Published in final edited form as:

Laryngoscope. 2018 January ; 128(1): 23–30. doi:10.1002/lary.26723.

What Drives Productivity Loss in Chronic Rhinosinusitis? A SNOT-22 Subdomain Analysis

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Abstract

Objectives—Previous studies have shown declines in productivity due to chronic rhinosinusitis (CRS) are correlated with disease-specific quality-of-life (QOL) measures. However, it is unclear which symptom domains contribute primarily to productivity loss. This investigation sought to assess the association between CRS-specific QOL subdomain impairment and productivity loss.

Study Design—Prospective, multi-institutional, observational cohort study.

Methods—198 patients with refractory CRS were enrolled between August, 2012 and June, 2015. Baseline QOL measures were obtained across five subdomains of the 22-item SinoNasal Outcome Test (SNOT-22). Lost productivity time was determined from patient-reported measures of annual absenteeism, presenteeism, and lost leisure time, and then monetized using annual daily wage rates from the 2012 U.S. National Census and 2013 Department of Labor statistics.

Results—Productivity losses correlated with impairments in both SNOT-22 psychological dysfunction ($R_s=0.428$, $p<0.001$), and sleep dysfunction domain scores ($R_s=0.355$, $p<0.001$). Higher SNOT-22 total scores also significantly correlated with increased monetized productivity losses ($R_s=0.366$, $p<0.001$). The mean annual productivity cost was \$11,820/patient; while patients with comorbid immunodeficiency (\$23,285/patient), tobacco use (\$23,195/patient), and steroid dependency (\$18,910/patient) reported higher than average annual productivity costs.

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Potential Conflicts of Interest: None

The abstract for this submission was accepted for oral presentation to The Triological Society meeting during the annual Combined Otolaryngology Spring Meetings in San Diego, California, USA, April 26-30th, 2017. **Abstract # 425.**

Level of Evidence: 2c

Financial Disclosures: Timothy L. Smith and Jess C. Mace are supported by a grant for this investigation from the National Institute on Deafness and Other Communication Disorders (NIDCD), one of the National Institutes of Health, Bethesda, MD., USA (R01 DC005805; PI/PD: TL Smith). Public clinical trial registration (www.clinicaltrials.gov) ID# NCT01332136. This funding organization did not contribute to the design or conduct of this study; collection, management, analysis, or interpretation of the data; preparation, review, approval or decision to submit this manuscript for publication. Luke Rudmik is a consultant for BioInspire (Peoria, AZ). There are no financial disclosures for Naweed Chowdhury.

Multivariate linear regression found maximum annual productivity costs in adjusted psychological (\$13,300/patient, $p<0.001$) and sleep dysfunction (\$9,275/patient, $p<0.001$) domains.

Conclusion—Impairments in sleep and psychological SNOT-22 domains correlate with productivity losses. Patients with comorbid immunodeficiency, smoking, and steroid dependency had higher than average productivity losses. Targeted management of psychological and sleep dysfunction in combination with standard symptom control may improve patient-centered care and reduce the annual economic burden of CRS.

MeSH Key Words

Sinusitis; Chronic Disease; Cost of Illness; Quality of Life; Paranasal Sinuses; Efficiency

Introduction

Chronic rhinosinusitis (CRS) is a poorly understood, multi-faceted disease process that manifests its impact in a variety of physical and emotional ways. Various validated patient-reported outcomes measures (PROMs) have attempted to quantify disease and symptom burden associated with CRS, one of the most common being the 22-item Sinonasal Outcomes Test (SNOT-22) survey instrument.¹ In addition to being an overall measure of CRS-specific quality-of-life (QOL), factor analysis of the SNOT-22 survey has previously identified five distinct symptom domains: rhinologic symptoms, extra-nasal rhinologic symptoms, ear/facial symptoms, sleep dysfunction, and psychological distress.² Earlier work has shown that CRS results in decreased daily work productivity, and that the degree of productivity loss is associated with a patient's baseline QOL status. This is not a trivial amount; in fact, productivity loss from CRS rivals that of many other chronic disease processes such as asthma, diabetes, and heart disease.³ Given this association, it is likely that impairments in each of the QOL domains represented within the SNOT-22 would differentially affect measures of productivity loss. For example, sleep disorders may induce a higher level of presenteeism on a more consistent basis, whereas pure rhinologic issues may cause sporadic, but frequent, absenteeism. As such, it is unclear what contribution each of the SNOT-22 domains provide to global productivity loss outcomes in CRS. In an environment where health care dollars are at a premium, differentiating which QOL domains associate with overall productivity loss can be useful for targeted symptom improvement in order to optimize patient-centered care and reduce further productivity losses to society.

Materials and Methods

Patient Population

Adult study participants (≥ 18 years of age) were prospectively enrolled between August, 2012 and June, 2015 into a non-randomized, multi-center, North American cohort evaluating various treatment outcomes for CRS. This cross-sectional investigation is a secondary data analysis of previously reported findings.⁴⁻⁷ Study participants were diagnosed with medically refractory CRS as defined by both the American Academy of Otolaryngology-Head and Neck Surgery and the European Position Paper on Rhinosinusitis and Nasal Polyposis 2012.^{8,9} Study participants had completed initial medical therapy including, but

not limited to: 240ml. of daily saline irrigation, at least one course of either topical corticosteroids (≥ 21 days) or trial of oral corticosteroid therapy (≥ 5 days), and at least one trial (≥ 14 days) of broad spectrum or culture-directed antibiotics. Enrollment procedures occurred after study participants underwent surgical counseling and voluntarily elected either appropriate, physician-directed, continued medical therapy (CMT) or endoscopic sinus surgery (ESS) as subsequent treatment modalities.

The Institutional Review Board (IRB) at each enrollment site governed investigational protocols and informed consent. Enrollment locations included sinus clinics within tertiary referral, academic hospital systems in the United States including: Oregon Health & Science University (OHSU; Portland, OR; IRB#7198), Stanford University (Palo Alto, CA; IRB#4947), the Medical University of South Carolina (Charleston, SC; IRB#12409), and the University of Calgary (Calgary, Alberta, Canada; IRB#E-24208). Patients were assured of minimal study risk, voluntary study consent, and that the standard of care would not be altered due to study participation.

Study participants provided a comprehensive medical and social history during baseline enrollment interviews and were asked to complete PROMs involving both symptom severity / QOL surveys and measures of productivity loss due to CRS. Additional measures of baseline disease severity, conducted per the standard of care, were used simultaneously for study purposes. The paranasal sinuses were diagnosed bilaterally using 0-30° rigid endoscopy (Karl Storz, Tuttlingen, Germany) and quantified by each enrolling physician using Lund-Kennedy staging (score range: 0-20) which quantifies visualized pathologic states within the paranasal sinuses including the presence and severity of nasal polyposis, discharge, edema, scarring, and crusting.¹⁰

High resolution computed tomography (CT) imaging was also utilized to evaluate preoperative sinonasal disease severity using contiguous images in both sagittal and coronal planes. Images were staged by the enrolling physician in accordance with the Lund-Mackay bilateral scoring system (score range: 0-24) which quantifies the severity of opacification in each sinus region.¹¹ Postoperative CT images were not collected due to elevated risk of radiation exposure and divergence from the standard of care. Higher scores on both staging systems represent worse intrinsic disease severity.

Exclusion Criteria

Study participants with comorbid cystic fibrosis or other primary ciliary dyskinesia diagnoses were excluded from analysis due to potential variations in global health and differential treatment considerations in the standard of care. Additional participants were excluded from the final cohort if they did not accurately complete all PROM surveys as instructed.

Patient-reported Outcome Measures

Study participants were asked to complete the 22-item SinoNasal Outcome Test (SNOT-22), a validated instrument developed to quantify sinonasal symptom severity (©2006, Washington University, St. Louis, MO).¹² Discrete item scores are measured using Likert scale responses (score range: 0–5) where higher scores indicate worse symptom severity as

follows: 0= 'No problem'; 5='Problem as bad as it can be'. Higher total scores on the SNOT-22 reflect worse daily functioning and/or symptom severity (score range: 0-110). The 22-items of the SNOT-22 survey have been categorized and summarized into 5 separate domains with minimal item cross-loading: rhinologic symptom domain (score range: 0-30), extra-nasal rhinologic symptom domain (score range: 0-15), ear / facial symptom domain (score range: 0-25), psychological dysfunction domain (score range: 0-35), and the sleep dysfunction domain (score range: 0-25).²

Productivity Outcomes and Monetization

To generate patient-specific productivity costs, the degree of lost productive time (LPT) was first measured, defined as the per-person work days lost due to refractory CRS. For this study we assumed the following average paid work time per patient: 8 hours per day, 5 days per week with 4 weeks of vacation per year (i.e. 48 paid work weeks and a total of 240 paid work days per year).

Based on current recall recommendations, absenteeism was quantified by asking both the number of full work days missed and the number of work hours missed due to CRS in the last 3 months.¹³⁻¹⁵ As defined above, a cumulative loss of 8 hours of work was equal to 1 full work day missed. Presenteeism was measured based on the Quantity and Quality Questionnaire.^{16,17} Patients were asked on average the percentage (%) of reduced daily work performance due to CRS in the last 3 months. Healthy baseline performance was assumed to be 100% productivity. It was also assumed that the average productivity level within the last 3 months was consistent over the course of the previous year. The annual number of work days missed due to CRS-related presenteeism was calculated using the following formula: $P = (E - A) * p$; where P is the number of missed work days due to presenteeism, E is the expected number of annual work days (ie. 240), A is the work days missed due to absenteeism, and p is the % reduced performance at work.¹⁵ Annual LPT was calculated by summing the work days lost from both presenteeism and absenteeism due to CRS.

Household productivity loss was calculated by asking patients how much time per day was consumed at home to care for their sinuses. It was assumed the potential household productivity/leisure time available for weekdays is 7 hours per day (5:00pm to 12:00am) and on weekend days it is 15 hours per day (9:00am to 12:00am) for 52 weekends per year. Therefore, 7 household hours lost per weekday or 15 household hours lost per weekend would equal one household work day lost. Household productivity is reported separately from paid work days missed since it has a different monetary valuation.

The human capital approach was then used to monetize productivity losses. To accurately reflect the productivity cost to society, we used the median annual US societal wage rate of \$30,853 based on the 2012 US National Census. Assuming 48 work weeks per year, at 40 hours per week and 8 hours per day, this produces a mean daily income of \$128.55 per patient.¹⁸ This value was used to monetize the paid work LPT. Household productivity loss was valued by assuming it was equal to the hourly wage of a housekeeper. Using the 2013 US Department of Labor statistics, the mean hourly wage rate for a housekeeper was \$10.49 which at 8 hours per day produced a daily household monetized LPT of \$90.91.¹⁹

Data Management and Statistical Analysis

De-identified participant study data was transferred to OHSU from each enrollment site for data compilation and final analysis. Study data was manually entered into a HIPAA compliant relational database (Access, Microsoft Corp., Redmond, WA) and statistical analyses were conducted using commercially available software (SPSS v.24, IBM Corp., Armonk, NY). Data normality was evaluated for ordinal and continuous measures to guide test selection. Two-tailed Spearman's correlation coefficients (R_s) were used to examine all associations between QOL measures and monetized productivity losses. Interpretations of correlation effect sizes followed conventional guidelines.²⁰ Kruskal-Wallis test statistics were used to compare productivity loss measures across SNOT-22 domain score categories.

Stepwise linear regression was used to identify significant risk factors associated with worse patient-reported productivity losses. Separate, preliminary models were built for each of the five SNOT-22 domain scores and the overall SNOT-22 score as independent exposures of interest. Additional model covariates were screened for univariate significance ($p < 0.200$) as either independent predictors or confounding factors. Final models used a manual forward selection ($p < 0.100$) and backwards elimination ($p < 0.050$) process with manual inclusion of and adjustment for enrollment site variation. Covariates resulting in an absolute change of $\pm 10\%$ in the effect estimate (β) of SNOT-22 scores was considered important confounding factors and remained in the model.^{21,22} Unadjusted β and adjusted β values, standard errors (SE), t-test statistics, and estimates of type-I error (p-values) are reported for each SNOT-22 domain score. The percentage of variance explained by each final model was calculated using coefficients of multiple determination (R^2).

Since SNOT-22 domain score ranges are different and involve some degree of survey item cross-loading², an accurate comparison of productivity cost by comparing adjusted β values was not possible, so a maximum annual impairment value was computed for each domain by multiplying their respective adjusted β by the highest possible score for that domain to obtain a single dollar value that allows for normalized comparison across domains.

Results

Final Study Population

A total of 198 study participants provided accurate and complete data for final analysis after exclusions for either comorbid cystic fibrosis or other primary ciliary dyskinesia ($n=26$) and incomplete survey responses during baseline enrollment interview ($n=74$). Final cohort characteristics, mean total and domain SNOT-22 scores, average monetized productivity losses, and clinical measures of disease severity are reported in Table 1.

Total Cohort Correlations between PROM scores

Correlations between continuous measures of QOL and productivity costs were evaluated for SNOT-22 total and domain scores. There was a significant correlation between SNOT-22 total scores and productivity cost ($R_s=0.366$; $p < 0.001$) (Figure 1). The two largest correlation coefficients were found between productivity cost and the psychological dysfunction domain score ($R_s=0.428$; $p < 0.001$) and the sleep dysfunction domain score

($R_s=0.355$; $p<0.001$); Figure 2). Significant, but weaker, correlations were found between productivity cost and the rhinologic symptom domain score ($R_s=0.217$; $p=0.002$), the extra-nasal rhinologic symptom domain score ($R_s=0.271$; $p<0.001$), the ear / facial symptom domain scores ($R_s=0.237$; $p=0.001$), and baseline endoscopy score ($R_s=0.145$; $p=0.042$).

Cohort Subgroup Correlations

Additional correlations between annual productivity cost and SNOT-22 total and domain scores were evaluated for independent patient subgroups (Table 2). All significant correlation coefficients ($p<0.050$) between SNOT-22 scores and annual productivity cost were found to be either weak or moderate in magnitude ($R_s<0.700$). Mean annual productivity costs were also determined for patient subgroups (Table 3), ranging between \$8,298 and \$23,285.

Additionally, mean annual productivity costs were evaluated across worsening SNOT-22 domain score categories (Table 4). The highest mean annual productivity costs were significantly ($p<0.050$) associated with each of the highest SNOT-22 domain scores, indicating higher average productivity losses relate with worse symptom severity with consistent effect. Multivariate linear regression was able to isolate mean annual productivity cost associated with single unit (1.0) increases in both SNOT-22 total scores and discrete domain scores (Table 5).

After adjustment for independent cofactors and comorbid conditions, every SNOT-22 domain score was significantly associated with various degrees of monetized productivity loss. Final models explained between 18% and 27% of total model variance (R^2) in the association between QOL and productivity loss. Maximal productivity losses for each domain were then computed as a standardized way of assessing the relative impact of impairment across domains using the adjusted β values from our linear regression model. For the rhinologic, extra-nasal rhinologic, and ear/facial symptom domains, the maximum mean annual productivity cost was \$8,340, \$8,775, and \$8,350 respectively. For the psychological and sleep domains, the potential maximum mean productivity cost was found to be \$13,300/year and \$9,275/year.

Discussion

Productivity loss constitutes an important component of the societal burden of disease, with the overall cost estimated to be \$260 billion in the United States (U.S.) alone.²³ In patients with refractory CRS who choose to undergo ESS, the annual indirect cost has been estimated to exceed \$13 billion in the US^{3,24}, or approximately 5% of that net productivity loss. While productivity measures are difficult to quantify in an increasingly service-based economy where output is not always materially defined²⁵, these findings nonetheless highlight the magnitude of economic impediment that chronic conditions like CRS may cause. Compounding this problem are rising direct costs, which are estimated to increase approximately 5.8% annually and predicted to account for 20% of the total U.S. gross domestic product by 2024.²⁶ While rising direct costs are subject to extrinsic factors like economic cycles, legislative changes, and health care utilization²⁷, indirect costs are often

related to disease-specific QOL impairments³ and thus can potentially be minimized through use of high value, patient-centered treatments.

In this study of 198 prospectively enrolled subjects with CRS, we expand on the current literature linking QOL impairment with productivity loss by investigating the contributions of discrete SNOT-22 symptom domains and patient comorbidity. Overall, the mean annual productivity cost across the entire cohort was approximately \$11,820/patient, while patients with comorbid immunodeficiency (~\$23,285/year), current tobacco use (~\$23,195/year), and corticosteroid dependency (~\$18,910/year) had statistically significant differences in productivity cost. Impairments in all five QOL domains of the SNOT-22 yielded significant associations with productivity loss, with psychological domain scores showing the strongest correlation, followed by sleep dysfunction. Interestingly, rhinologic symptom domain scores had the weakest correlation with reported lost productivity. These rankings are consistent with global assessments of lost productivity by health economists²⁸, who found that depression/mental illness was the second costliest chronic disease for U.S. employers in total expenditures and fourth costliest when looking at presenteeism alone, accounting for about 61% of the total economic cost.

Subgroup analysis of correlation coefficients across patient characteristics revealed some interesting trends. First, comorbid depression increased the strength of correlation between productivity cost and the rhinologic, extra-rhinologic, and ear-facial domain scores, suggesting that depression may be a potentiator of increased productivity loss. The effect was most notable in the ear-facial symptom domain, with a medium-to-large correlation coefficient between productivity and symptom severity in patients with comorbid depression ($R_s=0.654$; $p<0.001$; Table 2) compared to the overall cohort ($R_s=0.237$; $p=0.001$).²⁰ A similar potentiating effect was found in patients with comorbid GERD across all five symptom domains. Current alcohol use also appears to amplify the association between sleep dysfunction on productivity loss, which is perhaps not surprising given the links between alcohol consumption, sleep impairment, and next-day alertness.^{29,30}

Multivariate regression modelling supported significant bivariate associations between productivity cost and greater impairments in psychological and sleep domain scores after adjustment for additional independent cofactors. The highest adjusted β was noted in the extra-rhinologic symptom domain, with \$585 of productivity loss per unit. However, due to cross loading of domains and differential score ranges, the adjusted β was not considered to be an accurate comparison value across domains. Instead, the maximum productivity impact of each domain was used as an indicator of its relative weight. Similar to our univariate findings, the maximum productivity impact was highest for the psychological impairment domain followed by the sleep dysfunction domain, with annual costs of \$13,300/year and \$9,275/year respectively.

From a clinical perspective, this cross-sectional data suggests that much of the monetized productivity loss associated with CRS is related to non-rhinologic symptom domains. Therefore, from a purely economic perspective, minimizing indirect costs related to CRS may require addressing non-rhinologic aspects of the disease. Prior investigations of this cohort have shown that ESS improves cognitive impairment, psychological symptoms, and

sleep dysfunction in patients with CRS^{31–33}, so there is an important role for the otolaryngologist in improving these symptom domains while minimizing productivity loss overall.³⁴ However, in addition to postoperative CMT of rhinologic symptoms, collaboration with specialists in psychiatry, psychology, and sleep medicine may serve as adjunctive measures to improve productivity and optimize treatment of psychological and sleep issues.

Several limitations of the study are present. First, the final study cohort was selected from patients diagnosed with medically refractory CRS referred to academic rhinology practices for tertiary care. As such, results from this investigation may not be externally generalizable to the wider U.S. population with CRS. Second, the 90-day recall period inherent in the productivity loss measures used for this study may introduce some degree of recall bias. Third, patient-based productivity measures are approximations of personal, discernible value and are subject to some degree of subjective interpretation. As Western economies move away from tangible measures of productivity, such as manufacturing and farming, to intellectual and service-based sectors, it is becoming more difficult to estimate the lost value of these services due to various disease processes.²⁵ Lastly, there are well known inferential limitations with prevalence studies and the interpretation of any observed associations. While this study reveals statistically significant associations and consistency of effect across SNOT-22 domain scores, temporality cannot be determined and any measure of productivity loss may not be longitudinally durable over time in a dynamic, chronic disease process.

Conclusion

Impairments in sleep and psychological symptom domains strongly correlate with annual productivity cost. Patients with comorbid immunodeficiency, smoking, and steroid dependency had higher average productivity losses. Targeted management of psychological and sleep dysfunction in combination with standard symptom control may help to optimize patient-centered care and reduce the overall economic burden of CRS to society.

References

1. Rudmik L, Hopkins C, Peters A, Smith TL, Schlosser RJ, Soler ZM. Patient-reported outcome measures for adult chronic rhinosinusitis: A systematic review and quality assessment. *J Allergy Clin Immunol*. 2015; 136(6):1532–1540. [PubMed: 26654198]
2. DeConde AS, Bodner TE, Mace JC, Smith TL. Response shift in quality of life after endoscopic sinus surgery for chronic rhinosinusitis. *JAMA Otolaryngol Head Neck Surg*. 2014; 140(8):712–719. [PubMed: 25074504]
3. Rudmik L, Smith TL, Schlosser RJ, Hwang PH, Mace JC, Soler ZM. Productivity costs in patients with refractory chronic rhinosinusitis. *Laryngoscope*. 2014; 124(9):2007–2012. [PubMed: 24619604]
4. Smith TL, Mace JC, Rudmik L, et al. Comparing surgeon outcomes in endoscopic sinus surgery for chronic rhinosinusitis. *Laryngoscope*. 2017; 127(1):14–21. [PubMed: 27298069]
5. Ramakrishnan VR, Mace JC, Soler ZM, Smith TL. Examination of high-antibiotic users in a multi-institutional cohort of chronic rhinosinusitis patients. *Int Forum Allergy Rhinol*. Jan.2017 [Epub ahead of print]. doi: 10.1002/alr.21903
6. Levy JM, Mace JC, Rudmik L, Soler ZM, Smith TL. Low 22-item sinonasal outcome test scores in chronic rhinosinusitis: Why do patients seek treatment? *Laryngoscope*. 2017; 127(1):22–28. [PubMed: 27377575]

7. DeConde AS, Mace JC, Levy JM, Rudmik L, Alt JA, Smith TL. Prevalence of polyp recurrence after endoscopic sinus surgery for chronic rhinosinusitis with nasal polyposis. *Laryngoscope*. 2017; 127(3):550–555. [PubMed: 27859303]
8. Rosenfeld RM, Piccirillo JF, Chandrasekhar SS, et al. Clinical Practice Guideline (Update): Adult Sinusitis. *Otolaryngol Head Neck Surg*. 2015; 152(2 Suppl):S1–S39.
9. Fokkens WJ, Lund VJ, Mullol J, et al. European Position Paper on Rhinosinusitis and Nasal Polyps 2012. *Rhinol Suppl*. 2012; (23):1–298. 3 p preceding table of contents.
10. Lund VJ, Kennedy DW. Staging for rhinosinusitis. *Otolaryngol Head Neck Surg*. 1997; 117(3 Pt 2):S35–40. [PubMed: 9334786]
11. Lund VJ, Mackay IS. Staging in rhinosinusitis. *Rhinology*. 1993; 31(4):183–184. [PubMed: 8140385]
12. Hopkins C, Gillett S, Slack R, Lund VJ, Browne JP. Psychometric validity of the 22-item Sinonasal Outcome Test. *Clin Otolaryngol*. 2009; 34(5):447–454. [PubMed: 19793277]
13. Revicki DA, Irwin D, Reblando J, Simon GE. The accuracy of self-reported disability days. *Med Care*. 1994; 32(4):401–404. [PubMed: 8139304]
14. Severens JL, Mulder J, Laheij RJ, Verbeek AL. Precision and accuracy in measuring absence from work as a basis for calculating productivity costs in The Netherlands. *Soc Sci Med*. 2000; 51(2): 243–249. [PubMed: 10832571]
15. Zhang W, Bansback N, Anis AH. Measuring and valuing productivity loss due to poor health: A critical review. *Soc Sci Med*. 2011; 72(2):185–192. [PubMed: 21146909]
16. Brouwer WB, Koopmanschap MA, Rutten FF. Productivity losses without absence: measurement validation and empirical evidence. *Health Policy*. 1999; 48(1):13–27. [PubMed: 10539583]
17. Koopmanschap MA. PRODISQ: a modular questionnaire on productivity and disease for economic evaluation studies. *Expert Rev Pharmacoecon Outcomes Res*. 2005; 5(1):23–28. [PubMed: 19807557]
18. [Accessed February 26, 2017] US National Census: Income, Poverty, and Health Insurance Coverage in the United States: 2012. Available at: <http://www.census.gov/prod/2013pubs/p60-245.pdf>
19. [Accessed March 7, 2017] US Department of Labor: Occupational Employment Statistics. Available at: <http://www.bls.gov/oes/current/oes372012.htm>
20. Cohen, J. *Statistical Power Analysis for the Behavioral Sciences*. New York, NY: Routledge Academic; 1988.
21. Sullivan, L. *Essentials of Biostatistics in Public Health*. Riegelman, R., editor. Boston, MA: Jones and Bartlett Publishers; 2008.
22. Maldonado G, Greenland S. Simulation study of confounder-selection strategies. *Am J Epidemiol*. 1993; 138(11):923–936. [PubMed: 8256780]
23. Davis K, Collins SR, Doty MM, Ho A, Holmgren A. Health and productivity among U.S. workers. *Issue Brief (Commonw Fund)*. 2005; (856):1–10.
24. Smith KA, Orlandi RR, Rudmik L. Cost of adult chronic rhinosinusitis: A systematic review. *Laryngoscope*. 2015; 125(7):1547–1556. [PubMed: 25640115]
25. Matke S, Balakrishnan A, Bergamo G, Newberry SJ. A review of methods to measure health-related productivity loss. *Am J Manag Care*. 2007; 13(4):211–217. [PubMed: 17408341]
26. Keehan SP, Cuckler GA, Sisko AM, et al. National health expenditure projections, 2014–24: spending growth faster than recent trends. *Health Aff (Millwood)*. 2015; 34(8):1407–1417. [PubMed: 26220668]
27. Catlin, AC., Cowan, CA. Centers for Medicare and Medicaid Services. [Accessed March 6, 2017] History of Health Spending in the United States, 1960–2013. 2015. Available at: <https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/NationalHealthExpendData/Downloads/HistoricalNHEPaper.pdf>
28. Goetzel RZ, Long SR, Ozminkowski RJ, Hawkins K, Wang S, Lynch W. Health, absence, disability, and presenteeism cost estimates of certain physical and mental health conditions affecting U.S. employers. *J Occup Environ Med*. 2004; 46(4):398–412. [PubMed: 15076658]

29. Roehrs T, Roth T. Sleep, sleepiness, and alcohol use. *Alcohol Res Health*. 2001; 25(2):101–109. [PubMed: 11584549]
30. Yesavage JA, Leirer VO. Hangover effects on aircraft pilots 14 hours after alcohol ingestion: a preliminary report. *Am J Psychiatry*. 1986; 143(12):1546–1550. [PubMed: 3789207]
31. Alt JA, Mace JC, Smith TL, Soler ZM. Endoscopic sinus surgery improves cognitive dysfunction in patients with chronic rhinosinusitis. *Int Forum Allergy Rhinol*. 2016; 6(12):1264–1272. [PubMed: 27384037]
32. Levy JM, Mace JC, DeConde AS, Steele TO, Smith TL. Improvements in psychological dysfunction after endoscopic sinus surgery for patients with chronic rhinosinusitis. *Int Forum Allergy Rhinol*. 2016; 6(9):906–913. [PubMed: 27080574]
33. El Rassi E, Mace JC, Steele TO, Alt JA, Smith TL. Improvements in sleep-related symptoms after endoscopic sinus surgery in patients with chronic rhinosinusitis. *Int Forum Allergy Rhinol*. 2016; 6(4):414–422. [PubMed: 26678684]
34. Rudmik L, Smith TL, Mace JC, Schlosser RJ, Hwang PH, Soler ZM. Productivity costs decrease after endoscopic sinus surgery for refractory chronic rhinosinusitis. *Laryngoscope*. 2016; 126(3): 570–574. [PubMed: 26371457]

Figure 1. Linear association between SNOT-22 total scores and monetized productivity losses (n=198)

Figure 2. Linear association between SNOT-22 psychological dysfunction domain scores and monetized productivity losses (n=198)

Table 1
Patient characteristics and comorbidity of final study population with CRS (n=198)

Characteristics:	Mean [$\pm$ SD]	N (%)	Range [UB, LB]
Age (years)	47.7 [$\pm$ 15.4]		[18, 80]
Gender: Female ⁺		95 (48%)	
Race: White / Caucasian		163 (82%)	
African American		20 (10%)	
Asian		7 (4%)	
American Indian/Alaskan Native		2 (1%)	
Ethnicity: Hispanic / Latino		9 (5%)	
Previous sinus surgery		118 (60%)	
Treatment modality: ESS		158 (80%)	
CMT		40 (20%)	
Nasal polyposis		68 (34%)	
Asthma		71 (36%)	
Allergy (mRAST/skin prick confirmed)		111 (56%)	
Depression		20 (10%)	
Fibromyalgia		2 (1%)	
Immunodeficiency		6 (3%)	
Current tobacco use / smoker		11 (6%)	
Current alcohol use		82 (42%)	
Steroid dependency		21 (11%)	
Diabetes		18 (9%)	
GERD		37 (19%)	
Patient-report Outcome Measures:			
SNOT-22 total score	51.9 [$\pm$ 21.4]		[3, 106]
Rhinologic symptom domain	16.2 [$\pm$ 6.8]		[0, 30]
Extra-nasal rhinologic symptom domain	8.2 [$\pm$ 3.8]		[0, 15]
Ear / facial symptom domain	9.0 [$\pm$ 5.3]		[0, 23]
Psychological dysfunction domain	15.6 [$\pm$ 8.3]		[0, 35]
Sleep dysfunction domain	13.5 [$\pm$ 6.9]		[0, 25]
Productivity losses (monetized)	\$11,820 [$\pm$ \$10,349]		[\$0, \$49,059]
Clinical measures of disease severity:			
Endoscopy score	5.3 [$\pm$ 3.8]		[0, 18]
Computed tomography score	11.1 [$\pm$ 6.2]		[0, 24]

+, identified through self-report; CRS, chronic rhinosinusitis; SD, standard deviation; UB, upper bound; LB, lower bound; ESS, endoscopic sinus surgery; CMT, continued medical therapy; mRAST, modified radioallergosorbent testing; GERD, gastroesophageal reflux disease; SNOT-22, SinoNasal Outcome Test.

Table 2
Correlation coefficients between productivity cost and SNOT-22 total and domain scores between patient subgroupings (n=198)

Subgroups:	SNOT-22 total score	Rhinologic symptom domain		Extra-nasal rhinologic symptom domain		Ear / facial symptom domain		Psychological dysfunction domain		Sleep dysfunction domain	
	Rs	Rs	Rs	Rs	Rs	Rs	Rs	Rs	Rs	Rs	Rs
Male	0.392 *	0.231 *		0.270 *		0.228 *		0.511 *		0.338 *	
Female	0.344 *	0.224 *		0.258 *		0.236 *		0.333 *		0.364 *	
White/Caucasian	0.413 *	0.270 *		0.308 *		0.317 *		0.439 *		0.381 *	
African American	0.096	0.081		0.028		-0.273		0.209		0.376	
Asian	0.054	-0.464		0.148		-0.286		0.577		0.306	
American Indian/Alaska Native	----	----		----		----		----		----	
Hispanic/Latino	0.217	0.126		0.354		0.084		0.083		0.267	
Non-Hispanic/Latino	0.367 *	0.213 *		0.270 *		0.247 *		0.438 *		0.349 *	
Previous sinus surgery	0.411 *	0.202 *		0.280 *		0.205 *		0.427 *		0.279 *	
No previous sinus surgery	0.345 *	0.230 *		0.245 *		0.291 *		0.430 *		0.462 *	
Treatment modality: ESS	0.369 *	0.188 *		0.271 *		0.276 *		0.430 *		0.318 *	
Treatment modality: CMT	0.343 *	0.322 *		0.282		0.110		0.415 *		0.460 *	
Nasal polypsis	0.244 *	0.186		0.221		0.072		0.413 *		0.173	
Without nasal polypsis	0.439 *	0.312 *		0.300 *		0.308 *		0.444 *		0.442 *	
Asthma	0.390 *	0.229		0.380 *		0.277 *		0.472 *		0.388 *	
Without asthma	0.380 *	0.248 *		0.254 *		0.230 *		0.418 *		0.360 *	
Allergy	0.322 *	0.156		0.211 *		0.176		0.437 *		0.300 *	
Without allergy	0.432 *	0.308 *		0.343 *		0.333 *		0.430 *		0.420 *	
Depression	0.514 *	0.519 *		0.437 *		0.654 *		0.132		0.271	
Without depression	0.339 *	0.168 *		0.239 *		0.188 *		0.441 *		0.362 *	
Fibromyalgia	----	----		----		----		----		----	

Subgroups:	SNOT-22 total score	Rhinologic symptom domain	Extra-nasal rhinologic symptom domain	Ear / facial symptom domain	Psychological dysfunction domain	Sleep dysfunction domain
	Rs	Rs	Rs	Rs	Rs	Rs
Without fibromyalgia	0.368 *	0.221 *	0.272 *	0.241 *	0.429 *	0.356 *
Immunodeficiency	-0.429	-0.257	-0.395	-0.174	-0.464	-0.200
Without immunodeficiency	0.381 *	0.222 *	0.271 *	0.262 *	0.452 *	0.356 *
Current tobacco use / smoker	0.358	-0.032	0.442	0.342	0.259	0.325
No tobacco use	0.354 *	0.204 *	0.253 *	0.219 *	0.417 *	0.332 *
Current alcohol use	0.444 *	0.252 *	0.325 *	0.299 *	0.494 *	0.472 *
No alcohol use	0.313 *	0.165	0.216 *	0.203 *	0.414 *	0.309 *
Steroid dependency	0.487 *	0.035	0.280	0.474 *	0.478 *	0.407
Without steroid dependency	0.331 *	0.214 *	0.248 *	0.194 *	0.405 *	0.347 *
Diabetes mellitus	0.412	0.116	0.105	0.511 *	0.489 *	0.568 *
Without diabetes mellitus	0.354 *	0.216 *	0.288 *	0.211 *	0.413 *	0.337 *
GERD	0.562 *	0.444 *	0.523 *	0.393 *	0.516 *	0.526 *
Without GERD	0.317 *	0.162 *	0.223 *	0.202 *	0.407 *	0.315 *

SNOT-22, 22-item SinoNasal Outcome Test; Rs, Spearman's correlation coefficient; ESS, endoscopic sinus surgery; CMT, continued medical therapy; GERD, gastroesophageal reflux disease;

* indicates significant correlation ($p < 0.050$).

Table 3
Mean annual productivity cost per patient subgroup

Subgroups:	Mean annual productivity cost [$\pm$ SD]	Comparative differences p-value
Male	\$10,274	0.080
Female	\$13,496	
White/Caucasian	\$11,753	0.845
African American	\$13,422	
Asian	\$8,298	
American Indian/Alaska Native	\$9,776	
Hispanic/Latino	\$10,222	
Non-Hispanic/Latino	\$11,896	0.637
Previous sinus surgery	\$12,526	0.245
No previous sinus surgery	\$10,778	
Treatment modality: ESS	\$12,154	0.367
Treatment modality: CMT	\$10,497	
Nasal polyposis	\$9,845	0.303
Without nasal polyposis	\$12,853	
Asthma	\$10,782	0.333
Without asthma	\$12,400	
Allergy	\$11,599	0.863
Without allergy	\$12,102	
Depression	\$13,486	0.256
Without depression	\$11,632	
Fibromyalgia	\$12,491	0.577
Without fibromyalgia	\$11,813	
Immunodeficiency	\$23,285	0.011
Without immunodeficiency	\$11,462	
Current tobacco use / smoker	\$23,195	0.002
No tobacco use	\$11,162	
Current alcohol use	\$11,557	0.736
No alcohol use	\$12,096	
Steroid dependency	\$18,910	0.002
Without steroid dependency	\$10,979	
Diabetes mellitus	\$15,880	0.136
Without diabetes mellitus	\$11,414	
GERD	\$11,641	0.895
Without GERD	\$11,861	

SD, standard deviation; ESS, endoscopic sinus surgery; CMT, continued medical therapy; GERD, gastroesophageal reflux disease;

Table 4
Average monetized productivity losses across SNOT-22 domain score categories

SNOT-22 score categories:	Rhinologic symptom domain Mean [±SD]	Extra-nasal rhinologic symptom domain Mean [±SD]	Ear / facial symptom domain Mean [±SD]	Psychological dysfunction domain Mean [±SD]	Sleep dysfunction domain Mean [±SD]
0-5	\$4,777 [±\$8,138]	\$9,290 [±\$9,437]	\$9,296 [±\$10,307]	\$5,597 [±\$8,334]	\$6,414 [±\$8,269]
6-10	\$13,148 [±\$11,092]	\$11,765 [±\$10,410]	\$11,444 [±\$8,815]	\$9,944 [±\$10,967]	\$9,956 [±\$10,094]
11-15	\$12,420 [±\$10,268]	\$14,047 [±\$10,656]	\$12,797 [±\$10,089]	\$10,010 [±\$9,087]	\$11,796 [±\$9,315]
16-20	\$11,455 [±\$10,068]	----	\$14,770 [±\$11,143]	\$12,525 [±\$8,886]	\$13,968 [±\$10,892]
21-25	\$13,098 [±\$9,936]	----	\$21,428 [±\$16,632]	\$14,011 [±\$10,595]	\$16,178 [±\$11,245]
26-30	\$15,311 [±\$12,184]	----	----	\$20,146 [±\$9,644]	----
31-35	----	----	----	\$19,460 [±\$14,768]	----

SNOT-22, 22-item SinoNasal Outcome Test; SD, standard deviation.

Table 5

Multivariate linear regression modeling results of average monetized productivity loss associated with both SNOT-22 total score and domain score increases

Independent Modeling Outcomes:	Unadjusted β	SE	Adjusted β	Adjusted SE	p-value*	t-test statistic	R ²
SNOT-22 total score	\$163	\$33	\$144*	\$32	<0.001	4.50	0.238
Rhinologic symptom domain	\$270	\$108	\$278 [#]	\$109	0.011	2.55	0.184
Extra-nasal rhinologic symptom domain	\$659	\$186	\$585 ^{\$}	\$180	0.001	3.26	0.193
Ear / facial symptom domain	\$454	\$136	\$334 [@]	\$133	0.013	2.52	0.214
Psychological dysfunction domain	\$455	\$83	\$380 [^]	\$81	<0.001	4.68	0.273
Sleep dysfunction domain	\$482	\$101	\$371 ⁺	\$100	<0.001	3.73	0.244

B beta/effect estimate for each single unit change in predictive factors; SE, standard error; SNOT-22, 22-item SinoNasal Outcome Test; R², coefficient of multiple determination / explained adjusted model variance (%).

* p-value indicates significant predictive values after final model adjustments.

** adjusted for the following statistically significant or clinically relevant (p<0.100) independent cofactors/comorbidities: enrollment site, nasal polyposis, immunodeficiency, current tobacco use, and steroid dependent conditions.

[#] adjusted for the following statistically significant or clinically relevant (p<0.100) independent cofactors/comorbidities: enrollment site, nasal polyposis, immunodeficiency, current tobacco use, and steroid dependent conditions.

^{\$} adjusted for the following statistically significant or clinically relevant (p<0.100) independent cofactors/comorbidities: enrollment site, immunodeficiency, current tobacco use, and steroid dependent conditions.

[@] adjusted for the following statistically significant or clinically relevant (p<0.100) independent cofactors/comorbidities: enrollment site, nasal polyposis, immunodeficiency, current tobacco use, steroid dependent conditions, and baseline endoscopy score.

[^] adjusted for the following statistically significant or clinically relevant (p<0.100) independent cofactors/comorbidities: enrollment site, nasal polyposis, immunodeficiency, current tobacco use, steroid dependent conditions, and baseline endoscopy score.

⁺ adjusted for the following statistically significant or clinically relevant (p<0.100) independent cofactors/comorbidities: enrollment site, nasal polyposis, immunodeficiency, current tobacco use, steroid dependent conditions, and baseline endoscopy score.