

Economics of Chronic Rhinosinusitis

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Published online: 23 March 2017
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Abstract

Purpose of Review The objective of this article is to provide an updated review of the economic burden of chronic rhinosinusitis (CRS) and discuss how both medical and surgical interventions impact direct and indirect costs related to CRS. By understanding the economics of CRS, clinicians may improve the patient-centeredness of their care and help distinguish between low and high value interventions.

Recent Findings Direct costs related to CRS are primarily driven by outpatient physician visits, prescription medical therapy, and endoscopic sinus surgery (ESS). CRS produces large indirect costs and these costs often vary based on the severity of the patients CRS-specific QoL impairment. The overall direct cost related to CRS is estimated to range between \$10 and \$13 billion per year in the USA. The overall indirect cost related to CRS-related losses in work productivity is estimated to be in excess of \$20 billion per year.

Summary In the appropriate patients with refractory CRS, ESS provides significant reductions in both direct and indirect costs; however, continued medical therapy alone may be a high value intervention in select patients who have lower severity in their baseline QoL and work productivity.

Keywords Chronic sinusitis · Rhinosinusitis · Pharmacoeconomics · Cost · Economic · Burden of disease · Value of care

This article is part of the Topical Collection on *Rhinosinusitis*

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Introduction

Chronic rhinosinusitis (CRS) is a complex, heterogeneous inflammatory disease of the sinonasal cavities producing variable phenotypic severity profiles [1, 2]. A successful management plan for CRS often requires combinations of both topical and systemic medical therapies, and in select refractory cases, need for adjunctive surgery [3•, 4]. While CRS has been shown to have negative impacts on sinonasal symptoms [5], sleep [6], mood [7], and lower airway function [8], the primary patient-centered clinical endpoints of CRS are reductions in quality of life (QoL) [9] and work productivity [10]. Therefore, CRS not only has large direct treatment-related health care costs but also has substantial indirect costs to society resulting from lost work capabilities [11].

The purpose of this review is to highlight the economic burden of CRS along with the economic impact of both medical and surgical treatments. By understanding the economics of CRS, physicians may improve the value of care by appropriately utilizing scarce health care resources in the correct patient within an optimal time period [12, 13].

Burden of Disease: Prevalence Rate of CRS

Given that the diagnosis of CRS involves demonstration of both subjective symptom criteria and objective evidence of inflammation within the paranasal sinuses, there is no single diagnostic test that can be collected and quantified to provide an accurate diagnosis. This makes it challenging to define an accurate prevalence rate for CRS since determination depends on either population-based survey responses or administrative database coding, both of which have diagnostic limitations.

Prevalence estimates for CRS obtained from population-based survey responses may inappropriately increase the true prevalence rate since current evidence suggests that approximately 40 to 50% of “self-reported” CRS lacks objective evidence of inflammation using CT imaging and therefore do not have guideline-based CRS [14, 15]. Prevalence estimates obtained from using case definitions for CRS within administrative databases can also be flawed since the accuracy of diagnosis and coding at the primary care and emergency care level has been shown to be inaccurate [16–18]. Given these limitations, it is not surprising that currently reported prevalence estimates of CRS vary widely between 1 and 12% [19–22].

Five large population-based survey studies have assessed the prevalence of CRS [20, 22–25]. In 2003, a Canadian study surveyed 73,364 people and asked “if they have sinusitis diagnosed by a health professional.” The reported prevalence of CRS was 3.4% in males and 5.7% in females, but this study failed to discriminate between acute and chronic forms of rhinosinusitis and therefore likely overestimates the true prevalence of CRS. In 2011, the Global Allergy and Asthma European Network (GA²LEN) applied a strict symptom-based approach using the European Position Paper on Rhinosinusitis and nasal Polyps (EPOS) diagnostic criteria [26] to estimate the prevalence of CRS in Europe. This study surveyed 57,128 people from 12 European countries and reported a mean prevalence of CRS of 10.9% (range 6.9 to 27.1%) [20]. In 2011, Bhattacharyya evaluated the US-based Medical Expenditure Panel Survey (MEPS) database and reported a CRS prevalence rate of 4.9% [24]. In 2012, Pilan et al. surveyed and interviewed 2003 people within the Brazilian population and reported a CRS prevalence rate of 5.5% [25]. In 2014, Brackwell et al. published the summary of health statistics for US adults using a population-based survey delivered in 2012. “Sinusitis” was the ninth most condition in the USA with a prevalence rate of 12.1% [22]. However, apart from limitations in accuracy of diagnosing sinusitis based on patient-reported survey responses, the survey failed to differentiate between CRS and other forms of sinusitis such as acute viral and ABRS. Given the lack of demonstrated objective evidence of inflammation during survey responses, the mean rates from 3.4 and 12.1% may be overestimating the true prevalence of CRS.

From an economic perspective of the health care system, the prevalence rate obtained from administrative databases may provide a more accurate estimate for burden of disease since it only includes patients who utilize the health care system specifically for their CRS. In 2011, Bhattacharyya et al. evaluated the US-based MarketScan administrative database and reported a CRS prevalence rate of 2.3% [27]. In 2016, Xu et al. evaluated a Canadian-based administrative database and demonstrated that the prevalence of CRS seeking medical care was 2 to 3% [21]. In 2016, Akkina et al. evaluated an academic university health system database and reported a CRS prevalence rate of 1% [28].

While there are limitations with both population-based survey and administrative database approaches, evidence supports that the prevalence of CRS within the health care system is more accurately reported between 1 and 2.5% and the prevalence of CRS within the population may potentially reach a rate of 12% (Table 1).

Direct Costs of CRS

Direct costs refer to health care resources that are consumed to produce a unit of health output [29]. Between 1996 and 2013 in the USA, chronic upper respiratory diseases (as defined by CRS, allergic rhinitis, and sleep apnea) accounted for \$34.7 billion per year in health care costs (22nd overall) and were more costly than septicemia (\$33.9 billion per year; 23rd overall), asthma (\$32.5 billion per year; 24th overall), colorectal cancer (\$18.5 billion per year; 36th overall), and otitis media (\$8.8 billion per year; 55th most costly) [30].

When specifically evaluating CRS, direct costs tend to focus around three domains of resource consumption: (1) outpatient physician visits, (2) prescription medical therapy, and (3) surgery [31•]. Several studies have evaluated the overall direct cost of CRS, and the 2016 adjusted estimates appear to range between \$10 and \$13 billion per year in the USA (Fig. 1). In 2011, Bhattacharyya evaluated the US-based MEPS database and reported the overall direct cost of CRS to be approximately \$8.6 billion in 2008 USD (\$11.1 billion 2016 USD) [24]. In 2015, Caulley et al. evaluated the MEPS database and applied four different methods of estimation to quantify overall direct cost of CRS [31•]. Depending on which method was used to obtain cost estimates, the overall direct cost attributed to CRS approached \$12.5 billion per year in the USA.

Evaluating incremental direct costs is important to determine the cost directly attributable to a specific disease. Two recent studies took an incremental approach and quantified the direct cost specifically attributed to the management of CRS [24, 31•]. Both studies reported a similar incremental overall direct cost of managing CRS, which was approximately \$800 per patient per year (range \$772 and \$818) [24, 31•]. Outpatient physician visits accounted for the largest proportion of incremental direct costs (range \$346 and \$503 per year), followed by prescription medical therapy (incremental cost range \$397 to \$403 per year) (Fig. 1). Since emergency room visits and inpatient care are less common in the natural care cycle of CRS, incremental direct costs attributed to these resources were minimal, \$33 and –\$106 per patient per year, respectively [31•].

Surgical interventions represent a large direct cost to any health care system, and there is a call for surgeons to improve the appropriateness of surgical care in order to improve the value of health care delivery [32, 33]. Although not all patients with CRS require surgery, it is well accepted that endoscopic sinus surgery (ESS) can provide significant short- and long-

Table 1 Summary of prevalence rates for CRS

Study design	Country	Study (year)	Perspective	Prevalence rate of CRS
Administrative database	USA	Bhattacharyya et al. (2011) [27]	US health care system	2.3%
	USA	Akkina et al. (2016) [28]	Academic health care system	1.0%
	Canada	Xu et al. (2016) [21]	Canadian health care system	2.5%
Population-based survey	Canada	Chen et al. (2003) [23]	Canadian population	3.4% males and 5.7% females
	Europe	Hasten et al. (2011) [20]	European population	10.9%
	USA	Bhattacharyya (2011) [24]	US population	4.9%
	Brazil	Pilan et al. (2012) [25]	Brazilian population	5.5%
	USA	Blackwell et al. (2014) [22]	US population	12.1%

CRS chronic rhinosinusitis

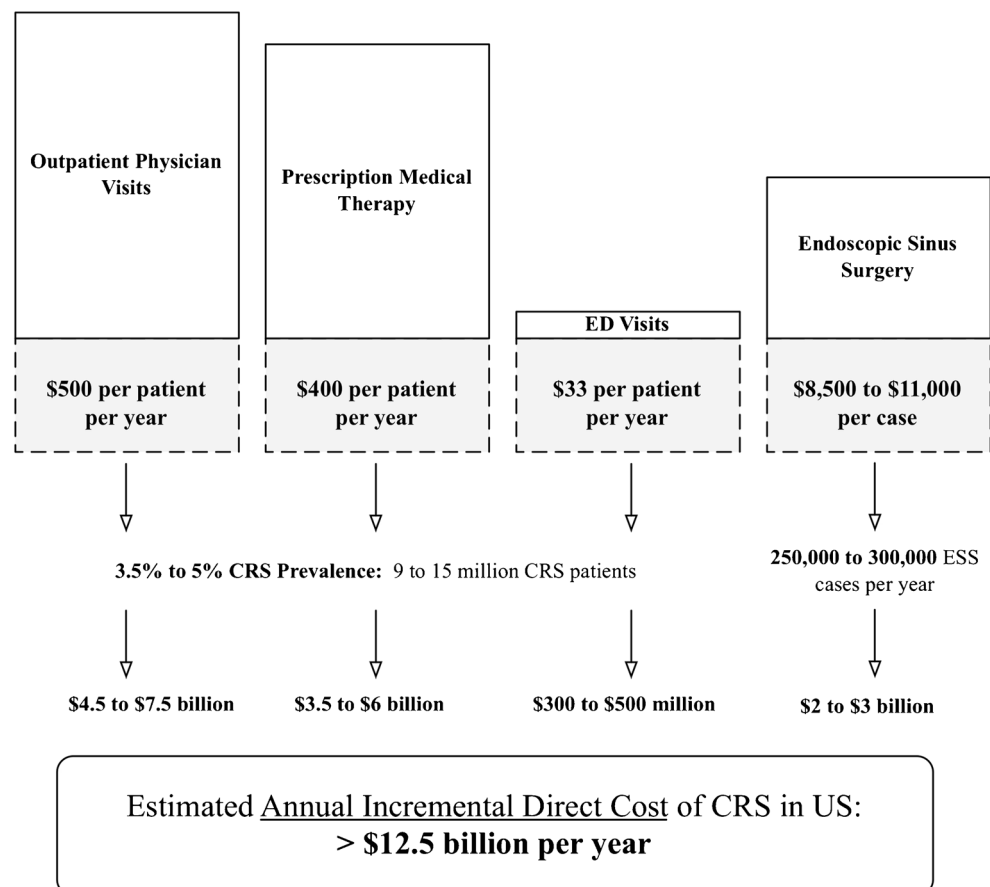
term benefit to patients with refractory CRS [34–36]. With over 250,000 ESS cases performed in the USA each year, ESS represents a large direct cost to the health care system. Several studies have quantified the direct cost of ESS from the perspective of different health care systems [37–46]. Based on the evidence, the direct cost of ESS in the USA ranges between \$8500 and \$11,000 2016 USD. When the cost of ESS was examined from the perspective of the Canadian, Taiwan, and Indian health care systems, the direct cost of ESS was lower with estimates reported to be \$3700, \$1900, and \$1100 2016 USD, respectively. Since the cost of ESS varied

widely between countries, it is important for future economic evaluations to include ESS costs that are specific to their local health care system.

Indirect Costs of CRS

Indirect costs are lost resources that are not the result of producing a unit of health output [29]. Indirect costs are commonly referred to as “productivity costs” since they typically result from lost work in the form of absenteeism (missed work) and

Fig. 1 Estimated annual incremental direct costs attributed to CRS in the USA



presenteeism (reduced productivity while at work). The primary disadvantage of lost work productivity is the reduction in how well a society uses its population inputs to produce usable outputs such as goods and services [47]. Therefore, the success of a given society is often linked to the health and functioning of its population. This makes work productivity an important clinical outcome to both assess and improve.

CRS tends to affect patients within their most productive work years between the ages of 30 and 50 years old. Therefore, the societal impacts of CRS tend to be large compared to other chronic diseases, such as osteoarthritis or macular degeneration, that tend to impact patients beyond their productive work years.

Three studies have evaluated the baseline indirect costs of CRS [48, 49, 50•]. In 2009 and 2012, Bhattacharyya evaluated two different national US-based administrative databases and quantified the baseline work impairment associated with CRS. On a population level, patients with CRS reported a mean absenteeism rate of 5.8 work days [48] and have an incremental increase of 1 work day missed per year compared to non-CRS-matched patients [49]. It is important to note that the CRS cohorts evaluated by Bhattacharyya included all patients with CRS and therefore will include a large proportion of patients with less severe phenotypes of CRS who were managed by primary care physicians and not referred for otolaryngology consultation. Including a large cohort of patients with less severe CRS will inherently produce a mean absenteeism that is better compared to CRS patients managed within otolaryngology practices. In 2014, Rudmik et al. prospectively evaluated a more select group of CRS patients, who were referred for otolaryngology consultation for failed medical therapy and were considered candidates for ESS. Outcomes from this more severe phenotypic cohort of patients with CRS demonstrated significantly larger indirect costs with a mean annual absenteeism and presenteeism rate of 25 and 40 days per patient, respectively. After applying a standard mean US annual wage rate, the annual indirect cost was \$10,077 per patient with refractory CRS [50•]. Furthermore, this study demonstrated that the degree of productivity cost was significantly associated with the degree of patient QoL impairment (i.e., larger QoL impairment being associated with larger productivity losses).

Overall, the degree of indirect costs related to CRS appears to be related to the phenotypic severity of CRS. Specifically, when productivity costs were evaluated on a population level, which included a majority of patients with milder phenotypes who do not receive ESS, the annual mean days missed from work is estimated to be 6 days [49]. This is in contrast to patients missing over 20 days per year in a cohort of patients with refractory CRS who had larger baseline reductions in their QoL and chose to undergo ESS [50•]. The indirect costs related to CRS are estimated to be in excess of \$20 billion per year in the USA (Fig. 2).

Medical Therapy Versus Endoscopic Sinus Surgery for CRS

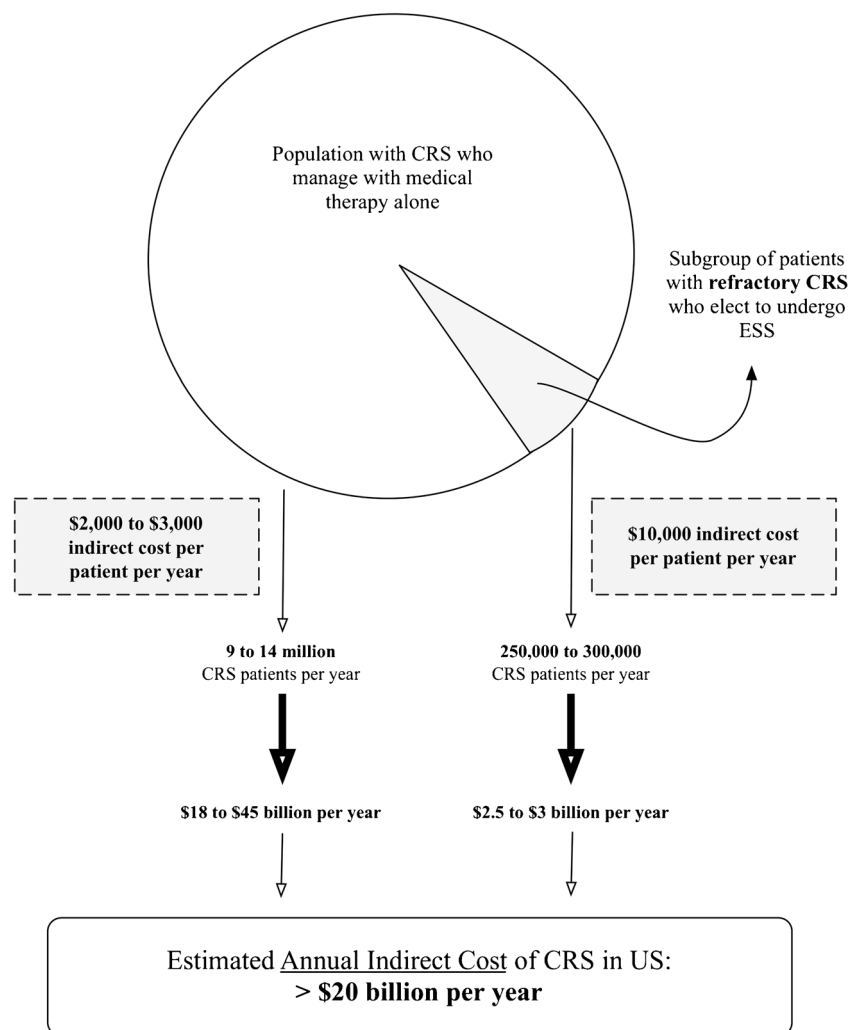
The goals of any successful management plan for CRS include reducing sinonasal mucosal inflammation and reconstitute normal physiologic function of the paranasal sinuses in order to improve patient quality of life and daily productivity. While there are a variety of treatment options for CRS [3•], the patient and physician are often faced with deciding between two broad management options: (1) continue with medical therapies alone or (2) perform ESS followed by post-operative medical therapy.

Based on the best available evidence, there is a subset of patients with CRS who will benefit from medical therapy alone, which is defined as patients receiving similar symptom and QoL improvements compared to those patients who receive ESS. For example, in a randomized trial in 2005, Alobid et al. demonstrated that CRS patients with large nasal polyps who were treated with a short course of oral corticosteroids followed by daily topical corticosteroid received similar clinical improvements to those patients who received ESS followed post-operative topical corticosteroids [51]. However, there remains a cohort of CRS patients who fail to improve with medical therapy alone [52, 53]. While predictive factors for treatment success continue to be evaluated, it appears that CRS patients with minimal impairment in their baseline QoL and work productivity may represent the most appropriate cohort to recommend medical therapy alone [54].

While the clinical effectiveness of ESS in the correct patient with medically refractory CRS is not controversial [36, 55], current indications for ESS are less defined and continue to be a topic of debate [56, 57]. To help reduce the uncertainty surrounding indications for ESS and improve the surgical decision-making process, recent appropriateness criteria for ESS in patients with uncomplicated CRS have been developed [58•]. Based on these criteria, an appropriate patient for ESS requires a minimum degree of quality of life impairment (SNOT-22 score >20), failed trial of defined medical therapies, and objective evidence of inflammation within the paranasal sinuses using computed tomography. While these criteria will continue to be refined based on new research, the criteria function to help select CRS patients who have the highest probability of receiving a successful outcome with surgery. This section will review the economic impact of providing either continued medical therapy alone or ESS during management of CRS.

Impact on Direct Costs

Reducing direct costs of health care, without negatively impacting clinical outcomes, is one strategy to improve value of care [59]. Several studies have evaluated how CRS-specific direct costs change after ESS [27, 44, 60, 61]. All studies have

Fig. 2 Estimated annual indirect cost related to CRS in the USA

shown that CRS-specific direct costs are reduced after ESS, and this outcome appears to be primarily driven by reductions in medication and physician visit utilization. After adjusting monetary outcomes for year of study design, the evidence supports that the mean preoperative annual direct cost of \$1500 to \$2700 per patient becomes reduced to a mean annual post-operative cost of \$600 to \$1200 per patient.

There have been no formal studies evaluating the change in CRS-specific direct costs before and after continued medical therapy alone. Despite the lack of evidence on this topic, it may be hypothesized that when medical therapy alone is able to successfully control a patient's QoL, then the baseline direct costs associated with their CRS management will remain stable. Future studies will need to evaluate how direct costs are impacted when CRS patients choose continued medical therapy alone.

Impact on Indirect Costs

As discussed earlier, it is important that clinical interventions reduce indirect costs in order to optimize the performance of a

society. Several studies have evaluated how both medical and surgical interventions impact indirect costs related to CRS [62–66]. In 2014, given prolonged elective surgical waitlists in Canada, Smith et al. was able to prospectively evaluate the impact of continued medical therapy alone in CRS patients who choose ESS but had to wait for surgery [53]. This study design provided a unique evaluation of continued medical therapy alone in a group of CRS patients with severe baseline reductions in QoL and work productivity who would typically undergo surgery within a couple months in other health care systems, such as the USA. After a mean of 6 months of continued medical therapy alone while waiting for ESS, the results demonstrated that work productivity significantly worsened (mean of 2.5 to 6.1 work days missed in last 90 days, $p = 0.02$). The follow-up study by Smith et al. demonstrated that when this same cohort of CRS patients received ESS, the work productivity significantly improved (mean of 6.1 to 0.2 work days missed in last 90 days, $p < 0.001$) [67].

In 2015, Rudmik et al. performed a prospective observational study that evaluated 38 patients with refractory CRS who made a preference-based decision to continue with

medical therapy alone [63]. The mean baseline annual indirect cost related to CRS in this cohort was \$3464 per patient. After continued medical therapy for a mean of 13 months, there was no significant change in the indirect costs (\$3464 compared to \$2730; $p = 0.736$). In 2016, Rudmik et al. prospectively evaluated the indirect costs in 27 patients with refractory CRS who made a preference-based decision to receive ESS [64]. In contrast to CRS patients who chose continued medical therapy, patients who choose to receive ESS had larger baseline indirect costs (\$9097 per patient). After a mean follow-up of 15 months after ESS, there was a significant reduction in the mean annual indirect cost from \$9097 to \$3301 per patient (annual net societal benefit of \$5796 per patient).

The outcomes from these studies highlight several important points. First, patient treatment selection appears to be associated with the severity of their baseline productivity impairment. Specifically, patients with better baseline work productivity (i.e., lower indirect costs) tended to select continued medical therapy alone as opposed to patients who had lower work productivity (i.e., high indirect costs) tended to select ESS. This is important because assessing the severity of baseline productivity impairment may assist clinicians in providing care that is focused on patient preferences for treatment.

A second important finding was that the severity of baseline productivity impairment helped to predict treatment success from either continued medical therapy alone or ESS. Specifically, patients who had better baseline

productivity were effectively managed with continued medical therapy alone, meaning their productivity level was maintained and did not get worse. Meanwhile, patients with poor baseline productivity got worse with continued medical therapy alone and then received significant improvements in productivity after undergoing ESS (Fig. 3). The relationship between baseline level of productivity impairment and degree of treatment success from either continued medical therapy alone or ESS was confirmed by two recent prospective studies [53, 67] and a recent cluster analysis study [68].

Lastly, the evidence supports a need to continue developing novel and targeted medical therapy interventions for patients with CRS. Specifically, despite CRS patients receiving the best available medical and surgical interventions, there were persistent post-treatment annual indirect costs of approximately \$2000 to \$3000 per patient. Current work on defining endotypes and development of novel biologic therapies may facilitate improved precision medicine for management of CRS [69–72].

In summary, CRS often reduces a patient's ability to function at work, and this creates indirect costs to society. The best available evidence suggests that the impact of ESS versus continued medical therapy alone on indirect costs often depends on the severity of the patients' baseline productivity level. Assessing the severity of productivity impairment may assist clinicians in counseling patients to their expected treatment outcomes and improve patient-centered care for CRS.

Fig. 3 Impact of medical therapy alone and ESS on indirect costs (work productivity) for CRS

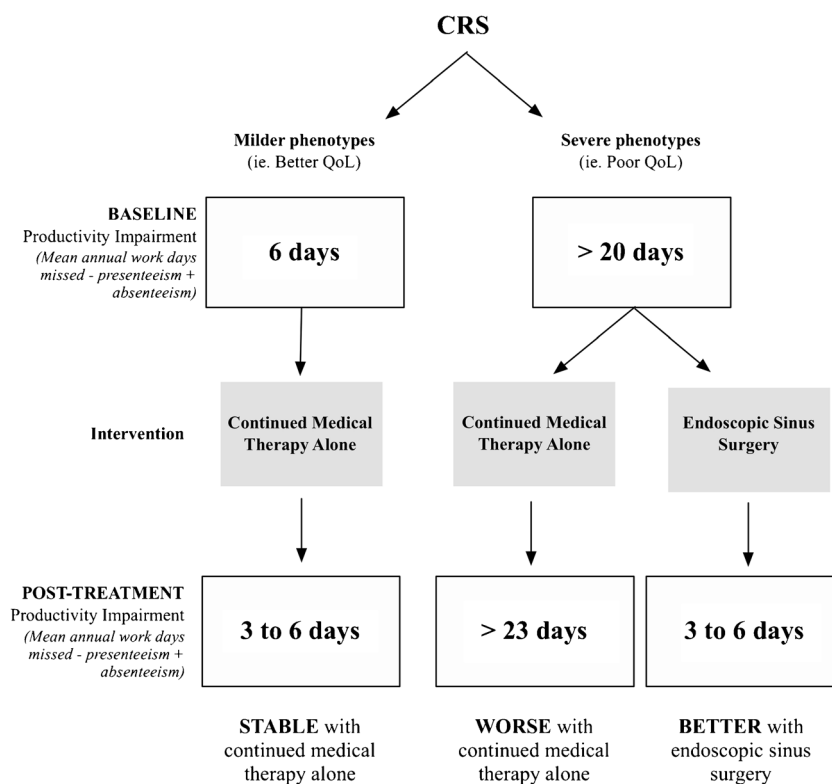


Table 2 Summary of economic evaluations for ESS versus continued medical therapy alone for refractory CRS

Study/year	Economic perspective	Methodology	Time horizon	Reference case discounting	Reference case ICER ^a	Certainty of outcomes based on PSA
Rudmik et al. 2015 [76]	US third-party payer	Markov decision-tree model	30 years	Cost = 3.5% Effectiveness = 0%	\$5901/QALY	74%
Scangas et al. 2016 [75]	US third-party payer	Markov decision-tree model	31 years	Cost = 3% Effectiveness = 3%	\$13,851/QALY	98%
Scangas et al. 2017 [74]	US third-party payer	Markov decision-tree model	36 years	Cost = 3% Effectiveness = 3%	\$5687/QALY	95%

ICER incremental cost-effectiveness ratio, PSA probabilistic sensitivity analysis, QALY quality-adjusted life year

^a The ICER represents the incremental costs (i.e., cost of the ESS treatment strategy – cost of the medical therapy-alone treatment strategy) divided by the incremental effectiveness (i.e., total number of QALYs from ESS treatment strategy – total number of QALYs from medical therapy-alone strategy). Therefore, the ICER represents the additional cost to obtain one additional QALY from using an ESS treatment strategy compared to medical therapy alone for CRS

Economic Evaluation: Incremental Cost-Effectiveness Ratio

To ensure that cost reduction strategies do not compromise quality of care, the costs of interventions should be put into context with the clinical benefit provided to patients. Economic evaluations are the comparative analysis of alternative interventions in terms of both their costs and clinical outcomes. While an in-depth discussion on economic evaluation is beyond the scope of this article, interested readers can review an article by Rudmik and Drummond, which provides an overview of important principles and methodology [73•]. Overall, the data provided from economic evaluations can provide several stakeholders with important information to assist in the efficient allocation of scarce health care resources.

There have been three recent economic evaluations analyzing ESS compared to continued medical therapy for refractory CRS [74–76]. All three studies took the perspective of the US third-party payer and developed a cohort-style, state transition, Markov decision-tree model with the primary outcome being the incremental cost-effectiveness ratio (ICER) of ESS compared to continued medical therapy. Each study used the quality-adjusted life year (QALY) as the effectiveness outcome, and the time horizon was 30 to 36 years. Overall, the outcomes from all three studies demonstrated that an ESS treatment strategy was more cost-effective than continued medical therapy alone for refractory CRS with 74 to 98% certainty for any willingness to pay threshold greater than \$20,000/QALY (Table 2).

An important limitation in all three economic evaluations evaluating ESS compared to continued medical therapy includes the lack of incorporating patient treatment preferences into the model. Unfortunately, the assumption that all patients with refractory CRS should be treated with the same treatment strategy is not patient-centered and

does not reflect real-world practice. To optimize patient-centered care for CRS, patients should be informed about their expected outcomes after treatment along with the potential risks and cost from surgery or continued medical therapy alone [77, 78]. When the patient is appropriately informed, then they can make a treatment decision based on their personal preferences. While individual patient treatment decisions often involve several factors, such as degree of personal risk aversion and out-of-pocket monetary cost, two disease-specific factors that have been shown to influence patient decision-making is the severity of their personal baseline QoL and productivity impairment [79]. Therefore, future economic evaluations would ideally evaluate the value of ESS and continued medical therapy using models where treatment strategies reflect patient preference as opposed to assuming that all CRS patients are treated with the same strategy.

Conclusions

Chronic rhinosinusitis is a common inflammatory disease that produces a large economic burden to health care systems around the globe. Direct costs are primarily driven by outpatient physician visits, prescription medical therapy, and ESS. CRS produces large indirect costs and these costs often vary based on the severity of the patients CRS-specific QoL impairment. In the correctly selected patient with refractory CRS, evidence supports that ESS is a high-value intervention and provides significant reductions in both direct and indirect costs; however, continued medical therapy alone may be a high-value intervention in select patients who have lower severity in their baseline QoL and productivity. To optimize the value of care, future studies should evaluate various patient-centered treatment strategies for CRS in order to provide the correct intervention to the correct patient within the correct time period.

Compliance with Ethical Standards

Conflict of Interest Dr. Rudmik declares no conflicts of interest relevant to this manuscript.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

Funding None.

Financial Disclosures Scientific advisory board for BioInspire and 480 Biomedical.

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- Of major importance

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