

Burden of illness: A systematic review of depression in chronic rhinosinusitis

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ABSTRACT

Background: Depression has been reported in patients with chronic rhinosinusitis (CRS), but its prevalence varies across studies, and uncertainty remains regarding the association with baseline disease severity and treatment outcomes.

Objective: To systematically assess the prevalence of depression in CRS and to review its relationship to baseline disease severity and outcomes after treatment.

Methods: A systematic review of the prevalence of possible depression was performed by using the available methods to diagnose depression, and the results were pooled. Studies that examined the relationship of depression on baseline disease severity and treatment outcomes were organized and reported individually.

Results: Thirteen studies met inclusion criteria for prevalence analysis. The prevalence of possible or likely depression in patients with CRS ranged from 11.0 to 40.0%, depending on the method of diagnosis and sensitivity of various depression instruments. Positive depression screening was consistently associated with worse CRS-specific quality of life (QOL), medication usage, and health care utilization, but there were no reliable CRS-specific factors to predict the presence of depression. Patients with possible depression who underwent medical or surgical treatment for CRS tended to have improvements in CRS-specific QOL but did not achieve the same degree of QOL as patients who were not depressed. Depression-specific QOL seemed to improve after treatment for CRS.

Conclusion: Positive depression screening was common in patients with CRS and had a negative association on the entire spectrum of QOL, health care utilization, and productivity. CRS-specific treatments were still beneficial in patients who seemed to be depressed and improved both depression-specific and CRS-specific QOL.

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The prevalence of physician-diagnosed depression in the United States is nearly 9%¹ and is the leading cause of disability among adults in high income countries.² Depression has a major effect on quality of life (QOL) and economic burden, with an estimated lost productivity cost of \$23 billion in 2011.³ In addition to major depression as a primary disorder, comorbid depression has been found in a variety of other chronic medical illnesses⁴ and often remains underdiagnosed because physicians and patients focus on the primary disease.

The presence of comorbid depression in chronic medical illness is often associated with negative health outcomes. For example, when comorbid depression is present in chronic obstructive pulmonary disease, it is associated with worse QOL, increased health care utilization, and even increased mortality.⁵ After coronary artery bypass, patients with depression have increased mortality and rehospitalization.⁴ Although the potential bidirectional nature of comorbid depression and poor outcomes makes causality difficult to determine, its strong association with negative outcomes is clinically relevant, both from a prognostic and treatment standpoint.

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Similar to other chronic illnesses, there is a reason to suspect that patients with chronic rhinosinusitis (CRS) have comorbid depression at a rate higher than population norms. However, estimating the true prevalence of comorbid depression and its potential impact in CRS is difficult for several reasons. First, patients with CRS are primarily treated by otorhinolaryngologists, who are experts in sinusitis management but who may not identify or address depressive symptoms. This reality is reflected in many CRS outcomes studies that fail to quantify depression. In addition, studies that depend only on a previous physician-given diagnosis of comorbid depression might underestimate the true prevalence of depression. Given preliminary reports of increased depression associated with CRS, it is critical for those who treat CRS to understand its true prevalence, as well as its impact on clinical presentation and treatment outcomes, to optimize care of our patients.

The goal of this review was to systemically evaluate the overall prevalence of depression in patients with CRS diagnosed both by physicians and through a variety of screening instruments. Secondary goals were to determine the association of comorbid depression on patients with CRS, potential factors that could alert clinicians to the presence of undiagnosed depression, and the relationship of comorbid depression on outcomes after treatment for CRS.

METHODS

Systematic Review of the Prevalence of Depression in CRS

Two reviewers (S.G., P.K.) independently performed a literature search by using PubMed (1947 to December 2015) and Scopus (1973 to November 2015) for studies that evaluated the prevalence of depression in the setting of CRS. The PubMed keywords and Medical Subject Heading terms used were “depression” or “depressive” and “rhinosinusitis” or “sinusitis” or “nasal” or “polyp.” Scopus (1999 to November 2015) was searched by using the terms “depression” or “depressive” and “rhinosinusitis” or “sinusitis” in the abstract and in the article title. Peer-reviewed articles in press were also included.

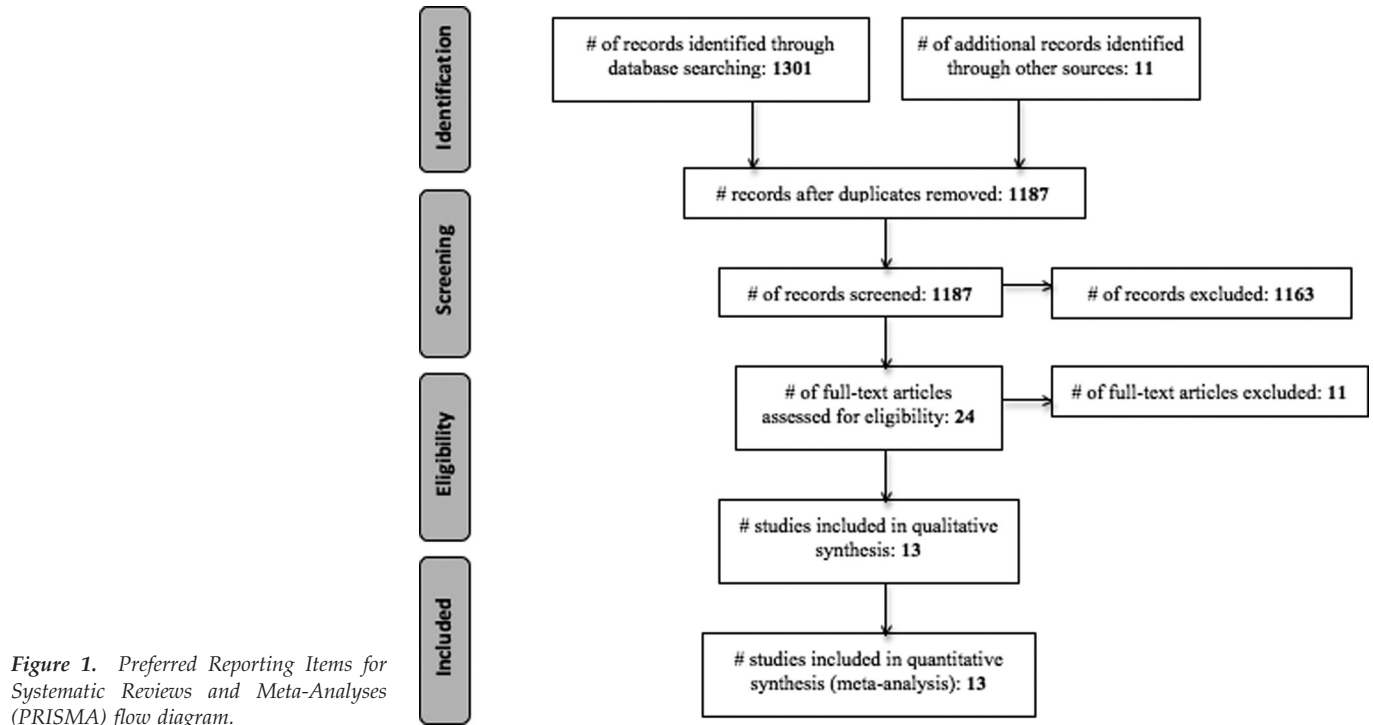


Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram.

Inclusion criteria required that all patients must have an explicit diagnosis of CRS by a physician. Self-reported CRS was excluded.

Depression assessments included a depression diagnosis by a previous physician or screening *via* validated questionnaires. Self-reported depression was excluded. Studies with mixed populations of patients with various sinonasal disorders were excluded unless data from patients with CRS could be isolated. Studies in which the frequency of depression was not provided or could not be deduced were also excluded. References from all identified studies were reviewed to determine if any additional articles were appropriate for inclusion. All articles were considered regardless of language. This study was considered exempt by the Medical University of South Carolina's institutional review board. The data from included studies were extracted and analyzed independently by two of us (S.G., Z.M.S.). The selected studies were categorized based on diagnostic method for depression. Categories included validated questionnaire and previous physician diagnosis. The combined prevalence of depression was calculated for each diagnostic method and reported as a summary frequency weighted by sample size.

Secondary Review of Depression Impacts

Data related to factors associated with depression in patients with CRS or the impact of comorbid depression on patient outcomes did not lend themselves to meta-analysis, given relative sparsity and heterogeneity. As such, these data were extracted from all the studies found during a previous literature search of depression in CRS, irrespective of whether they were included in prevalence estimates. Findings from these studies were tabulated and presented in an organized and descriptive fashion.

RESULTS

Systematic Review of a Positive Depression Screen Results in CRS

A total of 1187 articles were screened for eligibility, and 13 studies were selected based on inclusion-exclusion criteria. The search strat-

egy with flow diagram is presented per the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines⁶ (Fig. 1). These studies include a total of 2774 adult patients with CRS, with six studies that used the American Academy of Otolaryngology—Head and Neck Surgery criteria,^{7–12} four studies that used European Position Paper on Rhinosinusitis and Nasal Polyps criteria,^{13–16} two studies that used both the American Academy of Otolaryngology—Head and Neck Surgery and the European Position Paper on Rhinosinusitis and Nasal Polyps criteria,^{17,18} and one study that used physician diagnosis to determine CRS.¹⁹ With regard to depression, there were no studies that used strict Diagnostic and Statistical Manual of Mental Disorders, 4th Edition criteria.²⁰ Nine studies used a validated questionnaire to screen for depression,^{9,11,13–19} and four studies relied on a previous physician diagnosis.^{7,8,10,12}

There were four studies that used physician-diagnosed depression ($n = 631$ patients).^{7,8,10,12} All of these studies relied on patient report or medical record confirmation of other non-otolaryngologist physicians to make the diagnosis of depression. Two studies also required the use of antidepressants or psychologic counseling.^{7,8} The combined prevalence of depression for studies that used physician-diagnosed depression was 18.1% ($n = 114/631$), with a range from 13.4 to 25% (Table 1).^{7,8,10,12} Validated patient-reported questionnaires used to diagnose depression in the selected studies included the Hospital Anxiety and Depression Score (HADS), the 2-item Patient Health Questionnaire (PHQ2), the 9-item Patient Health Questionnaire (PHQ9), and the Beck Depression Inventory (BDI). All three questionnaires are self-reported scales used to determine the severity of depression by evaluating the frequency of depressive symptoms. Scoring can be variable, but, generally, the higher the score, the more severe the depression.

The HADS is a 14-item questionnaire used to determine severity of depression and anxiety by evaluating the frequency of depression and anxiety symptoms over a 1-week period. The seven questions related to depression are scored separately from the seven questions related to anxiety to give two individual scores. Four studies used the HADS questionnaire ($n = 495$ patients). The prevalence of depression varied, depending on the threshold used to define depression. The

Table 1 Prevalence of comorbid depression in patients with CRS

Study	CRS Diagnosis	Depression Diagnosis	Prevalence of Depression % (no./total)
Physician diagnosed			
Smith <i>et al.</i> , ¹² 2005	AAOHNS	Physician diagnosed	13.4 (16/119)
Brandsted and Sindwani ⁷ 2007	AAOHNS	Physician diagnosed	25 (27/106)
Mace <i>et al.</i> , ⁸ 2008	AAOHNS	Physician diagnosed	22.5 (23/102)
Smith <i>et al.</i> , ¹⁰ 2010	AAOHNS	Physician diagnosed	15.9 (48/302)
Mean (range), %			18.1 (13.4–25.0)
HADS			
Wasan <i>et al.</i> , ⁹ 2007	AAOHNS	HADS Moderate depression: 6–7 High depression: 8–21	9.1 (13/143) 14.7 (21/143)
Sahlstrand-Johnson <i>et al.</i> , ¹³ 2011	EPOS	HADS Possible depression: 8–10 Probable depression: 11–21	9.9 (17/171) 3.5 (6/171)
Tomoum <i>et al.</i> , ¹⁴ 2015	EPOS	HADS Possible depression: 8–10 Probable depression: 11–21	10.5 (13/124) 8.9 (11/124)
Nanayakkara <i>et al.</i> , ¹⁵ 2013	EPOS	HADS Depressed: 11–21	11.0 (6/57)
Mean (range), %			14.9 (11.0–23.8)
PHQ			
Schlosser <i>et al.</i> , ¹⁷ 2016	EPOS and AAOHNS	PHQ2 Depressed: >3	24.4 (167/685)
Davis <i>et al.</i> , ¹¹ 2005	AAOHNS	PHQ9 (threshold not specified)	25.2 (24/95)
Litvack <i>et al.</i> , ¹⁶ 2011	EPOS	PHQ9 Depressed: 10–27	25.0 (19/76)
Mean (range), %			24.5 (24.4–25.2)
BDI			
Jung <i>et al.</i> , ¹⁹ 2014	Physician	BDI Mild depression: 10–18 Moderate depression: 19–29 Severe depression: 30–63	36.0 (9/25) 4.0 (1/25) 0
Schlosser <i>et al.</i> , ¹⁸ 2016	EPOS and AAOHNS	BDI Depression: >14	31.0 (13/42)
Mean (range), %			34.3 (31.0–40.0)

CRS = Chronic rhinosinusitis; AAOHNS = American Academy of Otolaryngology—Head and Neck Surgery; HADS = Hospital Anxiety and Depression Score; EPOS = European Position Paper on Rhinosinusitis and Nasal Polyps; PHQ = Patient Health Questionnaire; BDI = Beck Depression Inventory.

study that used the lowest cutoff, of ≥ 6 , reported the highest prevalence, of 23.8%.⁹ Two studies used a cutoff of 8 points, which resulted in prevalences that ranged from 15.4 to 19.4%.^{13,14} The strictest study used ≥ 11 points as a cutoff and, not surprisingly, resulted in the lowest prevalence, of only 11%.¹⁵ (Table 1). The overall prevalence of depression in CRS that used HADS was 14.9%, with a range from 11.0 to 23.8%, depending on the threshold used to define depression (Table 2).

The PHQ consists of two (PHQ2) or nine (PHQ9) questions by using a Likert scale, and patients are asked to consider the frequency of symptoms over a 2-week period. The only study to use PHQ2 was also the largest ($n = 685$ patients) and reported a prevalence of 24.4%.¹⁷ (Table 1). Two studies used PHQ9, and both reported a prevalence of 25% (Table 1). Overall, 856 patients were studied by using the PHQ questionnaires with a prevalence of $\sim 25\%$, regardless of whether the two-item or nine-item version was used. The BDI consists of 21 multiple-choice questions, each scored from 0 to 3 for a total of 63 possible points. Two studies that fit the criteria for this systematic review used the BDI. The first study used a validated Japanese version of the BDI-II, which was revised from the original BDI in 1996 to correspond with the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition criteria.^{19,20} A score of ≥ 10 was used to define depression, which resulted in a prevalence of mild depression to be 36%, moderate depression to be 4%, and severe depression to be 0%. The combined prevalence, therefore, was 40% (Table 1). The

other BDI study used a cutoff of ≥ 14 to diagnose depression and found a prevalence of 31.0%.¹⁸ Among the nine studies that used validated questionnaires,^{9,11,13–19} the prevalence of depression ranged from 11.0 to 40.0%. As seen from both the HADS and BDI data, the score used to define depression varied among the studies, and the lower thresholds for defining depression resulted in higher prevalences (Table 1).

Factors Associated with a Positive Depression Screen Result in Patients with CRS

Given the high prevalence of depression in CRS, we then examined factors that may aid clinicians in detecting depression in their patients (Table 2). With regard to demographics, depression was associated with female sex in two studies,^{8,19} whereas three studies failed to detect an association.^{7,13,18} In general, other demographic factors, such as age and race, were uniformly not associated with depression. In addition, there were no comorbidities consistently associated with depression. Asthma and fibromyalgia results were mixed, whereas allergic rhinitis, chronic obstructive pulmonary disease, and smoking were not associated with depression in any study. Six studies^{7,8,12,14,16,17} examined CRS-severity factors by using endoscopy and/or computed tomography, and none found an association with depression. Reports on the impact of polyp status and revision surgery were mixed.

Table 2 Impact of comorbid depression on CRS presentation

Study	Associated Factors	CRS Symptoms	CRS Utilization
Davis <i>et al.</i> , ¹¹ 2005		Patients with depression had worse SNOT-16 scores.	
Smith <i>et al.</i> , ¹² 2005	Depression not associated with CT or endoscopy		
Brandsted and Sindwani ⁷ 2007	Depression associated with septal deviation and GERD	Patients with depression had worse pain, energy, and daily activity scores compared with patients with CRS and without depression	Patients with depression had similar medication usage to patients without depression
	No association with age, sex, allergy, polyps, CT, or previous ESS	Other CRS symptoms and duration of symptoms similar	
Wasan <i>et al.</i> , ⁹ 2007	Depression associated with anxiety	Patients with depression had higher oropharyngeal, systemic, and total symptom scores	Patients with depression used more antibiotics and had more missed workdays and provider visits
Mace <i>et al.</i> , ⁸ 2008	Depression associated with female sex; no association with age, race, asthma, polyps, smoking, allergy, CT, or endoscopy	Patients with depression had worse RSDI scores, worse medication subscale of CSS	
Litvack <i>et al.</i> , ¹⁶ 2011	Depression associated with less asthma (10.5 vs 42.1%). Depression not associated with CT or endoscopy	Depressed patients had worse RSDI and SF-36 No association with CSS	
Sahlstrand-Johnson <i>et al.</i> , ¹³ 2011	Depression not associated with sex or age; 21% CRSsNP with possible or probable depression vs 11% CRSwNP but not statistically different	Depression (HADS) associated with worse total SNOT-22 score	
Nanayakkara <i>et al.</i> , ¹⁵ 2013		Depression (HADS) was associated with total SNOT-22 score and nose-specific symptoms	
Jung <i>et al.</i> , ¹⁹ 2014	Depression (BDI) worse in female patients; no association with age	BDI score was inversely correlated with olfaction <i>via</i> TDI	
Tomoum <i>et al.</i> , ¹⁴ 2015	Depression not associated with endoscopy score	HADS depression score was associated with worse total RSDI	
Chung <i>et al.</i> , ²¹ 2015		Depression (SCL-90-R) worse in CRSwNP with anosmia vs CRSwNP with hyposmia or normosmia	
Schlosser <i>et al.</i> , ¹⁸ 2016	Depression (BDI) was worse in physician-diagnosed depression, fibromyalgia, asthma; CRSsNP had higher prevalence BDI-diagnosed depression and worse BDI scores than controls; no association with age, sex, race		
Schlosser <i>et al.</i> , ¹⁷ 2016	Depression associated with less alcohol and with revision surgery (53.9 vs 38.0%); no association with asthma, fibromyalgia, COPD, polyps, CT, endoscopy, allergy, smoking status	Patients with depression had worse total SNOT-22 and RSDI scores across all subdomains	Patients with depression had more missed productivity, worse sleep (PSQI scores), and more oral antibiotic, oral steroid, and oral decongestant use

CRS = Chronic rhinosinusitis; SNOT-22 = 22-item Sino-Nasal Outcome Test; SNOT-16 = 16-item Sino-Nasal Outcome Test; CT = computed tomography; GERD = gastroesophageal reflux disease; ESS = endoscopic sinus surgery; RSDI = Rhinosinusitis Disability Index; CSS = chronic sinusitis survey; CRSsNP = chronic rhinosinusitis without nasal polyposis; HADS = Hospital Anxiety and Depression Score; BDI = Beck Depression Inventory; TDI = threshold, discrimination, identification (range 0–48); SCL-90-R = Symptom Checklist-90-Revised; CRSwNP = chronic rhinosinusitis with nasal polyposis; COPD = chronic obstructive pulmonary disease; PSQI = Pittsburgh Sleep Quality Index; SF-36 = short-form health survey.

Table 3 Impact of depression on outcomes

Study	CRS and General QOL Outcome	Depression Outcome
Smith <i>et al.</i> , ¹² 2005	Patients with depression had significant improvement in RSDI but had worse pre- and postoperative RSDI scores, and less improvement when on RSDI than patients without depression Patients with depression had less endoscopic improvement	
Davis <i>et al.</i> , ¹¹ 2005	Patients with depression had significant improvement in SNOT-16 scores after surgery but began and finished with worse scores than patients without depression	The rate of PHQ9 diagnosed depression decreased from 25% before surgery to 11% after ESS
Brandsted and Sindwani ⁷ 2007	Patients with depression did not improve with medication usage, CRS-specific (CSS), or general QOL (SF-8) scores; patients with depression had improvements in headache and facial pain	
Mace <i>et al.</i> , ⁸ 2008	Patients with depression had improved RSDI, CSS, and endoscopy after surgery; a similar degree of improvement to patients without depression but began and finished with lower RSDI	
Smith <i>et al.</i> , ¹⁰ 2010	Depression was not associated with likelihood of achieving MCID of RSDI or CSS.	
Litvack <i>et al.</i> , ¹⁶ 2011	Patients with depression improved RSDI after ESS the same degree as patients without depression	Depression scores (PHQ9) improved after ESS
Katotomichelakis <i>et al.</i> , ²² 2014		Greatest improvement in BDI in CRSwNP and hyposmics and/or anosmics Smoking associated with less improvement in BDI
Schlosser <i>et al.</i> , ¹⁷ 2016	Improvement in PHQ2 with medical or surgical therapy for CRS correlated with improvement in total SNOT-22, PSQI, missed productivity and oral antibiotic usage	PHQ2 scores improved after ESS or medical treatment to similar degree in all outcomes CRSsNP was associated with increased odds of achieving MCID in PHQ2 with medical or surgical treatment

CRS = Chronic rhinosinusitis; QOL = quality of life; RSDI = Rhinosinusitis Disability Index; SNOT-22 = 22-item Sino-Nasal Outcome Test; SNOT-16 = 16-item Sino-Nasal Outcome Test; PHQ = Patient Health Questionnaire; ESS = endoscopic sinus surgery; CSS = chronic sinusitis survey; SF = short form; MCID = minimal clinically important difference; BDI = Beck Depression Inventory; CRSwNP = chronic rhinosinusitis with nasal polyposis; PSQI = Pittsburgh Sleep Quality Index; CRSsNP = chronic rhinosinusitis without nasal polyposis; SF-8 = 8-item short-form health survey.

When depression is present in CRS, it is consistently associated with worse CRS-specific QOL as measured by a variety of instruments, including the Rhinosinusitis Disability Index, the 22-item Sino-Nasal Outcome Test, and the Chronic Sinusitis Survey. Three studies examined baseline medication usage, productivity, or physician visits, and found that comorbid depression was uniformly associated with worse performance across each of these metrics (Table 2).^{7,9,17} Two studies^{19,21} reported worse baseline olfaction in patients with CRS and depression, although one of these studies was limited to patients with CRS with nasal polyposis.²¹

Impact of Depression on Outcomes

Six studies report that CRS-specific metrics improved after endoscopic sinus surgery in patients with comorbid depression,^{8,10–12,16,17} whereas one study failed to find improvement⁷ in this population (Table 3). Whether patients with depression have the same degree of improvement after endoscopic sinus surgery as do patients without depression is unclear. The majority of studies indicated that patients with depression start and end with worse CRS-specific QOL than patients without depression but that their absolute level of improvement (*i.e.*, change from baseline) is similar. One study examined medical therapy for CRS and found that it also improves 22-item

Sino-Nasal Outcome Test in patients with depression, similar to endoscopic sinus surgery.¹⁷

Four studies examined depression-specific outcomes after CRS-specific medical or surgical therapy, and all found improvement in depression.^{11,16,17,22} These studies aimed to determine whether treatment of CRS specifically would impact comorbid depression secondarily. Overall, there are limited data, but it seems that treatment of CRS results in a mean improvement in depression scores. The greatest improvement in depression-specific outcomes seems to be in those with olfactory dysfunction and nonsmokers. The impact of nasal polyps was beneficial to depression outcomes in one study of patients with CRS with nasal polyposis,²² whereas another study found increased odds of achieving a minimal clinically important difference in patients with CRS without nasal polyposis.¹⁷ The data that support depression-specific improvement are limited, and most studies were not designed to investigate this outcome in a comprehensive fashion.

DISCUSSION

Depression seems to be a comorbid condition in CRS, with a prevalence of up to 40%. The criterion standard for diagnosing depression involves detailed evaluation by a mental health expert by using Diagnostic and Statistical Manual of Mental Disorders, 4th

Edition criteria.²⁰ Unfortunately, we were unable to find any studies that used such strict diagnostic criteria but had to rely on screening instruments and previous physician diagnosis of depression that may aid otolaryngologists in identifying this important comorbidity. We found that, as screening instruments become more detailed and as thresholds for defining depression are lowered, they detect an increasing prevalence of possible depression, above and beyond that seen based solely on existing physician diagnosis. This finding indicated that comorbid depression was likely undiagnosed and underappreciated in this patient population.

The U.S. Preventive Services Task Force recommends screening and treatment of depression in primary care settings with PHQ or HADS instruments.² O'Connor et al.²³ report that screening instruments demonstrate sensitivity of 80–90% and specificity of 70–85%. This obviously varies widely, depending on the demographics of the population being studied, the screening instrument used, and the thresholds used for each of the various instruments. The expected rate of depression in a general primary care setting is much lower than what we found across CRS populations, which indicated that routine screening of the CRS population would have even greater utility. Although U.S. Preventive Services Task Force recommendations were not specific to CRS populations, it was apparent that some sort of screening would be worthwhile to help identify undiagnosed depression.² Further work is clearly needed to determine the optimal screening tool and ideal thresholds that balance sensitivity and specificity in a CRS population, confirmed by psychiatric evaluation. However, simple two-item questionnaires, *e.g.*, the PHQ2, seem to be a reasonable start for screening. Use of this instrument can be efficiently integrated into intake questionnaires both at baseline and follow-up time points. Although screening instruments are not sufficient for a definitive diagnosis of depression, those with positive screening results can be referred to a mental health expert for a more detailed assessment and determination of depression treatment.²³

When positive depression screening results occur in patients with CRS, all the studies demonstrated a negative association with CRS-specific QOL. Impaired global health outcomes even extended to medication usage, productivity, and physician visits. The true economic impact of comorbid depression in CRS is unknown but is likely to be millions of dollars each year. Unfortunately, there were no demographic, comorbid, or CRS-specific factors that reliably predicted the presence or severity of depression, which indicated that physicians must continue to rely on screening instruments or clinical examination. In addition, we were unable to comment on the impact of the treatment of depression with counseling and/or antidepressants. Only two studies reported use of these depression-specific therapies, and medications used and compliance were not reported.^{7,8} CRS patients with untreated depression may experience poorer QOL when compared to those undergoing depression counseling or pharmacotherapy.

There are a number of potential mechanisms to explain the increased prevalence of depression in CRS. Previous studies showed a wide spectrum of systemic effects in patients with CRS, including sleep dysfunction, anxiety, and cognitive impairment.^{14,24,25} All of these systemic morbidities can increase the likelihood of depression, and the relationship among these systemic disorders is complex.²⁶ In addition, patients with CRS may feel socially isolated due to sinonasal symptoms, such as impaired olfaction and/or taste, nasal obstruction, and drainage. Similar to other chronic illnesses, patients with CRS have to spend significant time with physician visits and health care activities, *e.g.*, sinus lavage.²⁷ This lost recreational time likely results in frustration and potential depression. Also, in other chronic illnesses, a systemic inflammatory hypothesis has been proposed, which links inflammatory cytokine levels to depression severity.²⁶ Cancer patients are known to have elevated levels of systemic interleukin 6 and 1 β that correlate with fatigue and behavioral symptoms, and similar increases in circulating proinflammatory cytokines may contribute to depression associated with other illnesses, including

multiple sclerosis, rheumatic disease, asthma, and allergies.²⁶ The systematic inflammatory hypothesis has not yet been studied in CRS.

The relationship of comorbid depression with CRS outcomes is complex. Similar to studies of comorbid depression in other chronic illnesses,^{4,5} most studies in CRS demonstrate that patients with depression still improve after treatment but may not achieve equivalent long-term outcomes. Put another way, patients with depression may improve to a similar relative degree, but their QOL remained below that of patients without depression. This finding certainly has implications for prognosis and patient counseling regarding long-term expectations. The potential bidirectional association of depression and CRS makes it difficult to determine why patients may fail to achieve similar long-term QOL levels as peers without depression. One could hypothesize that depression is a secondary outcome of a particularly severe phenotype of CRS or, alternatively, that ongoing depression impacts patient-reported QOL, independent of CRS severity. Regardless, more study is required to parse out these mechanisms and develop treatment recommendations.

CONCLUSION

Depression is commonly associated with CRS and likely underdiagnosed in many patients. It is associated with worse QOL and likely poorer absolute outcomes after CRS treatment. To obtain optimal posttreatment results, it is critical that we gain a better understanding of depression in CRS and develop strategies to treat this important comorbidity.

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