.4)	n=8 Mean (SD) = 42.4 (7.1)	0.818
	Abnormal	n=12 Mean (SD) = 34.9(12.5)	n=58 Mean (SD) = 31.1 (11.7)	0.314
P-Value		0.017	0.010	

QOD-NS: Questionnaire of Olfactory Disorders Negative Statements; T: Threshold; D: Discrimination; I: Identification.

Table 5

ROC Analysis of QOD-NS Ability to Detect Olfactory Dysfunction

Area Under the Curve (AUC)	Std. Error	Asymptotic Sig.	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
.770	.053	<0.000	.667	.873

Olfactory Dysfunction if QOD	Sensitivity	Specificity	Youden's Index
7.0	0.000	1.000	0.000
9.0	0.011	1.000	0.011
10.5	0.023	1.000	0.023
11.5	0.046	1.000	0.046
12.5	0.057	1.000	0.057
13.5	0.080	1.000	0.080
14.5	0.115	1.000	0.115
16.0	0.126	1.000	0.126
17.5	0.138	1.000	0.138
19.5	0.149	1.000	0.149
21.5	0.172	1.000	0.172
22.5	0.184	1.000	0.184
23.5	0.218	1.000	0.218
24.5	0.253	1.000	0.253
25.5	0.253	0.955	0.207
26.5	0.276	0.955	0.230
27.5	0.310	0.955	0.265
28.5	0.333	0.955	0.288
30.0	0.368	0.909	0.277
31.5	0.391	0.909	0.300
32.5	0.402	0.909	0.311
33.5	0.425	0.909	0.334
34.5	0.471	0.909	0.380
35.5	0.494	0.909	0.403
36.5	0.517	0.864	0.381
37.5	0.563	0.818	0.381
38.5	0.609	0.818	0.427
39.5	0.621	0.773	0.393
40.5	0.667	0.727	0.394
41.5	0.678	0.682	0.360
42.5	0.701	0.682	0.383
43.5	0.713	0.591	0.304

Olfactory Dysfunction if QOD	Sensitivity	Specificity	Youden's Index
44.5	0.747	0.591	0.338
45.5	0.805	0.545	0.350
46.5	0.828	0.500	0.328
47.5	0.885	0.500	0.385
48.5	0.920	0.273	0.192
49.5	0.966	0.227	0.193

ROC: Receiver Operating Characteristics; QOD-NS: Questionnaire of Olfactory Disorders Negative Statements