Received: 11 August 2022 | Accepted: 29 October 2022

DOI: 10.1111/coa.14013

ORIGINAL ARTICLE

WILEY

# Tobacco use increases the risk of chronic rhinosinusitis among patients undergoing endoscopic sinus surgery

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**Funding information**
National Cancer Institute, Grant/Award Number: P30 CA2014; National Center for Research Resources, Grant/Award Number: R01 RR021746

## Abstract

**Background:** Although it has been postulated that tobacco use, as well as other environmental exposures, may contribute to chronic rhinosinusitis (CRS), the data remain limited. Here, we utilised a large state population database to assess the association between tobacco use and CRS prevalence among patients undergoing endoscopic sinus surgery (ESS).

**Methods:** Employing a case–control study design, the Utah Population Database was queried for patients age >18 with a diagnosis of CRS and tobacco use who underwent ESS between 1996 and 2018. Smoking status was compared between patients with CRS ($n = 34\,350$) and random population controls matched 5:1 on sex, birth year, birthplace, time residing in Utah, and pedigree (i.e., familial) information ($n = 166\,020$). Conditional logistic regression models were used for comparisons between CRS patients and their matched controls. All analyses were repeated, additionally adjusting for race, ethnicity, tobacco use, asthma history, and interaction between tobacco use and asthma history.

**Results:** A total of 200 370 patients were included in the final analysis. Patients with CRS were significantly more likely to demonstrate a history of tobacco use than controls (19.6% vs. 15.0%; $p < .001$), with an adjusted odds ratio (aOR) of 1.42, 95% confidence interval 1.37–1.47; $p < .001$. More patients with CRS and comorbid asthma used tobacco (19.5%) than controls with asthma (15.0%; $p < .001$).

**Conclusion:** History of tobacco use may portend increased risk for the development of CRS among patients undergoing ESS compared to healthy controls.

KEYWORDS
chronic rhinosinusitis, endoscopic sinus surgery, smoking, tobacco

## 1 | INTRODUCTION

Chronic rhinosinusitis (CRS) is a common condition affecting approximately one in seven Americans, with a severe impact on quality of life and a large societal cost.[1] The negative impact on patient quality of life and health is similar or even more severe than congestive heart failure, angina, chronic obstructive pulmonary disease, and back pain.[2] Despite the impact that this condition has on individual health and society, the aetiology remains unclear as it is a multifactorial disease with many predisposing factors.

Among the many potential factors thought to contribute to an increased risk of CRS are tobacco use, as well as other environmental exposures.[3] However, studies surrounding CRS and tobacco use have suffered from poor study design, small sample sizes and inadequate definitions of CRS, leading to significant heterogeneity and conflicting results. Moreover, prior studies have been performed primarily in

  

non-US populations, such as South Korea, China, and most recently, the United Kingdom.[4–10] Finally, prior studies have not accounted for the potential confounding impact of comorbid asthma when evaluating the role of tobacco use on CRS prevalence. Patients with asthma are more likely to be smokers of tobacco compared to the healthy public (up to 27%[11] vs. 14%[12] in the general public), and the literature has repeatedly demonstrated that a large proportion of patients with CRS have concomitant asthma.[13]

We hypothesized that a history of tobacco use would increase the risk of CRS. Focusing on a large, US-based database, and utilising a case–control study design, we sought to characterise this relationship between tobacco use and CRS and test the aforementioned hypothesis.

**Key points**

1. Tobacco use is among the many potential factors thought to contribute to an increased risk of chronic rhinosinusitis (CRS).
2. However, data is limited.
3. Studies surrounding CRS and tobacco use suffer from poor study design, small sample sizes, and inadequate definitions of CRS, leading to heterogeneity and conflicting results.
4. Most of these data are based on non-US populations and epidemiologic in nature.
5. Utilising a case–control study design and a US-based population, the present investigation demonstrated that a history of tobacco use may portend an increased risk for the development of CRS among patients undergoing endoscopic sinus surgery compared to healthy controls.

## 2 | METHODS

### 2.1 | Utah Population Database

The Utah Population Database (UPDB) contains 42 million records spanning several decades, representing 11 million individuals who have ever resided in Utah, as well as their ancestors identified from genealogical records. Of these, 7 million individuals are linked to statewide clinical data contributed by the Utah Department of Health and the University of Utah Healthcare system of clinics and hospitals. Records on hospitalizations, ambulatory surgeries, and emergency department visits span from 1996 to the present.[14] The institutional review board (IRB) of the University of Utah and the Utah Resource for Genetic and Epidemiologic Research approve this population-based investigation. An IRB waiver of consent and authorization were obtained. We utilised UPDB data resources for this study as previously described,[14–16] and followed the written reporting guideline for this study. The comprehensive and longitudinal nature the database provides a unique opportunity to assess the relationship between various risk factors, including tobacco use, and CRS as compared to individually matched population controls, while maintaining anonymity of medical datasets linked to the UPDB by providing investigators with a non-identifying study identifier unique to each approved protocol.[17]

### 2.2 | Study population

#### 2.2.1 | Case definition

Electronic medical records within UPDB were queried for patients age 18 and older with an index diagnosis of CRS between 1996 and 2017.[15] Patients were included in the study if they satisfied the following criteria:

1. CPT (Current Procedural Terminology) endoscopy code 31231 *AND* at least one or more ICD-9/10 diagnosis codes for: chronic rhinosinusitis without nasal polyposis (CRSsNP): ICD-9473.0-473.9; ICD-10 J32.0-J32.9 *or* chronic rhinosinusitis with nasal polyposis (CRSwNP): ICD-9471.x; ICD-10 J33.0-J33.
2. CPT sinus surgery code: 30115, 30110, 31233, 31237, 31254, 31255, 31256, 31267, 31276, 31287, 31288, 31253, 31257, 31259

Of note, patient diagnoses/procedures in 2015 were excluded due to the inability to link these health records to other administrative records. Cases were excluded if they had the following known diagnoses that can be secondary causes of CRS: cystic fibrosis (ICD-9 277.x, ICD-10 E84.x), malignant sinonasal neoplasms (ICD-9 160.0-160.9, ICD-10 C30.0), inverted papilloma (ICD-9 212.0, ICD-10 D14.0), and a history of head or facial trauma (ICD-9 801.0-804.9; ICD-10 S01-S09), cerebrospinal fluid leak (ICD-9 349.81; ICD-10 G96.0), ganulomatosis with polyangitis (ICD-9 446.4; ICD-10 M31.3x), sarcoidosis (ICD-9 135.x; ICD-10 D86.x), churg-strauss syndrome (ICD-9 446.4; ICD-10 M30.1), HIV/AIDS (any HIV illness) (ICD-9 42; ICD-10 B20.x), injury to blood vessels of the head and neck (Carotid ICD-9 900.00-900.03, multiple vessels ICD-9 900.82, specified vessels ICD-9 900.89, and CSF rhinorrhea ICD-9 349.81; ICD-10 S15.x, J34.89), or history of aspirin exacerbated respiratory disease (ICD-9 V14.6, ICD-10 Z88.6). Patients were excluded if there was no documentation of patient gender, or if the date of last follow-up in the UPDB preceded the date of first surgery. This excluded patient records that may have documentation errors and ensure that we have adequate follow-up.

#### 2.2.2 | Control selection

Control patients (i.e., no history of CRSwNP or CRSsNP) were randomly selected from the Utah population and individually matched to cases in a 5:1 target ratio (actual 4.8:1) based on sex, birth year,

**TABLE 1** Baseline demographic data comparing patients with chronic rhinosinusitis (CRS) with their matching controls

| | Controls ($N = 166\,020$) | CRS ($N = 34\,350$) | $p$ Value |
|---|---|---|---|
| Gender | | | .737 |
| Female | 84 662 (51.0%) | 17 482 (50.9%) | |
| Male | 81 358 (49.0%) | 16 868 (49.1%) | |
| Race | | | <.001 |
| White/Caucasian | 149 123 (89.8%) | 31 945 (93.0%) | |
| African American | 730 (0.4%) | 81 (0.2%) | |
| Asian | 1716 (1.0%) | 216 (0.6%) | |
| American Indian/Alaska Native | 1082 (0.7%) | 46 (0.1%) | |
| Native Hawaiian/Pacific Islander | 609 (0.4%) | 57 (0.2%) | |
| Other/multiple races | 6199 (3.7%) | 1129 (3.3%) | |
| Not available | 6561 (4.0%) | 876 (2.6%) | |
| Ethnicity | | | <.001 |
| Not Hispanic/Latino | 123 576 (74.4%) | 27 095 (78.9%) | |
| Hispanic/Latino | 16 519 (10.0%) | 2490 (7.2%) | |
| Not available | 25 925 (15.6%) | 4765 (13.9%) | |
| Asthma | 10 646 (6.4%) | 7837 (22.8%) | <.001 |
| Allergy | 3010 (1.8%) | 2476 (7.2%) | <.001 |
| Tobacco use | 24 946 (15.0%) | 6699 (19.5%) | <.001 |
| Born in Utah | | | <.001 |
| Yes | 99 008 (59.6%) | 20 521 (59.7%) | |
| No | 51 159 (30.8%) | 11 541 (33.6%) | |
| Unknown | 15 853 (9.5%) | 2288 (6.7%) | |
| Nasal polyposis | | | <.001 |
| Yes | 0 (0) | 20 026 (58.3%) | |
| No | 166 020 (100.0%) | 14 324 (41.7%) | |

*Note*: Demographic characteristics of CRS vs. controls were compared using *t*-tests for continuous variables and chi-square tests for categorical variables.

birthplace (i.e., Utah or other), time residing in Utah, and pedigree (i.e., familial) information in relation to CRSwNP or CRSsNP cases. We required controls to reside in Utah at least until the matching case's first CRS diagnosis. This requirement was necessary to ensure that the controls did not have any diagnosis history of CRS in Utah. Matching by 'familial information' indicates that cases and controls were matched by the minimum of pedigree information (i.e., if cases were singleton, controls could be singleton; if cases were not singleton, controls had to have at least a first degree relative who was informative; that is, alive and living in Utah after 1 January 1996). The control subject randomisation was performed using sampling without replacement. Risk factors associated with occurrence of CRS were compared between cases and controls.

## 2.3 | Demographics and exposures

The following demographic information was collected for each patient: age at index case diagnosis, gender, race/ethnicity, birthplace (in Utah or outside of Utah). Exposure status for diagnosis history of allergies, asthma, and tobacco use were determined from electronic medical records in UPDB from 1996 to 2017. A diagnosis of tobacco use was searched utilising the following codes for tobacco/nicotine use: ICD-9 V15.82 and ICD-10 Z87.891. Patients with asthma were defined as anyone who were diagnosed with ICD-9493.x or ICD-10 J45.x. The presence of allergy diagnoses was confirmed using ICD-9 477 or ICD-10 J30.

## 2.4 | Study outcome

The primary outcome of this study was diagnosis of CRS requiring endoscopic sinus surgery (ESS), as defined above from the medical record (1996–2017), among individuals with and without a diagnosis history of tobacco use.

## 2.5 | Statistical analysis

Demographic characteristics and tobacco smoking status was compared across cases and controls, using *t*-tests for continuous variables and chi-squared tests for categorical variables. Conditional logistic

**TABLE 2** Tobacco use among patients with chronic rhinosinusitis (CRS) vs. matching controls with respect to sex and nasal polyposis

| | 5:1 controls | | CRS | | | CRSsNP | | | CRSsNP | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Personal use of tobacco | *N* | % | *N* | % | *p* Value | *N* | % | *p* Value | *N* | % | *p* Value |
| Total subjects | 166 020 | 100.0 | 34 350 | 100.0 | | 14 310 | 100 | | 20 040 | 100 | |
| Gender | | | | | .737 | | | .826 | | | .802 |
| Men | 81 358 | 49.0 | 16 868 | 49.1 | | 6588 | 46.0 | | 10 280 | 51.3 | |
| Women | 84 662 | 51.0 | 17 482 | 50.9 | | 7722 | 54.0 | | 9760 | 48.7 | |
| Tobacco use | | | | | <.001 | | | <.001 | | | <.001 |
| Exposed | 24 946 | 15.0 | 6699 | 19.5 | | 2707 | 18.9 | | 3992 | 19.9 | |
| Unexposed | 141 074 | 85.0 | 27 651 | 80.5 | | 11 603 | 81.1 | | 16 048 | 80.1 | |
| Tobacco use in men | | | | | <.001 | | | <.001 | | | <.001 |
| Exposed | 13 410 | 16.5 | 3627 | 21.5 | | 1349 | 20.5 | | 2278 | 22.2 | |
| Unexposed | 67 948 | 83.5 | 13 241 | 78.5 | | 5239 | 79.5 | | 8002 | 77.8 | |
| Tobacco use in women | | | | | <.001 | | | <.001 | | | <.001 |
| Exposed | 11 536 | 13.6 | 3072 | 17.6 | | 1358 | 17.6 | | 1714 | 17.6 | |
| Unexposed | 73 126 | 86.4 | 14 410 | 82.4 | | 6364 | 82.4 | | 8046 | 82.4 | |

*Note*: *p* Values were calculated from chi-square tests comparing CRS patients to their matching controls.
Abbreviations: CRSsNP, chronic rhinosinusitis without nasal polyposis; CRSwNP, chronic rhinosinusitis with nasal polyposis.

regression models were used for comparisons between CRS patients and their matched controls. All analyses were repeated, additionally adjusting for race, ethnicity, tobacco use, asthma history, and interaction between tobacco use and asthma history. Statistical analysis was performed using R software version 4.0.1.

## 3 | RESULTS

### 3.1 | Demographics

A total of 200 370 patients (34 350 CRS and 166 020 controls) were included in the final analysis (Table 1). The mean age at first CRS diagnosis was 43.9 with 58.3% of CRS patients demonstrating nasal polyposis. A larger proportion of the CRS cases were White/Caucasian and non-Hispanic/Latino compared to controls ($p < .001$). Similarly, significantly more CRS patients exhibited a history of asthma, allergy, and tobacco use ($p < .001$).

### 3.2 | Tobacco use among controls versus patients with CRS

A significantly larger amount of CRS patients demonstrated a personal history of tobacco use (19.5%) than matched controls (15.0%; $p < .001$; Table 2). This association between tobacco use and a CRS diagnosis was seen in both males and females, as well as in CRSsNP and CRSwNP (Table 2). The risk of CRS in the setting of tobacco use demonstrated an unadjusted odds ratio (OR) of 1.38 [confidence interval (CI) 1.34–1.42; $p < .001$; Table 3]. Compared to tobacco non-users without a history of asthma, the CRS risk among tobacco users without a history of asthma was 1.42-fold, while the CRS risk among smokers with an asthma was 3.60-fold (Tables S1 and A1). Among non-smokers with asthma, CRS risk was 5.21-fold (Tables S1 and A1). Finally, among the CRS with asthma (CRS-A) cases, there was a greater proportion of patients with a personal history of tobacco use (23.3%) compared to controls with asthma (15.6%) (Table 1).

## 4 | DISCUSSION

Most of the current data examining the relationship between active smoking and CRS is based in epidemiologic studies (mainly from Asia and the United Kingdom). The impact of findings from these investigations is hampered by inherent limitations related to survey style epidemiologic studies, including incomplete diagnostic criteria to characterise CRS.[18] The variable definition of CRS across this literature has resulted in significant heterogeneity.[18] Most studies do not have physician diagnoses, but rather incorporate self-reported diagnoses, which can significantly overestimate the true prevalence of disease.[9] Furthermore, findings from existing studies are often contradictory—some demonstrate an association between tobacco smoking and CRS prevalence,[4–8] while others do not.[9,10,19] Finally, few (limited) attempts have even been made to examine this relationship in the US population.[20] It is important to acknowledge these limitations in the existing literature and work to address them; if overlooked, they can lead to overreaching conclusions about the definitive nature of the positive association between tobacco smoking and CRS prevalence.[21]

In the present study, we used physician diagnoses of CRS based on ICD-9 and ICD-10 codes to fill in the knowledge gap left behind by study design deficits and a lack of US-based investigations in the prior

**TABLE 3** Association of chronic rhinosinusitis (CRS) with history of tobacco use—an *unadjusted* logistic regression analysis accounting for matching on sex and birth year

| | All patients[a] | | | Men[a] | | | Women[a] | | |
|---|---|---|---|---|---|---|---|---|---|
| | OR | 95% CI | *p* Value | OR | 95% CI | *p* Value | OR | 95% CI | *p* Value |
| | Risk of CRS vs. controls | | | | | | | | |
| Likelihood ratio test | 413.2, $p < 2e{-}16$ | | | 239.1, $p < 2e{-}16$ | | | 175.3, $p < 2e{-}16$ | | |
| Tobacco history | | | | | | | | | |
| Exposed | 1.38 | 1.34–1.42 | <.001 | 1.40 | 1.34–1.46 | <.001 | 1.35 | 1.30–1.41 | <.001 |
| Unexposed | Reference | | | Reference | | | Reference | | |
| | Risk of CRSsNP vs. controls | | | | | | | | |
| Likelihood ratio test | 147.3, $p < 2e{-}16$ | | | 75.81, $p < 2e{-}16$ | | | 71.64, $p < 2e{-}16$ | | |
| Tobacco history | | | | | | | | | |
| Exposed | 1.35 | 1.29–1.41 | <.001 | 1.36 | 1.27–1.46 | <.001 | 1.34 | 1.25–1.43 | <.001 |
| Unexposed | Reference | | | Reference | | | Reference | | |
| | Risk of CRSwNP vs. controls | | | | | | | | |
| Likelihood ratio test | 267.2, $p < 2e{-}16$ | | | 164.4, $p < 2e{-}16$ | | | 103.9, $p < 2e{-}16$ | | |
| Tobacco history | | | | | | | | | |
| Exposed | 1.40 | 1.34–1.45 | <.001 | 1.43 | 1.35–1.50 | <.001 | 1.37 | 1.29–1.45 | <.001 |
| Unexposed | Reference | | | Reference | | | Reference | | |

*Note*: Unadjusted (i.e., accounting for sex and age) conditional logistic regression models were used for comparison between CRS patients [i.e., all CRS cases, CRS without nasal polyposis (CRSsNP), CRS with nasal polyposis (CRSwNP)] and their matching controls.
Abbreviations: CI, confidence interval; OR, odds ratio.
[a]See Table 2 for sample size for each of these categories.

literature. Our study was unique in that it was able to achieve a large sample size without the traditional design of a survey-based epidemiologic survey, due to the incorporation of a large, statewide database, as well as implementation of a study design that accounted for comorbid asthma. These study design differences may explain why, unlike some of the survey-based, epidemiologic studies, our data demonstrate a significant association between tobacco use and prevalence of CRS with or without comorbid asthma, with an adjusted OR of 1.42, representing an over 40% increase in risk.

The use of self-reported or non-physician CRS diagnoses, or otherwise limited implementation of recommended subjective and objective diagnostic criteria for CRS,[22,23] has the potential to misconstrue the true prevalence of disease and is also subject to recall bias. Nevertheless, this is a common limitation of survey-based studies, which represent most of the current data on CRS and tobacco use. Indeed, several large survey studies in Europe and Asia have utilised this study design to conclude that CRS is more common among tobacco users and non-users (i.e., tobacco use is an independent risk factor for development of CRS).[4–8] However, these studies suffer from the aforementioned limitations to varying degrees.

Only a single database study was undertaken in the United States by Lieu et al. in 2000; although the authors noted a relative risk of 1.18 associated with cigarette smoking, this study was again significantly hindered by reliance on a self-reported diagnosis of CRS (i.e., symptoms of 'sinusitis or sinus problems' in the last 12 months). Chen et al. performed a similar national database study in Canada and found an association between active smoking and CRS, but again, the study design was hindered by a self-reported diagnosis of CRS.

It is less common to come across studies that have successfully incorporated physician and/or complete diagnostic criteria in their evaluation of CRS and tobacco use. The two major studies to have done so utilised the Chronic Rhinosinusitis Epidemiology Study (CRES) data in the United Kingdom, incorporating the EPOS 2012 symptomatic guidelines and either endoscopic or CT evidence of CRS to render a physician diagnosis of CRS. Both studies, with limited sample sizes ranging from 1400 to 1700 patients, demonstrated no significant association between tobacco smoking and a diagnosis of CRS.[10] An earlier study out of Korea by Min et al. similarly combined a large epidemiology study design with both subjective and objective (nasal endoscopy) diagnostic criteria of CRS in a population of 9000 Korean participants to likewise conclude a lack of association between tobacco smoking and prevalence of CRS.[19]

In contrast to the present investigation, these three studies, which also utilised comprehensive criteria/physician diagnoses for CRS, demonstrated no significant relationship between CRS and tobacco use. It is important to note that although the results from our study differ from those outlined in the CRES studies and by Min et al., they are in alignment with the larger collection of non-US epidemiologic studies.[4–8] A possible reason for this observation may lie in the significantly larger sample size, longitudinal nature (1996–2017 in the present study vs. 2007–2013 in CRES studies and 1991 in Min et al.)[9,10,19] and/or different baseline levels of smoking in the respective populations. For example, our study included 166 000 matched

non-CRS controls and an additional 34 000 patients with a CRS diagnosis; this is a much larger sample size than either the CRES or Min et al. studies.[9,10,19] It is possible that if the differences between CRS patients and healthy controls are small, a larger sample size such as ours is necessary to tease out these differences. Furthermore, all patients included in our analysis underwent ESS for their CRS. It is possible that these cases represent more severe disease that cannot be managed medically, which may be unique from the patient population examined in the CRES studies.

There are several key limitations to our study that should be acknowledged. First, the ICD-9 and ICD-10 codes used to diagnose tobacco use include all forms of tobacco consumption, including smoking, chewing, snuffing, and so forth. Existing data in the literature demonstrates that of the individuals in the United States who use tobacco, the vast majority smoke (14% of the US population), rather than consume it in a smokeless fashion (2.4% of the US population).[12,24] Nevertheless, the present manuscript interprets our data as tobacco used in any form and does not imply that *only* smoking tobacco is associated with risk of developing CRS. Second, we were limited by our database, in our ability to characterise duration of use, as well as former versus current tobacco use. Third, we cannot ignore the potential for inaccurate coding at the time the time of initial diagnostic documentation. However, the CRS diagnoses codes used here have been previously validated through chart review.[15,16] Furthermore, although ICD-9 codes tobacco codes were shown to be effective in identifying an individual's smoking status,[25] we acknowledge there is potential for underreporting of tobacco use. Fourth, the rates of tobacco use in the state of Utah are not representative of the remainder of the United States, as the prevalence of cigarette smoking is the lowest in the state of Utah compared to the rest of the United States (7.9% vs. 14% in 2019).[12] It is possible that in areas that have higher rates of tobacco use, the association with a CRS diagnosis may be even greater. Finally, due to the large sample size of the present study, there is a potential for statistical over-powering, which may highlight statistical differences that are not necessarily clinically relevant. Despite these limitations, the large sample size of the present investigation, along with a case–control study design and incorporation of physician, rather than self-reported diagnoses of CRS, help fill a knowledge gap regarding the impact of tobacco use on the prevalence of CRS. Future studies should consider evaluating the role of tobacco use on revision rates of ESS in CRS to further understand the impact of tobacco on CRS outcomes.

## 5 | CONCLUSION

The risk of a CRS diagnosis is increased by more than 40% among tobacco users undergoing ESS compared to matched controls, independent of asthma status.

### AUTHOR CONTRIBUTIONS

**Amarbir S. Gill:** Conceptualization; data interpretation; manuscript writing; revisions. **Huong Meeks:** Data analysis; data interpretation; revisions. **Karen Curtin:** Data analysis; data interpretation; revisions. **Kerry Kelly:** Data interpretation; revisions. **Jeremiah A. Alt:** Conceptualizations; data analysis; data interpretation; revisions.

### ACKNOWLEDGEMENTS

This study was supported by the Department of Surgery, 'blinded for review'. The authors thank the Pedigree and Population Resource of 'blinded for review', 'blinded for review' (funded in part by the 'blinded for review' Cancer Foundation) for its role in the ongoing collection, maintenance, and support of the Utah Population Database (UPDB). The authors also acknowledge partial support for the UPDB through grant P30 CA2014 from the National Cancer Institute, 'blinded for review' and from the 'blinded for review' program in Personalised Health. The authors thank the 'blinded for review' Center for Clinical and Translational Science (funded by NIH Clinical and Translational Science Awards) and 'blinded for review' Information Technology Services and Biomedical Informatics Core for establishing the Master Subject Index between the UPDB and the 'blinded for review' Health Sciences Center. This research was supported by the NCRR grant, 'Sharing Statewide Health Data for Genetic Research' (R01 RR021746, G. Mineau, PI) with additional support from the Utah State Department of Health and the 'blinded for review'.

### CONFLICT OF INTEREST

Kerry Kelly is the co-founder and co-owner of Tetrad Network Sensor Solutions. Jeremiah A. Alt is a consultant for OptiNose, GM, Medtronic, and GSK. Other authors declare no conflict of interest.

### PEER REVIEW

The peer review history for this article is available at https://publons.com/publon/10.1111/coa.14013.

### DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

### ETHICS STATEMENT

Local institutional review board approval was obtained before commencing this study and conducted in accordance with all relevant guidelines and regulations. An IRB waiver of consent and authorization were obtained.

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## SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

**How to cite this article:** Gill AS, Meeks H, Curtin K, Kelly K, Alt JA. Tobacco use increases the risk of chronic rhinosinusitis among patients undergoing endoscopic sinus surgery. Clinical Otolaryngology. 2023;48(3):414–22. https://doi.org/10.1111/coa.14013

## APPENDIX A

**TABLE A1** Expansion of Table S1 parameters

| (a) All CRS patients | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Covariate** | **Est** | **SE** | ***Z*** | ***p* Value** | **RR** | **LL** | **UL** |
| Tobacco use: Yes (vs. no) | 0.35 | 0.02 | 19.57 | 0 | 1.42 | 1.37 | 1.47 |
| White: No (vs. yes) | −0.38 | 0.03 | −12.9 | 0 | 0.69 | 0.65 | 0.73 |
| White: Unknown (vs. yes) | −0.37 | 0.04 | −9.26 | 0 | 0.69 | 0.64 | 0.75 |
| Hispanic: Yes (vs. no) | −0.4 | 0.02 | −16.78 | 0 | 0.67 | 0.64 | 0.7 |
| Hispanic: Yes (vs. unknown) | −0.07 | 0.02 | −3.59 | 0 | 0.93 | 0.9 | 0.97 |
| Asthma: Yes (vs. no) | 1.65 | 0.02 | 84.21 | 0 | 5.21 | 5.01 | 5.41 |
| Tobacco use × asthma | −0.72 | 0.04 | −18.65 | 0 | | | |
| **(b) Male CRS patients only** | | | | | | | |
| **Covariate** | **Est** | **SE** | ***Z*** | ***p* Value** | **RR** | **LL** | **UL** |
| Tobacco use: Yes (vs. no) | 0.36 | 0.02 | 14.88 | 0 | 1.43 | 1.36 | 1.5 |
| White: No (vs. yes) | −0.36 | 0.04 | −8.55 | 0 | 0.7 | 0.65 | 0.76 |
| White: Unknown (vs. yes) | −0.47 | 0.06 | −8.47 | 0 | 0.63 | 0.56 | 0.7 |
| Hispanic: Yes (vs. no) | −0.51 | 0.04 | −14.23 | 0 | 0.6 | 0.56 | 0.64 |
| Hispanic: Yes (vs. unknown) | −0.13 | 0.03 | −5.03 | 0 | 0.87 | 0.83 | 0.92 |
| Asthma: Yes (vs. no) | 1.75 | 0.03 | 54.59 | 0 | 5.74 | 5.39 | 6.11 |
| Tobacco use × asthma | −0.68 | 0.06 | −11.46 | 0 | | | |
| **(c) Female CRS patients only** | | | | | | | |
| **Covariate** | **Est** | **SE** | ***Z*** | ***p* Value** | **RR** | **LL** | **UL** |
| Tobacco use: Yes (vs. no) | 0.35 | 0.03 | 12.94 | 0 | 1.42 | 1.34 | 1.49 |
| White: No (vs. yes) | −0.4 | 0.04 | −9.76 | 0 | 0.67 | 0.62 | 0.73 |
| White: Unknown (vs. yes) | −0.24 | 0.06 | −4.17 | 0 | 0.79 | 0.7 | 0.88 |
| Hispanic: Yes (vs. no) | −0.3 | 0.03 | −9.48 | 0 | 0.74 | 0.7 | 0.79 |
| Hispanic: Yes (vs. unknown) | 0 | 0.03 | −0.13 | .898 | 1 | 0.95 | 1.05 |
| Asthma: Yes (vs. no) | 1.59 | 0.02 | 64.12 | 0 | 4.91 | 4.67 | 5.15 |
| Tobacco use × asthma | −0.77 | 0.05 | −14.7 | 0 | | | |
| **(d) All CRSsNP patients** | | | | | | | |
| **Covariate** | **Est** | **SE** | ***Z*** | ***p* Value** | **RR** | **LL** | **UL** |
| Tobacco use: Yes (vs. no) | 0.33 | 0.03 | 11.95 | 0 | 1.39 | 1.32 | 1.47 |
| White: No (vs. yes) | −0.46 | 0.05 | −9.96 | 0 | 0.63 | 0.58 | 0.69 |
| White: Unknown (vs. yes) | −0.4 | 0.06 | −6.44 | 0 | 0.67 | 0.59 | 0.76 |
| Hispanic: Yes (vs. no) | −0.49 | 0.04 | −13.28 | 0 | 0.61 | 0.57 | 0.66 |
| Hispanic: Yes (vs. unknown) | −0.12 | 0.03 | −4.21 | 0 | 0.88 | 0.84 | 0.94 |
| Asthma: Yes (vs. no) | 1.42 | 0.03 | 45.13 | 0 | 4.14 | 3.89 | 4.4 |
| Tobacco use × asthma | −0.67 | 0.06 | −10.79 | 0 | | | |
| **(e) Male CRSsNP patients only** | | | | | | | |
| **Covariate** | **Est** | **SE** | ***Z*** | ***p* Value** | **RR** | **LL** | **UL** |
| Tobacco use: Yes (vs. no) | 0.33 | 0.04 | 8.58 | 0 | 1.39 | 1.29 | 1.5 |
| White: No (vs. yes) | −0.47 | 0.07 | −6.91 | 0 | 0.62 | 0.54 | 0.71 |
| White: Unknown (vs. yes) | −0.51 | 0.09 | −5.71 | 0 | 0.6 | 0.51 | 0.72 |
| Hispanic: Yes (vs. no) | −0.59 | 0.06 | −10.21 | 0 | 0.55 | 0.5 | 0.62 |
| Hispanic: Yes (vs. unknown) | −0.19 | 0.04 | −4.49 | 0 | 0.83 | 0.76 | 0.9 |

(Continues)

**TABLE A1** (Continued)

| (e) Male CRSsNP patients only | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Covariate** | **Est** | **SE** | ***Z*** | ***p* Value** | **RR** | **LL** | **UL** |
| Asthma: Yes (vs. no) | 1.45 | 0.05 | 26.52 | 0 | 4.25 | 3.82 | 4.73 |
| Tobacco use × asthma | −0.65 | 0.1 | −6.36 | 0 | | | |
| **(f) Female CRSsNP patients only** | | | | | | | |
| **Covariate** | **Est** | **SE** | ***Z*** | ***p* Value** | **RR** | **LL** | **UL** |
| Tobacco use: Yes (vs. no) | 0.33 | 0.04 | 8.35 | 0 | 1.39 | 1.29 | 1.51 |
| White: No (vs. yes) | −0.45 | 0.06 | −7.23 | 0 | 0.64 | 0.57 | 0.72 |
| White: Unknown (vs. yes) | −0.28 | 0.09 | −3.24 | .001 | 0.75 | 0.64 | 0.89 |
| Hispanic: Yes (vs. no) | −0.42 | 0.05 | −8.63 | 0 | 0.66 | 0.6 | 0.72 |
| Hispanic: Yes (vs. unknown) | −0.06 | 0.04 | −1.58 | .113 | 0.94 | 0.87 | 1.02 |
| Asthma: Yes (vs. no) | 1.41 | 0.04 | 36.51 | 0 | 4.09 | 3.79 | 4.41 |
| Tobacco use × asthma | −0.69 | 0.08 | −8.65 | 0 | | | |
| **(g) All CRSwNP patients** | | | | | | | |
| **Covariate** | **Est** | **SE** | ***Z*** | ***p* Value** | **RR** | **LL** | **UL** |
| Tobacco use: Yes (vs. no) | 0.37 | 0.02 | 15.57 | 0 | 1.44 | 1.38 | 1.51 |
| White: No (vs. yes) | −0.32 | 0.04 | −8.48 | 0 | 0.73 | 0.67 | 0.78 |
| White: Unknown (vs. yes) | −0.35 | 0.05 | −6.75 | 0 | 0.71 | 0.64 | 0.78 |
| Hispanic: Yes (vs no) | −0.33 | 0.03 | −10.7 | 0 | 0.72 | 0.68 | 0.76 |
| Hispanic: Yes (vs. unknown) | −0.03 | 0.02 | −1.12 | .262 | 0.97 | 0.93 | 1.02 |
| Asthma: Yes (vs. no) | 1.8 | 0.03 | 71.35 | 0 | 6.04 | 5.75 | 6.34 |
| Tobacco use × asthma | −0.75 | 0.05 | −15.16 | 0 | | | |
| **(h) Male CRSwNP patients only** | | | | | | | |
| **Covariate** | **Est** | **SE** | ***Z*** | ***p* Value** | **RR** | **LL** | **UL** |
| Tobacco use: Yes (vs. no) | 0.38 | 0.03 | 12.24 | 0 | 1.46 | 1.37 | 1.55 |
| White: No (vs. yes) | −0.29 | 0.05 | −5.43 | 0 | 0.75 | 0.68 | 0.83 |
| White: Unknown (vs. yes) | −0.45 | 0.07 | −6.3 | 0 | 0.64 | 0.56 | 0.73 |
| Hispanic: Yes (vs. no) | −0.46 | 0.05 | −10.04 | 0 | 0.63 | 0.58 | 0.69 |
| Hispanic: Yes (vs. unknown) | −0.1 | 0.03 | −2.84 | .004 | 0.91 | 0.85 | 0.97 |
| Asthma: Yes (vs. no) | 1.91 | 0.04 | 47.88 | 0 | 6.75 | 6.24 | 7.29 |
| Tobacco use × asthma | −0.7 | 0.07 | −9.55 | 0 | | | |
| **(i) Female CRSwNP patients only** | | | | | | | |
| **Covariate** | **Est** | **SE** | ***Z*** | ***p* Value** | **RR** | **LL** | **UL** |
| Tobacco use: Yes (vs. no) | 0.36 | 0.04 | 9.9 | 0 | 1.44 | 1.34 | 1.54 |
| White: No (vs. yes) | −0.36 | 0.05 | −6.62 | 0 | 0.7 | 0.63 | 0.78 |
| White: Unknown (vs. yes) | −0.21 | 0.08 | −2.77 | .006 | 0.81 | 0.7 | 0.94 |
| Hispanic: Yes (vs. no) | −0.21 | 0.04 | −4.99 | 0 | 0.81 | 0.75 | 0.88 |
| Hispanic: Yes (vs. unknown) | 0.04 | 0.04 | 1.26 | .208 | 1.05 | 0.98 | 1.12 |
| Asthma: Yes (vs. no) | 1.72 | 0.03 | 52.84 | 0 | 5.59 | 5.24 | 5.96 |
| Tobacco use × asthma | −0.81 | 0.07 | −11.78 | 0 | | | |