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A Population-Based Study Investigating Chronic Rhinosinusitis and the Incidence of Asthma

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Objectives/Hypothesis: Chronic rhinosinusitis (CRS) is an inflammatory disease of the paranasal sinuses, associated with reduced health-related quality of life and increased utilization of healthcare services. Chronic upper and lower respiratory diseases often coexist, although the extent to which CRS is associated with developing asthma remains unclear. To investigate the effect of CRS on receiving a subsequent diagnosis of asthma, we used data from a previously conducted national, longitudinal survey.

Methods: Respondents from the Canadian National Population Health Survey from 1998/1999 to 2010/2011 were used. Data were analyzed from 11,555 (66.9%) subjects, $\geq$ 19 years of age and reporting no asthma at baseline. Respondents were reviewed for 12 years to determine the cumulative incidence of asthma. Logistic regression was used to estimate the effect of CRS on the development of asthma, adjusting for age, gender, body mass index, cigarette smoking, and food- or nonfood-related allergies.

Results: During the 12-year study period, 6.0% (95% confidence interval [CI] [95% CI]: 5.4%–6.7%) of respondents developed asthma. Baseline CRS (odds ratio [OR]: 2.7, 95% CI: 1.9–3.9), female gender (OR: 1.4, 95% CI: 1.1–1.8), and allergies (OR: 2.6, 95% CI: 2.1 – 3.3) were significantly associated with developing asthma. After adjustment, respondents with CRS were significantly more likely to develop asthma than non-CRS counterparts (OR: 2.0, 95% CI: 1.4–2.9).

Conclusion: Results indicate that one in 13 individuals with CRS will be subsequently diagnosed with asthma. Given the economic burden and use of healthcare services associated with asthma, providers managing CRS may consider increased awareness and subsequent treatment for asthma.

Key Words: Chronic rhinosinusitis, asthma, longitudinal.

Level of Evidence: 4.

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INTRODUCTION

Asthma is a highly prevalent chronic respiratory disease that affects nearly 8.5% of Canadians over the age of 12 years.[1] Asthma is characterized by shortness of breath, chest tightening, wheezing, and coughing.[2] Asthma may precipitate from exercise, environmental and occupational-related exposures, or manifest secondary to lower respiratory tract infections.[3–6] Similarly, inflammation of the lower respiratory tract in response to circulating allergens can result in bronchoconstriction, increased production of mucus, and restricted airflow into the lungs.[2,7] Among Canadians, asthma is associated with increased hospitalizations, emergency department visits, physician visits, and usage of prescription medications.[8] Asthma results in a high economic burden at population and patient levels.[8] With regard to psychosocial health, previous studies have reported increased levels of depression, anxiety, and attempted suicide in addition to worse health-related quality of life among individuals with asthma.[8–10]

There are multiple etiological factors associated with asthma that include sinonasal pathology.[2,4,7] Allergic rhinitis has been shown to present concurrently and contribute to the development of asthma, as reported in a previously conducted population-based study.[11] These conditions share common pathological mechanisms with regard to the release of inflammatory cells and cytokines.[12] These findings support the notion that the upper and lower respiratory tracts function as an integrated system and often respond to similar stimuli.[7] Chronic rhinosinusitis (CRS) is an advanced form of sinonasal pathology that is characterized by long-standing inflammation of the nose and paranasal sinuses.[13] The prevalence of CRS in Canada is 5.7% and ranges from 2% to 16% in the United States.[14–16] Major symptoms of CRS include nasal congestion, obstruction, discharge, facial pain or pressure, and loss of smell.[13] CRS may present in the absence of allergic rhinitis and in response to infectious or noninfectious factors.[7] Previous studies have identified cross-sectional associations between CRS and asthma.[14,17–20] In Canada, Chen et al. used a representative sample of the population and found that individuals with CRS commonly reported living with concurrent asthma .[14]

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Although previous studies have established coassociation between upper and lower respiratory tract pathology[14,21] and suggest that asthma may precede CRS diagnosis,[22] the extent to which CRS contributes to the incidence of asthma is unclear. This warrants further study in consideration of the extensive impact of asthma on patient health-related quality of life, comorbidities, healthcare utilization, and expenditure.[8] Early and comprehensive management of CRS may play a role in reducing the likelihood of developing asthma. The purpose of this study was to investigate the likelihood of developing asthma between individuals with or without CRS over a 12-year observational period. This study utilized data from a representative sample of the Canadian population collected from 1998/1999 to 2010/2011.

MATERIALS AND METHODS

Data Source

The present study was based on longitudinal data collected in the National Population Health Surveys (NPHS), conducted by Statistics Canada (Ottawa, Ontario, Canada). A description of the NPHS design, sampling method, questionnaire, and execution can be found elsewhere.[23] To summarize, the NPHS is a population-based cohort drawn from a representative community sample of 17,276 Canadian individuals. Respondents participating in the NPHS were longitudinally surveyed every 2 years to collect information related to socioeconomic and demographic factors, chronic health conditions, lifestyle and healthcare utilization. The target population for the NPHS consisted of household residents above the age of 12 years and excluded individuals on Aboriginal reserves or Crown land, residents of health institutions. Full-time members of the Canadian Forces Bases were excluded, in addition to individuals from remote areas of Ontario and Quebec. Trained employees of Statistics Canada primarily conducted face-to-face interviews at the start of the longitudinal evaluation and followed predominantly with telephone interviews at each subsequent biennial survey. Response rates decreased from 88.3% in 1998/1999 to 69.7% in 2010/2011. Individuals less than 19 years of age were excluded from the present study.

Definition of Explanatory and Outcome Variables

Chronic Rhinosinusitis. Inquiry of the presence or absence of chronic health conditions considered as long-term conditions was conducted for each participant. Chronic health conditions presented or were expected to last greater than 6 months and required to have been diagnosed by a health professional. In the NPHS, chronic health conditions included CRS and was determined from participant responses during the corresponding 1998/1999 interview. Respondents answering the following question affirmatively were considered to have CRS: "Do you have rhinosinusitis diagnosed by a health professional?" Individuals affirming or refuting CRS diagnosis in 1998/1999 were included, and respondents were excluded if CRS status was unknown or not reported. The analytic sample consisted of CRS-positive and CRS-negative participants in 1998/1999 and reviewed until 2010/2011.

Asthma. Participants were specifically questioned about the diagnosis of asthma during the chronic health conditions portion of the NPHS interview. To determine the primary outcome, respondents answering both of the following questions affirmatively were considered to be asthmatic: "Do you have asthma diagnosed by a health professional?" and "Have you had any asthma symptoms or asthma attacks in the past 12 months?" Responses were evaluated at subsequent biennial surveys from 1998/1999 to 2010/2011. To ensure respondents with concurrent CRS and asthma at baseline (i.e., 1998/1999) were not included in the analytic sample, individuals affirming asthma, reporting a history of asthma, or indicating use of asthma medications were excluded.

Use of Asthma Medications. The use of asthma medications was considered as the secondary outcome. Respondents affirming the following question were considered to use asthma medications: "In the past month, did you take asthma medications such as inhalers and nebulizers?" Participants were excluded if a response was not provided. As described above, responses were evaluated throughout the 12-year evaluation period. Individuals using asthma medications at baseline were excluded.

Covariates

A review of existing literature was completed to identify potential confounding factors related to the prevalence of asthma. Covariates were defined from participant responses provided at baseline of the evaluation period. Age was grouped into 5-year categories (19–24, 25–29, 30–34, 35–39, 40–44, 45–49, 50–54, 55–59, 60–64, 65–69, and $\geq$ 70 years), and gender consisted of dichotomous distinction between male and female. Cultural or racial origin was defined as Caucasian, Aboriginal, or respondents identifying themselves other than Caucasian or Aboriginal (i.e., black, Korean, Filipino, Japanese, Chinese, South Asian, South East Asian, Arab/West Asian, Latin American, multiple race respondents). Income was categorized into respondents reporting personal income $20,000 or more and less than $20,000. Highest level of education was defined as postsecondary graduation, some postsecondary, secondary school graduation, and less than secondary school graduation. Body mass index (BMI), defined as weight (kg)/height (m^2), was separated into four categories: underweight ($<$ 18.5), normal weight (18.5–24.9), overweight (25.0–29.0), and obese ($>$ 30.0). Cigarette smoking was categorized into current, former, and never-smokers. Current smokers included respondents who reported current daily or occasional cigarette smoking. Former smokers consisted of respondents having indicated previous daily or occasional smoking. All other individuals with no history of cigarette smoking were considered as never-smokers. Allergies were assessed by responses to inquiries related to food or nonfood-related allergies. Participants were excluded if a response was not provided.

Statistical Analysis

The cumulative incidence (total number of new asthma cases/total population at risk), attributable risk (AR; incidence of asthma given CRS-positive, incidence of asthma given CRS-negative), number needed to treat (NNT; 1/AR), and odds ratio (OR; odds of asthma given CRS-positive; odds of asthma given CRS-negative) were reported. The observation period was separated into tertiles: 4-year (1998/1999–2002/2003), 8-year (1998/1999–2006/2007), and 12-year (1998/1999–2010/2011). Respondents with multiple affirmations of asthma were counted once (i.e. at date of first report) and restricted from the at-risk population for subsequent incidence estimates. Logistic regression was used to describe the independent effect of CRS on the incidence of asthma or use of asthma medications. Unadjusted and adjusted models were fitted for the cumulative incidence of asthma and use of asthma medications. All covariates were added to a preliminary multivariable logistic regression model. Income and highest level of education were significantly collinear; therefore, income was included in the subsequent analysis and highest level of education was excluded. All remaining covariates were added to a secondary multivariable logistic regression model. To establish parsimony and minimize overfitting, cultural or racial origin and

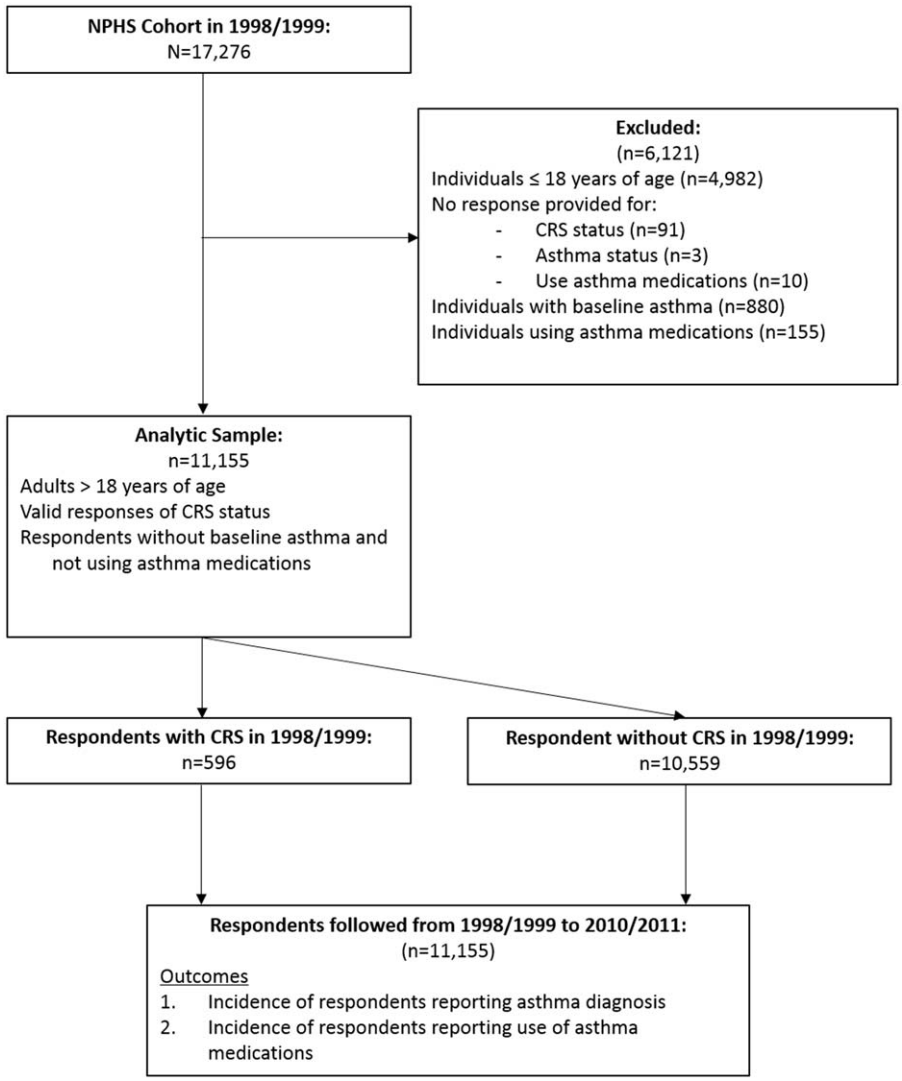

Fig. 1. Flow diagram of respondents included and excluded for investigation of the effect of chronic rhinosinusitis on developing asthma, based on observations from the Canadian National Population Health Surveys, Canada, 1998/1999–2010/2011. CRS = chronic rhinosinusitis; NPHS = Canadian National Population Health Survey.

income were not retained in the final multivariable regression model because these covariates did not yield significantly different regression estimates whether included or excluded. The final multivariable regression model included age, gender, BMI, cigarette smoking, and allergies. All estimates of association and 95% confidence intervals (CIs) were weighted according to the sampling weights provided by Statistics Canada. Weighting was performed to ensure effect estimates were representative of the NPHS sampling method and to provide appropriate estimates of variance. Statistical analysis was completed using SAS Version 9.3 (SAS Institute Inc., Cary NC).

RESULTS

The study cohort consisted of 11,155 respondents having met the inclusion criteria (Fig. 1). Respondents were primarily female (59.6%), between the ages of 30 to 64 years (77.4%), and of normal BMI (52.6%). The majority of respondents were cigarette smokers (63.4%), consisting of former (39.5%) and current smokers (24.1%). At baseline, the prevalence of CRS was 5.3% (95% CI: 4.7%–5.9%), and participants reporting concurrent CRS and asthma (0.9%, 95% CI: 0.7–1.1) in 1998/1999 were excluded from the analytic sample.

From 1998/1999 to 2010/2011, the cumulative incidence of asthma was 6.0% (95% CI: 5.4%–6.7%). The proportion of incidence asthma cases was greater during the initial 4-year tertile (2.7%, 95% CI: 2.3%–3.2%) than subsequent tertiles (8-year: 2.0%, 95% CI: 1.7%–2.5%; 12-year: 1.3%, 95% CI: 1.1%–1.7%). Throughout the overall evaluation period, respondents with CRS were significantly more likely to develop asthma than respondents without CRS (OR: 2.7, 95% CI: 1.9–3.9; AR: 8.2%, 95% CI: 4.1%–12.3%). One in 13 individuals with CRS were subsequently diagnosed with asthma within the evaluation period (NNT: 13, 95% CI: 8–24). Individuals with CRS were more likely to develop asthma in the initial 4 years of evaluation (1998/1999–2002/2003 OR: 3.9, 95% CI: 2.5–6.2). The cumulative likelihood of developing asthma was also associated with allergies, gender, and obesity (Table I). After adjusting for age, gender, BMI, cigarette smoking and allergies, respondents with CRS were more likely to develop asthma than non-CRS counterparts (adjusted OR: 2.0, 95% CI: 1.4–2.9).

TABLE I.
Comparison of Baseline Sociodemographics Compared Between Respondents With or Without CRS, Based on Observations from the National Population Health Surveys, Canada, 1998/1999–2010/2011.

Characteristics	Respondents Identified With CRS (n = 596) Relative frequency (%)	Respondents Identified Without CRS (n = 10,559) Relative frequency (%)	OR (95% CI)
Age Category (years)			1.06 (1.01–1.11)*
19–24	5.95	8.97	Reference
25–29	2.71	6.88	
30–34	8.94	9.99	
35–39	12.21	13.75	
40–44	17.14	14.17	
45–49	13.99	12.12	
50–54	10.60	9.83	
55–59	10.27	7.63	
60–64	7.64	6.53	
65–69	6.98	4.58	
70+	3.57	5.56	
Gender			
Male	32.96	47.84	Reference
Female	67.04	52.16	1.87 (1.44–2.41)
Cultural or Racial Origin			
Other than Caucasian or Aboriginal†	2.95	5.08	Reference
Caucasian	95.57	93.57	1.76 (0.99–3.06)
Aboriginal	1.10	1.13	1.69 (0.59–4.82)
Income			
$20,000 or more	79.33	77.88	Reference
Less than $20,000	16.87	18.33	0.90 (0.68–1.20)
Not stated or refused	3.80	3.79	0.98 (0.58–1.67)
Highest Level of Education			
Postsecondary graduation	33.04	29.67	Reference
Some postsecondary	25.59	25.20	0.92 (0.69–1.19)
Secondary school graduation	17.58	14.32	1.10 (0.80–1.52)
Less than secondary school graduation	23.79	30.81	0.69 (0.52–1.00)
BMI Category			
Normal weight (18.5–24.9)	48.66	56.51	Reference
Underweight (< 18.5)	9.62	9.83	1.14 (0.74–1.74)
Overweight (25.0–29.0)	24.51	25.76	1.11 (0.82–1.49)
Obese (> 30.0)	17.21	7.91	2.53 (1.79–3.58)
Allergy			
No	39.76	75.20	Reference
Yes	60.24	24.80	4.59 (3.59–5.90)
Cigarette Smoking			
Never	36.56	38.13	Reference
Current	24.28	24.06	1.05 (0.77–1.45)
Former	39.16	37.81	1.80 (0.82–1.43)

*Represents OR per 5-year increase in age.
†Includes cultural or racial origins: black, Korean, Filipino, Japanese, Chinese, South Asian, South East Asian, Arab/West Asian, Latin American, multiple race respondents.
Bold text: Statistically significant odds ratios having 95% CIs that do not include 1 (i.e., *P* value less than 0.05). BMI = body mass index; CI = confidence interval; CRS = chronic rhinosinusitis; OR = odds ratio.

From 1998/1999 to 2010/2011, respondents with CRS were significantly more likely to use asthma medications than counterparts without CRS (OR: 3.1, 95% CI: 2.3–4.2, AR: 14.2%, 95% CI: 9.2%–19.2%) (Table II). One in eight individuals with CRS reported having used asthma medication within the evaluation period (NNT: 8, 95% CI: 5–11). Individuals with CRS were more likely to use asthma medications in the initial 4 years of evaluation (1998/1999 to 2002/2003 OR: 4.8, 95% CI: 3.2 – 7.2) than onward (2004/2005 to 2010/2011 OR: 1.4, 95% CI: 0.9–2.3).

TABLE II.
Unadjusted and Adjusted* Odds Ratios and 95% Confidence Intervals for 12-Year Cumulative Incidence of Asthma and Use of Asthma Medication in Relation to Baseline Chronic Rhinosinusitis, National Population Health Surveys, Canada, 1998/1999–2010/2011.

	OR of Developing Asthma (95% CI)		OR of Using Asthma Medications (95% CI)	
Characteristics	Unadjusted	Adjusted	Unadjusted	Adjusted
Chronis Rhinosinusitis				
Yes	2.7 (1.9–3.9)	2.0 (1.4–2.9)*	3.1 (2.3–4.2)	2.4 (1.8–3.3)*
No	Reference		Reference	
Age				
Per 5-year category†	0.9 (0.9–1.0)	0.9 (0.9–1.0)	1.0 (1.0–1.1)	1.0 (1.0–1.1)
19–24 years	Reference		Reference	
Gender				
Female	1.4 (1.1–1.8)	1.3 (1.0–1.6)	1.3 (1.1–1.6)	1.2 (1.0–1.5)
Male	Reference		Reference	
BMI				
Underweight (< 18.5)	0.8 (0.5–1.3)	0.7 (0.5–1.1)	1.3 (0.9–1.7)	1.2 (0.9–1.6)
Overweight (25.0–29.0)	0.8 (0.6–1.1)	0.9 (0.7–1.2)	0.9 (0.8–1.2)	0.9 (0.7–1.2)
Obese (> 30.0)	1.3 (0.9–2.0)	1.2 (0.8–1.8)	1.5 (1.1–2.1)	1.3 (0.9–1.8)
Normal weight (18.5–24.0)	Reference		Reference	
Cigarette Smoking				
Current	0.9 (0.8–1.3)	0.9 (0.7–1.2)	1.6 (1.2–2.0)	1.7 (1.3–2.2)
Former	1.0 (0.7–1.2)	1.0 (0.8–1.3)	1.4 (1.1–1.7)	1.4 (1.1–1.8)
Never	Reference		Reference	
Allergy				
Yes	2.6 (2.1–3.3)	2.3 (1.8–2.9)	1.9 (1.6–2.3)	1.7 (1.4–2.1)
No	Reference		Reference	

*Adjusted for age, gender, body mass index, cigarette smoking, and allergy. Reference group are CRS-negative, males, normal weight, nonsmokers and nonallergic respondents.
†Age categories: 19–24, 25–29, 30–34, 35–39, 40–44, 45–49, 50–54, 55–59, 60–64, 65–69, 70+ years.
Bold text: Statistically significant ORs having 95% CIs that do not include 1 (i.e., *P* value less than 0.05).
BMI = body mass index; CI = confidence interval; CRS = chronic rhinosinusitis; OR = odds ratio.

The use of asthma medications was also associated with allergies, gender, obesity, and cigarette smoking. After adjusting for age, gender, BMI, cigarette smoking, and allergies, respondents with CRS were more likely to use asthma medications than non-CRS counterparts (adjusted OR: 2.4, 95% CI: 1.8–3.3) (Table II).

DISCUSSION

CRS is a debilitating chronic disease that is associated with significantly reduced health-related quality of life, productivity, and increased healthcare utilization.[24–26] Similarly, asthma is a multifactorial chronic respiratory disease that has extensive clinical and economic impact on patients and the healthcare system.[8] Although often independently evaluated and managed, CRS and asthma commonly coexist.[14,17,27] This has been attributed to the integrated functionality and response of the upper and lower respiratory tract to analogous stimuli.[7,28–30] Several studies have shown coexistent associations between CRS and asthma,[14,21] and that asthma may precede CRS.[22] However, the extent to which CRS is associated with subsequent development of asthma is unclear. In the present study, the relationship between CRS and the likelihood of developing asthma was evaluated using a representative sample of Canadians. Unadjusted estimates indicate that one in 13 individuals with CRS will be subsequently diagnosed with asthma. Adjusting for potential confounders, individuals with CRS are two times more likely to be diagnosed with asthma than non-CRS counterparts. With regard to medications, one in eight individuals with CRS will subsequently initiate nebulizers or inhalers to treat asthma symptoms. After adjustment, individuals with CRS are 2.4 times more likely to use asthma medications than non-CRS counterparts. The increased likelihood of using asthma medication may be attributed to the greater proportion of smokers reporting the use of nebulizers and inhalers, when adjusted for potential confounders.

Although these results suggest a temporal relationship between CRS and asthma, alternative explanations can be considered. Atopy, allergic, and nonallergic rhinitis are reported among individuals with CRS and have been linked with the incidence of asthma.[11,31,32] Toren et al. performed a nested case-control study of 15,813 individuals and found that cases with asthma were over five times more likely to present with rhinitis symptoms prior to asthma diagnosis.[11] The risk of adult-onset asthma was higher among nonatopic individuals with rhinitis than atopic counterparts.[11] Following this, Shaaban et al. performed a longitudinal study of 6,461 individuals and

reported that risk of developing asthma was greater among those with allergic rhinitis than nonallergic rhinitis or atopy alone.[31] It is important to note that rhinitis and atopy may contribute to the results found in the present study. Specific questions pertaining to rhinitis and atopy were not included in the NPHS[23]; as a result, these factors could not be adequately measured. However, the NPHS survey incorporated specific questions related to food- and nonfood-related allergies, and these factors were included in the multivariable analysis. Given the significant association between allergies observed in the present study, it is reasonable to consider that this categorization method included individuals with allergic rhinitis and atopy.

One limitation of the aforementioned studies is the inability to consider the persistent symptomatology and role of physician diagnosis in CRS.[11,31] In these studies, rhinitis was defined as symptoms of nasal congestion or frequent occurrences of sneezing, and atopy was defined as nasal allergies[11] or nonspecific allergies.[31] CRS is a persistent inflammatory disease of the paranasal sinuses that requires subjective and objective evidence for diagnosis.[33,34] Given this, the link between CRS and the development of asthma warrants further study. The utility of the NPHS in this context is specific questioning regarding previously diagnosed chronic health conditions that include CRS and asthma. Several hypothesizes could explain the results observed in the present study. Chronic inflammation of the paranasal sinuses or nasal polyposis may contribute to nasal obstruction and prevent filtration of inspired air into the lungs, increasing the frequency of potentially exacerbating allergens.[7] The paranasal sinuses may operate as a reservoir of infectious factors such as microorganisms, bacterial antigens, and biofilms, which may migrate from the upper to lower respiratory tract.[7] Alternatively, individuals with CRS and asthma may represent a subgroup of patients with common tissue remodeling characteristics that increases the likelihood of coassociation. [35] It is also important to consider that CRS and asthma may have manifested concurrently, but asthmatic symptomatology was not clinically appreciable at the time of CRS diagnosis. This may explain that the incidence of asthma diagnosis was higher during the initial 4 years from baseline than onward. It is plausible that CRS may not have been the singular risk factor and that asthmatic pathology was already present but yet to be formally diagnosed by a physician. Tan et al. found that individuals with newly diagnosed CRS often presented with premorbid asthma when compared to healthy controls. These findings, in addition to those discussed earlier, suggest a bidirectional relationship and may allude to a subgroup of individuals with inflammatory and remodeling patterns that increase the likelihood of coexistent CRS and asthma.[22,35]

Despite this, respondents with concurrent physician-diagnosed asthma or use of asthma medications at baseline were excluded from this study. This established a respondent cohort where respondents did not have asthma at baseline and were evaluated at subsequent interviews to determine new asthma diagnoses. The outcome was determined from patient responses to specific questioning about physician-diagnosed asthma, which is a limitation of the present analysis. As described by the Canadian Thoracic Society, the reference standard for asthma diagnosis in adults includes a comprehensive clinical history, reduced pulmonary function with improvement after bronchodilator use, and a positive methacholine or exercise challenge tests.[36] Although, these criteria would have reduced the frequency of misclassification bias, they are not feasible to ascertain in large-scale, population-based studies.[37] The present study is limited by its retrospective nature and potential for recall bias because categorization of the explanatory and outcome variables were dependent on respondents self-reporting physician diagnosed CRS and asthma. Given these limitations, temporal associations are presented with prudency, and causality cannot be concluded. Excluding cultural or racial origin, income, and highest level of education (due collinearity with income) from the adjusted analysis, for the purposes of achieving parsimony, may have underestimated the potentially confounding effects of ethnicity and socioeconomic status on the incidence of newly diagnosed asthma or use of asthma medication. However, these covariates were only removed because the multivariable regression model did not yield significantly different regression estimates when these covariates were included.

Presently, there is a paucity of studies prospectively investigating the incidence of asthma among individuals with CRS. The results of the present study are similar to a previously performed nested case-control study; Hirsh et al. found that individuals with CRS were nearly three times more likely to develop asthma in 5 years than healthy controls.[38] The relationship between CRS and comorbid disease is an area that warrants further evaluation because individuals with CRS are more likely to access healthcare services that are not restricted to otolaryngologists. Chung et al. found that Taiwanese individuals with CRS were more likely to access otolaryngology and nonotolaryngology outpatient services, in addition to more days spent as inpatients.[39] This was complemented by greater outpatient and inpatient costs than non-CRS controls.[39] These findings, in addition to a previously performed investigation of healthcare utilization of Canadians,[24] suggest that CRS results in a significant impact on healthcare services and expenditure. Given the likelihood of developing asthma among individuals with CRS, this may contribute to an increase in the frequency of physician and emergency department visits and prescription medication usage. Healthcare providers managing individuals with CRS may consider regular surveillance of asthma symptoms for earlier diagnosis and to potentially reduce healthcare services utilization. Future long-term, longitudinal cohort studies of individuals with CRS are required to investigate the validity of this hypothesis and identify the contributing factors to the increased access of healthcare services.

CONCLUSION

In the present study, the incidence of asthma was evaluated in a representative sample of the Canadian population. From baseline, individuals with CRS were significantly more likely to develop asthma and use

asthma medications than non-CRS counterparts. These results indicate that CRS is a risk factor contributing to the development of asthma. Early and comprehensive management of CRS may be considered to reduce the likelihood of asthma incidence. Evidence of temporality would be strengthened from longitudinal investigations objectively measuring asthma symptoms and pulmonary function and performing challenge tests among nonasthmatic individuals with CRS. Future prospective studies following newly diagnosed individuals with CRS are warranted to investigate the interaction of airway remodeling mediators that may differentiate CRS phenotypes, risk of asthma, and potential bidirectional pathogenesis between the upper and lower respiratory tracts.

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BIBLIOGRAPHY

1. Statistics Canada. Asthma, by sex, provinces and territories. *Gov Canada.* 2014. Available at: http://www.statcan.gc.ca/tables-tableaux/sum-som/l01/cst01/health50a-eng.htm. Accessed June 12, 2015.
2. Chen Y, Johansen H, Thillaiampalam S, Sambell C. Asthma. *Health Reports.* 2005;16(2):43–46. Available at: http://www.statcan.gc.ca/pub/82-625-x/2013001/article/11834-eng.htm. Accessed October 8, 2013.
3. Arif AA, Delclos GL, Lee ES, Tortolero SR, Whitehead LW. Prevalence and risk factors of asthma and wheezing among US adults: an analysis of the NHANES III data. *Eur Respir J* 2003;21:827–833. doi:10.1183/09031936.03.00054103a.
4. Toren K, Blanc PD. Asthma caused by occupational exposures is common—a systematic analysis of estimates of the population-attributable fraction. *BMC Pulm Med* 2009;9:7. doi:10.1186/1471-2466-9-7.
5. Liu T, Valdez R, Yoon PW, Crocker D, Moonesinghe R, Khoury MJ. The association between family history of asthma and the prevalence of asthma among US adults: National Health and Nutrition Examination Survey, 1999–2004. *Genet Med* 2009;11:323–328. doi:10.1097/GIM.0b013e31819d3015.
6. Backman K, Piippo-Savolainen E, Ollikainen H, Koskela H, Korppi M. Adults face increased asthma risk after infant RSV bronchiolitis and reduced respiratory health-related quality of life after RSV pneumonia. *Acta Paediatr* 2014;103:850–855. doi:10.1111/apa.12662.
7. Krouse JH, Brown RW, Fineman SM, et al. Asthma and the unified airway. *Otolaryngol Head Neck Surg* 2007;136(suppl 5):S75–S106. doi:10.1016/j.otohns.2007.02.019.
8. Ismaila AS, Sayani AP, Marin M, Su Z. Clinical, economic, and humanistic burden of asthma in Canada: a systematic review. *BMC Pulm Med* 2013;13:70. doi:10.1186/1471-2466-13-70.
9. Barker E, Kolves K, De Leo D. The relationship between asthma and suicidal behaviours: a systematic literature review. *Eur Respir J* 2015;46:96–106. doi:10.1183/09031936.00011415.
10. Lavoie KL, Bacon SL, Barone S, Cartier A, Ditto B, Labrecque M. What is worse for asthma control and quality of life: depressive disorders, anxiety disorders, or both? *Chest* 2006;130:1039–1047. doi:10.1378/chest.130.4.1039.
11. Toren K, Olin A-C, Hellgren J, Hermansson B-A. Rhinitis increase the risk for adult-onset asthma—a Swedish population-based case-control study (MAP-study). *Respir Med* 2002;96:635–641. doi:10.1053/rmed.2002.1319.
12. Pawankar R. Allergic rhinitis and asthma: are they manifestations of one syndrome? *Clin Exp Allergy* 2006;36:1–4. doi:10.1111/j.1365-2222.2006.02420.x.
13. Rosenfeld RM, Andes D, Bhattacharyya N, et al. Clinical practice guideline: adult sinusitis. *Otolaryngol Head Neck Surg* 2007;137(suppl 3):S1–S31. doi:10.1016/j.otohns.2007.06.726.
14. Chen Y, Dales R, Lin M. The epidemiology of chronic rhinosinusitis in Canadians. *Laryngoscope* 2003;113:1199–1205. doi:10.1097/00005537-200307000-00016.
15. Blackwell DL, Lucas JW, Clarke TC. Summary health statistics for U.S. adults: national health interview survey, 2012. *Vital Health Stat 10.* 2014;260:1–161. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24819891. Accessed March 2, 2015.
16. Halawi AM, Smith SS, Chandra RK. Chronic rhinosinusitis: epidemiology and cost. *Allergy Asthma Proc* 2013;34:328–334. doi:10.2500/aap.2013.34.3675.
17. Jarvis D, Newson R, Lotvall J, et al. Asthma in adults and its association with chronic rhinosinusitis: the GA2LEN survey in Europe. *Allergy* 2012;67:91–98. doi:10.1111/j.1398-9995.2011.02709.x.
18. Lin DC, Chandra RK, Tan BK, et al. Association between severity of asthma and degree of chronic rhinosinusitis. *Am J Rhinol Allergy* 2011;25:205–208. doi:10.2500/ajra.2011.25.3613.
19. Seybt MW, McMains KC, Kountakis SE. The prevalence and effect of asthma on adults with chronic rhinosinusitis. *Ear Nose Throat J* 2007;86:409–411. Available at : http://www.ncbi.nlm.nih.gov/pubmed/17702323. Accessed October 8, 2013.
20. Shi JB, Fu QL, Zhang H, et al. Epidemiology of chronic rhinosinusitis: results from a cross-sectional survey in seven Chinese cities. *Allergy* 2015;70:533–539. doi:10.1111/all.12577.
21. Chung SD, Chen PY, Lin HC, Hung SH. Comorbidity profile of chronic rhinosinusitis: a population-based study. *Laryngoscope* 2014;124:1536–1541. doi:10.1002/lary.24581.
22. 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. doi:10.1016/j.jaci.2013.02.002.
23. Peaudet MP, Chen J, Perez C, Ross N. National Populatoin Health Survey Overview 1996/1997. *Stat Canada* 1998;1:82–567. Available at: http://publications.gc.ca/Collection-R/Statcan/82-567-XIB/0009882-567-XIE.pdf. Accessed November 4, 2013.
24. Macdonald KI, McNally JD, Massoud E. The health and resource utilization of Canadians with chronic rhinosinusitis. *Laryngoscope* 2009;119:184–189. doi:10.1002/lary.20034.
25. Durr DG, Desrosiers MY, Dassa C. Impact of rhinosinusitis in health care delivery: the Quebec experience. *J Otolaryngol* 2001;30:93–97.
26. Gliklich RE, Metson R. The health impact of chronic sinusitis in patients seeking otolaryngologic care. *Otolaryngol Head Neck Surg* 1995;113:104–109.
27. Chung S-D, Chen P-Y, Lin H-C, Hung S-H. Comorbidity profile of chronic rhinosinusitis: a population-based study. *Laryngoscope* 2014;124:1536–1541. doi:10.1002/lary.24581.
28. De Benedictis FM, Bush A. Rhinosinusitis and asthma: epiphenomenon or causal association? *Chest* 2009;136(suppl 5):e30.
29. Pakdaman MN, Luong A. The links between chronic rhinosinusitis and asthma. *Curr Opin Otolaryngol Head Neck Surg* 2011;19:218–223. doi:10.1097/MOO.0b013e32834500a8.
30. Kariyawasam HH, Rotiroti G. Allergic rhinitis, chronic rhinosinusitis and asthma: unravelling a complex relationship. *Curr Opin Otolaryngol Head Neck Surg* 2013;21:79–86. doi:10.1097/MOO.0b013e32835ac640.
31. Shaaban R, Zureik M, Soussan D, et al. Rhinitis and onset of asthma: a longitudinal population-based study. *Lancet* 2008;372:1049–1057. doi:10.1016/S0140-6736(08)61446-4.
32. Dixon AE, Kaminsky D, Holbrook JT, Wise R, Shade DM, Irvin CG. Allergic rhinitis and sinusitis in asthma: differential effects on symptoms and pulmonary function. *Chest* 2006;130:429–435. doi:10.1378/chest.130.2.429.
33. Desrosiers M, Evans G, Keith PK, et al. Canadian clinical practice guidelines for acute and chronic rhinosinusitis. *Allergy Asthma Clin Immunol* 2011;7:2. doi:10.1186/1710-1492-7-2.
34. Fokkens WJ, Lund VJ, Mullol J, et al. European position paper on rhinosinusitis and nasal polyps 2012. *Rhinol Suppl* 2012:3 p preceding table of contents, 1–298.
35. Frieri M. Asthma linked with rhinosinusitis: an extensive review. *Allergy Rhinol* 2014;5:41–49. doi:10.2500/ar.2014.5.0083.
36. Lougheed MD, Lemiere C, Ducharme FM, et al. Canadian Thoracic Society 2012 guideline update: diagnosis and management of asthma in preschoolers, children and adults. *Can Respir J* 2012;19:127–164.
37. Chen Y, Dales R, Tang M. Obesity may increase the incidence of asthma in women but not in men: *Am J Epidemiol* 2002;155:191–197.
38. Hirsch G, Yan XS, Sundaresan S, et al. Five-year risk of incident disease following a diagnosis of chronic rhinosinusitis. *Allergy* 2015. doi:10.1111/all.12759. Epub ahead of print.
39. Chung S-D, Hung S-H, Lin H-C, Lin C-C. Healthcare service utilization among patients with chronic rhinosinusitis: a population-based study. *Laryngoscope* 2014;124:1285–1289. doi:10.1002/lary.24500.