

# Workplace Indirect Cost Impacts of Nasal and Sinus Symptoms and Related Conditions

Jordan R. Kuiper, MS, Annemarie G. Hirsch, PhD, MPH, Karen Bandeen-Roche, PhD, Agnes S. Sundaresan, MD, MPH, Bruce K. Tan, MD, Robert C. Kern, MD, Robert P. Schleimer, PhD, and Brian S. Schwartz, MD, MS

**Objective:** Evaluate associations of nasal and sinus and related symptoms, as well as selected health conditions which produce those symptoms, with total lost productive time (LPT) at work in the past 2 weeks. **Methods:** We used a cross-sectional analysis of 2402 currently working subjects. Self-reported physician diagnoses, condition statuses measured with standardized instruments, and symptom-based factor scores from an exploratory factor analysis were used in survey weighted log-binomial regression. **Results:** Pain and pressure, nasal blockage and discharge, and asthma and constitutional symptom factor scores as well as self-reported allergic rhinitis were associated with higher total LPT. Individuals who met operationalized criteria for multiple health conditions, especially chronic rhinosinusitis, had the greatest total LPT. **Conclusions:** Better management of these symptoms, and awareness of how they impact an individual's ability to perform job-functions in the workplace, could improve overall productivity.

**Keywords:** ENT, epidemiology, productivity, symptoms, workplace

Cost is an important component in determining the overall burden of a disease,<sup>1</sup> often broken-down into two primary sources: direct and indirect. Direct costs include expenditures related to the medical treatment and care received for a condition while indirect costs are commonly characterized by daily life and employment impacts of a condition. In the workplace, indirect costs often include absenteeism (missing work due to health conditions)

and presenteeism (reduced productivity and performance at work due to health conditions), which are jointly referred to as total lost productive time (LPT).<sup>2</sup> Acute conditions, like influenza, often have more indirect costs than direct costs,<sup>1,3</sup> whereas chronic conditions, like diabetes, have larger direct costs.<sup>4</sup>

Chronic rhinosinusitis (CRS) is an upper respiratory condition characterized by inflammation of the nasal and paranasal sinuses,<sup>5-7</sup> that is estimated to affect nearly 12% of the adult US population,<sup>7</sup> and incurs \$22 to \$32 billion in total costs yearly.<sup>8,9</sup> The European Position Paper on Rhinosinusitis and Nasal Polyps symptom-based criteria (CRS<sub>s</sub>) is commonly used for CRS classification in epidemiologic studies.<sup>5</sup> Individuals with CRS<sub>s</sub> have been shown to have severe, persistent, and bothersome symptoms<sup>10</sup> that would be expected to impact workplace productivity. Previous studies have shown CRS to result in increased absenteeism<sup>11-17</sup> and presenteeism<sup>12,15,17,18</sup> with estimates as high as 24.6 and 38.8 days per year, respectively.<sup>18</sup> These studies have focused on individuals in the more severe spectrum of disease with many focused solely on recalcitrant or refractory CRS after surgery.<sup>15,17,18</sup>

To date, no study has evaluated the workplace impacts of CRS across the full spectrum of disease in a general population representative sample. CRS is often comorbid with several conditions (eg, allergic rhinitis [hay fever], asthma, migraine headache)<sup>19,20</sup> and the nasal and sinus symptoms (NSS) used in CRS<sub>s</sub> criteria often occur from these conditions as well. Further, these conditions have been shown to increase absenteeism,<sup>21-25</sup> presenteeism,<sup>21-25</sup> and total LPT.<sup>26,27</sup> Several of these conditions with overlapping symptoms are diagnosed solely on the basis of symptoms (eg, migraine headache), while others have additional evidence that can assist diagnosis (eg, pulmonary function tests, skin allergy testing, sinus computed tomography scan). Treatment for some of these conditions itself can have side effects that themselves impact work. Few prior studies have attempted to disentangle whether aspects of the diagnosis itself, which could capture the impact of treatment side effects, or the specific associated symptoms, were most associated with increased LPT.<sup>12,17</sup>

Given the lack of general population-based epidemiologic studies of NSS due to CRS and related conditions with workplace impacts, the overarching objective of this study was to identify risk factors for LPT in a generalizable, population-based sample. To accomplish this objective, we used electronic health records (EHR) of subjects who had a primary care provider from Geisinger, a healthcare system in over 40 counties in central and northeastern Pennsylvania; these subjects are representative of the general population for the region.<sup>28</sup>

## MATERIALS AND METHODS

### Study Overview

We performed a cross-sectional analysis using responses to the final questionnaire in a longitudinal study of subjects focused on NSS and CRS, described elsewhere.<sup>7,29</sup> Briefly, we sequentially mailed five self-administered questionnaires from April 2014 through December 2015 to a stratified random sample of primary care patients of Geisinger. Details of items included in questionnaires are described

From the Department of Environmental Health and Engineering (Mr Kuiper, Dr Hirsch, Dr Schwartz); Department of Epidemiology and Health Services Research, Geisinger, Danville, Pennsylvania (Dr Hirsch, Dr Sundaresan, Dr Schwartz); Department of Biostatistics (Dr Bandeen-Roche), Johns Hopkins University Bloomberg School of Public Health, Baltimore, Maryland; Department of Otolaryngology Head and Neck Surgery (Dr Tan, Dr Kern, Dr Schleimer); and Division of Allergy and Immunology, Department of Medicine (Dr Tan, Dr Kern, Dr Schleimer), Northwestern University Feinberg School of Medicine, Chicago, Illinois.

**Clinical Significance:** Pain and pressure, nasal blockage and discharge, and asthma and constitutional symptom factors were associated with increased total lost productive time. Increased awareness of how symptoms and health conditions impact workplace productivity could motivate improved symptom management to reduce workplace impacts.

**Author contributions:** All authors participated in drafting/revision of the manuscript, final approval of the manuscript, and interpretation of findings. All authors agree to be accountable for all aspects of the work. J.R.K., A.G.H., A.S.S., B.K.T., R.C.K., R.P.S., and B.S.S. were involved in the conception and design of the study. J.R.K., A.G.H., K.B.R., and B.S.S. acquired and analyzed the data.

This study was supported in part by grant U19AI106683 (Chronic Rhinosinusitis Integrative Studies Program [CRISP]) from the National Institutes of Health, and by a grant from the National Institute for Occupational Safety and Health (T42 OH0008428) to the Johns Hopkins University Education and Research Center for Occupational Safety and Health.

The authors declare they have no actual or potential competing financial interests. Supplemental digital contents are available for this article. Direct URL citation appears in the printed text and is provided in the HTML and PDF versions of this article on the journal's Web site ([www.joem.org](http://www.joem.org)).

Address correspondence to: Brian S. Schwartz, MD, MS, Johns Hopkins Bloomberg School of Public Health, 615 N. Wolfe Street, Room W7041, Baltimore, MD 21205 ([bschwar1@jhu.edu](mailto:bschwar1@jhu.edu)).

Copyright © 2019 American College of Occupational and Environmental Medicine

DOI: 10.1097/JOM.0000000000001636

elsewhere.<sup>29</sup> Briefly, the four questionnaires following baseline were used to understand seasonal exacerbations of NSS and were sent in approximately 4 months intervals. This study was approved by the Institutional Review Board (IRB) of Geisinger, which has an IRB Authorization Agreement with the Johns Hopkins Bloomberg School of Public Health. Health Insurance and Accountability Act authorization and written informed consent waivers were approved by the IRB.

### Sampling Method and Study Population

A description of the sampling method has been previously reported.<sup>7</sup> Electronic health records (EHR) were utilized to categorize individuals into three groups based on International Classification of Disease-9 and Current Procedural Terminology codes for allergic rhinitis, asthma, CRS, nasal polyps, and sinus procedures. We over-sampled individuals with CRS, nasal polyp, allergic rhinitis, and asthma diagnostic codes, as well as racial/ethnic minorities.<sup>7</sup> Of the 23,700 individuals randomly selected to participate in the longitudinal study, 7847 responded to the baseline survey and 4600 responded to the final follow-up questionnaire.

### Primary Independent Variables

We first operationalized definitions and analytic variables for the primary independent variables of interest, including condition statuses and symptoms.

#### CRS Classification

We used the CRS<sub>s</sub> criteria for categorizing individuals with CRS as previously reported.<sup>7,10,29</sup> CRS<sub>s</sub> status (referred to as CRS) was determined using self-reported frequency (in the past 3 months) of the cardinal CRS symptoms (nasal blockage, green or yellow discharge [anterior or posterior], smell loss, and facial pain or pressure) at each questionnaire. These symptoms were self-reported using a five-point Likert scale (“never,” “once in a while,” “some of the time,” “most of the time,” and “all of the time”). Symptoms reported at least “most of the time” were considered towards CRS<sub>s</sub> criteria. Individuals were assigned into three CRS status groups: “never” (did not meet current CRS<sub>s</sub> criteria at any questionnaire), “past” (met criteria at a prior questionnaire but not at the last one), and “current” (met criteria at last one).

#### Self-Reported Physician Diagnoses and Migraine Headache Status

Self-reported physician diagnosis of hay fever and asthma were ascertained at baseline. Migraine status was operationalized as a binary indicator and determined using standardized and validated methods.<sup>29,30</sup>

#### Symptom Factor Scores

Factor scores were estimated from five factors using factor weights and methods previously described.<sup>31</sup> Briefly, three EFA models were performed using 3535 subjects with responses to baseline, 6 months, and 16-month (final) questionnaires. Indicators included in the EFA were 37 self-reported symptoms in the categories of nasal and sinus; ear and eye; asthma; constitutional symptoms (ie, fever, headache, fatigue); and allergy symptoms. Five factors were identified by the EFA models as pain and pressure; blockage and discharge; asthma and constitutional; smell loss; and ear and eye symptoms. Factor weights from the 16-month questionnaire EFA were used to estimate factor scores as previously reported.<sup>31</sup> Larger scores indicated greater reporting of symptoms relevant to the specific factor and were standardized by z-transformation to allow for comparisons of factors.

#### Dependent Variables: Absenteeism, Presenteeism, and Lost Productive Time

Questions from the Work and Health Interview<sup>32</sup> were only included in the 16-month questionnaire, using a 2-week recall

period. Subjects were instructed to complete the work-related questions only if they were currently working. Questions ascertained the average number of days worked per week and hours worked per day, which were then combined to calculate the average total hours worked in the prior 2 weeks. NSS-specific absenteeism was operationalized from two questions: “How many workdays did you miss in the past two weeks because you were not feeling well?” and “How many of the workdays in the past two weeks were missed due to nasal and sinus symptoms?” We estimated lost productivity while at work (presenteeism) due to NSS in two components. We first estimated presenteeism days with responses to two questions: “On how many days in the past two weeks did you go to work when not feeling well?” and “On the days in the past two weeks you were not feeling well at work how many were due to your nasal and sinus symptoms?” We then estimated an “impact index” as workplace ability and function while having NSS using responses to five Likert scale questions (Supplemental Digital Content Table S1, <http://links.lww.com/JOM/A571>). Each of the five questions were scored from 0 to 1 (1 = all of the time; 0.75 = most of the time; 0.50 = about half of the time; 0.25 = some of the time; 0 = none of the time) and the final index score was the mean of the five questions. Finally, the product of presenteeism days and the impact index provided the total number of NSS-specific presenteeism days. Both absenteeism and presenteeism were converted from days to hours using estimated hours worked per 2-week period. Lastly, total LPT was estimated by adding NSS-specific absenteeism and presenteeism for each subject.

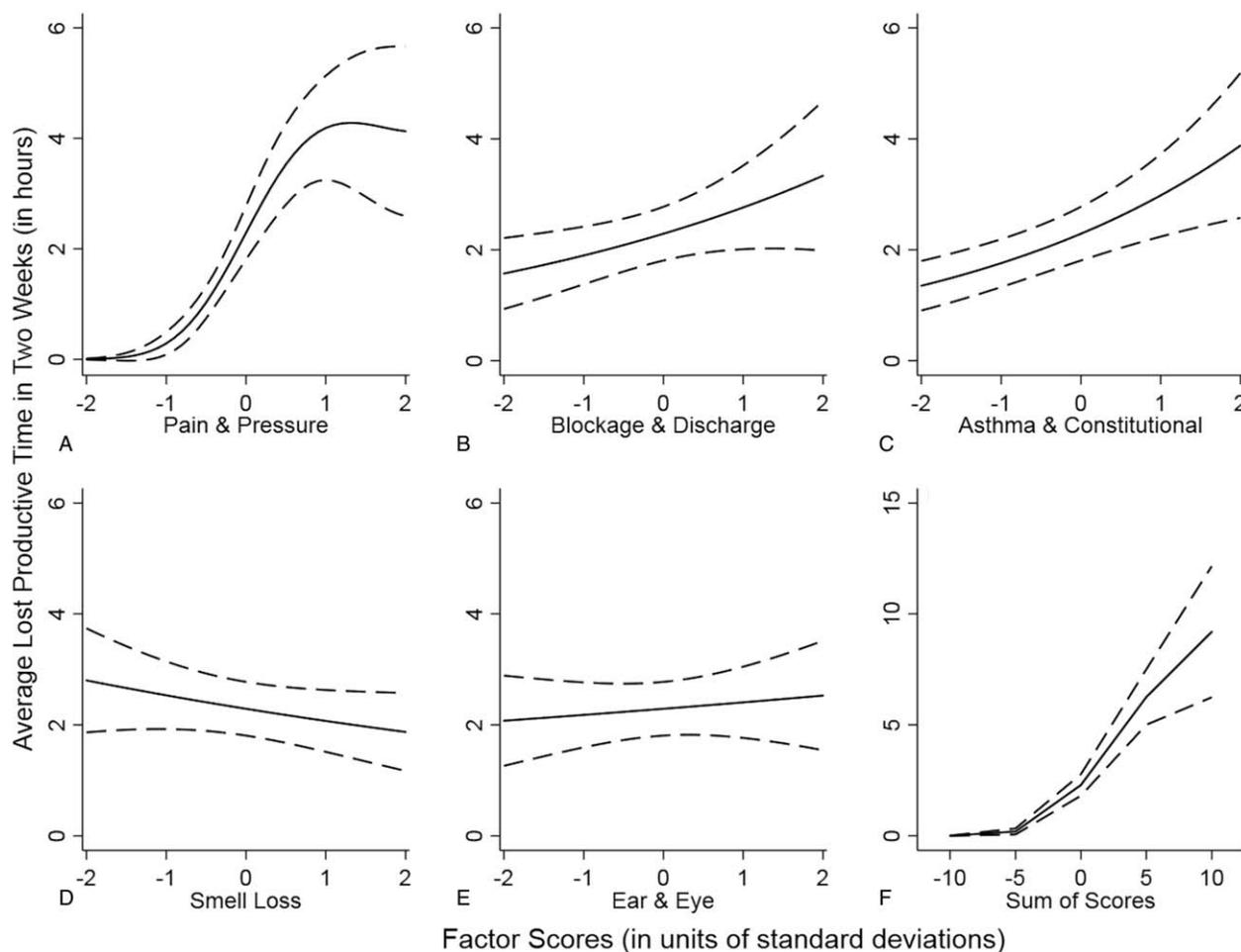
### Statistical Analyses

The primary goals of the analysis were to evaluate whether: (1) symptom-based factor scores from an exploratory factor analysis (EFA)<sup>31</sup> of a range of symptoms from several related conditions (ie, asthma, CRS, hay fever, migraine headache) were more strongly associated with total LPT than were operationalized or self-reported physician diagnoses of these conditions; and (2) estimate and compare average total LPT within subgroups based on CRS and other health conditions to characterize subgroups with higher average total LPT.

Of the 4600 subjects who responded to the final questionnaire, 2402 had classifiable CRS status and reported currently working and were therefore included in the analysis. Relations between variables as well as distributions were assessed and missing data on selected covariates were multiply imputed as done previously.<sup>29</sup> For adjusted estimates of total LPT, three log-binomial regression models were assessed: model 1 evaluated symptom factors; model 2 evaluated condition statuses (eg, physician-reported hay fever); and model 3 (fully-adjusted) evaluated symptoms and conditions. The outcome in these models was a proportion defined by: the number of work-hours attributed to LPT (numerator) over the average total number of hours worked (denominator), in a 2-week period.

Potential covariates were selected from prior studies and a priori theory and included age (years, centered, and scaled per 5-years), sex, race/ethnicity (white vs non-white), receipt of Medical Assistance (a surrogate for family socioeconomic status),<sup>33</sup> body mass index (BMI, kg/m<sup>2</sup>), Charlson comorbidity index (centered),<sup>34</sup> smoking status (never, former, current), and education (high school education or less, some college, 4 or more years of college). Non-linearity in continuous covariates was assessed, resulting in a cubic function for pain and pressure.

To better understand associations observed in the regression models, we estimated LPT over a range of factor score values (Fig. 1) and in subgroups based on CRS and health conditions using average adjusted predictions (ie, predictive margins<sup>35</sup>) derived from the fully-adjusted model (Fig. 2). Hereafter, we refer to these values as average expected total LPT (AET-LPT). While effect



**FIGURE 1.** Adjusted average total lost productive time (in hours) in 2 weeks, by standardized factor scores and sum of factor scores, estimated in the source population. LPT estimates are presented across  $\pm 2$  standard deviations for each of five symptom factors: (A) pain and pressure; (B) blockage and discharge; (C) asthma and constitutional; (D) smell loss; (E) ear and eye; and (F) the sum of the five factor scores. LPT, lost productive time.

estimates from regression models are useful in understanding adjusted relations of covariates with the outcome, this latter approach provides tangible estimates of the expected outcome for, as examples, specific subgroups of people or for different values of specified covariates.

Models were weighted using methods previously described<sup>29</sup> and included use of sampling<sup>7,10</sup> and inverse-probability of censoring weights (IPCW).<sup>29</sup> As done previously,<sup>7,10,29</sup> full weights were used in estimation of descriptive statistics whereas truncated weights were used in regression modeling. Adequacy of model fit was assessed by inspecting residuals, influence, and leverage, with one observation ultimately removed from final models. Models with and without this observation were substantively comparable, yet non-linearity of pain and pressure factor score was attenuated when the observation was included. Statistical analyses were performed using STATA v15.1 (StataCorp, College Station, TX) and R v3.4.1 (R Foundation for Statistical Computing, Vienna, Austria; www.r-project.org) software packages.

**Sensitivity Analyses**

We did not include CRS status in model 3 since questions used to operationalize CRS<sub>s</sub> were also included in the factors, thereby inducing a linear dependency. However, we did test an

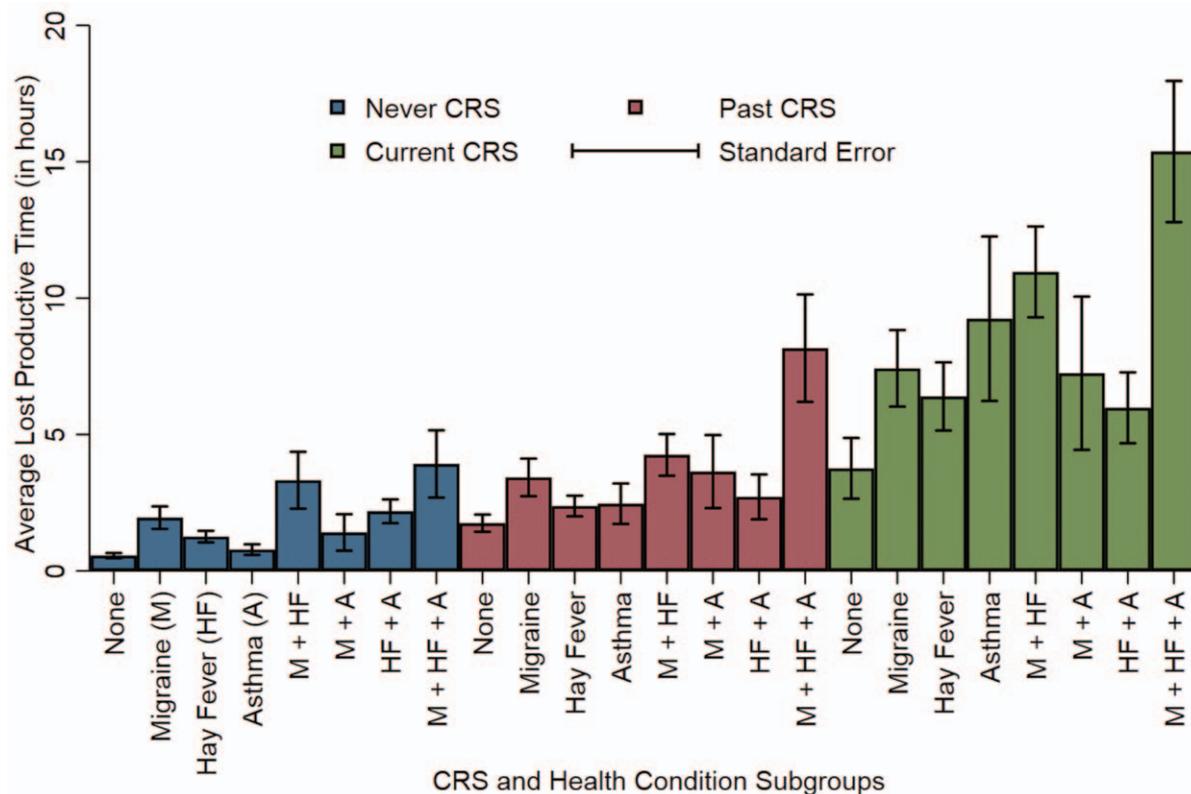
additional model in which we included CRS status as a covariate. We also assessed sensitivity of observed effect estimates (for model 3) to sampling weights by comparing estimates from unweighted, truncated, and fully weighted models.

**RESULTS**

**Description of Study Population**

Of the 2402 working subjects, a total of 134, 775, and 790 subjects had any hours of absenteeism, presenteeism, and total LPT in the prior 2 weeks, respectively. The mean (standard error) absenteeism, presenteeism, and total LPT in the past 2 weeks was 0.40 (0.10), 1.45 (0.17), and 1.86 (0.21) hours, respectively. Compared with subjects included in the study, excluded subjects tended to be older, less healthy (ie, larger Charlson comorbidity index), and more likely to receive Medical Assistance (Supplemental Digital Content Table S2, <http://links.lww.com/JOM/A571>).

Population-estimated (survey weighted) descriptive information for the study sample showed persons with LPT were younger, more likely to be women, had more comorbidities, and were more likely to have past or current CRS (Table 1). Average factor scores were estimated in the source population, both overall and in CRS and health condition subgroups (ie, migraine headache, hay fever,



**FIGURE 2.** Adjusted average total lost productive time (in hours) in 2 weeks, by CRS<sub>s</sub> and health condition subgroups, estimated in the source population. Estimates based on fully-adjusted model (model 3) associations. CRS<sub>s</sub>, symptoms that meet European Position Paper on Rhinosinusitis definition for CRS symptoms.

asthma, and combinations [Supplemental Digital Content Figure S1, <http://links.lww.com/JOM/A571>].

**Adjusted Estimates of Workplace Impacts**

In an adjusted model with symptom factor scores, three factors were associated with total LPT: pain and pressure, blockage and discharge, and asthma and constitutional (model 1, Table 2). In the next model, factor scores were removed and condition status for various health conditions were added; in this model, migraine, physician-diagnosed hay fever, and past and current CRS were associated with increased hours of total LPT (model 2, Table 2). In the fully-adjusted model, factor scores and health condition status were included together; pain and pressure, blockage and discharge, and asthma and constitutional factors, as well as hay fever, remained associated with total LPT (model 3, Table 2). Generally, estimates and inferences were substantively unchanged when different sampling weights were used (or omitted) (Supplemental Digital Content Table S3, <http://links.lww.com/JOM/A571>) or when CRS status was added to model 3 (Supplemental Digital Content Table S4, <http://links.lww.com/JOM/A571>).

We further evaluated associations of each factor with total LPT by estimating AET-LPT using score values within ±2 standard deviations, controlling for covariates (model 3, Table 2 and Fig. 1A–E). AET-LPT for a one standard deviation increase from the mean pain and pressure factor score would be 4.19 (95% CI: 3.25, 5.13) hours, while a decrease would be 0.29 (95% CI: 0.08, 0.49) hours (Fig. 1A). Similarly, AET-LPT for a blockage and discharge factor score one standard deviation above or below the mean would be 2.76 (95% CI: 2.01, 3.52) and 1.90 (95% CI: 1.38, 2.42) hours, respectively (Fig. 1B). AET-LPT for a one standard

deviation increase from the mean asthma and constitutional factor score would be 2.98 (95% CI: 2.24, 3.73) hours, while a decrease would be 1.76 (95% CI: 1.33, 2.19) hours (Fig. 1C). Using the sum of all factor scores as an aggregate measure of all NSS and related symptoms, AET-LPT among subgroups with a score of 0, 5, or 10 would be 2.29 (95% CI: 1.81, 2.78), 6.25 (95% CI: 5.00, 7.50), and 9.20 (95% CI: 6.24, 12.2) hours, respectively (Fig. 1F).

Finally, to understand how associations with symptoms and LPT are represented in subgroups of individuals with these symptoms, we estimated AET-LPT within subgroups based on CRS and health conditions, using the fully-adjusted model (Fig. 2). Overall, the current CRS subgroup would be expected to have the most AET-LPT, 7.47 hours (95% CI: 6.11, 8.82) in 2 weeks. Current CRS subgroups with comorbid asthma, hay fever, or migraine would have an AET-LPT of 9.25 (95% CI: 3.34, 15.2), 6.40 (95% CI: 3.95, 8.85), and 7.42 (95% CI: 4.67, 10.2) hours, respectively. Lastly, the current CRS subgroup with all three comorbidities would have an AET-LPT of 15.4 (95% CI: 10.3, 20.5) hours (Fig. 2).

**DISCUSSION**

In this first general population-based study of the workplace impacts of nasal, sinus, and related symptoms due to CRS and comorbid conditions, several findings were notable. We identified three symptom domains using factor scores that were associated with total LPT, specifically pain and pressure, blockage and discharge, and asthma and constitutional, with the strongest association for pain and pressure. Before inclusion of these factor scores, past or current CRS, hay fever, and migraine were each associated with total LPT but only hay fever was associated with total LPT when factor scores were included.

**TABLE 1.** Population-Estimated Characteristics Based on Study Sample (n = 2402)

Selected Variables	Means (95% Confidence Intervals)/Medians (IQR)*		
	No LPT (n = 1612) <sup>†</sup>	LPT >0 (n = 790)	P-Value
Hours worked per day; mean	8.33 (8.12–8.54)	8.52 (8.24–8.80)	0.31
Days worked per 2-week period; mean	9.68 (9.49–9.87)	10.2 (9.91–10.5)	<b>0.003</b>
Age (in yrs); mean	48.4 (47.0–49.8)	43.9 (41.7–46.0)	<b>0.001</b>
Body mass index (BMI; kg/m <sup>2</sup> ); mean	29.4 (28.7–30.0)	29.0 (27.9–30.2)	0.62
Charlson comorbidity index; mean	0.79 (0.72–0.86)	1.16 (0.97–1.33)	<b>0.001</b>
Blockage and discharge; median (IQR)	–0.77 (0.91)	0.18 (1.17)	<b>&lt;0.001</b>
Pain and pressure; median (IQR)	–0.82 (0.55)	0.15 (1.58)	<b>&lt;0.001</b>
Asthma and constitutional; median (IQR)	–0.75 (–0.71)	0.16 (1.31)	<b>&lt;0.001</b>
Smell loss; median (IQR)	–0.77 (0)	0.24 (2.19)	<b>&lt;0.001</b>
Ear and eye; median (IQR)	–0.71 (1.07)	0.22 (1.36)	<b>&lt;0.001</b>
Column percentages (95% confidence intervals)			
Sex (female), n = 1496	59.7 (55.0–64.4)	75.8 (69.1–82.4)	<b>&lt;0.001</b>
Race/ethnicity (non-white), n = 157	3.73 (3.29–4.17)	5.59 (3.79–7.40)	0.09
Medical assistance (ever received) <sup>‡</sup> , n = 137	5.70 (3.09–8.32)	10.3 (5.43–15.1)	0.10
CRS <sub>s</sub> status (16-month) <sup>§</sup>			
Never, n = 1034	74.7 (70.9–78.4)	45.4 (37.2–53.6)	<b>&lt;0.001</b>
Past, n = 915	19.5 (16.1–22.8)	32.9 (25.7–40.0)	<b>0.001</b>
Current, n = 453	5.88 (3.89–7.87)	21.7 (15.9–27.5)	<b>&lt;0.001</b>
Physician diagnosed asthma, n = 573	8.82 (6.82–10.8)	23.6 (17.4–29.7)	<b>&lt;0.001</b>
Physician diagnosed hay fever, n = 1169	26.2 (22.4–30.0)	54.4 (46.2–62.6)	<b>&lt;0.001</b>
Migraine headache status, n = 523	11.2 (8.06–14.3)	36.0 (28.2–43.8)	<b>&lt;0.001</b>

Bold indicates statistical significance at P < 0.05.

CRS, chronic rhinosinusitis; CRS<sub>s</sub>, symptoms that meet European Position Paper on Rhinosinusitis definition for CRS symptoms; HER, electronic health record; LPT, lost productive time; NSS, nasal and sinus symptoms.

\*Estimates derived using survey weighted methods; P-values based on F-ratios, except factor scores, which are based on Mann–Whitney–Wilcoxon U test.

<sup>†</sup>LPT estimated using the sum of self-reported days missed and present while ill (in which work productivity was affected) due to NSS.

<sup>‡</sup>Medical assistance is determined from the EHR and is a proxy for family socioeconomic status.

<sup>§</sup>CRS status determined using self-reported symptoms relevant to CRS<sub>s</sub> at all observed time-points; never CRS = never met CRS<sub>s</sub> criteria over follow-up; past CRS = met CRS<sub>s</sub> criteria at some point in lifetime or over follow-up, but did not meet criteria at time of 16-month follow-up; current CRS = met CRS<sub>s</sub> criteria at time of 16-month follow-up.

**TABLE 2.** Adjusted Log-Binomial Regression Models of Total Lost Productive Time (in hours) in 2 weeks, by Symptom Factor Scores (Model 1), Selected Conditions (Model 2), and Both (Model 3), Estimated in the Source Population<sup>a</sup>

Covariates	Exponentiated β-Coefficients <sup>b</sup> (95% Confidence Interval)		
	Model 1	Model 2	Model 3 <sup>b</sup>
Pain and pressure factor score (FS) <sup>c</sup>			
Linear term	3.38 (2.42–4.71)*		3.31 (2.37–4.61)*
Squared term <sup>d</sup>	0.47 (0.31–0.71)*		0.48 (0.32–0.73)*
Cubic term <sup>d</sup>	1.16 (1.02–1.32)**		1.15 (1.02–1.31)**
Blockage and discharge FS	1.21 (1.01–1.45)**		1.21 (1.02–1.43)**
Asthma and constitutional FS	1.31 (1.16–1.50)*		1.30 (1.14–1.48)*
Smell loss FS	0.92 (0.80–1.06)		0.90 (0.78–1.04)
Ear and eye FS	1.08 (0.91–1.28)		1.05 (0.89–1.24)
Migraine status (Ref: no)		1.83 (1.31–2.55)*	1.24 (0.94–1.64)
Physician diagnosed hay fever (Ref: no)		1.61 (1.19–2.19)**	1.30 (1.00–1.70)**
Physician diagnosed asthma (Ref: no)		1.22 (0.87–1.72)	1.20 (0.88–1.63)
CRS <sub>s</sub> status (Ref: never) <sup>e</sup>			
Past		1.62 (1.10–2.38)**	
Current		4.24 (2.85–6.29)*	

CRS, chronic rhinosinusitis; CRS<sub>s</sub>, symptoms that meet European Position Paper on Rhinosinusitis definition for CRS symptoms; EHR, electronic health record; LPT, lost productive time; NSS, nasal and sinus symptoms.

<sup>a</sup>Estimates derived using survey weighted methods; outcome is a proportion represented by total LPT as the numerator and average total hours worked in a 2-week period as the denominator; all models additionally adjusted for: age (centered; scaled by 5 years), sex, race/ethnicity, medical assistance, body mass index (centered), Charlson comorbidity index (centered), smoking status, and education.

<sup>b</sup>To avoid linear dependency between current CRS status and the symptom factor scores, CRS<sub>s</sub> status was not retained in the final version of model 3 in which all other estimates are based on; estimates for CRS status are only derived from model 2.

<sup>c</sup>Factor scores were standardized (z-transformed) with units of SDs; entered model as continuous variables.

<sup>d</sup>Allowed for non-linearity in association.

<sup>e</sup>CRS status determined using self-reported symptoms relevant to CRS<sub>s</sub> at all observed time-points; never CRS = never met CRS<sub>s</sub> criteria over follow-up; past CRS = met CRS<sub>s</sub> criteria at some point in lifetime or over follow-up, but did not meet criteria at time of 16-month follow-up; current CRS = met CRS<sub>s</sub> criteria at time of 16-month follow-up.

\*P-value: <0.001

\*\*P-value: <0.05.

We attempted to determine which aspect of a condition was the key determinant of workplace impact by including both symptom factors and condition indicators in the same model. While condition status also encompasses symptoms (as they are generally the basis for diagnosis) it further includes willingness to seek medical care, disease control, medical or surgical treatments (which may affect reported symptoms), and side effects of treatments. By including both measures into a single model, we attempted to disentangle the workplace impacts of symptoms from the other aspects of the studied health conditions. Our results suggest that symptoms are more important than other features of these health conditions, with the symptoms of pain and pressure having a strong association with total LPT.

The finding with the pain and pressure factor is consistent with that of a prior study of CRS and LPT in a tertiary care sample, in which facial pain was found to be highly correlated with workplace presenteeism and total LPT, even with adjustment for total sino-nasal outcomes test (SNOT)-22 scores (which includes nasal and sinus, fatigue, and allergy symptoms) and confounding variables.<sup>12</sup> The results of both studies suggest that facial pain is associated with LPT even after accounting for differences in co-occurring symptoms. Our observed association between nasal blockage and discharge and total LPT is also supported by a study of SNOT-22 domains and indirect costs among individuals with refractory CRS, where increases in monetary costs were associated with a one standard deviation increase in extra-nasal rhinologic symptoms (eg, nasal discharge).<sup>17</sup> Asthma, particularly poorly controlled, has reportedly been associated with workplace impacts,<sup>23,24</sup> and our association of the asthma and constitutional factor with total LPT is consistent with prior literature. Our lack of an association for the smell loss factor score is also consistent with a recent study of olfactory dysfunction and total LPT among individuals with recalcitrant CRS using an objective measure of smell loss.<sup>36</sup>

Current CRS was associated with more total LPT than never or past CRS. Symptoms of blockage and discharge as well as facial pain and pressure are used in CRS<sub>s</sub> criteria for current CRS classification. Given this dependence on these symptoms for classification, it is perhaps unsurprising that current CRS was associated with total LPT in a model which only included conditions, since several studies of mainly tertiary care populations have shown CRS to influence workplace productivity among persons with it.<sup>12,15,18</sup> It is important to note the association of current CRS was attenuated when symptom factor scores were included in the same model. While this could be due to modest collinearity, it may also imply that it was the symptom-based components of current CRS classification which drove its association with total LPT, as opposed to aspects of medical and/or surgical treatments.

Hay fever was the only condition to remain associated with LPT in the fully-adjusted model. We speculate that only individuals with the most severe hay fever symptoms would seek medical care and thus have a physician diagnosis; however, the observation could also be due to side effects of some allergy medications, which have been associated with LPT.<sup>37</sup>

Estimates of total LPT share similarities with previous findings. A prior study of total LPT among migraineurs found a range of 0.98 to 4.07 and 0.83 to 4.95 hours of total LPT per week among white women and men, respectively, ages 45 to 54 years.<sup>27</sup> Our study estimates are comparable. A pain and pressure symptom factor score one standard deviation above average predicted 4.19 hours of total LPT per 2 weeks (~2.10 hours per week), while migraineurs with no history of CRS and other comorbidities were predicted to have 1.95 hours of total LPT per 2 weeks (~0.98 hours per week). Our study also found results differing from prior studies. For example, a study of CRS estimated an average workplace impact of 63.4 days of total LPT per year (507.2 hours assuming

8-hour work periods) among persons with CRS.<sup>18</sup> The discrepancy is likely because the latter study was only of persons with refractory CRS selected from tertiary-referral centers, so represents the most extreme end of the disease spectrum.

Our study had several strengths. This is the first study, to our knowledge, to estimate and compare the workplace impacts of several conditions in a general population-based sample including CRS subjects with the full spectrum of disease, not only those cared for in tertiary care referral facilities. We examined symptom-based factors and evaluated their associations with total LPT with and without inclusion of specific health conditions in the models, disentangling the role of symptoms and other features of the health conditions on total LPT.

This study also had limitations. We did not have occupational information (eg, job title) for the subjects included in this study. We were thus unable to incorporate job type in analyses. We were also unable to account for differences in workplace culture and workplace policies (eg, sick time, personal time off without having to provide medical documentation, light duty) that could differentially influence how symptomatic conditions could be translated into absence time and presenteeism. Finally, we studied self-reported physician diagnoses, self-reported symptoms, and conditions based on standardized screening instruments, but were not able to include objective evidence of inflammation in our CRS definition.

In this first population-based study of NSS and other symptoms from CRS and related health conditions, we found that rigorously estimated factor scores in the domains of pain and pressure, nasal blockage and discharge, and asthma and constitutional symptoms were associated with increased total LPT. Awareness for how these symptoms may impact a person's ability to perform necessary job functions, as well as better management of symptoms, may ultimately lead to improved workplace productivity.

## REFERENCES

1. Jo C. Cost-of-illness studies: concepts, scopes, and methods. *Clin Mol Hepatol*. 2014;20:327–337.
2. Stewart WF, Ricci JA, Chee E, et al. Lost productive work time costs from health conditions in the United States: results from the American Productivity Audit. *J Occup Environ Med*. 2003;45:1234–1246.
3. Putri W, Muscatello DJ, Stockwell MS, et al. Economic burden of seasonal influenza in the United States. *Vaccine*. 2018;36:3960–3966.
4. Goetzl RZ, Long SR, Ozminkowski RJ, et al. Health, absence, disability, and presenteeism cost estimates of certain physical and mental health conditions affecting U.S. employers. *J Occup Environ Med*. 2004;46:398–412.
5. Fokkens WJ, Lund VJ, Mullol J, et al. European position paper on rhinosinusitis and nasal polyps 2012. *Rhinol Suppl*. 2012;2012:3. preceding table of contents, 1–298. [published Online First: 2012/07/07].
6. Orlandi RR, Kingdom TT, Hwang PH, et al. International consensus statement on allergy and rhinology: rhinosinusitis. *Int Forum Allergy Rhinol*. 2016;6(suppl):S22–S209.
7. Hirsch AG, Stewart WF, Sundaesan AS, et al. Nasal and sinus symptoms and chronic rhinosinusitis in a population-based sample. *Allergy*. 2017;72:274–281.
8. Smith KA, Orlandi RR, Rudmik L. Cost of adult chronic rhinosinusitis: a systematic review. *Laryngoscope*. 2015;125:1547–1556.
9. Rudmik L. Economics of chronic rhinosinusitis. *Curr Allergy Asthma Rep*. 2017;17:20.
10. Sundaesan AS, Hirsch AG, Young AJ, et al. Longitudinal evaluation of chronic rhinosinusitis symptoms in a population-based sample. *J Allergy Clin Immunol Pract*. 2018;6:1327.e3–1335.e3.
11. Bhattacharyya N. The economic burden and symptom manifestations of chronic rhinosinusitis. *Am J Rhinol*. 2003;17:27–32.
12. Smith KA, Ashby S, Orlandi RR, et al. The price of pain in chronic rhinosinusitis. *Int Forum Allergy Rhinol*. 2018;8:907–912.
13. Sahlstrand-Johnson P, Hopkins C, Ohlsson B, et al. The effect of endoscopic sinus surgery on quality of life and absenteeism in patients with chronic rhinosinusitis - a multi-centre study. *Rhinology*. 2017;55:251–261.

14. Sahlstrand-Johnson P, Ohlsson B, Von Buchwald C, et al. A multi-centre study on quality of life and absenteeism in patients with CRS referred for endoscopic surgery. *Rhinology*. 2011;49:420–428.
15. Rudmik L, Smith TL, Mace JC, et al. Productivity costs decrease after endoscopic sinus surgery for refractory chronic rhinosinusitis. *Laryngoscope*. 2016;126:570–574.
16. Campbell AP, Hoehle LP, Phillips KM, et al. Smoking: an independent risk factor for lost productivity in chronic rhinosinusitis. *Laryngoscope*. 2017;127:1742–1745.
17. Chowdhury NI, Mace JC, Smith TL, et al. What drives productivity loss in chronic rhinosinusitis? A SNOT-22 subdomain analysis. *Laryngoscope*. 2018;128:23–30.
18. Rudmik L, Smith TL, Schlosser RJ, et al. Productivity costs in patients with refractory chronic rhinosinusitis. *Laryngoscope*. 2014;124:2007–2012.
19. Tan BK, Chandra RK, Pollak J, et al. Incidence and associated premorbid diagnoses of patients with chronic rhinosinusitis. *J Allergy Clin Immunol*. 2013;131:1350–1360.
20. Hirsch AG, Yan XS, Sundaresan AS, et al. Five-year risk of incident disease following a diagnosis of chronic rhinosinusitis. *Allergy*. 2015;70:1613–1621.
21. Blanc PD, Trupin L, Eisner M, et al. The work impact of asthma and rhinitis: findings from a population-based survey. *J Clin Epidemiol*. 2001;54:610–618.
22. Vandenplas O, Vinnikov D, Blanc PD, et al. Impact of rhinitis on work productivity: a systematic review. *J Allergy Clin Immunol Pract*. 2018;6:1274.e9–1286.e9.
23. Sadatsafavi M, Rousseau R, Chen W, et al. The preventable burden of productivity loss due to suboptimal asthma control: a population-based study. *Chest*. 2014;145:787–793.
24. Hiles SA, Harvey ES, McDonald VM, et al. Working while unwell: workplace impairment in people with severe asthma. *Clin Exp Allergy*. 2018;48:650–662.
25. Messali A, Sanderson JC, Blumenfeld AM, et al. Direct and indirect costs of chronic and episodic migraine in the United States: a web-based survey. *Headache*. 2016;56:306–322.
26. Stewart WF, Wood GC, Razzaghi H, et al. Work impact of migraine headaches. *J Occup Environ Med*. 2008;50:736–745.
27. Stewart WF, Bruce C, Manack A, et al. A case study for calculating employer costs for lost productive time in episodic migraine and chronic migraine: results of the American Migraine Prevalence and Prevention Study. *J Occup Environ Med*. 2011;53:1161–1171.
28. Casey JA, Cosgrove SE, Stewart WF, et al. A population-based study of the epidemiology and clinical features of methicillin-resistant *Staphylococcus aureus* infection in Pennsylvania, 2001–2010. *Epidemiol Infect*. 2013;141:1166–1179.
29. Kuiper JR, Hirsch AG, Bandeen-Roche K, et al. Prevalence, severity, and risk factors for acute exacerbations of nasal and sinus symptoms by chronic rhinosinusitis status. *Allergy*. 2018;73:1244–1253.
30. Lipton RB, Dodick D, Sadovsky R, et al. A self-administered screener for migraine in primary care: the ID Migraine validation study. *Neurology*. 2003;61:375–382.
31. Cole M, Bandeen-Roche K, Hirsch AG, et al. Longitudinal evaluation of clustering of chronic sinonasal and related symptoms using exploratory factor analysis. *Allergy*. 2018;73:1715–1723.
32. Stewart WF, Ricci JA, Leotta C, et al. Validation of the work and health interview. *Pharmacoeconomics*. 2004;22:1127–1140.
33. Casey JA, Curriero FC, Cosgrove SE, et al. High-density livestock operations, crop field application of manure, and risk of community-associated methicillin-resistant *Staphylococcus aureus* infection in Pennsylvania. *JAMA Intern Med*. 2013;173:1980–1990.
34. Charlson ME, Pompei P, Ales KL, et al. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis*. 1987;40:373–383.
35. Graubard BI, Korn EL. Predictive margins with survey data. *Biometrics*. 1999;55:652–659.
36. Schlosser RJ, Storck KA, Rudmik L, et al. Association of olfactory dysfunction in chronic rhinosinusitis with economic productivity and medication usage. *Int Forum Allergy Rhinol*. 2017;7:50–55.
37. Ricci JA, Chee E, Lorandeanu AL, et al. Fatigue in the U.S. workforce: prevalence and implications for lost productive work time. *J Occup Environ Med*. 2007;49:1–10.