

Direct costs of adult chronic rhinosinusitis by using 4 methods of estimation: Results of the US Medical Expenditure Panel Survey

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Background: Chronic rhinosinusitis (CRS) is an inflammatory disease that affects 2% to 16% of the US population. Despite its increasing prevalence, there are currently limited data in the literature evaluating the economic burden of this disease.

Objective: This study aimed to determine the direct health care costs of CRS from the perspective of the US government.

Methods: A prevalence-based approach was used to estimate cost of illness for CRS from the 2011 Medical Expenditure Panel Survey database by using a 4-part model: (1) an estimated sum of all health care expenditures, (2) an attribution model for disease-specific estimation of expenditures, (3) an estimation based on a propensity score model, and (4) estimated disease-specific expenditure by using a linear regression-based approach. A disease prevalence of 3.5% was used.

Results: The mean CRS-specific annual expenditure was \$5955 (95% CI, \$5087-\$6823) by using method 1 compared with \$5560 (95% CI, \$4689-\$6431) by using method 2 and \$5560 (95% CI, \$4653-\$6467) by using method 3. The annual expenditure, as estimated by using method 4, was \$5589 (95% CI, \$4986-\$6192). Ambulatory expenses accounted for the largest proportion of expenditures, followed by prescription and in-hospital expenses. **Conclusions:** This study provided a range of estimates of the direct medical expenditures associated with CRS. We demonstrated that the economic burden attributable to this disease was an estimated \$60.2 to \$64.5 billion US dollars in 2011, with a wide variation in the total and incremental direct expenditures depending on the type of estimation model used and the prevalence assumed. (J Allergy Clin Immunol 2015;■■■:■■■-■■■.)

Key words: Chronic rhinosinusitis, cost, direct medical expenditures, rhinosinusitis treatment, Medical Expenditure Panel Survey

Abbreviations used

CCI: Charlson Comorbidity Index
COI: Cost of illness
CRS: Chronic rhinosinusitis
GLM: Generalized linear model
ICD: International Classification of Diseases
MEPS: Medical Expenditure Panel Survey
USD: US dollars

Chronic rhinosinusitis (CRS) refers to an inflammatory condition of the nasal passage and paranasal sinuses that has been present for at least 8 weeks.¹⁻⁴ It is an increasingly common diagnosis encountered in primary care, allergy, and otolaryngology practices, with an estimated prevalence of 5% in Canada and 2% to 16% in the United States.⁵⁻⁷ CRS has been found to have a significant effect on a patient's physical and mental health status that parallels that of arthritis, inflammatory bowel disease, asthma, and cancer.^{2,8-11} Studies have revealed a CRS diagnosis to be associated with 73 million restricted activity days and 24 million patient visits in the American patient population, placing it among the top 10 disabling chronic conditions and identifying it as a correspondingly high consumer of health care resources.^{12,13}

Health policy reform is closely associated with the economic analysis of disorders to establish judicious use of resources. Despite the prevalence of CRS and its debilitating effect on patients' quality of life, there have been limited studies evaluating the economic burden of this disease. Ray et al¹⁴ revealed that \$5.8 billion in health care expenditures was attributable to CRS in the United States in 1996. In this particular study the authors used the Delphi technique in their cost of illness (COI) assessment. In 2011, Bhattacharyya¹⁵ used the Medical Expenditure Panel Survey (MEPS) to identify the incremental health care use and expenditure associated with CRS in the United States in 2007 by using only 1 estimation model (ie, a generalized linear model [GLM] or regression model).¹⁵ The study noted a significant increase in incremental health care expenditures associated with this patient population from 1996, with an estimated \$8.6 billion in national health care expenditures. Smith et al¹⁶ recently concluded that the overall cost of CRS to US society was \$22 billion, but this was based on a recent systematic review evaluating available COI evidence for CRS in the literature. The conclusions of that particular review are limited to the best available evidence, as opposed to providing a new and more accurate cost estimation.

Accurate COI studies based on more recent cost data are pivotal for informed planning of health care budgets and research investments, as well as for formulating cost-effectiveness

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analyses.^{17,18} Such estimates are currently lacking for CRS. Therefore the purpose of this study was to provide accurate estimates of the US direct health care costs for CRS treatment by using the latest (2011) MEPS with 4 established cost estimation protocols.

METHODS

This was a cross-sectional study based on the 2011 MEPS database, the most recent calendar year available at the time of the study. The MEPS database is a survey conducted annually by the federal Agency for Health and Research Quality. The survey captures a large population of noninstitutionalized civilians in the United States through a series of 5 interviews conducted over 2.5 years. It is designed to specifically assess health care costs in the United States by collecting population-based information on health care expenditures, insurance coverage and methods of payment, demographics, and medical conditions. The weighted survey results represent the cost expenditures of the collective US population.¹⁹

Direct medical expenditures were estimated by using a prevalence-based approach. Prevalence, as used in the analytic stage of this study, was estimated from the respondents reporting CRS in the MEPS 2011 data set based on their International Classification of Diseases (ICD) 9 codes.

The full-year consolidated data set was merged with the following data sets from the 2011 year to extract the medical expenses: medical conditions, prescribed medicines, home health, hospital inpatient, emergency department visits, outpatient visits, office-based medical provider visits, and other medical expenses. The ICD was used to identify adult respondents (>18 years of age) with CRS (ICD-9-CM code 473.X). As specified by the parameters of MEPS, patients in this study had to have been given a diagnosis of CRS by a physician. The remaining respondents were categorized as subjects without CRS. The primary outcome of the study was direct medical expenditures associated with CRS at a person and population level.^{19,20}

Akobundu et al²¹ described 4 estimation methods used for direct medical expenditures: (1) a summation of all medical expenditures, (2) a summation of all medical expenditures attributable to a disease in a person with the disease, (3) the incremental expenditures between the population with a disease and a matched sample of control subjects without the disease, and (4) the incremental expenditures associated with a population with the disease, as estimated by a linear regression model through a coefficient that compares subjects with and without the disease.^{20,21}

We used these 4 analytic methods to estimate health expenditures of CRS. In the summation model, we first calculated a summation of all health care expenditures from all patients with CRS. A descriptive analysis was also performed to describe health expenditures based on sociodemographics and other covariates. The respondents with a medical event associated with CRS were identified, and consideration was given to all medical expenditures associated with these patients.

The second method, the attribution model, involved identification of disease-specific expenditures by using an attribution model. In this model consideration was restricted to direct medical expenditures related to the patient population affected by CRS, as outlined by specific parameters. The health care subgroups specifically under study included inpatient, emergency department, outpatient, office-based, home health, and pharmacy expenses.

The third method, the propensity score model, involved computing total and incremental medical expenditures in subjects with and without CRS. This was established by using a propensity score matching technique. We calculated propensity scores for each population. Subjects without and with CRS were matched according to propensity scores, and incremental expenditures were estimated. The covariates included in the propensity score estimation were age, sex, race, education, region, health insurance status, asthma diagnosis, socioeconomic status, health status, and patient comorbidities. Comorbidities were accounted for through the Charlson Comorbidity Index (CCI). The D'Hoore et al²² adaptation of the CCI was selected for this study because it could be easily applied to the MEPS data files given it uses the 3-digit ICD code system. The comorbidities given weighted consideration in this format of the CCI included myocardial infarction,

congestive heart failure, peripheral vascular disease, dementia, cerebrovascular disease, chronic pulmonary disease, connective tissue disease, gastric ulcer disease, mild liver disease, diabetes, hemiplegia, moderate or severe renal disease, any tumor, leukemia, lymphoma, liver disease, and metastatic tumor.

The final method, the regression model, was based on a GLM. The regression model provided the opportunity to control for several covariates in the estimation process. Differences in the demographic characteristics of the CRS and control groups, including age, sex, race, education, region, health insurance status, asthma diagnosis, socioeconomic status, health status, and comorbidities, were adjusted for in a GLM with log link function and gamma distribution. All *a priori* covariates met our definition of confounding and were included in the final model. We initially modeled other comorbidities of CRS, including depression, sleep disturbances, and associated otologic comorbidities (eg, otitis media with effusion and Eustachian tube dysfunction), as linear functions of annual cost, but this did not improve our model fit. As such, these covariates were not included in the final model. The regression model can become biased by the skewed distribution of the cost data.²³ Therefore a GLM framework was used. Appropriate distribution was identified by using the modified Park test. Model performance was assessed with the Pearson correlation test and the Pregibon link test.

The estimated expenditures were then multiplied by the population weight to create a national estimate of medical expenditures associated with CRS. We assumed a disease prevalence of 3.5% based on the sample population of patients with CRS in the MEPS database for 2011. All costs are reported in 2011 US dollars (USD).

All analyses were performed with SAS version 9.4 (SAS Institute, Cary, NC) and STATA version 12 (StataCorp, College Station, Tex) software. The analysis accounted for sampling weights, stratification, and clustering, as provided by the MEPS data set to ensure the results reflect a nationally representative sample.

RESULTS

In this study 1,170 (3.5%) respondents in the MEPS database experienced CRS in 2011 compared with 32,475 respondents who did not have CRS (Table I). The mean age of patients with CRS was 36 years for male and 43 years for female patients. The majority of patients with CRS in this sample population were female (63.8%).

The mean annual expenditure caused by CRS was \$5955 (95% CI, \$5087-\$6823) by using the summation model. This model accounted for all health care expenditures in this patient population.

The annual direct medical cost of CRS was \$5560 (95% CI, \$4689-\$6431) per respondent, as estimated by using the attribution model. The largest component of expenditures for patients with CRS was office-based expenditures and constituted \$1615 per person per annum and comprised 32.4% of total expenses. Other expenditures of sizeable economic burden were prescription expenditures at 28.1% and hospital inpatient and outpatient expenses (including surgery) at 24.5% and 9.3%, respectively (Table II). Ambulatory care expenses associated with CRS, including office-based, hospital outpatient, and emergency department visits, were associated with \$2425 in direct expenses and 43.0% of total annual medical expenditures in patients with CRS.

After adjusting for age, sex, race, education, insurance, region, income, marital status, health status, and CCI (the propensity score model), patients with CRS incurred an annual expenditure of \$5560 (95% CI, \$4653-\$6467). The adjusted annual incremental expenditure associated with CRS was \$364 ($P < .58$).

TABLE I. Descriptive statistics on the sociodemographic, health status, and expenditure variables in MEPS adult respondents with and without CRS

Demographic characteristics of study population	CRS		P value
	No (n = 32,475)	Yes (n = 1,170)	
Age (y)			<.001
Male (mean)	36.3	35.8	
Female (mean)	37.9	42.9	
Sex (%)			<.0001
Male	48.2	36.2	
Female	51.8	63.8	
Race (%)			<.0001
White	68.9	80.6	
Black	20.8	14.6	
Asian	7.1	1.6	
Other	3.2	3.2	
Hispanic			<.0001
Hispanic	29.5	11.5	
Not Hispanic	70.5	88.5	
Asthma status (%)			<.0001
Yes	9.4	16.6	
No	90.6	83.3	
Region (%)			.3458
Northeast	15.8	11.8	
Midwest	19.4	26.8	
South	37.6	41.8	
West	26.5	19.6	
Marital status (%)			<.0001
Married	34.5	44.3	
Unmarried	65.5	55.7	
Insurance status (%)			<.0001
Private	52.2	73.4	
Public	30.7	20.4	
Uninsured	17.1	6.2	
Self-reported health (%)			<.0001
Excellent	32.2	22.6	
Very good	30.5	33.4	
Good	25.7	28.2	
Fair	8.3	11.4	
Poor	2.3	4.2	
Income status (%)			<.0001
High income	15.6	24.4	
Medium income	16.0	21.8	
Low income	15.8	15.6	
Poor	36.8	23.3	
Near poor	15.9	14.9	
Education (%)			<.0001
No degree	33.8	21.0	
GED/high school diploma	23.3	22.7	
Bachelor's degree or higher	32.5	51.0	
Inapplicable/unavailable	10.4	5.2	
CCI score (mean)	1.54	1.74	<.0001

Based on the regression model, the total annual expenditure for the CRS population was estimated at \$5589 (95% CI, \$4986-\$6192), as seen in Table III. This was significantly higher (\$1152, $P < .0001$) than the total annual expenditure for the non-CRS population, which was estimated at \$4437 (95% CI, \$4260-\$4614).

Table III depicts the total and incremental national expenditures caused by CRS, as estimated by using the 4 models. The total direct COI associated with CRS in the United States for

TABLE II. Total annual direct COI (2011 USD) of CRS by category of service (attribution model)

Direct cost of illness by category	CRS	Non-CRS
Total	5560	4742
Office based	1683	1180
Prescription	1563	1160
Inpatient hospital	1364	1470
Outpatient hospital	520	454
ED	222	189
Home health	112	194
Other	96	96

ED, Emergency department.

2011 was estimated to be \$60.2 to \$64.5 billion USD. The incremental annual expenditures associated with CRS were estimated at \$3.9 to \$12.5 billion USD.

DISCUSSION

This study revealed direct health care costs of CRS in the United States by using the 2011 MEPS database, which has become a useful resource for the purpose of estimating COI.¹⁹ This was the first study to provide a range for the annual direct medical expenditures of CRS based on a nationally representative sample of the US population. Our study demonstrated that the diagnosis of CRS was associated with an annual cost of \$5560 to \$5955 per patient. The results of the study revealed that office-based expenses were the primary driver of total annual expenditures associated with CRS, followed closely by expenditures because of prescription medications. This might be as a result of the frequent disease exacerbations and the general difficulty controlling patients' symptoms that lead to patient medical visits and medication prescription.

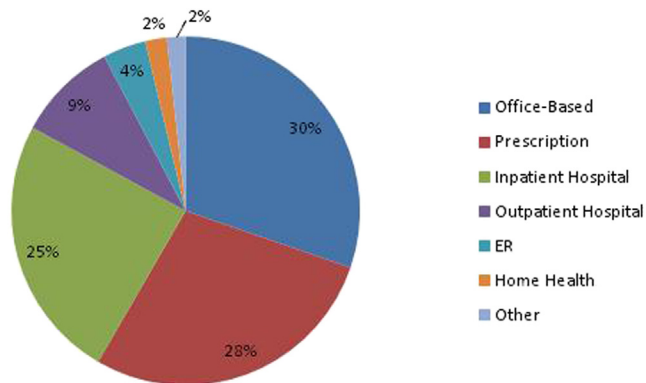
The summation model accounted for total all-cause health care costs in patients with CRS and estimated a total annual expenditure of \$5955. Summation models represent simple analytic approaches to estimates of total expenditures for the affected prevalence.²⁴ They account for costs associated with any medical event in patients with CRS. The obvious limitation in this model stems from the risk of accounting for costs unrelated to CRS. This model does not attempt to isolate costs attributable to the disease, as seen in the attribution, propensity score, and regression models, but rather with the respondent.²⁰ As such, the estimated annual cost expenditure of \$5955 per respondent has the potential to overestimate the expenditures attributed to CRS.

The attribution model revealed an annual total expenditure of \$5560 per respondent. This model isolated the component expenses caused by CRS before proceeding with a summation of expenses (Fig 1). Estimation protocols using this model have the additional benefit of estimating costs that are restricted to CRS-attributable spending. The additional costs associated with comorbidities would not be accounted for in this model if they were not coded appropriately, resulting in underestimation of the total annual expenditure. Expenses related to CRS, such as expenses caused by the psychological burden of disease, that are not coded as attributable to CRS in the MEPS data set would be overlooked and would not be accounted for in the annual expenditure.^{20,25} These comorbidities have been found to be prevalent in this population and could carry significant weight with respect

TABLE III. Total expenditures for CRS, as estimated by using 4 COI methodologies

Expenditures for CRS	Per person per annum (mean $\pm$ SE)		US total national expense by prevalence of CRS*	US incremental national expense by prevalence of CRS*
	CRS	No CRS		
Total expenditures				
Summation model	\$5955 $\pm$ \$440	\$5008 $\pm$ \$144	\$64.5 billion	
Attribution model	\$5560 $\pm$ \$442	\$4743 $\pm$ \$143	\$60.2 billion	
Incremental expenditures				
Propensity score model	\$5560 $\pm$ \$462	\$5195 $\pm$ \$422	\$60.2 billion	\$3.9 billion
GLM model	\$5589 $\pm$ \$306	\$4437 $\pm$ \$90	\$60.6 billion	\$12.5 billion

*Prevalence of CRS estimated from prevalence of CRS in MEPS respondents (3.5%).

**FIG 1.** Direct medical expenditures (2011 USD) of CRS by type of service (attribution model). ER, Emergency department.

to the comorbidities that are associated with CRS.¹¹ Ray et al¹⁴ reported that 12% of expenses associated with asthma, chronic otitis media, and Eustachian tube dysfunction were associated with the diagnosis and treatment of comorbid acute and chronic sinusitis.

The propensity score model is intended to establish disease-specific costs by using an algorithm that adjusts for confounders among control and case patients, such that the 2 cohorts are matched according to propensity scores. The model accounts for covariates that can affect CRS, as described in the study design. The annual mean direct expenditure associated with CRS was \$5560 when the propensity score model was performed. The incremental expenditure, as estimated by using this model, was \$364. Matching models, such as propensity score matching, reduce the overt bias that confounding factors have on the direct expenditures being estimated in observational studies.²⁶ Furthermore, this model is particularly useful for diseases in which there are few outcomes per covariate adjustment variable. Propensity scores are also intuitive to readers given that they resemble the features of randomized controlled trials.²³ However, the propensity score model is susceptible to underestimation of rare events. As such, disease groups should not represent less than 10% of the overall population.²⁶ The prevalence of CRS varies in the literature but is estimated at 3.5% in this study and could thus potentially bias the results obtained in the propensity score model.

The regression model was the GLM approach. This model provided an alternate method of adjusting for confounders and revealed a total direct cost of \$5589 and an incremental cost of \$1152. The regression model with the appropriate variance function is particularly useful in modeling highly skewed cost

data. The relevant diagnostic tests, as described in the study design, were used in this study to ensure the most appropriate model specification when the GLM framework was used. Regression models are unfortunately still susceptible to bias because of unobservable factors that could alter the final estimation product.

With an estimated prevalence of 3.5%, expenditures associated with the treatment of patients with CRS were estimated to be \$60.2 to 64.5 billion USD in 2011. This total expense accounted for 4.5% to 4.8% of the overall expenditures for US health care in 2011.¹⁹ The incremental national expenditure caused by CRS was estimated at \$3.9 to \$12.5 billion USD. This constituted 0.30% to 0.94% of the total US health care budget for 2011.

In this study the estimated prevalence of CRS for the United States in 2011 was 3.5% based on the sample population represented in the MEPS survey results. The expenditures reported by the sample population in the MEPS data set were weighted to permit derivation of national estimates of US disease expenditure. The prevalence of CRS varies extensively in the literature but can be estimated to lie within the range of 2% to 16% in the United States.⁷ By using the CRS prevalence estimates in the literature, this would provide an estimated incremental cost for CRS of \$2.3 to \$57.4 billion USD in 2011 based on the propensity score and regression models.

Compared with the published literature, our results are substantially higher than the previously established estimates of the economic burden of CRS based on the respective estimation models. Ray et al¹⁴ estimated the direct expenditures caused by CRS at \$5.8 billion USD. This study used a Delphi technique to determine the number of medical encounters caused by CRS; however, the prevalence used in the study was not explicitly reported.¹⁴ Bhattacharyya¹⁵ analyzed the 2007 survey results of the MEPS database and identified a national incremental health care cost of \$8.6 billion per year at a prevalence of 4.9%. This study used a regression model to establish direct cost estimation for patients with CRS. The results of our study confirm a continued upward trend of the direct medical costs associated with CRS by using our regression model. However, the absolute increase is highly sensitive to the estimated prevalence of CRS; our study used a conservative prevalence estimate. The majority of expenditures were associated with ambulatory expenses in both studies, which is similar to the results reported in our study.

The MEPS database has been used extensively as a resource to analyze costs associated with various medical conditions and therapies. However, as comprehensive as this database is for COI analyses, there are limitations associated with this survey. One of the important limitations of the MEPS database is its failure to accurately account for prevalence of a disease within a population. Patients must be able to self-identify at least 1

medical condition to be included in the medical conditions component of the MEPS survey. This has the potential to limit the external validity of the results because patients who did not self-report symptoms consistent with CRS but who had an underlying diagnosis would not be accounted for in the database. This could result in underestimation of the prevalence and overall economic burden of CRS.^{15,19} In contrast, this has the potential to inflate costs as well because of survey respondents misreporting diagnoses.²⁷ This issue has been recognized as a weakness of many administrative databases, and there are currently no databases that provide costing data for CRS that have examined the accuracy of diagnosis (Macdonald et al, unpublished data). However, the potential for this in our study is reduced by the verification of self-reported patient conditions by physicians and hospitals in the MEPS survey.¹⁹

Furthermore, the MEPS database limits expenses per visit to one primary diagnosis based on the ICD-9-CM. As a result, CRS contributing to comorbidities or patient encounters would not be accounted for in the tabulated expenses.¹⁴ This will also lead to aggregation of costs related to conditions.²⁷ In the context of this study, the costs related to CRS would include costs related to CRS with nasal polyposis. Furthermore, Hsu et al²⁸ identified limitations in the diagnostic accuracy of CRS using billing codes in isolation. Objective confirmation of the diagnosis of CRS by using a nasal endoscopy or computed tomographic imaging is necessary to improve the accuracy of phenotyping CRS.²⁸ The propensity score and regression models adjusted for patients' comorbidities based on medical conditions that required a medical assessment annually and were represented in the 2011 MEPS database. Although this would not be an exhaustive representation of patients' comorbidities, this is a widely accepted method of establishing comorbidities to ensure that the models accurately adjusted for active medical conditions that could contribute to patients' expenditures for 2011.

Finally, the MEPS database also limits the population of respondents to noninstitutionalized civilians. Unfortunately, this results in exclusion of high-cost populations, such as persons living in nursing homes.²⁷

These cost estimations are a reflection of the economic burden of CRS in the United States based on the MEPS respondents. Given that several components must be considered in the estimation of the national cost of an illness, such as country-level differences in health care resource allocation, prevalence of CRS, and diagnostic criteria, a direct generalization of the expenses cannot be made to other countries. A country-by-country comparison would need to be made to estimate differences in economic burden of disease at an international level.

There are additional limitations introduced into this study because of the observational design of prevalence-based COI studies. As a chronic condition, CRS expenses are dependent on cumulative costs based on disease progression. However, this would not be accounted for in a point estimate of medical expenditures, as captured by a prevalence-based approach. This could be rectified in the future with a longitudinal study of cumulative costs to better estimate long-term economic burden. It is also important to note that this study focused on direct expenditures associated with CRS. Given the chronic nature and long-term disability of patients with CRS, total costs for chronic illnesses should account for indirect and intangible costs. Indirect costs include loss of productivity and disability by patients and their caregivers as a result of illness or treatment.

Intangible costs refer to the psychosocial consequences and quality-of-life decrements.²³ Incorporation of these additional costs into a COI approach would undoubtedly increase the estimated total expenditure of a disease.

In conclusion, the economic burden of CRS continues to demonstrate an upward trend. We identified an incremental direct cost of \$3.9 to \$12.5 billion USD for CRS treatment. The upper limit of our estimate is considerably higher than the previously published adjusted cost. This might indicate that the direct cost of CRS has been previously underestimated. Furthermore, as shown in this study, different techniques can cause modest variability in COI estimates. Given the significant clinical and economic burden associated with CRS, it is essential that there be accurate data to reflect the needs of the current patient population and to effectively contribute to decision analysis in health policy reform.

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Clinical implications: Direct medical expenditures for CRS treatment are increasing and currently range from \$5560 to \$5955 per person annually, resulting in a total expenditure of \$60.6 to \$64.9 billion USD per year.

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