

# Classification of Chronic (1) Rhinosinusitis—Working Toward Personalized Diagnosis

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### **KEYWORDS**

- Chronic rhinosinusitis Precision medicine Personalized medicine Microbiome
- Cluster analysis 
  Phenotype 
  Endotype 
  Epidemiology

### **KEY POINTS**

- The costs of chronic rhinosinusitis (CRS) are massive and increasing, with an estimated 4.5% of total US health care expenditures devoted to CRS care in 2011.
- Stratification of CRS by polyp status and baseline clinical history is not predictive of treatment outcomes.
- Baseline lost productivity, age, and the Sinonasal Outcome Test-22 score can effectively stratify patients into 5 distinct clusters with distinct responses to endoscopic sinus surgery.
- Genotypic data that can be discerned by an in-clinic taste test are associated with surgical outcomes in patients with CRS without nasal polyps.
- Baseline microbiomic data are associated with clinical phenotypes as well as surgical outcomes.

## INTRODUCTION

Medicine as a whole is at the precipice of a revolution. The crucible of unprecedented advances in big data and financial and political pressure to provide increasingly efficient care are fueling these rapid changes. Management of CRS is particularly

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susceptible to these changes for various reasons. Although CRS is a devastating disease, it is not life threatening, and in the modern era, the value of treatments has to be justified. It is also a hugely expensive disease, with some estimates placing the direct costs at 4.5% of the entire health care expenditure.<sup>1</sup> Given that patients with medically recalcitrant disease that undergo endoscopic sinus surgery (ESS) fail to make clinically significant improvements approximately one-fourth of the time,<sup>2</sup> there will be pressure on clinicians to refine these outcomes and justify the costs.

CRS is also now recognized as a complex multifactorial disease with a poorly understood interplay between anatomy, microbiome, and innate immunity that yields the common final pathway of 2 of 4 cardinal symptoms with characteristic endoscopic and radiographic findings.<sup>3</sup> New technological advances in all of these fields will help to refine outcomes, but will also require the clinician to be more facile in increasingly sophisticated technologies. Identification of patients who are good and bad surgical candidates will increasingly be demanded of the physician by patients, politicians, and payers.

This article covers the financial pressures that are driving the demand for a more efficient delivery of care, as well as the informatics and technical advances that are facilitating these refinements.

#### Epidemiology

A large range in prevalence of CRS is likely, due to variation of epidemiologic methods. Large questionnaire-based studies avoid the pitfalls of geographic variation and support US and European rates of CRS at approximately 10%. Confirmation of the veracity of the questionnaire-based methodology with clinical evaluations supports the accuracy of this methodology.

Understanding the true prevalence of a disease such as CRS is a critical yet challenging endeavor. Accurate prevalence estimates facilitate judicious application of research, as well as industry and health care resources in addressing CRS, and thus it behooves patients, the medical profession, and society to accurately document its prevalence. It is somewhat confusing to find that the literature on CRS reflects a wide range of prevalence, at 2% to 15%.<sup>4,5</sup> The range of prevalence is in part driven by the underlying methodology of the epidemiologic study: large-scale questionnaire evaluations and small-scale clinical evaluations.

#### **Questionnaire-Based Evaluations**

It has been a relatively recent development that broadly accepted diagnostic criteria for CRS have been adopted.<sup>3,6</sup> Epidemiologic studies, therefore, that predate modern definitions are limited by a lack of sensitivity and specificity and are not directly comparable. Although modern definitions of CRS require both subjective patient-reported symptoms along with physician-reported radiographic and/or endoscopic endpoints, there are practical limitations in obtaining large, population-level studies that include radiographic and endoscopic endpoints. Given these inherent limitations, a current examination of the literature places the true US prevalence of CRS at approximately 10%.<sup>7</sup>

Several national surveys support this number. The US National Health Interview Survey was carried out in 2012 and is the largest of these surveys.<sup>7</sup> It included 234,921 adults and 12.1% of subjects reported having been given the diagnosis of sinusitis by a health care provider in the preceding year. This likely is an overestimate of CRS rates, since the questionnaire did not clarify whether the diagnosis given was for acute or chronic disease. However, the 2008 Global Allergy and Asthma European Network questionnaire-based survey included 57,128 respondents based on the

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