

Understanding the Clinical and Economic Burden of Chronic Rhinosinusitis with Nasal Polyposis (CRSwNP)

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Clinical Discussions with:



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Overview of Chronic Rhinosinusitis with Nasal Polyposis (CRSwNP) and Disease Burden

Chronic rhinosinusitis with nasal polyposis (CRSwNP) is a chronic inflammatory disease that can affect quality of life.¹ It is characterized by the development of polypoid growths that start in the sinus and eventually extend into the nose, resulting in persistent symptoms such as congestion, stuffiness, nasal discharge, pain or facial pressure, impairment or loss of sense of smell, and fatigue.^{2,3} Patients with CRSwNP represent only 20% to 25% of the CRS population but have more severe disease and consume more healthcare resources.³⁻⁷

Nasal polyps are believed to arise in the nasal mucosa due to the contribution of chronic type 2 inflammation.^{1,2} Activated epithelial cells and type 2 inflammatory cytokines—including interleukin (IL)-4, IL-5, and IL-13—as well as local immunoglobulin E (IgE) contribute to the persistent underlying inflammation associated with the development of CRSwNP.⁸⁻¹⁰ In addition, CRSwNP is often associated with other atopic comorbidities driven by type 2 inflammation, including allergic rhinitis (~66%) and asthma (~55%).^{11,12} In patients with chronic inflammation, the risk for nasal polyps increases significantly in the presence of inflammatory bowel disease (17.5%), atopic dermatitis (16.5%), and asthma (22%).¹¹

Patients with CRSwNP often have reduced quality of life because of an impaired sense of smell, and they may face other comorbid conditions. A retrospective analysis of data from the National Comparative Audit of Surgery for Nasal Polyposis and Chronic Rhinosinusitis found that nasal congestion was the most prevalent individual symptom (93.5%) associated with CRSwNP. Subsequently, the third most prevalent symptom was waking up tired (69.9%), as patients with this CRSwNP often suffer from sleep disturbances and a lack of sleep.¹³

Cost Considerations

In a 2015 study, researchers sought to estimate the cost burden of CRSwNP. They systematically searched eight

commonly used medical databases and categorized 44 articles based on seven domains: overall healthcare cost (direct and indirect), resource utilization, medical management strategies, overall procedure cost of endoscopic sinus surgery (ESS), intraoperative technologies, ESS litigation, and diagnostics. Overall CRSwNP-related healthcare costs ranged from \$6.9 billion to \$9.9 billion in 2014 U.S. dollars. The authors reported “substantial” direct and indirect costs related to this condition.¹⁴

More recently, an observational, retrospective, case-control study published in 2019 used the Truven Health MarketScan U.S. claims database to determine costs associated with CRSwNP. While patients undergoing surgery have the highest mean per-patient per year cost (\$26,000), even patients with CRSwNP who do not undergo surgery have a significant cost burden (\$13,000).¹⁵

Treatment Considerations for CRSwNP

Some treatment options for patients with CRSwNP can include nasal saline and steroid irrigation, maintenance intranasal corticosteroids, antibiotics, oral corticosteroids, and surgery.² While short-term (1–3 weeks) use of oral corticosteroids can reduce the polyp size and improve patient symptoms, the benefits subside when steroids are tapered off. A literature review assessed randomized, controlled trials comparing a short course (up to 21 days) of oral corticosteroids with placebo or no treatment. The researchers found that corticosteroids increased the risk for gastrointestinal disturbances (risk ratio [RR], 3.45; 95% confidence interval [CI], 1.11–10.78) and insomnia (RR, 3.63; 95% CI, 1.10–11.95) compared with placebo or no treatment.^{16,17}

The British Society for Allergy & Clinical Immunology guidelines on the management of rhinosinusitis and CRSwNP advise that oral corticosteroids should be used briefly (for 5–10 days). According to the guidelines, “Oral corticosteroids should be used briefly and always in combination with a

topical nasal corticosteroid. A suggested regimen for adults is 0.5 mg/kg given orally in the morning for 5–10 days and is used for: severe nasal obstruction, short-term rescue medication for uncontrolled symptoms on conventional pharmacotherapy, [and] medical polypectomy.” Long-term exposure to oral corticosteroids can result in adverse events and is not recommended.¹⁶⁻¹⁹

Once traditional treatment options no longer provide benefit due to symptom persistence and polyp recurrence, many patients will undergo surgery, during which the polyps are removed and paranasal sinuses are cleared of inflamed edematous tissue. However, following surgery, some patients may fail to achieve long-term control due to further polyp recurrence and persistent symptoms (see **FIGURE**).^{1,2}

An Unmet Need

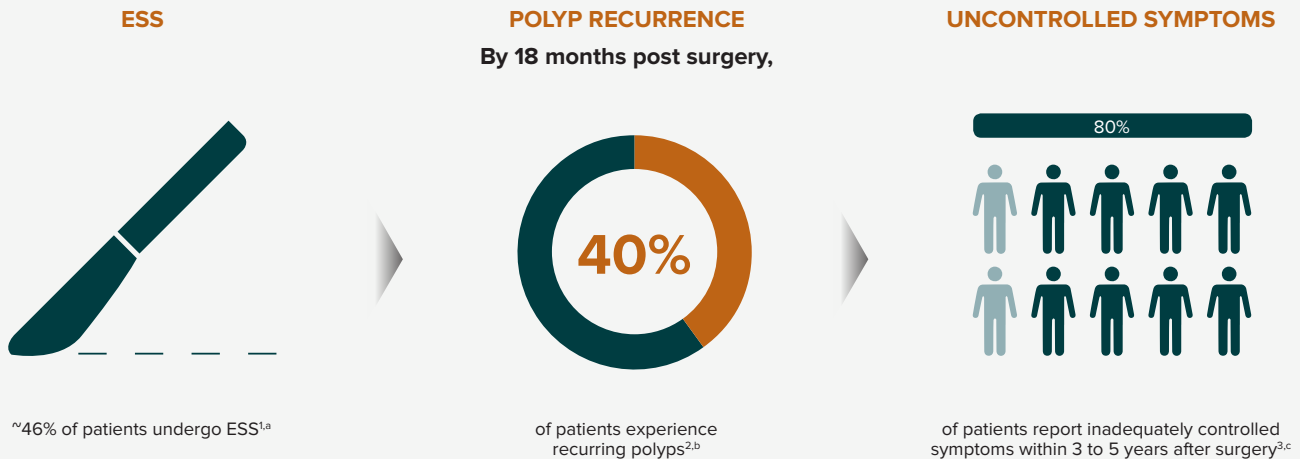
A small portion of the CRSwNP population is in need of a nonsurgical option. Approximately 90,000 patients are uncontrolled despite recent oral corticosteroids or prior surgery and approximately 55,000 are uncontrolled despite prior surgery.^{20,21} The GALEN study found that 59% of patients who undergo surgery will undergo revision surgery, and nearly 23% of patients will undergo four or more revision surgeries.¹

A prospective, multicenter cohort study found that polyp recurrence is common after surgery: Polyps recurred after approximately 18 months in an estimated 40% of patients. Surgical removal of nasal polyps and inflamed sinus mucosal tissue does not address the cause of the underlying inflammation and processes leading to polyp formation, thus polyps recur, and revision surgery is often needed.¹⁰

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FIGURE. Many Patients Fail to Achieve Long-Term Control

After ESS, polyp recurrence and persistent symptoms continue to impact patients' lives and healthcare services



ESS, endoscopic sinus surgery

^aA total of 869 patients from the Global Allergy and Asthma European Network (GALEN) study;¹ ^bProspective, multicenter cohort of adult patients undergoing ESS for medically recalcitrant CRSwNP performed between August 2004 and February 2015. N=197 and N=129 at 6 and 18 months, respectively;² ^cThe levels of control corresponded to mean total VAS (visual analog scale), SNOT-22 (sinonasal symptoms, sinonasal outcome test), and SF-36 (short form) scores (n=389). Inadequately controlled patients were partially controlled or not controlled.³

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“CRSwNP is a disease with high burden to the patient and the society; however, tools to define disease severity and identify factors impacting on pharmacoeconomics are not well defined yet. The influence of disease subtype and patterns of inflammation and comorbidities on burden and costs need to be defined, and treatment approaches need to be evaluated

in terms of appropriateness,” according to the International Consensus (ICON) on Chronic Rhinosinusitis, a collaborative statement from the International Collaboration in Asthma, Allergy and Immunology. Additional treatment options are needed for this patient population.²²

Clinical Insights



William W. Busse, MD, professor of medicine in the Section of Allergy, Pulmonary, and Critical Care Medicine at the University of Wisconsin School of Medicine and Public Health, provides insights on CRSwNP from a clinical perspective.

Q: Can you discuss the treatment approach for patients with CRSwNP? As disease severity and symptoms progress, what are patients' options?

A: This is a disease that occurs very frequently in conjunction with asthma, and it has very significant healthcare burdens for patients. People do not feel well, and they have repetitive episodes of what appear to be sinus infections. They have difficulty with their sense of smell and nasal congestion. They don't sleep well at night. The condition can significantly interfere with their normal lifestyle and compromises well-being.

The way to approach this problem has been considerably difficult. Currently, we don't know why patients develop nasal polyps. Current treatment consists, primarily, of topical application of nasal corticosteroids at baseline, but this approach has a limited benefit. Despite the use of topical nasal steroids, which may be effective in rhinosinusitis and other conditions of the nose, they do not seem to have much of an effect on the size of the nasal polyps.

Thus, other forms of treatment are required, and this often consists of systemic corticosteroids, which can lead to a reduction in the size of the nasal polyps, return of sense of smell and taste, and provide a general feeling of symptom relief. However, polyps persist, and the occurrence rate can be quite variable.

Because of this, surgery is often required, and patients need repetitive

episodes of corticosteroids to control the polyp growth. Surgery can provide symptom relief, but for many of these individuals, the polyps reoccur. Overall, the treatment options are very limited.

Q: Are there any concerns with or limits to how often patients can be treated with corticosteroids? Are there any risk factors with using these agents in the long term?

A: There are considerable risks with long-term use or even repetitive short-term use of corticosteroids. The repetitive use of systemic corticosteroids puts patients at risk for other diseases like diabetes, loss of bone mineralization, and hypertension.²³ Most of us feel there should be a time limit on the frequency with which patients use corticosteroids.

Q: Will patients experience a difference in disease management or treatment if they are seen by an allergist versus and ENT (ear, nose, and throat) specialist?

A: It is highly dependent upon the medical practice situation. I'm an allergist, and we don't perform surgery. It's a stepwise approach—usually an allergist sees the patient first, then in conjunction with a consultation with an ENT surgeon. In my practice, we work very closely with our otolaryngologist. Since our current forms of treatment are limited, we will refer the patient to an ENT for the consideration of surgery.

“CRSwNP can be very insidious, but it can have a profound effect, so awareness is key. Many patients go for a length of time without receiving care and tend to live with this for extended periods of time.”

—William W. Busse, MD

Q: As you mentioned, CRSwNP is associated with other atopic comorbidities such as asthma. Does this complicate or change patient treatment or management?

A: I think the data strongly indicate that the association of CRSwNP and asthma is a very distinct phenotype in patients with asthma. These individuals tend to have more severe disease and require a higher dosage of medications to control their asthma. Through mechanisms that are not entirely clear, the presence of CRSwNP with asthma leads to disease that is more difficult to treat and tends to have greater disease morbidity.

Q: Can you describe the surgical approach for patients with CRSwNP?

A: I'm not a surgeon, but I think the surgical approach is highly variable

depending upon the extensiveness of the nasal polyps and the experience of the ENT surgeon. Some surgeons tend to use an apparatus that attaches to the polyps, pulls them down, and pulverizes them. I think this allows for more extensive removal of the polyps. It seems to be a more extensive procedure as far as long-term benefits. Another approach that seems to be safe is where the polyps are resected.

Q: How often and why do patients sometimes experience recurrence after surgery?

A: The major problem is that polyps can reoccur, and the majority of patients undergo multiple surgeries. Over the years, I've had patients who have required 15 to 20 polyp removals. These are extreme cases, but I think they underline the problem with nasal

polyps. Repetitive surgeries can lead to increased risks. The benefits of doing surgery becomes more limited with each subsequent surgery.

Our understanding of this is very limited. We don't know why polyps develop or recur. We do know there is a type 2 inflammatory process that begins in the sinuses, extends to the nasal passages, and causes blockage.

Q: How does this disease affect patients?

A: This is a disease with tremendous morbidity. Patients just don't feel well. This really interferes with a normal lifestyle. It also interferes with sleep patterns, and these patients are profoundly fatigued as a consequence.

I think this condition tends to be underdiagnosed, and recognition of it is important. Physicians must take a look in the patient's nose and recognize any polyps in there. One of the heralding symptoms of this condition is a loss of smell.

CRSwNP can be very insidious, but it can have a profound effect, so awareness is key. Many patients go for a length of time without receiving care and tend to live with this for extended periods of time.

From the Payer Side



Edmund Pezalla, MD, MPH, founder and CEO of Enlightenment Bioconsult, LLC, and former vice president of pharmaceutical policy and strategy at Aetna, provides insights on CRSwNP from a payer perspective.

Q: Can you discuss the treatment options for patients with CRSwNP? What are the benefits and challenges associated with the different treatment options from a payer perspective?

A: The treatment has two parts. One is the treatment of the polyps themselves, which can be done with nasal or oral steroids. This seems to be the usual first-line approach. In addition, CRSwNP can occur with chronic rhinosinusitis, partly due to blockage of appropriate drainage. This too can be

treated with steroids and sometimes antibiotics if there is also a suspected infection. However, this doesn't have any impact on the polyps and doesn't treat the underlying problem.

In terms of surgical options, you could either remove the polyps or you can remove them and also do sinus drainage and open up the sinus passages, which is a broader procedure.

There are one or two nasal steroid products that are indicated for this condition. They are relatively inexpensive

and nowhere near as invasive as surgery. The same goes for the oral steroids. We don't want patients on oral steroids for a long time, but a brief exposure to a high-enough dose can improve the situation.

However, these medical treatments are temporary, and the polyps don't always go away. A surgical approach can have longer-lasting outcomes, but the need for subsequent surgery is high in this setting.

such as functional ESS can be more invasive and expensive, and patients' recovery is longer, which may result in the need for additional medication and added costs.

Q: For patients who undergo one or more revision surgeries, what is the budget impact?

A: Patients tend to get more extensive subsequent surgeries. A secondary

These patients have various allergy symptoms, so if you're treating all of these things, you should look to reduce the amount of drugs patients receive. You don't want patients overdoing it on steroids.

Q: What are your recommended goals for long-term management of this patient population?

A: Payers generally don't have guidelines for treatment. We have endorsed the GINA (Global Initiative for Asthma) guidelines for asthma, and we assume that surgeons follow guidelines from the appropriate surgical societies in terms of treatment algorithm and type of surgery.

The goal for patients with CRSwNP is to have basically no symptoms. We want patients to be able to breathe normally and not have recurrent sinus infections or chronic rhinitis. For patients who also have asthma, we want to see a reduction in exacerbations, an improvement in pulmonary function, and fewer episodes of emergency care. ●

“Patients tend to get more extensive subsequent surgeries. A secondary surgery can take longer and be more difficult, which requires additional insurance codes.”

—Edmund Pezalla, MD, MPH

Q: What are the costs associated with patient management and the treatment options for CRSwNP?

A: From a payer point of view, there are the usual costs associated with diagnosis and early management. Primary care physicians are familiar with nasal and oral steroids. At the start, there are costs related to doctor visits, radiographs, or X-rays of the sinuses, as well as the cost of steroids and antibiotics. So far, none of this is too expensive, but it's starting to add up.

What happens more often is that the patient doesn't get better. They then go to see an ENT who does an endoscopy and is now considering surgical options. They might try the steroids again, but they're also doing more X-rays, a magnetic resonance imaging scan, or a computed tomography scan. Now the diagnostic costs are starting to add up.

There are different kinds of surgical options. A polypectomy is relatively inexpensive, and patients recover fairly quickly. But other sinus surgeries

surgery can take longer and be more difficult, which requires additional insurance codes. It's always harder to go in and do a revision. For patients with chronic disease, it becomes more difficult and expensive.

Q: Often, patients have other inflammatory conditions like asthma. How are patients with both conditions managed?

A: There are multiple overlapping symptoms that can make it difficult to control the asthma.

Patients with asthma are often treated with some form of steroids. They may also receive inhaled corticosteroids plus a long-acting beta-agonist or leukotriene inhibitor. There are some generic options, but many of these agents are branded, so it can be expensive to treat these patients.

It's not clear whether treating the polyps will improve asthma control, but for some patients, reducing the chronic sinusitis probably has an impact. Together, these conditions start to become more expensive.

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Dr. Busse is a professor of medicine in the Section of Allergy, Pulmonary, and Critical Care Medicine at the University of Wisconsin School of Medicine and Public Health. Dr. Busse's research has focused on the mechanism of asthma with particular interests in eosinophilic inflammation and rhinovirus-induced asthma for which he has had long-standing National Institutes of Health support, as well as lung-brain interactions in asthma. He is a diplomat of the American Board of Internal Medicine and American Board of Allergy and Clinical Immunology. Dr. Busse received the Folkert Belzer Life Achievement Award in 2004, the American Thoracic Society Award for Scientific Accomplishments in 2005, the Citation Award for Achievement from the University of Wisconsin School of Medicine and Public Health in 2008, and the American Thoracic Society Foundation Breathing for Life Award in 2014.

Dr. Pezalla is the founder and chief executive officer of Enlightenment Bioconsult, LLC, a strategic payer consultancy advising biopharmaceutical firm on access, technology assessment, and drug evaluation in the U.S. market. His clients include established pharmaceutical firms and emerging companies with innovative therapies. Dr. Pezalla served nine years as vice president of pharmaceutical policy and strategy for Aetna and four years as vice president of clinical services for RxSolutions. He is a member of the MIT Center for Biomedical Innovation NEW Drug Development ParadIGmS project and was a member of the inaugural class of scholars-in-residence at the Duke-Margolis Center for Health Policy.

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