Acute exacerbations of chronic rhinosinusitis: The current state of knowledge

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Abstract
Objectives: Acute exacerbations of chronic rhinosinusitis (AECRS) are distinct from baseline symptomatology related to chronic rhinosinusitis (CRS). In this review, we seek to examine the literature on AECRS to synthesize the definition, epidemiology, pathophysiology, treatment, and impact of AECRS on CRS patients.

Methods: A comprehensive narrative review of the scientific literature, identified by searching PubMed from inception through April 2022, was performed.

Results: AECRS is defined in consensus guidelines as a worsening of chronic sinus disease symptomatology, with a return to baseline, typically after intervention with systemic antibiotics and/or corticosteroids. The working definition used across the literature, however, is broad and heterogeneous. The pathophysiology of AECRS is incompletely understood but is hypothesized to include an interplay of environmental and patient-specific factors. AECRS have been found to have a negative impact on quality-of-life measures, independent of baseline CRS symptomatology, and impact how patients and physicians view overall disease control. Treatment for AECRS includes oral antibiotics and systemic corticosteroids, although their efficacy for AECRS is unclear. Appropriate use of medical and surgical treatment for CRS can reduce the frequency of AECRS.

Conclusions: AECRS are a distinct entity in CRS patients and should be independently assessed when evaluating patients for CRS control. The efficacy of systemic medication usage for AECRS is currently unclear, but appropriate medical management of baseline CRS can reduce the frequency of AECRS. More research is needed to further understand this phenomenon, including a more precise and prospective definition, defined epidemiology, and how to appropriately treat.

Level of Evidence: 5

KEYWORDS
acute exacerbations, chronic rhinosinusitis, oral antibiotics, review, sinus infections, systemic corticosteroids
Chronic rhinosinusitis (CRS) is an inflammatory disease of the sinonasal cavity. This disease impacts patients via (1) a decrease in quality of life (QoL) due to chronic sinonasal symptomatology and their acute exacerbations (AEs); and (2) may lead to increased morbidity and even mortality via exacerbations of pulmonary disease, orbital manifestations, or intracranial complications. CRS affects ~1%-5% of the general population worldwide and is associated with direct healthcare costs in the tens of billions of US dollars every year. These estimates of yearly expense are even higher when including indirect costs such as lost work productivity.

Asthma exacerbations have been shown to be due to pathophysiologic processes that are distinct from the mechanisms of the baseline disease. Asthma exacerbations are both a cause of significant morbidity and mortality and are a major driver of healthcare expenditure. Given the impact that exacerbations of lower airway inflammatory disease have on patients, it can be hypothesized that acute exacerbations of CRS (AECRS) may also have a distinct manifestation in the upper airway, leading to a significant impact on patients.

Despite their potentially important role, AECRS have only recently been the focus of study. Historically, the definition of an AECRS has been broad and variable across the literature. Consensus guidelines on CRS have simply defined AECRS as transient worsening of symptom intensity that returns to baseline on its own or, more typically, after intervention with antibiotics and/or systemic corticosteroids. Although descriptive and largely capturing the main essence of the AECRS, this definition is vague and retrospective, which ultimately prevents reliable prospective capture of these events. Nevertheless, studies using proxy measures of AECRS, for example the need for rescue medications, have demonstrated the many possible ways that AECRS may impact CRS patients.

Given the rapidly expanding literature on AECRS demonstrating their very significant impact on CRS patients, the objective of this review is to collect and synthesize contemporary knowledge on the epidemiology, pathophysiology, treatment, and impact of AECRS.

The objective of this article is to provide a narrative review on AECRS with a focus on definition, epidemiology, pathophysiology, impact on the patient, and treatment. With those goals in mind, the MEDLINE and PubMed Central databases were queried for studies and review articles that addressed the objective of this review. Searches were performed between April and May 2022 using primary search terms including “chronic rhinosinusitis,” “exacerbations,” “bacteriology,” “viral infections,” “antibiotics,” and “systemic corticosteroids.” The references of identified articles were also searched for pertinent articles.

In the absence of definitive objective or quantitative criteria, consensus guideline documents have described an AECRS as a transient worsening of symptom intensity in CRS patients with return to baseline symptomatology, typically after intervention with antibiotics and/or systemic corticosteroids. This definition, however, is problematic as it relates to the study of AECRS because it is retrospective in nature, which precludes prospective detection (and therefore direct study), and it has the potential to be inconsistent and unreliable in detecting AECRS because it is not based on any objective or quantitative criteria. As a result, the definitions of AECRS are heterogeneous across the literature, in particular in the setting of studies that require quantitative characterization of AECRS.

Some studies have defined an AECRS as any acute worsening of sinonasal symptomatology reported by the patient, whereas others have followed this definition but used quantitative validated patient-reported outcomes to verify worsening symptomatology. Other studies have used surrogate measures of AECRS to quantify AECRS frequency, such as the frequency of sinus infections and/or frequency of rescue medication (i.e., antibiotics or oral corticosteroids).

Finally, endoscopic findings have also been used to define AECRS in the literature. Evidence of mucopurulent drainage on endoscopy is frequently used, particularly in studies on the bacteriology of AECRS. Interestingly, a recent study defined AECRS as a recurrence of nasal polyposis in their retrospective study of corticosteroid use in a subset of post-surgical CRS with nasal polyps (CRSwNP) patients.

Despite their heterogeneity, definitions of AECRS in the literature are uniformly limited by their lack of overall predictive ability. Although measures such as use of rescue medications may be quite specific for AECRS, they are likely not sensitive, as they do not capture episodes that are not treated with rescue medications. Similarly, although symptom-based criteria may be sensitive for AECRS, they likely have poor specificity in that not every transient worsening of CRS symptoms would necessarily be categorized as an AECRS. More specifically, the time course or duration that distinguishes an AE from random fluctuation in symptoms has not been clarified in the literature and thus is subject to patient interpretation as well as differences in physician prescribing practices. Finally, the majority of AECRS definitions are retrospective in nature and rely on patient recall of the AECRS (e.g., their symptomatology or medication usage) introducing recall bias in the majority of studies on this phenomenon.

The incidence of AECRS in CRS patients is highly variable and dependent on individual factors such as comorbidities (e.g., asthma and aeroallergen hypersensitivity) as well as environmental factors such as seasonality or exposures. A large epidemiological study reported that 25.9% of CRS patients may have experienced at least one AECRS in the last 12 months. Another study found that after endoscopic sinus
surgery (ESS), 15% of CRS patients experienced at least one AECRS over a 14 months period.22 Studies looking into temporal trends have shown that AECRS peaks during the winter months.21,25 This has been validated using the frequency of internet search trends in the Northern and Southern Hemispheres, as well as in English and non-English speaking countries.26 Although aeroallergen hypersensitivity has been shown to be a disease modifier in CRS,1,2 studies into temporal trends have not supported an increase in AECRS during “peak allergy seasons,” or transitions between seasons.26

In a similar vein to study of the asthma exacerbation-prone phenotype, work has been done to study CRS patients who have frequent AECRS or an exacerbation-prone phenotype.27 We have previously proposed that AECRS-prone be defined as having at least 4 AECRS episodes in a 12 months period18 based on previous guidelines indicating that at least 1 rescue medication in 3 months was an indication of uncontrolled CRS.1 In a retrospective review of over 3000 patients with CRS, 19.3% were found to have meet this criteria for exacerbation-prone CRS, with at least 4 AECRS (defined by an antibiotic course prescribed for worsening sinus symptoms) over a 12 months period.19 Our prior work found that the exacerbation-prone phenotype of CRS was associated with high sinonasal symptom burden (defined by a 22-item Sinonasal Outcome Test [SNOT-22] score >23) and comorbid asthma but negatively associated with nasal polyps.18 A more recent study by Kwah et al. found that the exacerbation-prone phenotype of CRS was associated with increased BMI, nonwhite race, female sex, eosinophil count of at least 150 cells/ml, and presence of comorbidities (asthma, allergic rhinitis, autoimmune disease, and any drug or antibiotic allergy).19 Additionally, increased burden of disease on sinus CT also predicted more frequent AECRS episodes.19 A history of ESS has also been suggested to be associated with more frequent AECRS, perhaps a reflection of those patients’ medically recalcitrant CRS at baseline.21 Understanding the population with exacerbation-prone CRS may assist clinicians in determining how to appropriately counsel patients and potentially which patients may require more aggressive treatment to keep their CRS controlled.

The association between comorbid asthma and frequency of AECRS supports the unified airway hypothesis suggesting that inflammatory changes in the lower airways exacerbate the upper airways and vice versa.18,19 Furthermore, AECRS-related metrics can be used to assess asthma disease control independent from baseline CRS symptom severity. For example, AECRS frequency was found to be independently associated with asthma control level, regardless of baseline CRS symptom severity.15

Association between migraine and AECRS has also been previously reported,21 suggesting that cephalgia may influence the perception of AECRS or the possibility that overlapping symptoms are inappropriately attributed to AECRS. However, another study has reported no association between migraine or other headache disorders and an exacerbation-prone CRS phenotype.18 Further study of this relationship is needed to better understand how migraine and AECRS may be related.

5 PATHOPHYSIOLOGY

As the pathophysiology of CRS is heterogeneous, AECRS pathophysiology is hypothesized to be heterogeneous as well, with many different factors leading to increased sinonasal symptomatology. Proposed etiologies include inhaled irritants (such as aeroallergens or pollutants), dysregulation of the innate or adaptive immune system, mucociliary dysfunction, or microbial bacterial infection.

A healthy epithelial barrier is important in the innate defense against AECRS. Immunologic differences in CRS patients compared to healthy controls have been found both at baseline and during AEs. IL-6 is increased in nasal secretions in CRSwNP patients at baseline, suggesting a proinflammatory disposition that further increases during AECRS. During AEs in CRSwNP patients, levels of IL-5, IL-6, and eosinophil major basic protein further elevate in nasal secretions, implicating an increase in local type 2 immunological responses and eosinophilic inflammation as compared to controls without CRS.28 Furthermore, a systemic immune response has been identified during AEs in CRSwNP patients in addition to local inflammatory changes within the nose. During AEs, serum levels of vascular endothelial growth factor and granulocyte-macrophage colony stimulating factor significantly increase compared to corresponding patients’ baselines and healthy control patients.28 The exact role of these changes has yet to be determined, however, and thus further research is warranted to investigate the immune response during AECRS, both in CRSwNP and CRS without nasal polyps (CRSsNP) patients.

Type 2 cytokines produced during AECRS can mechanically weaken the epithelial barrier and increase permeability, thus leading to a susceptibility for microbial invasion and infection.20,28 Furthermore, baseline epithelial inflammation in CRS can be exacerbated by viral infections and the subsequent host response, further diminishing epithelial function.29 Cho et al. found that CRS patients have a higher proportion of respiratory viruses and are more likely to have multiple viral pathogens detected in their nasal secretions and mucosa compared with non-CRS controls.30 This study was performed in patients who were not experiencing AEs, however, suggesting that chronic inflammation in CRS may in itself predispose to infection with respiratory viruses.30 The role of viral infections in AECRS pathophysiology is supported by the finding of worldwide temporal trends, which show a two-fold increase in AECRS during the winter months; a time of increased respiratory viral infections.25,26 Viruses implicated in the development of AECRS are respiratory syncytial virus, influenza virus, coronavirus, parainfluenza virus, rhinovirus, and enterovirus.1,2,30 The development of AECRS is a complex process, however, and thus there is disagreement regarding how significant the contribution of viruses is in the pathophysiology of AECRS.29

Although the role of bacteria in CRS is not completely elucidated and remains a topic of debate, antibiotics are often used to treat AEs to return CRS symptoms to their baseline severity.6,31 Bacteria implicated in AECRS based on endoscopically guided cultures often include noncolonizing pathogenic bacteria.22 During AEs, one or a few pathogens become overrepresented compared to colonizing bacteria23 and this includes species such as Staphylococcus aureus,
coagulase-negative staphylococci, Staphylococcus Pneumonia, Pseudomonas, and Haemophilus influenzae, which are commonly found in cultures obtained during AECRS, in both pre-ESS and post-ESS patients. Additionally, anaerobic bacteria are commonly present during AECRS, although they are not always sought out in microbiological studies. It is important to note that the bacterial makeup in AECRS is more varied than the causative organisms implicated in acute rhinosinusitis, which are most commonly S. pneumonia, H. influenzae, and Moraxella catarrhalis. There are no consistent differences in the sinonasal microbiota during AEs occurring in patients with CRSwNP versus CRSsNP versus acute fungal rhinosinusitis.

Studies of sinus microbiota both pre- and post-AE have elucidated how antibiotic therapy affects the microbiome in post-ESS patients. Specifically, antibiotic treatment leads to a decrease in abundance in sinonasal bacteria but an increase in bacterial diversity. Additionally, in a study by Yaniv et al., the majority of CRS patients studied showed a change in bacterial isolates cultured from AECRS over their lifetime. Furthermore, biofilm-forming bacteria are very common as a dominant cultured species from the sinuses in the setting of an AECRS. In one study of middle meatal cultures obtained from patients experiencing AECRS, 76.7% of cultured bacteria formed biofilms in vitro. Biofilms are notable in that they confer resistance to the effects of antibiotics and normal mucociliary clearance compared to free-floating, planktonic bacteria. These points have important treatment implications that will be discussed later in this review.

Overall, more research is needed to clarify the pathophysiology of AECRS. In particular, there are knowledge gaps with respect to the role of mucociliary dysfunction, viral infections, and aeroallergens as instigating factors for AECRS. Furthermore, characterization of the mucosal inflammatory milieu in patient subpopulations that are more prone to frequent AECRS may also help shed light on the pathophysiology of AECRS.

6 | IMPACT OF AECRS ON CRS PATIENTS

AECRS is a distinct clinical entity that should be assessed separately from baseline CRS symptomatology. Although the baseline CRS disease state alone has an impact on QoL and productivity, the frequency of self-reported episodes of AEs in CRS patients has been shown to be an independent predictor of decreased general health-related QoL. AECRS can also lead to lost productivity regardless of baseline CRS symptom severity, with this effect found to be most prominent among asthmatics. Moreover, AECRS frequency, as defined by systemic medication usage, has been found to be associated with asthma-related emergency department usage, which can serve as a predictor of asthma-related mortality.

Furthermore, surrogate measures of AECRS, such as CRS-related systemic medication (i.e., antibiotics and oral corticosteroids) use, are significantly associated with decreased CRS-related and general health-related QoL. This effect holds true despite individual patient characteristics, such as the presence of comorbidities and the presence of polyps, over 3 and 12 months time periods. With each incremental increase in systemic medication usage for CRS, there is an associated incremental decrease in QoL measures, which may be a reflection of the cumulative burden that recurrent AECRS have on patients.

Finally, AECRS also impact how patients and providers view control of their disease. In the European Position Paper on Rhinosinusitis guideline’s definition of CRS disease control, systemic rescue medication use impacts the level of control and impacts overall treatment decisions. In contrast, prior research suggests that patients most strongly correlate their baseline symptomatology—in particular nasal symptomatology—as measured by SNOT-22 score with their perception of disease control. However, a recent qualitative study found that AECRS are incorporated into a patient’s perception of their own disease control. Separately, physicians were shown to use the frequency of systemic corticosteroid and oral antibiotic courses used, in addition to baseline symptomatology, to inform their understanding of an individual patient’s global CRS control. With increased AECRS frequency and decreased control of disease, patients are more likely to experience escalated treatment for their CRS including ESS and adjuvant medical treatment.

7 | TREATMENT OF AECRS

Although antibiotics are frequently used for the treatment of AECRS, the data are inconclusive regarding their efficacy. There is a single randomized control trial to date examining the use of antibiotics in AECRS. When comparing the use of a 14 day course of amoxicillin/clavulanate (amox/clav) for AECRS, antibiotics did not change the clinical course of AECRS compared to placebo. Amox/clav provided adequate coverage in 82% of specimens but there was no significant difference in symptom evolution or endoscopic scores with antibiotic use measured at the 14-day time point (with efficacy at earlier time points not measured). Post-treatment middle meatal cultures were obtained in both the placebo and antibiotic groups showing that the majority of bacterial growth was not eradicated, even after antibiotic treatment. It is important to note that both treatment arms had significant improvement in symptoms regardless of treatment or bacterial eradication. In addition, this trial had a small sample size, with only 22 patients in the treatment group, and 11 in the placebo group.

Yan et al. compared the use of culture-directed antibiotics versus empiric antibiotic therapy in AECRS. This study found that there was no QoL benefit from the use of culture-directed antibiotics although there was an improvement in long-term (1–6 months post-treatment) endoscopic scores with the use of cultures to guide therapy. However, this study was limited by its retrospective nature and differences in baseline patient characteristics between groups. Another study prospectively followed patients after ESS and found that when culturing purulent sinus drainage during AEs, 75% of post-ESS patients revealed de novo growth of noncolonizing bacteria compared to previous culture. A separate study found that in patients experiencing recurrent episodes of AECRS, cultured bacterial isolates
changed in 68% of patients over the course of their disease process, requiring a change in antibiotic choice—when chosen based on prior culture data—40% of the time. Thus, empiric antibiotics based on past culture data (e.g., cultures obtained during surgery or prior AEs) may be misleading. At this time, the evidence does not strongly support the use of antibiotics in AECRS and current clinical practice guidelines do not make any explicit recommendations for antibiotic use in AECRS. More research is needed in this topic to make an evidence-based recommendation. If antibiotics are to be used, however, it is important to practice antibiotic stewardship and consider that antibiotic resistance is high in patients experiencing AECRS.

Sabino et al. showed that both free-floating, planktonic bacteria and bacterial biofilms demonstrate high antibiotic resistance profiles in patients with AECRS. Although planktonic bacterial resistance can provide an indicator for treatment of biofilms, close to 20% of planktonic bacteria susceptible to a particular antibiotic produce resistant biofilms. Taken together, this data suggests the importance of culture-directed therapy as opposed to use of empiric antibiotics or choosing an antibiotic based on past culture results. Ultimately, however, no strong recommendation is currently made by any guidelines regarding the use of antibiotics in AECRS based on the available evidence.

In patients with resistant bacterial strains, there may be a future benefit to bacteriophage therapy. Bacteriophages are viruses that infect and destroy bacteria. In one study, 46% of post-ESS patients carried bacterial isolates that demonstrated mechanisms of antibiotic resistance. However, 81% of these strains were found to be sensitive to bacteriophage therapy. Some phages have the benefit of being able to penetrate biofilms and are more highly selective than antibiotics, which may have the secondary benefit of contributing to a healthier microbiome by only targeting pathogenic bacteria. It is important to note, however, that bacteriophage therapy is not routinely used in the United States despite being shown to be generally safe and well-tolerated.

Although treatment with systemic corticosteroids is common in AECRS and is used as a surrogate measure defining AECRS, there is a paucity of data supporting this therapeutic approach to AECRS. Short-term courses of oral corticosteroids can be successfully used to reduce the sinonasal symptoms and polyp burden seen in CRSwNP patients. A small study investigating the use of systemic corticosteroids in a pediatric population with CRSsNP showed improved symptomatology and radiographic CRS burden with use of oral corticosteroids plus antibiotics compared to placebo plus antibiotics. Neither of these studies, however, specifically addressed the use of systemic corticosteroids during AEs. Importantly, current consensus guidelines do not make any recommendations regarding the use of systemic corticosteroids for treatment of AECRS.

Reflecting the practice of empiric use of corticosteroids for AECRS, triamcinolone acetonide/carboxymethylcellulose foam instilled into the sinuses during AEs in post-ESS CRSwNP patients has been studied as an alternative to systemic corticosteroids. Reduction in the use of systemic corticosteroids is important as even short-term courses of corticosteroids can lead to significant side effects. Courses <30 days have been associated with increased rates of sepsis, venous thromboembolism, and fractures, even at lower steroid doses (e.g., <20 mg/day of prednisone equivalent doses). Chaudhry et al. found that the local instillation of triamcinolone acetonide/carboxymethylcellulose foam significantly reduced systemic corticosteroid prescriptions for AECRS and was well tolerated, even in patients with comorbidities such as diabetes mellitus. This was examined in a retrospective fashion in a single rhinology practice, and thus its use needs to be studied in a more robust fashion prior to recommendations being made regarding its efficacy.

Finally, many other remedies exist, which patients or treating healthcare providers may employ in the treatment of AECRS. Although this is certainly not an exhaustive list, these possible treatments include over the counter medications such as decongestants and mucolytics, hypertonic saline irrigations, topical antibiotic irrigations, vibration therapy, acupuncture, or other complementary medicine therapy. Yet, no studies exist on the use of these aforementioned therapies and AECRS, leaving much to be discovered.

8 | IMPACT OF TREATMENT OF CRS ON AECRS

The mainstay of CRS treatment targets sinonasal inflammation and includes nasal saline irrigations and intranasal corticosteroids. It has been shown that appropriate medical management of CRS reduces systemic medication use in CRS, which may be a reflection of decreased AECRS.

ESS is often recommended for CRS patients with medically recalcitrant disease. Schlosser et al. found that post-ESS, both CRSsNP and CRSwNP patients reduced their systemic medication usage at 6-months follow up, reflecting possible reduction in AECRS. Specifically, CRSsNP patients reduced both systemic antibiotics and oral corticosteroid usage, whereas CRSwNP patients saw a reduction in systemic corticosteroid use alone. In a recent randomized control trial, evaluating ESS and medical therapy for CRS compared to medical therapy alone, fewer patients in the ESS plus medical therapy group experienced AECRS. Furthermore, the ESS plus medical therapy group used less than half of the cumulative mean dose of systemic corticosteroids as the medical therapy group.

Type 2 inflammation is one of the dominant etiologies of CRS in North America and Western Europe. Biologics, consisting of monoclonal antibodies, targeting type 2 inflammation are now approved by United States Food and Drug Administration for the treatment of CRSwNP, although their use for type-2 CRSsNP may be on the horizon. Prior to the dedicated use of biologics for CRSwNP, however, the impact of biologics on CRS was primarily seen as a secondary benefit in the use of biologics for the treatment of asthma in asthmatic CRS patients. One retrospective study showed that biologic use in a population of CRS patients (both with and without polyps) with comorbid asthma significantly reduced both antibiotic use and oral corticosteroid use for AECRS.
(49% and 60% reduction, respectively). In specific patients reporting frequent AECRS (defined as three or more antibiotic courses in the last year), there was a highly significant 62% reduction in antibiotic use for AECRS with the use of biologics. Although biologics are not currently approved for CRSwNP, they can be a useful, yet expensive, adjunct in CRSwNP patients and have been shown to reduce AECRS. Recent trials specifically studying the efficacy of biologics for the treatment of CRSwNP have also documented that their use is associated with decreased systemic corticosteroid usage for CRSwNP again suggesting decreased AECRS. Taken together, appropriate medical and surgical management of CRS leads to a decrease in AECRS, at least as measured via the proxy of systemic rescue medication usage.

8.1 | Limitations

The current consensus guideline definition of AECRS is necessarily vague because accurate, reliable, objective, and quantitative criteria of AECRS do not yet exist. As a result, however, there is heterogeneity in how this phenomenon is defined in research studies and in clinical practice. This heterogeneity and lack of precise, prospective definitions makes it hard to compare study to study and hard to diagnose AECRS in real time. Many studies of AECRS are based on patient recall rather than prospectively collected data regarding AEs. Additionally, the variation in endpoints used in studies limits the ability to draw strong conclusions. There is also a paucity of literature on AECRS outside of otolaryngology and allergy journals and therefore healthcare providers at primary care offices, urgent care offices, and emergency departments are at a disadvantage when treating these patients. Importantly, there is a lack of randomized control trials to guide treatment in AECRS. Future directions in AECRS research should focus on establishing a specific definition of AEs for use in prospective studies to allow better comparison of results. Randomized control trials studying the treatment of AECRS would be helpful to assist in developing strong evidence-based guidelines to aid clinicians.

9 | CONCLUSION

AECRS are a distinct entity and should be independently assessed when evaluating patients for CRS control. Proxy measures for AECRS that are commonly used include the frequency of “sinus infections” perceived by patients as well as their CRS-related antibiotic and systemic corticosteroid use. AECRS decreases CRS-related and general health-related QoL regardless of baseline CRS severity. Although AECRS is often treated with antibiotics, the data regarding the causality of bacterial infection is conflicting. Despite this, given the high antibiotic resistance in this population, culture-directed therapy should be strongly considered by the treating physician if antibiotics are to be prescribed for AECRS. Additionally, there is a paucity of data supporting the use of systemic corticosteroids in AECRS. However, appropriate medical management of baseline CRS can reduce the frequency of AECRS. Furthermore, ESS in medically uncontrolled CRS patients or the addition of biologics in severe, refractory CRSwNP patients can reduce the cumulative use of corticosteroids in these populations suggesting their benefits in reducing AECRS.

CONFLICT OF INTEREST

No conflicts of interest to report.

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REFERENCES

1. Fokkens WJ, Lund VJ, Hopkins C, et al. European position paper on Rhinosinusitis and nasal polyps 2020. Rhinology. 2020;58(Suppl S29):1-464. doi:10.4193/Rhin20.600
2. Orlandi RR, Kingdom TT, Smith TL, et al. International consensus statement on allergy and rhinology: rhinosinusitis 2021. Int Forum Allergy Rhinol. 2021;11(3):213-739. doi:10.1002/air.22741
3. Hoehle LP, Phillips KM, Bergmark RW, Caradonna DS, Gray ST, Sedaghat AR. Symptoms of chronic rhinosinusitis differentially impact general health-related quality of life. Rhinol J. 2016;54(4):316-322. doi:10.4193/Rhinol16.211
4. Phillips KM, Hoehle LP, Bergmark RW, Caradonna DS, Gray ST, Sedaghat AR. Acute exacerbations mediate quality of life impairment in chronic Rhinosinusitis. J Allergy Clin Immunol Pract. 2016;5(2):422-426. doi:10.1016/j.jaip.2016.09.015
5. Phillips KM, Bergmark RW, Hoehle LP, Caradonna DS, Gray ST, Sedaghat AR. Chronic rhinosinusitis exacerbations are differentially associated with lost productivity based on asthma status. Rhinology. 2018;56(4):323-329. doi:10.4193/Rhin18.033
6. Yamasaki A, Hoehle LP, Phillips KM, et al. Association between systemic antibiotic and corticosteroid use for chronic rhinosinusitis and quality of life. Laryngoscope. 2018;128(1):37-42. doi:10.1002/lary.26778
7. Speth MM, Hoehle LP, Phillips KM, Caradonna DS, Gray ST, Sedaghat AR. Changes in chronic rhinosinusitis symptoms differentially associate with improvement in general health-related quality of life. Ann Allergy Asthma Immunol. 2018;121(2):195-199. doi:10.1016/j.anai.2018.05.029
8. Sedaghat AR, Kuan EC, Scadding GK. Epidemiology of chronic Rhinosinusitis: prevalence and risk factors. J Allergy Clin Immunol Pract. 2022;29:1395-1403. doi:10.1016/j.jaip.2022.01.016
9. Rudmik L. Economics of chronic Rhinosinusitis. Curr Allergy Asthma Rep. 2017;17(4):20. doi:10.1007/s11882-017-0690-5
10. Wahid NW, Smith R, Clark A, Salam M, Philpott CM. The socioeconomic cost of chronic rhinosinusitis study. Rhinology. 2020;58(2):112-125. doi:10.4193/Rhin19.424
11. Smith KA, Rudmik L. Medical therapy, refractory chronic rhinosinusitis, and productivity costs. Curr Opin Allergy Clin Immunol. 2017;17(1):5-11. doi:10.1097/ACI.0000000000000329
12. Rodrigo GJ, Rodrigo C, Hall JB. Acute asthma in adults. Chest. 2004;125(3):1081-1102. doi:10.1378/chest.125.3.1081
13. Castillo JR, Peters SP, Busse WW. Asthma exacerbations: pathogenesis, prevention, and treatment. J Allergy Clin Immunol. 2017;139(4):918-927. doi:10.1016/j.jaci.2017.05.001
14. Ivanova JI, Bergman R, Binnbaum HG, Colice GL, Silverman RA, McLaurin K. Effect of asthma exacerbations on health care costs among asthmatic patients with moderate and severe persistent asthma. J Allergy Clin Immunol. 2012;129(5):1229-1235. doi:10.1016/j.jaci.2012.01.039
48. Desrosiers M, Mannent LP, Amin N, et al. Dupilumab reduces systemic corticosteroid use and sinonasal surgery rate in CRSwNP. *Rhinology*. 2021;59(3):301-311. doi:10.4193/Rhin20.415

49. Gevaert P, Omachi TA, Corren J, et al. Efficacy and safety of omalizumab in nasal polyposis: 2 randomized phase 3 trials. *J Allergy Clin Immunol*. 2020;146(3):595-605. doi:10.1016/j.jaci.2020.05.032

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