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The Prevalence of Olfactory Dysfunction in Chronic Rhinosinusitis

Preeti Kohli, BA¹, Akash N. Naik, BA¹, E. Emily Harruff, BS¹, Shaun A. Nguyen, MD, MA¹, Rodney J. Schlosser, MD^{1,2}, and Zachary M. Soler, MD, MSc¹

¹Department of Otolaryngology – Head and Neck Surgery, Medical University of South Carolina, Charleston, SC, USA

²Department of Surgery, Ralph H. Johnson, VA Medical Center, Charleston, SC, USA

Abstract

Objective—Many studies have reported that olfactory dysfunction frequently occurs in chronic rhinosinusitis (CRS) populations; however, the prevalence and degree of olfactory loss has not been systematically studied. The aims of this study are to use combined data to report the prevalence of olfactory dysfunction and to calculate weighted averages of olfactory test scores in CRS patients.

Data Sources—A search was conducted in PubMed and Scopus, following the methods of Preferred Reporting Items for Systematic Review and Meta-Analysis guidelines.

Review Methods—Studies reporting the prevalence of olfactory dysfunction using objective measures or olfactory test scores using validated scales were included.

Results—A total of 47 articles were included in systematic review and 35 in the pooled data analysis. The prevalence of olfactory dysfunction in chronic rhinosinusitis was found to be 30.0% using the Brief Smell Identification Test, 67.0% using the 40-item Smell Identification Test, and 78.2% using the total Sniffin' Sticks score. Weighted averages $\pm$ standard deviation of olfactory test scores were 25.96 $\pm$ 7.11 using the 40-item Smell Identification Test, 8.60 $\pm$ 2.81 using the Brief Smell Identification Test, 21.96 $\pm$ 8.88 using total Sniffin' sticks score, 5.65 $\pm$ 1.51 using Sniffin' Sticks threshold, 9.21 $\pm$ 4.63 using Sniffin' Sticks discrimination, 9.47 $\pm$ 3.92 using Sniffin' Sticks Identification, and 8.90 $\pm$ 5.14 using the questionnaire for olfactory disorders-negative statements.

Conclusion—In chronic rhinosinusitis populations, a significant percentage of patients experience olfactory dysfunction and mean olfactory scores are within the dysosmic range.

Keywords

olfaction; smell; chronic rhinosinusitis; sinusitis; prevalence

Correspondence: Preeti Kohli, BA, Department of Otolaryngology – Head and Neck Surgery, Medical University of South Carolina, 135 Rutledge Ave, MSC 550, Charleston, SC 29425, USA. Telephone: 516-713-9934; Fax: (843) 792-0546; pkohli89@gmail.com.

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Introduction

Chronic rhinosinusitis (CRS) affects nearly one in eight adults in the United States¹ and is a leading causes of olfactory dysfunction worldwide.^{2,3} Clinicians are increasing focus towards olfactory impairment, a cardinal symptom used to diagnose CRS, due to its direct and indirect effects on behavior, nutritional status, and environmental safety.⁴ A recent study even linked smell loss to increased mortality, a finding not seen with hearing or vision loss.⁵ Understanding the scope of CRS-related olfactory dysfunction benefits multiple stakeholders, including patients, physicians, researchers, and healthcare policy-makers.

Many studies have reported olfactory dysfunction frequently occurs in CRS populations; however, the prevalence and degree of olfactory loss has not been systematically studied. Population-based studies separating olfactory dysfunction by etiology sometimes use imprecise proxies such as “sinus infections” or “nasal congestion” which do not necessarily translate into a formal diagnosis of CRS.^{6,7} In addition, studies exploring olfaction in CRS often use differing test methods, making direct comparisons difficult.

The main objective of this study was to perform a systematic review with meta-analysis and pooled data analysis on of the prevalence and degree of olfactory dysfunction, respectively, in patients with CRS. The secondary aim was to review patient-specific factors which might impact olfaction within CRS, including demographics, CRS-specific disease severity measures, and comorbidities.

Methods

Literature search strategy

A comprehensive literature search of PubMed (1947 - November 2015) and Scopus (1973- November 2015) was conducted on November 29, 2015. The full search term for PubMed was (“Smell”[Mesh] OR smell* OR “Olfaction Disorders”[Mesh] OR olfact* OR Anosmi* OR “Olfactory Perception”[Mesh] OR Hyposmi* OR “Odors”[Mesh] OR odor*) AND (rhinosinusitis OR sinusitis). The full search term for Scopus was (smell* OR olfact* OR Anosmi* OR Hyposmi* OR odor*) and (rhinosinusitis OR sinusitis). Language and date filters were not applied with the intention of generating a broad list of potential studies. Figure 1 highlights the search strategy used in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.⁸ Reference lists of all obtained articles were examined for additional studies meeting inclusion criteria. Two authors (P.K. and E.E.H.) independently conducted the database searches. The resulting studies were reviewed first using titles and abstracts and then full manuscripts. Each included study was evaluated for quality using the Oxford Center for Evidence-Based Medicine (OCEBM) criteria.⁹

Inclusion/exclusion criteria

Patients in each included study must have been diagnosed with CRS using specified diagnostic criteria, such as characteristic symptoms and/or imaging, although this was allowed to vary across individual studies. Included studies had to present data on

quantitative olfactory loss using a validated scale or report the prevalence of olfactory dysfunction using an objective testing measure. Articles were excluded if the overall cohort included non-CRS patients that could not be separated. Studies that preferentially enrolled patients with olfactory disturbances were excluded, as were reviews and individual case reports. In instances where multiple studies were clearly published from an overlapping cohort of patients, the largest and/or most recent study was utilized so as not to include duplicate data in weighted estimates.

Data extraction and statistical analysis

Data was extracted from studies meeting inclusion criteria by 3 authors (P.K., A.N.N., and E.E.H.) using standardized forms. Extracted information included: criteria used to diagnose CRS, demographic information, CRS-specific disease severity metrics, comorbidities, mean and standard deviation (SD) of any reported olfactory measures, and prevalence of olfactory dysfunction. Continuous variables were summarized by the mean $\pm$ standard deviation. Nominal variables were summarized by percentage. A meta-analysis of proportions was performed to combine prevalence estimates. Heterogeneity across studies was assessed using the I^2 statistic. If the heterogeneity test was significant, p-value for a random effects model was used. If the heterogeneity test was non-significant, p-value for fixed effects model was used. The use of a fixed or random effect model is indicated as “fixed” or “random” in the results section. Means and SDs for combination of olfactory test data was weighted according to study sample sizes. Data is presented first for studies presenting composite measures of objective olfactory function, followed by those that evaluated identification or threshold tests, and lastly those that used alternative measures of olfaction. Ninety-five percent confidence intervals extracted from studies were converted to SDs according to Cochrane guidelines.¹⁰ Independent t-tests were used to compare differences between polyp groups. A p value of <0.05 was considered statistically significant for all statistical tests. All analyses were performed using MedCal 16.4.3 (MedCalc Software bvba, Belgium)

Risk bias assessment

Included articles were assessed for bias risk using two domains of the Quality in Prognosis Studies tool that are relevant to prevalence studies: study participation (risk of selection bias) and outcome measurement (risk of outcome bias).¹¹ Each domain was subjectively evaluated (ranked as low, moderate, or high) and provided in the respective tables (Table 1-3). For risk of selection bias, the major criteria used to evaluate studies included: 1) method of CRS diagnosis (greater bias in studies that did not use established guidelines), 2) type of treatment, if any, the cohort elected (greater bias in studies only providing data on patients electing surgery), and 3) single vs. multi-institutional studies (greater bias in single institution studies). Minor criteria included characteristics such as whether the enrollment process was described, if sampling time frame was described, and if co-morbidities between patients with and without olfactory dysfunction were described. For risk of outcome bias, studies that used a validated measure of olfaction and described the testing process and scoring were ranked as low bias studies. Studies using non-validated measures of olfaction were ranked as higher levels of bias.

Results

Search characteristics

The database search yielded 871 citations of which 231 full manuscripts were reviewed and 47 fulfilled inclusion/exclusion criteria (Figure 1). Table 1, 2, and 3 provide a summary of all included articles. Within all studies, 5,197 CRS patients were identified. Included studies were either prospective, longitudinal cohorts or cross-sectional in design (level of evidence 3).⁹

Olfactory dysfunction – combined prevalence estimates and pooled means

Composite scores

Sniffin' Sticks – Total Threshold/Discrimination/Identification (TDI) score: Three studies in CRS mixed¹²⁻¹⁴ reported the prevalence of olfactory dysfunction using the total TDI score. Olfactory status using Sniffin' Sticks total score is classified as 15 anosmic, 30 hyposmic, >30 normosmic.¹⁵ The combined prevalence of normosmics, hyposmics, anosmics, and overall olfactory dysfunction in CRS mixed patients was 21.77% ($I^2 = 69.20\%$; random), 46.03% ($I^2 = 0.00\%$; fixed), 28.92% ($I^2 = 9.46\%$; fixed), and 78.23% ($I^2 = 69.20\%$; random), respectively (Table 1, Figure 2). Four studies in CRS mixed^{12,14,16,17} presented TDI total scores, yielding a population of 253 patients. Pooled TDI score was 21.96 ± 8.88 , which falls into hyposmic range (Table 4).

Two studies in chronic rhinosinusitis with nasal polyps (CRSwNP)^{18,19} reported the prevalence of olfactory dysfunction using the total TDI. The combined prevalence of normosmics, hyposmics, anosmics, and overall olfactory dysfunction was 6.32% ($I^2 = 96.81\%$; random), 33.20% ($I^2 = 97.06\%$; random), 56.81% ($I^2 = 98.64\%$; random), and 93.68% ($I^2 = 96.81\%$; random), respectively (Table 1). Four studies in CRSwNP¹⁸⁻²¹ presented TDI total scores, yielding a population of 233 patients. Pooled TDI score was 15.58 ± 6.49 , which falls into hyposmic range. CRS mixed had significantly higher total TDI scores than CRSwNP patients (21.96 ± 8.88 vs 15.58 ± 6.49 , $p < 0.0001$) (Table 4).

Connecticut Chemosensory Clinical Research Center (CCCRC) test—Two studies in CRS mixed^{22,23} and 1 study in CRSwNP²⁴ reported the prevalence of olfactory dysfunction using CCCRC, which includes both threshold and identification measures. Because enough studies did not provide raw number of patients, combined prevalence in CRS mixed patients could not be calculated, however, prevalence estimates from individual studies are reported in Table 1. Weighted combination of olfactory scores was also unable to be performed due to variations in olfactory testing procedures between studies.

Identification

40-Item Smell Identification Test (SIT-40): Four studies in CRS mixed²⁵⁻²⁸ reported the prevalence of olfactory dysfunction using SIT-40. The combined prevalence of normosmics, hyposmics, anosmics, and overall olfactory dysfunction was 34.39% ($I^2 = 0.00\%$; fixed), 43.96% ($I^2 = 0.00\%$; fixed), 21.90% ($I^2 = 0.00\%$; fixed), and 67.00% ($I^2 = 58.46\%$; fixed), respectively (Table 2, Figure 3).

Olfactory status using SIT-40 is classified as: 0-5 malingering, 6-19 anosmic, 20-33 hyposmic, and 34-40 normosmic.²⁹ Twelve studies presented SIT-40 scores amenable to combination analysis, yielding a population of 1576 CRS mixed patients.^{26,30-39} Pooled SIT-40 score was 25.96 ± 7.11 , which falls in the hyposmic range (Table 4).

Brief Smell Identification Test (B-SIT): Three studies in CRS mixed⁴⁰⁻⁴² reported the prevalence of olfactory dysfunction using B-SIT. Normosmia using B-SIT is classified as a score ≥ 9 normosmia.⁴³ The combined prevalence of olfactory dysfunction was 29.97% ($I^2=91.12\%$; random) (Table 2).

Three studies presented B-SIT scores amenable to combination analysis, yielding a population of 520 CRS mixed patients.^{40,42,44} Pooled B-SIT score was 8.60 ± 2.81 , which falls into abnormal olfactory range (Table 4).

Sniffin' Sticks – identification: Six studies in CRS mixed^{12,14,16,45-47} and 2 studies in CRSwNP^{18,19} presented standard 16-odor identification scores, yielding a population of 899 and 187 patients, respectively. Olfactory dysfunction using the 16-odor Sniffin' Sticks identification test is defined as scores ≤ 11 .⁴⁸ Pooled identification scores were significantly higher in CRS mixed patients when compared to CRSwNP (9.47 ± 3.92 vs 6.04 ± 3.14 , $p<0.0001$) although both were abnormal (Table 4).

Three studies in CRS mixed⁴⁹⁻⁵¹ and 2 studies in chronic rhinosinusitis without nasal polyps (CRSsNP)^{52,53} presented modified 12-odor identification scores, yielding a population of 245 and 53 patients, respectively. Olfaction is classified using 12-odor Sniffin' Sticks identification test as: 0-6 anosmic, 7-10 hyposmic, 11-12 normosmic.⁵⁴ Pooled identification scores were non-significantly higher in CRS mixed patients when compared to CRSsNP (8.06 ± 3.06 vs 7.25 vs 1.52 , $p=0.0617$) although both were in hyposmic range (Table 4).

Threshold

Sniffin' Sticks: Threshold: Six studies in CRS mixed^{12,14,16,55-57} and 2 studies in CRSwNP^{18,19} presented threshold scores, yielding a population of 386 and 187 patients, respectively. Olfactory dysfunction using Sniffin' Sticks threshold tests is defined as ≤ 6.00 in males and ≤ 6.50 in females. Pooled threshold scores were significantly higher in CRS mixed patients when compared to CRSwNP (5.65 ± 1.51 vs 2.28 ± 2.11 , $p<0.0001$) although both were abnormal (Table 4).

Butanol Threshold Test (BTT)—Three studies in CRS mixed^{44,58,59} reported the prevalence of olfactory dysfunction using BTT (Table 3). The combined prevalence of normosmic, hyposmics, anosmics, and overall olfactory dysfunction was 21.80% ($I^2=36.43\%$; fixed), 31.21% ($I^2=82.88\%$; random), 46.29% ($I^2=79.12\%$; random), and 78.21% ($I^2=36.43\%$; fixed), respectively. Weighted combination of olfactory scores was unable to be performed due to variations in testing procedure.

Other threshold tests—One study of 28 CRS mixed patients reported the prevalence of hyposmia using the Phenylethyl Alcohol (PEA) test as 42.9%.⁶⁰ One study of 25 CRS mixed patients reported the prevalence of anosmia using the Olfactometer Threshold Test

(T&T) as 32%.⁶¹ One study of 115 CRS mixed patients reported the prevalence of normosmia, hyposmia, and anosmia as 16%, 52%, and 31%, respectively, using a non-validated threshold test⁶² (Table 3).

Alternative measures of olfaction

Sniffin' Sticks - Discrimination: Three studies in CRS mixed^{12,14,16} and 2 studies in CRSwNP^{18,19} presented discrimination scores, yielding a population of 189 and 187 patients, respectively. Olfactory dysfunction using Sniffin' Sticks discrimination is defined as ≤ 10 .¹⁵ Pooled discrimination scores were significantly higher in CRS mixed patients when compared to CRSwNP (9.21 ± 4.63 vs 6.48 ± 3.46 , $p < 0.0001$) although both were abnormal (Table 4).

European Test of Olfactory Capabilities (ETOC)—One study in 30 CRSwNP patients reported the prevalence of normosmia, hyposmia, and anosmia as 6.7%, 30.0%, and 63.3%, respectively, using ETOC⁶³ (Table 3).

Questionnaire of Olfactory Disorders – Negative Statements (QOD-NS)—Two studies in CRS mixed patients presented QOD-NS scores in 213 patients.^{12,13} QOD-NS scores range from 0 (poor smell) to 51 (normal smell).⁶⁴ The pooled QOD-NS score was 8.90 ± 5.14 (Table 4).

Factors associated with olfactory dysfunction

Given the high prevalence of olfactory dysfunction in CRS, we examined included studies for factors that may help clinicians identify patients at highest risk of smell loss. Twenty-three of the 47 included studies reported predictors. Among demographic factors, higher age was most frequently associated with poorer smell with 7 studies reporting this association.^{12,19,27,40,47,50,65} Two studies did not find any association between age and olfactory dysfunction.^{59,66} Within CRS-specific factors, a higher Lund-Mackay (LM) CT score was most frequently associated with poorer smell with 11 studies reporting this relationship.^{18,21,27,38,40,52,59,66–69} Remaining studies did not examine this association. Among co-morbid factors impacting smell, nasal polyposis was most frequently associated with olfactory dysfunction with 10 studies reporting an association.^{12,22,27,32,40,47,62,65–67} Remaining studies did not examine this relationship.

Discussion

This study systematically reviewed olfactory impairment in CRS and estimated the prevalence of olfactory dysfunction in CRS to be 29.97% using B-SIT, 67.00% using SIT-40, and 78.23% using total TDI score. Weighted means of each composite and individual olfactory measure fell into the range for olfactory dysfunction, further confirming its high prevalence in CRS populations. Additionally, the pooled QOD-NS score of 8.90 suggests that smell loss significantly impacts the quality of life of CRS patients, including social, physical, and emotional well-being.

Given these findings, we reviewed studies for factors associated with olfactory dysfunction. Higher LM CT scores were most frequently associated with poorer smell. Inflammatory

changes apparent on CT scans are caused by nasal discharge, edema, or polyps, which restrict the flow of odorant-permeated air in the nasal passages.⁷⁰ Inflammation can also produce structural changes to the pseudostratified columnar epithelium, which contains bipolar neurons, disrupting the propagation of signals to the olfactory bulb and primary sensory cortex.⁷⁰ Nasal polyposis was the most frequently associated co-morbidity in patients with olfactory dysfunction. Nasal polyps are physical barriers to odorants, and the ongoing inflammation associated with this subgroup could contribute to permanent neuroepithelial damage. Higher age was the most frequent demographic factor to be associated with poorer smell and is previously well-studied.^{7,71,72}

The prevalence of olfactory impairment is sub-group and test-dependent. CRSwNP groups experienced higher levels of olfactory dysfunction than CRS mixed populations. While prevalence estimates using TDI and SIT-40 were comparable, B-SIT led to a much lower value. Even though B-SIT may be more clinically feasible, it likely underestimates true olfactory dysfunction in CRS populations. Prior studies by Alt et al. and Deconde et al. agree B-SIT lacks sensitivity in classifying degree of identification loss.^{40,43} The combination analysis of olfactory scores (Table 4), in which B-SIT came closest to the normosmic cut-off out of all the composite olfactory measures, support this hypothesis. Given the goal of testing to maximize sensitivity, when possible, Sniffin' Sticks and SIT-40 are preferred methods of olfactory measurement.

The prevalence of olfactory dysfunction using total TDI score was slightly higher than SIT-40. This difference may be because the Sniffin' Sticks tests all three components of olfaction while SIT-40 tests only identification. In Table 4, we found CRS-related olfactory dysfunction to impact each sub-component of TDI, highlighting that a comprehensive olfactory assessment may have greater ability to detect olfactory impairment than any single component. Lotsch et al. conducted a study in idiopathic Parkinson's disease (IBD) patients using Sniffin' Sticks and found test sensitivity to increase as more sub-components were used.⁷³ The mechanism and degree to which each of these sub-components is affected in CRS remains unknown and is an area of further study. However, it is possible that relying solely on identification may underestimate the prevalence of olfactory dysfunction.

Strengths of this study include its systematic design, broad coverage of testing methodologies, and relatively large sample sizes for the most common metrics. As with all reviews, the study was restricted to available data which limited some conclusions. This was particularly true for the CRSsNP population, which was not reported as a separate and distinct subgroup in most studies. There is also inherent selection and/or publication bias since most patients enrolled into studies were seeking treatment for CRS. Although representative of patients presenting for clinical care, it may not be generalizable to all patients with CRS, particularly those with milder and less symptomatic disease. Although an effort was made to minimize redundancy by using only the largest or most recent studies from cohort studies, it remains possible that some studies overlapped in terms of the included patients.

Conclusion

A significant percentage of CRS patients experience olfactory dysfunction and mean olfactory scores of CRS cohorts are well within the dysosmic range. Age, inflammatory changes on CT, and nasal polyps are the most common factors associated with olfactory dysfunction across studies.

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References

1. Rosenfeld RM, Piccirillo JF, Chandrasekhar SS, et al. Clinical Practice Guideline (Update): Adult Sinusitis. *Otolaryngol Head Neck Surg*. 2015; 152(2 suppl):S1–S39. DOI: 10.1177/0194599815572097
2. Croy I, Nordin S, Hummel T. Olfactory disorders and quality of life--an updated review. *Chem Senses*. 2014; 39(3):185–194. DOI: 10.1093/chemse/bjt072 [PubMed: 24429163]
3. Lee WH, Wee JH, Kim D-K, et al. Prevalence of subjective olfactory dysfunction and its risk factors: korean national health and nutrition examination survey. *PLoS One*. 2013; 8(5):e62725.doi: 10.1371/journal.pone.0062725 [PubMed: 23671628]
4. Wang L, Walker VE, Sardi H, Fraser C, Jacob TJC. The correlation between physiological and psychological responses to odour stimulation in human subjects. *Clin Neurophysiol*. 2002; 113(4): 542–551. <http://www.ncbi.nlm.nih.gov/pubmed/11955999>. [PubMed: 11955999]
5. Schubert CR, Fischer ME, Pinto AA, et al. Sensory Impairments and Risk of Mortality in Older Adults. *J Gerontol A Biol Sci Med Sci*. Mar.2016 doi: 10.1093/gerona/glw036
6. Rawal S, Hoffman HJ, Bainbridge KE, Huedo-medina TB, Duffy VB. Prevalence and Risk Factors of Self-Reported Smell and Taste Alterations: Results from the 2011-2012 U.S. National Health and Nutrition Survey (NHANES). 2015; 00:1–8. DOI: 10.1093/chemse/bjv057
7. Bhattacharyya N, Kepnes LJ. Contemporary assessment of the prevalence of smell and taste problems in adults. *Laryngoscope*. 2015; 125(5):1102–1106. DOI: 10.1002/lary.24999 [PubMed: 25369790]
8. Moher D, Liberati A, Tetzlaff J, Altman DG. PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *J Clin Epidemiol*. 2009; 62(10): 1006–1012. DOI: 10.1016/j.jclinepi.2009.06.005 [PubMed: 19631508]
9. Durieux N, Pasleau F, Howick J. OCEBM Levels of Evidence Working Group. The Oxford 2011 Levels of Evidence. Group. 2011; 1(version):5653. <http://www.cebm.net/index.aspx?o=1025>.
10. Higgins, JPT., Altman, DG. *Cochrane Handbook for Systematic Reviews of Interventions*. Version 5.1.0 [Updated March 2011]. The Cochrane Collaboration, 2011. Higgins, JPT., Green, S., editors. 2011.
11. Hayden JA, van der Windt DA, Cartwright JL, Côté P, Bombardier C. Assessing bias in studies of prognostic factors. *Ann Intern Med*. 2013; 158(4):280–286. DOI: 10.7326/0003-4819-158-4-201302190-00009 [PubMed: 23420236]
12. Katotomichelakis M, Simopoulos E, Tripsianis G, et al. Predictors of quality of life outcomes in chronic rhinosinusitis after sinus surgery. *Eur Arch Otorhinolaryngol*. 2014; 271(4):733–741. DOI: 10.1007/s00405-013-2626-6 [PubMed: 23842603]
13. 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]

14. Thamboo A, Chang BA, Habib AR, et al. The effect of two sphenoidotomy approaches on the sense of smell: trans-ethmoidal versus trans-sphenoethmoidal. *Rhinology*. 2014; 52(3):281–287. DOI: 10.4193/Rhin13.106 [PubMed: 25271535]
15. 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 Oto-Rhino-Laryngology*. 2007; 264(3): 237–243. DOI: 10.1007/s00405-006-0173-0
16. Reyhler G, Colbrant C, Huart C, et al. Effect of three-drug delivery modalities on olfactory function in chronic sinusitis. *Laryngoscope*. 2015; 125(3):549–555. DOI: 10.1002/lary.24937 [PubMed: 25224684]
17. Wallwork B, Coman W, Mackay-Sim A, Greiff L, Cervin A. A double-blind, randomized, placebo-controlled trial of macrolide in the treatment of chronic rhinosinusitis. *Laryngoscope*. 2006; 116(2):189–193. DOI: 10.1097/01.mlg.0000191560.53555.08 [PubMed: 16467702]
18. Chung JH, Lee YJ, Kang TW, et al. Altered Quality of Life and Psychological Health (SCL-90-R) in Patients With Chronic Rhinosinusitis With Nasal Polyps. *Ann Otol Rhinol Laryngol*. 2015; 124(8):663–670. DOI: 10.1177/0003489415576181 [PubMed: 25743178]
19. Katotomichelakis H, Tripsianis G, Simopoulou M, Papathanassiou J, Danielides VMG. Biometric predictive models for the evaluation of olfactory recovery after endoscopic sinus surgery in patients with nasal polyposis. *Am J Rhinol Allergy*. 2010; 24:276–280. DOI: 10.2500/ajra.2010.24.3476 [PubMed: 20819466]
20. Gudziol D, Abolmaali N, Gerber J, Rombaux P, Hummel TVB. Increasing olfactory bulb volume due to treatment of chronic rhinosinusitis—a longitudinal study. *Brain*. 2009; 132:3096–3101. <http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L35555520>. [PubMed: 19773353]
21. Konstantinidis M, Kaidoglou K, Constantinidis J, Gudziol VW. Olfactory mucosa in nasal polyposis: implications for FESS outcome. *Rhinology*. 2010; 48:47–53. DOI: 10.4193/Rhin09.102 [PubMed: 20502735]
22. Sanchez-Vallecillo MV, Fraire ME, Baena-Cagnani C, Zernotti ME. Olfactory dysfunction in patients with chronic rhinosinusitis. *Int J Otolaryngol*. 2012; 2012:327206.doi: 10.1155/2012/327206 [PubMed: 22685462]
23. Shin SH, Park JY, Sohn JH. Clinical value of olfactory function tests after endoscopic sinus surgery: A short-term result. *Am J Rhinol*. 1999; 13(1):63–66. <http://www.scopus.com/inward/record.url?eid=2-s2.0-0032605133&partnerID=40&md5=d672cc6897d4900acd9ad5ea30e58135>. [PubMed: 10088032]
24. Baradaranfar MH, Ahmadi ZS, Dadgarnia MH, et al. Comparison of the effect of endoscopic sinus surgery versus medical therapy on olfaction in nasal polyposis. *Eur Arch Otorhinolaryngol*. 2014; 271(2):311–316. DOI: 10.1007/s00405-013-25536 [PubMed: 23700266]
25. Guss J, Doghramji L, Reger C, Chiu AG. Olfactory dysfunction in allergic rhinitis. *ORL J Otorhinolaryngol Relat Spec*. 2009; 71(5):268–272. DOI: 10.1159/000242429 [PubMed: 19797935]
26. Litvack JR, Mace JC, Smith TL. Olfactory function and disease severity in chronic rhinosinusitis. *Am J Rhinol Allergy*. 2009; 23(2):139–144. DOI: 10.2500/ajra.2009.23.3286 [PubMed: 19401037]
27. Soler ZM, Sauer DA, Mace JC, Smith TL. Ethmoid histopathology does not predict olfactory outcomes after endoscopic sinus surgery. *Am J Rhinol Allergy*. 2010; 24(4):281–285. DOI: 10.2500/ajra.2010.24.3477 [PubMed: 20819467]
28. Sugiyama K, Matsuda T, Kondo H, et al. Postoperative olfaction in chronic sinusitis: smokers versus nonsmokers. *Ann Otol Rhinol Laryngol*. 2002; 111(11):1054–1058. [PubMed: 12450184]
29. Doty RL, Yousem DM, Pham LT, Kreshak AA, Geckle R, Lee WW. Olfactory dysfunction in patients with head trauma. *Arch Neurol*. 1997; 54(9):1131–1140. <http://www.ncbi.nlm.nih.gov/pubmed/9311357>. [PubMed: 9311357]
30. Bhandarkar ND, Smith TL, M JC. The impact of osteitis on disease severity measures and quality of life outcomes in chronic rhinosinusitis. *Int Forum Allergy Rhinol*. 2011; 1:372–378. DOI: 10.1002/alr.20068 [PubMed: 22028948]

31. Friedman M, Hamilton C, Samuelson CG, et al. Dead Sea salt irrigations vs saline irrigations with nasal steroids for symptomatic treatment of chronic rhinosinusitis: a randomized, prospective double-blind study. *Int Forum Allergy Rhinol*. 2012; 2(3):252–257. DOI: 10.1002/alr.21003 [PubMed: 22337474]
32. Jiang R-S, Kuo L-T, Wu S-H, Su M-C, Liang K-L. Validation of the applicability of the traditional Chinese version of the University of Pennsylvania Smell Identification Test in patients with chronic rhinosinusitis. *Allergy Rhinol (Providence)*. 2014; 5(1):28–35. DOI: 10.2500/ar.2014.5.0084 [PubMed: 25199144]
33. Jiang KL, Wu SH, Su MC, Chen WK, Lu FJ, RS L. Electrolyzed acid water nasal irrigation after functional endoscopic sinus surgery. *Am J Rhinol Allergy*. 2014; 28:176–181. DOI: 10.2500/ajra.2014.28.4015 [PubMed: 24717957]
34. Kondo H, Matsuda T, Hashiba M, Baba S. A study of the relationship between the T&T olfactometer and the University of Pennsylvania Smell Identification Test in a Japanese population. *Am J Rhinol*. 1998; 12(5):353–358. [PubMed: 9805536]
35. Lund M, Scadding GK, VJ H. Functional endoscopic sinus surgery in the management of chronic rhinosinusitis. An objective assessment. *J Laryngol Otol*. 1991; 105:832–835. [internal-pdf://3180808612/Lund-1991-Functionalendoscopicsinussurgery.pdf](#). [PubMed: 1753193]
36. Pinto JM, Mehta N, DiTineo M, Wang J, Baroody FM, Naclerio RM. A randomized, double-blind, placebo-controlled trial of anti-IgE for chronic rhinosinusitis. *Rhinology*. 2010; 48(3):318–324. DOI: 10.4193/Rhin09.144 [PubMed: 21038023]
37. Saedi B, Sadeghi M, Yazdani N, Afshari A. Effectiveness of FESS in Smell Improvement of Sinusitis Patients. *Indian J Otolaryngol Head Neck Surg*. 2013; 65(Suppl 2):283–287. DOI: 10.1007/s12070-011-0439-8
38. Soler ZM, Pallanch JF, Sansoni ER, et al. Volumetric computed tomography analysis of the olfactory cleft in patients with chronic rhinosinusitis. *Int Forum Allergy Rhinol*. 2015; 5(9):846–854. DOI: 10.1002/alr.21552 [PubMed: 26010298]
39. Soler ZM, Wittenberg E, Schlosser RJ, Mace JC, Smith TL. Health state utility values in patients undergoing endoscopic sinus surgery. *Laryngoscope*. 2011; 121(12):2672–2678. DOI: 10.1002/lary.21847 [PubMed: 22034223]
40. Alt JA, Mace JC, Buniel MCF, Soler ZM, Smith TL. Predictors of olfactory dysfunction in rhinosinusitis using the brief smell identification test. *Laryngoscope*. 2014; 124(7):E259–E266. DOI: 10.1002/lary.24587 [PubMed: 24402746]
41. DeConde AS, Alt JA, Schlosser RJ, Smith TL, Soler ZM, M JC. Comparative effectiveness of medical and surgical therapy on olfaction in chronic rhinosinusitis: a prospective, multi-institutional study. *Int Forum Allergy Rhinol*. 2014; 4:725–733. DOI: 10.1002/alr.21350 [PubMed: 25044658]
42. Hajjij A, Mace JC, Soler ZM, Smith TL, Hwang PH. The impact of diabetes mellitus on outcomes of endoscopic sinus surgery: a nested case-control study. *Int Forum Allergy Rhinol*. 2015; 5(6):533–540. DOI: 10.1002/alr.21495 [PubMed: 25913815]
43. DeConde AS, Mace JC, Alt JA, Schlosser RJ, Smith TL, Soler ZM. Comparative effectiveness of medical and surgical therapy on olfaction in chronic rhinosinusitis: a prospective, multi-institutional study. *Int Forum Allergy Rhinol*. 2014; 4(9):725–733. DOI: 10.1002/alr.21350 [PubMed: 25044658]
44. Kim JH, Choi HN, Park SY, BG O. Simple assessment of olfaction in patients with chronic rhinosinusitis. *Acta Otolaryngol*. 2015; 135:258–263. DOI: 10.3109/00016489.2014.974288 [PubMed: 25625195]
45. Chang H, Lee HJ, Mo J-H, Lee CH, Kim J-W. Clinical implication of the olfactory cleft in patients with chronic rhinosinusitis and olfactory loss. *Arch Otolaryngol Head Neck Surg*. 2009; 135(10):988–992. DOI: 10.1001/archoto.2009.140 [PubMed: 19841336]
46. Schriever VA, Gupta N, Pade J, Szewczynska M, Hummel T. Olfactory function following nasal surgery: a 1-year follow-up. *Eur Arch Otorhinolaryngol*. 2013; 270(1):107–111. DOI: 10.1007/s00405-012-1972-0 [PubMed: 22382399]
47. Pade TJH. Olfactory function following nasal surgery. *Laryngoscope*. 2008; 118:1260–1264. DOI: 10.1097/MLG.0b013e318170b5cb [PubMed: 18438263]

48. 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]
49. Ek A, Middelveldt RJM, Bertilsson H, et al. Chronic rhinosinusitis in asthma is a negative predictor of quality of life: results from the Swedish GA(2)LEN survey. *Allergy.* 2013; 68(10):1314–1321. DOI: 10.1111/all.12222 [PubMed: 24107218]
50. Gudziol V, Hummel C, Negoias S, Ishimaru T, Hummel T. Lateralized differences in olfactory function. *Laryngoscope.* 2007; 117(5):808–811. DOI: 10.1097/MLG.0b013e3180330092 [PubMed: 17473673]
51. Minwegen F, Thomas JP, Bernal-Sprekelsen M, Dazert S, Minovi A. Predictive value of disease severity on self-reported rating and quantitative measures of olfactory function outcomes after primary endoscopic sinus surgery. A prospective study. *Rhinology.* 2014; 52(4):437–443. DOI: 10.4193/Rhin14.043 [PubMed: 25479229]
52. Konstantinidis S, Printza A, Vital V, Ferekidis E, Constantinidis JIT. Olfactory dysfunction in nasal polyposis: correlation with computed tomography findings. *ORL J Otorhinolaryngol Relat Spec.* 2007; 69:226–232. DOI: 10.1159/000101543 [PubMed: 17409781]
53. Lind H, Joergensen G, Lange B, Svendstrup F, Kjeldsen AD. Efficacy of ESS in chronic rhinosinusitis with and without nasal polyposis: a Danish cohort study. *Eur Arch Otorhinolaryngol.* Jun.2015 doi: 10.1007/s00405-015-3667-9
54. Videler WJ, Badia L, Harvey RJ, et al. Lack of efficacy of long-term, low-dose azithromycin in chronic rhinosinusitis: a randomized controlled trial. *Allergy.* 2011; 66(11):1457–1468. DOI: 10.1111/j.1398-9995.2011.02693.x [PubMed: 21884529]
55. Elsharif BN, Hamad MH, Hugentobler M, Bahig SM, Gamaa AM, Lacroix JS, HS L. Olfactory function and nasal nitric oxide. *Clin Otolaryngol.* 2007; 32:356–360. DOI: 10.1111/j.1749-4486.2007.01534.x [PubMed: 17883555]
56. Klimek L, Hummel T, Moll B, Kobal G, Mann WJ. Lateralized and bilateral olfactory function in patients with chronic sinusitis compared with healthy control subjects. *Laryngoscope.* 1998; 108(1 Pt 1):111–114. [PubMed: 9432078]
57. Ottaviano G, Marioni G, Giacomelli L, et al. Smoking and chronic rhinitis: effects of nasal irrigations with sulfurous-arsenical-ferruginous thermal water: A prospective, randomized, double-blind study. *Am J Otolaryngol.* 2012; 33(6):657–662. DOI: 10.1016/j.amjoto.2012.03.002 [PubMed: 22521235]
58. Min YS, Song BH, Cho YS, Lee KS, YG Y. Recovery of nasal physiology after functional endoscopic sinus surgery: olfaction and mucociliary transport. *ORL J Otorhinolaryngol Relat Spec.* 1995; 57:264–268. <http://www.karger.com/Article/Abstract/276755>. [PubMed: 8587779]
59. Kim BG, Kang JM, Shin JH, Choi HN, Jung YH, Park SY. Do sinus computed tomography findings predict olfactory dysfunction and its postoperative recovery in chronic rhinosinusitis patients? *Am J Rhinol Allergy.* 29(1):69–76. DOI: 10.2500/ajra.2015.29.4120
60. Cowart BJ, Flynn-Rodden K, McGeady SJ, Lowry LD. Hyposmia in allergic rhinitis. *J Allergy Clin Immunol.* 1993; 91(3):747–751. [PubMed: 8454797]
61. Ikeda K, Kondo Y, Sunose H, et al. Subjective and objective evaluation in endoscopic sinus surgery. *Am J Rhinol.* 1996; 10(4):217–220. <http://www.scopus.com/inward/record.url?eid=2-s2.0-0005687666&partnerID=40&md5=eb8bf4cd45bd1fe45d0eaede8aec2b9c>.
62. Delank KW, Stoll W. Olfactory function after functional endoscopic sinus surgery for chronic sinusitis. *Rhinology.* 1998; 36(1):15–19. [PubMed: 9569436]
63. Vandenhende-Szymanski C, Hochet B, Chevalier D, Mortuaire G. Olfactory cleft opacity and CT score are predictive factors of smell recovery after surgery in nasal polyposis. *Rhinology.* 2015; 53(1):29–34. DOI: 10.4193/Rhin14.160 [PubMed: 25756075]
64. Frasnelli J, Hummel T. Olfactory dysfunction and daily life. *Eur Arch Otorhinolaryngol.* 2005; 262(3):231–235. DOI: 10.1007/s00405-004-0796-y [PubMed: 15133691]
65. Litvack JR, Fong K, Mace J, James KE, Smith TL. Predictors of olfactory dysfunction in patients with chronic rhinosinusitis. *Laryngoscope.* 2008; 118(12):2225–2230. DOI: 10.1097/MLG.0b013e318184e216 [PubMed: 19029858]

66. Saedi M, Yazdani N, Afshari ABS. Effectiveness of FESS in Smell Improvement of Sinusitis Patients. *Indian J Otolaryngol Head Neck Surg.* 2013; 65:283–287. DOI: 10.1007/s12070-011-0439-8
67. Lind G, Lange B, Svendstrup F, Kjeldsen ADHJ. Efficacy of ESS in chronic rhinosinusitis with and without nasal polyposis: a Danish cohort study. *Eur Arch Otorhinolaryngol.* 2015; doi: 10.1007/s00405-015-3667-9
68. Elsherif HS, Landis BN, Hamad MH, et al. Olfactory function and nasal nitric oxide. *Clin Otolaryngol.* 2007; 32(5):356–360. DOI: 10.1111/j.1749-4486.2007.01534.x [PubMed: 17883555]
69. Vandenhende-Szymanski B, Chevalier D, Mortuaire GCH. Olfactory cleft opacity and CT score are predictive factors of smell recovery after surgery in nasal polyposis. *Rhinology.* 2015; 53:29–34. DOI: 10.4193/Rhin14.160 [PubMed: 25756075]
70. Thompson CF, Kern RC, Conley DB. Olfaction in Endoscopic Sinus and Skull Base Surgery. *Otolaryngol Clin North Am.* 2015; 48(5):795–804. DOI: 10.1016/j.otc.2015.05.007 [PubMed: 26117298]
71. Doty RL, Shaman P, Applebaum SL, Giberson R, Sikorski L, Rosenberg L. Smell identification ability: changes with age. *Science.* 1984; 226(4681):1441–1443. <http://www.ncbi.nlm.nih.gov/pubmed/6505700>. [PubMed: 6505700]
72. Murphy C, Schubert CR, Cruickshanks KJ, Klein BEK, Klein R, Nondahl DM. Prevalence of olfactory impairment in older adults. *JAMA.* 2002; 288(18):2307–2312. DOI: 10.1001/jama.288.18.2307 [PubMed: 12425708]
73. Lötsch J, Reichmann H, Hummel T. Different odor tests contribute differently to the evaluation of olfactory loss. *Chem Senses.* 2008; 33(1):17–21. DOI: 10.1093/chemse/bjm058 [PubMed: 17761724]
74. Fokkens WJ, Lund VJ, Mullol J, et al. EPOS 2012: European position paper on rhinosinusitis and nasal polyps 2012. A summary for otorhinolaryngologists. *Rhinology.* 2012; 50(1):1–12. DOI: 10.4193/Rhino50E2 [PubMed: 22469599]
75. Gudziol V, Buschhüter D, Abolmaali N, Gerber J, Rombaux P, Hummel T. Increasing olfactory bulb volume due to treatment of chronic rhinosinusitis--a longitudinal study. *Brain.* 2009; 132(Pt 11):3096–3101. DOI: 10.1093/brain/awp243 [PubMed: 19773353]
76. Reyckner G, Colbrant C, Huart C, et al. Effect of three-drug delivery modalities on Olfactory function in chronic sinusitis. *Laryngoscope.* 2014; 125(3):549–555. DOI: 10.1002/lary.24937 [PubMed: 25224684]
77. 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]
78. Thamboo BA, Habib AR, Manji J, Hathorn I, Sunkaraneni V, Javer AAC. The effect of two sphenoidotomy approaches on the sense of smell: trans-ethmoidal versus trans-sphenoethmoidal. *Rhinology.* 2014; 52:281–287. DOI: 10.4193/Rhin13.106 [PubMed: 25271535]
79. Desrosiers M, Evans GA, Keith PK, et al. Canadian clinical practice guidelines for acute and chronic rhinosinusitis. *J Otolaryngol Head Neck Surg.* 2011; 40(Suppl 2):S99–S193. <http://www.ncbi.nlm.nih.gov/pubmed/21658337>. [PubMed: 21658337]
80. Otolaryngol Head Neck Surg; Report of the Rhinosinusitis Task Force Committee Meeting; Alexandria, Virginia. August 17, 1996; 1997. p. S1–S68. <http://www.ncbi.nlm.nih.gov/pubmed/9380416>
81. Shin JY, Sohn JH, SH P. Clinical value of olfactory function tests after endoscopic sinus surgery: a short-term result. *Am J Rhinol.* 1999; 13:63–66. [PubMed: 10088032]
82. Benninger MS, Ferguson BJ, Hadley JA, et al. Adult chronic rhinosinusitis: definitions, diagnosis, epidemiology, and pathophysiology. *Otolaryngol Head Neck Surg.* 2003; 129(3 Suppl):S1–S32. <http://www.ncbi.nlm.nih.gov/pubmed/12958561>. [PubMed: 12958561]
83. Rosenfeld RM, Andes D, Bhattacharyya N, et al. Clinical practice guideline: adult sinusitis. *Otolaryngol Head Neck Surg.* 2007; 137(3 Suppl):S1–S31. DOI: 10.1016/j.otohns.2007.06.726 [PubMed: 17761281]

84. Litvack JR, Mace JC, Smith TL. Olfactory function and disease severity in chronic rhinosinusitis. *Am J Rhinol Allergy*. 23(2):139–144. DOI: 10.2500/ajra.2009.23.3286
85. Soler E, Schlosser RJ, Mace JC, Smith TL, ZM W. Health state utility values in patients undergoing endoscopic sinus surgery. *Laryngoscope*. 2011; 121:2672–2678. DOI: 10.1002/lary.21847 [PubMed: 22034223]
86. Sugiyama T, Kondo H, Mitsuya S, Hashiba M, Murakami S, Baba SKM. Postoperative olfaction in chronic sinusitis: Smokers versus nonsmokers. *Ann Otol Rhinol Laryngol*. 2002; 111:1054–1058. [internal-pdf://3876935514/Sugiyama-2002-Postoperativeolfactioninchron.pdf](#). [PubMed: 12450184]
87. Schriever N, Pade J, Szevczynska M, Hummel T, VA G. Olfactory function following nasal surgery: a 1-year follow-up. *Eur Arch Otorhinolaryngol*. 2013; 270:107–111. DOI: 10.1007/s00405-012-1972-0 [PubMed: 22382399]
88. Fokkens W, Lund V, Bachert C, et al. European position paper on rhinosinusitis and nasal polyposis. *Rhinology*. 2005; 18:1–88.
89. Bardaranfar MH, Ranjbar Z, Dadgarnia MH, et al. The effect of an absorbable gelatin dressing impregnated with triamcinolone within the olfactory cleft on polypoid rhinosinusitis smell disorders. *Am J Rhinol Allergy*. 2014; 28(2):172–175. DOI: 10.2500/ajra.2014.28.4016 [PubMed: 24717956]

Figure 1.
PRISMA diagram outlining search strategy

Figure 2.
Meta-analysis of prevalence of olfactory dysfunction using composite Sniffin' Sticks score

Figure 3.
Meta-analysis of prevalence of olfactory dysfunction using 40-item Smell Identification Test (SIT-40)

Table 1

Characteristics of included studies using composite olfactory tests

Reference	Diagnostic method CRS	Olfaction measure	Factors associated with Olfactory Dysfunction	n	Prevalence OD % (n) Risk Bias Assessment
Sniffin' Sticks: TDI					
Chung et al. (2015) ¹⁸	EPOS 2012 ⁷⁴	SS: T, D, I, TDI	LM CT score SNOT-20 score Depression (SCL-90-R) Anxiety sx (SCL-90-R) Phobia sx (SCL-90-R)	71 CRSwNP	TDI - N: 20% (14) H: 55% (39) A: 25% (18) RSB – moderate; ROB - low
Gudziol et al. (2009) ⁷⁵	Physician dx	SS: TDI	NR	19 CRSwNP	NR RSB – high ROB - low
Katotomichelakis et al. (2010) ¹⁹	Physician dx	SS: T, D, I, TDI	Older Age Duration of olfactory loss Prior sinus surgery ASA intolerance	116 CRSwNP	T – H: 23% (27) A: 77% (89) D – H: 16% (19) A: 84% (97) I – H: 15% (17) A: 85% (99) TDI – H: 15% (17) A: 85% (99) RSB – high; ROB - low
Katotomichelakis et al. (2014) ¹²	EPOS 2012	SS: T, D, I, TDI QOD-NS	Older Age Female Non-smokers Lower SES NP Asthma history ASA intolerance	111 CRS mixed	TDI - N: 24.3% (27) H: 43.3% (48) A: 32.4% (36) RSB – moderate; ROB - low
Konstantinidis et al. (2010) ²¹	Physician dx	SS: TDI	LM-CT score Prior sinus surgery Duration of CRS Moderate/severe inflammation (olfactory/ respiratory mucosa biopsy)	27 CRSwNP	NR RSB – high; ROB - low

Reference	Diagnostic method CRS	Olfaction measure	Factors associated with Olfactory Dysfunction	n	Prevalence OD % (n) Risk Bias Assessment
Reychler et al. (2015) ⁷⁶	Physician dx	SS: T, D, I, TDI	NR	30 CRS mixed	NR RSB – low; ROB - low
Simopoulos et al. (2012) ⁷⁷	Physician dx	Sniff Sticks: TDI QOD-NS	Female Depression (BDI) Anxiety (ZAS) SF-36	102 CRS mixed	TDI - N: 33.3% (34) H: 44.2% (45) A: 22.5% (23) RSB – low; ROB - low
Thamboo et al. (2014) ⁷⁸	Canadian clinical practice guidelines 2011 ⁷⁹	SS: T,D,I, TDI	NR	1) 24 CRS mixed (trans-ethmoid surgery) 2) 24 CRS mixed (trans-sphenoid-moid surgery)	1) N: 13% (3) H: 54% (13) A: 33% (8) 2) N: 8% (2) H: 58% (14) A: 33% (8) RSB – moderate; ROB - low
Wallwork et al. (2006) ¹⁷	AAO-HNS 1997 ⁸⁰	SS: TDI	NR	29 CRS mixed (Roxithromycin) 35 CRS mixed (placebo)	NR RSB – low; ROB - low
Summary - CRS mixed: N: 21.77% (range 8-33.3%); H: 46.03% (range 43.3-58%); A: 28.92% (range 22.5-33%); overall OD: 78.23% CRSwNP: N: 6.32% (range 0-20%); H: 33.20% (range 15-55%); A: 56.81% (range 25-85%); overall OD: 93.68%					
Baradaranfar et al. (2014) ²⁴	Physician dx	CCCRC	NR	1) 30 surgical CRSwNP 2) 30 medical CRSwNP	1) N: 3.33% (1) H: 53.33% (16) A: 43.33% (13) 2) N: 0% (0) H: 43.33% (13) A: 56.67% (17) RSB – low; ROB - low
Sanchez-Vallecillo et al. (2012) ²²	Physician dx	CCCRC	Smokers NP Asthma AR Septal deviation Turbinate hypertrophy	33 CRS mixed total 1) 18-39 yo 2) 40-64 yo 3) Age>65 yo	1) N: 9% H: 73% A: 18% 2) H: 63% A: 37% 3) H: 67% A: 33% RSB – high; ROB - low
Shin et al. (1999) ⁸¹	Physician dx	CCCRC	Graded OMU CT score	50 CRS mixed	N: 0% (0) H: 40% (20) A: 60% (30)

Reference	Diagnostic method CRS	Olfaction measure	Factors associated with Olfactory Dysfunction	n	Prevalence OD % (n) Risk Bias Assessment
Summary – CRS mixed: Range OD 91-100% RSB – high; ROB - low					

CRS: chronic rhinosinusitis; CRSwNP: chronic rhinosinusitis with nasal polyps; OD: olfactory dysfunction; AAO-HNS: American Academy of Otolaryngology and Head and Neck Surgery; CCCRC: Connecticut Chemosensory Clinical Research; N: normosmic; H: hyposmic; A: anosmic; NR: not reported; T: threshold; D: discrimination; I: identification; EPOS: European Position Paper on Sinusitis; AR: allergic rhinitis; SS: Sniffin' Sticks; NP: Nasal polyps; OMU: Osteomeatal Unit; LM CT: Lund-Mackay computed tomography; SNOT-20: 20-item Sinonasal Outcome Test; SCL-90-R: Symptom Checklist-90-Revised; SF-36: Short Form-36 Health Survey; BDI: Beck Depression Inventory; ZAS: Zung Anxiety Scale; SES: socioeconomic status; ASA: Acetylsalicylic Acid; AR: sx: symptoms; dx: disease; RSB: Risk of Selection Bias; ROB: Risk of Outcome Bias

Table 2

Characteristics of included studies using identification olfactory tests

Reference	Diagnostic method CRS	Olfaction measure	Factors associated with Olfactory Dysfunction	n	Prevalence OD % (n) Risk Bias Assessment
SIT-40					
Bhandarkar et al. (2011) ³⁰	RTP ⁸²	SIT-40	Osteitis	1) 79 CRS mixed Osteitis 2) 111 CRS mixed Non-osteitis	NR RSB – moderate; ROB - low
Friedman et al. (2012) ³¹	AAO-HNS 2007 ⁸³	SIT-40	NR	1) 55 CRS mixed steroid/hyper-tonic saline irrigations 2) 59 CRS mixed dead sea salt irrigations	NR RSB – low; ROB - low
Guss et al. (2009) ²⁵	Physician dx	SIT-40	NR	10 CRS with AR	N: 50% (5) H: 40% (4) A: 10% (1) RSB – low; ROB - low
Jiang et al. (2014) ³²	Physician dx	SIT-40	NP	100 CRS 48 CRSsNP 52 CRSwNP	NR RSB – low; ROB - low
Jiang et al. (2014) ³³	AAO-HNS 2003 ⁸²	SIT-40 STT	NR	36 CRS mixed (EAW) 35 CRS mixed (NS) 39 CRS mixed	NR RSB – moderate; ROB - low
Kondo et al. (1998) ³⁴	Physician dx	SIT-40	NR	36 CRS mixed	NR RSB – low; ROB - low
Litvack et al. (2009) ^{65,84,*}	AAO-HNS 2003	SIT-40	Older age Smokers NP Asthma	367 CRS mixed	N: 33% (122) H: 45% (166) A: 22% (79) RSB – moderate; ROB - low
Lund et al. (1991) ³⁵	Physician dx	SIT-40	NR	24 CRS mixed	NR RSB – high; ROB - low

Reference	Diagnostic method CRS	Olfaction measure	Factors associated with Olfactory Dysfunction	n	Prevalence OD % (n) Risk Bias Assessment
Pinto et al. (2010) ³⁶	AAO-HNS 2003	SIT-40	NR	7 CRS mixed (placebo) 7 CRS mixed (anti-IgE)	NR RSB – high; ROB - low
Saedi et al. (2013) ⁶⁶	Physician dx	SIT-40	LM CT OMU obstruction NP Extent of dx during surgery	89 CRS mixed	NR RSB – high; ROB - low
Soler et al. (2015) ³⁸	AAO-HNS 2007	SIT-40	LM CT score OC opacification	199 CRS mixed	NR RSB – moderate; ROB - low
Soler et al. (2010) ²⁷	AAO-HNS 2003	SIT-40	Age Male LM CT score LK endoscopy NP Asthma ASA intolerance AR	101 CRS mixed	N: 36.6% (37) H: 39.6% (40) A: 23.8% (24) RSB – moderate; ROB - low
Soler et al. (2011) ⁸⁵	AAO-HNS 2007	SIT-40	NR	232 CRS mixed	NR RSB – moderate; ROB - low
Sugiyama et al. (2002) ⁸⁶	Physician dx	SIT-40	NR	37 CRS mixed	OD: 83.8% (31) RSB – high; ROB - low
Summary - CRS mixed: N: 34.39% (range 33-50%); H: 43.96% (range 39.6-45%); A: 21.90% (range 10-23.8%); overall OD: 67.00%					
B-SIT					
Alt et al. (2014) ⁴⁰	AAO-HNS 2007	B-SIT	Older age LM CT score LK endoscopy score	1) 260 CRSsNP 2) 152 CRSwNP	1) OD: 16.9% (44) 2) OD: 52% (79) RSB – low; ROB - low

Reference	Diagnostic method CRS	Olfaction measure	Factors associated with Olfactory Dysfunction	n	Prevalence OD % (n) Risk Bias Assessment
			SNOT-22 RSDI emotional Prior sinus surgery NP ASA intolerance Asthma Recalcitrant disease		
Deconde et al. (2014) ⁴³	AAO-HNS 2007	B-SIT	Thick nasal discharge (SNOT-22) Nasal airway obstruction (SNOT-22/RSDI)	1) 222 CRS mixed surgical 2) 58 CRS mixed medical	1) OD: 29.7% (66) 2) OD: 29.3% (17) RSB – low; ROB - low
Hajjij et al. (2015) ⁴²	AAO-HNS 2007	B-SIT	NR	1) 20 CRS mixed (DM) 2) 20 CRS mixed (non-DM)	1) OD: 30% (6) 2) OD: 20% (4) RSB – moderate; ROB - low
Summary – CRS mixed: Overall OD: 29.97% (range 16.9-52%)					
Sniffin' Sticks: I					
Ek et al. (2013) ⁴⁹	EPOS 2012	SS: I (12 odor)	NR	110 CRS mixed	NR RSB – low; ROB - low
Gudziol et al. (2007) ⁵⁰	Prior dx	SS: I (12 odors; 7 anosmia)	Older Age	765 CRS mixed	A: 29.28% (224) RSB – low; ROB - low
Konstantinidis et al. (2007) ⁵²	Physician dx	SS: I (12 odor)	Male LM CT score Damm CT segmentation grading	31 CRSwNP	NR RSB – high; ROB - low
Lind et al. (2015) ⁶⁷	EPOS 2012	SS: I (12 odor)	LM CT score LK endoscopy score NP	1) 97 CRS 2) 75 CRSsNP 3) 22 CRSwNP	NR RSB – moderate; ROB - low

Reference	Diagnostic method CRS	Olfaction measure	Factors associated with Olfactory Dysfunction	n	Prevalence OD % (n) Risk Bias Assessment
Minwegen et al. (2014) ⁵¹	EPOS 2012	SS: I (12 odor)	NR	1) LM CT 7 – 17 CRS mixed 2) LM CT 8 – 21 CRS mixed	NR RSB – moderate; ROB - low
Pade and Hummel (2008) ⁴⁷	Physician dx	SS: I	Older age NP ASA Intolerance Eosinophilia	387 CRS mixed	NR RSB – high; ROB - low
Schrieffer et al. (2013) ⁸⁷	Physician dx	SS: I	NR	113 CRS mixed	NR RSB – high; ROB - low

CRS; chronic rhinosinusitis; CRSwNP: chronic rhinosinusitis with nasal polyposis; CRSsNP: chronic rhinosinusitis without polyposis; SIT-40: 40-item Smell Identification Test; B-SIT: Brief Smell Identification Test; OD: olfactory dysfunction; AAO-HNS: American Academy of Otolaryngology and Head and Neck Surgery; N: normosmic; H: hyposmic; A: anosmic; NS: normal saline; RTF: Rhinosinusitis Task Force; NR: not reported; I: identification; EPOS: European Position Paper on Sinusitis; AR: allergic rhinitis; EAW: electrolyzed acid water; SS: Sniffin' Sticks; NP: Nasal polyps; OMU: Osteomeatal Unit; OC: Olfactory Cleft; LM CT: Lund-Mackay computed tomography; LK: Lund-Kennedy; ASA: Acetylsalicylic Acid; AR: allergic rhinitis; sx: symptoms; dx: disease; RDSI: Rhinosinusitis Disability Index; DM: diabetes mellitus; SNOT-22: 22-item Sinonasal Outcome Test; RSB: Risk of Selection Bias; ROB: Risk of Outcome Bias

* predictors extracted from 2008 study using same cohort

Table 3

Characteristics of included studies using threshold and alternative olfactory tests

Reference	Diagnostic method	CRS	Olfaction measure	Factors associated with Olfactory Dysfunction	n	Prevalence OD % (n) Risk Bias Assessment
Sniffin' Sticks: T						
Elsherif et al. (2007) ⁶⁸	EPOS 2005 ⁸⁸		SS: T	LM CT score Nasal nitric oxide concentrations	64 CRS mixed	NR RSB – moderate; ROB - low
Klimek et al. (1998) ⁵⁶	Physician dx		SS: T	NR	63 CRS mixed	NR RSB – low; ROB - low
Ottaviano et al. (2012) ⁵⁷	Physician dx		SS: T	NR	35 CRS mixed (sulfur water) 35 CRS mixed (NS)	NR RSB – low; ROB - low
BTT						
Baradaranfar et al. (2014) ⁸⁹	Physician dx		BTT	NR	1) 30 CRSwNP ESS; triamcinol-one 2) 30 CRSwNP ESS; NS	1) N: 0% (0) H 27% (8) A: 73% (22) 2) N: 0% (0) H 43.33% (13) A: 56.67% (17) RSB – high; ROB - low
Kim et al. (2015) ⁵⁹	AAO-HNS 2007		BTT	LM CT OC/OMC obstruction	97 CRS mixed	N: 16.5% (16) H: 29.9% (29) A: 53.6% (52) RSB – moderate; ROB - low
Kim et al. (2015) ⁴⁴	AAO-HNS 2007		BTT B-SIT	NR	68 CRS mixed	N: 27.9% (19) H: 19.1% (13) A: 52.9% (36) RSB – moderate; ROB - low
Min et al. (1995) ⁵⁸	Physician dx		BTT	NR	80 CRS mixed	N: 22% (18) H: 45% (36) A: 33% (26) RSB – high; ROB - low
Summary – CRS mixed: N: 21.80 % (range 16.5-27.9%); H: 31.21% (range 19.1-45%); A: 46.29% (range 33-53.6%); overall OD: 78.21%						
Other threshold measures						
Cowart et al. (1993) ⁶⁰	Physician dx		PEA threshold test	NR	28 CRS mixed	H: 12 (42.9%) RSB – low; ROB - moderate

Reference	Diagnostic method	CRS	Olfaction measure	Factors associated with Olfactory Dysfunction	n	Prevalence OD % (n) Risk Bias Assessment
Delank 1998 ⁶²	Physician dx		threshold ^d /discrimination ^b	NP	115 CRS mixed	N: 16% (19) H: 52% (60) A: 31% (36) RSB – high; ROB - moderate
Ikeda et al. (1996) ⁶¹	Physician dx		T&T	NR	25 CRS mixed	A: 32% (8) RSB – high; ROB - low
Summary - CRS mixed : Range OD: 32-83%						
Alternative olfactory tests						
Vandenhende-Szymanski et al. (2015) ⁶⁹	EPOS 2012		ETOC	LM CT score OC opacity Prior sinus surgery	30 CRSwNP	N: 6.7% (2) H: 30.0% (9) A: 63.3% (19) RSB – moderate; ROB - low

CRS: chronic rhinosinusitis; CRSwNP: chronic rhinosinusitis with nasal polyposis; OD: olfactory dysfunction; AAO-HNS: American Academy of Otolaryngology and Head and Neck Surgery; N: normosmic; H: hyposmic; A: anosmic; BTT: Butanol Threshold Test; B-SIT: Brief Smell Identification Test; NR: not reported; T: threshold; EPOS: European Position Paper on Sinusitis; PEA: Phenylethyl alcohol; SS: Sniffin' Sticks; STT: Smell Threshold Test; T&T: Olfactometer Threshold Test; ETOC: European Test of Olfactory Capabilities; NP: Nasal polyps; OMU: Osteomeatal Unit; OC: Olfactory Cleft; LM CT: Lund-Mackay computed tomography; LK: Lund-Kennedy; sx: symptoms; dx: disease; RSB: Risk of Selection Bias; ROB: Risk of Outcome Bias

^a 6 scaled dilutions of dimethylsulfide and 2-phenylethanol;

^b 8 odorants; participant identifies different odorant of 3 presented odors

Table 4

Pooled olfactory scores across studies

Olfactory measure	Classification OD	CRS mixed (n)	Olfactory score (SD) - CRS mixed	CRSwNP (n)	Olfactory score (SD) - CRSwNP	P-value
SIT-40	Normosmic: 34-40 Hyposmic: 20-33 Anosmic: 6-19 Malingering: 0-5	1576	25.96 (7.11)	n/a	n/a	n/a
B-SIT	Normosmic: 9	520	8.60 (2.81)	n/a	n/a	n/a
TDI total score (SS)	Normosmic: >30 Hyposmic: 30 Anosmic: 15	253	21.96 (8.88) 21.95988142	233	15.58 (6.49)	<0.0001
T (SS)	OD: 6.00 (males) OD: 6.50 (females)	386	5.65 (1.51)	187	2.28 (2.11)	<0.0001
D (SS)	OD: 10	189	9.21 (4.63)	187	6.48 (3.46)	<0.0001
I (SS)	OD: 11	899	9.47 (3.92)	187	6.04 (3.14)	<0.0001
				CRSSsNP (n)	Olfactory score (SD) - CRSSsNP	
I (SS - modified 12 odor)	Normosmic: 11-12 Hyposmic: 7-10 Anosmic: 0-6	245	8.06 (3.06)	53	7.25 (1.52)	0.0617
QOD-NS	0 (poor smell) to 51 (normal smell)	213	8.90 (5.14)	n/a	n/a	n/a

SIT-40: 40-item smell identification; CRS: chronic rhinosinusitis; CRSwNP: chronic rhinosinusitis with nasal polyps; CRSSsNP: chronic rhinosinusitis without polyps;