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Associations of environmental and community features with radiologic sinus inflammation in Pennsylvania, USA

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Background: Chronic rhinosinusitis is a disease of the nasal and sinus mucosa with direct and indirect costs for individuals and society, including the risk of transition to lower airway diseases. Using electronic health records from the Geisinger Health System in Pennsylvania, we evaluated associations of environmental and community features as surrogates for aeroallergens with radiologic sinus inflammation, an objective finding of chronic rhinosinusitis.

Methods: In a nested case–control study using electronic health records data, we included individuals aged 18–80 years from 2008 to 2018, with two encounters in the 4 years before their index date, and residence in a 38-county study region. We identified cases (n = 2,382) with radiologic sinus inflammation using a validated text algorithm applied to sinus computed tomography scan reports. Controls (n = 11,910) were frequency-matched on age, sex, and year of encounter. Exposures were assigned based on the residential address within latency and duration windows. We used logistic regression with robust standard errors clustered on community to estimate odds ratios and 95% confidence intervals while adjusting for confounding variables.

Results: Cases and controls had a mean (SD) age of 49.5 (15.3) years, were predominantly non-Hispanic White (96%), and had a mean (SD) contact time with the Geisinger Health System of 5.88 (3.29) years. We found independent associations of greater urbanization, higher greenness, higher cumulative growing degree days, and lower precipitation with increased odds of radiologic sinus inflammation. Residence in higher density urban areas (compared with rural) was strongly associated (odds ratio [95% confidence interval]) with radiologic sinus inflammation (1.70 [1.31, 2.21]).

Conclusions: Higher cumulative growing degree days, greater urbanization, lower precipitation, and higher greenness had robust associations with radiologic sinus inflammation. Findings reflect the complexity of environmental and community risk factors that directly and indirectly influence radiologic sinus inflammation, including both aeroallergens and air pollutants. Risk of this objective finding of chronic rhinosinusitis could increase with continued climate change-driven variation in weather and land use.

Keywords: rhinosinusitis; environmental epidemiology; aeroallergens; electronic health records

Introduction

Chronic rhinosinusitis is an inflammatory disease of the nasal and sinus mucosa with 5%–12% prevalence in the United States[1–3] and numerous risk factors for development, progression, and exacerbation.[3–5] Chronic rhinosinusitis has significant impacts on quality of life,[6–8] carries high costs for individuals and society,[9,10] and increases the risk for development of serious lower respiratory diseases, including bronchiectasis and asthma.[11–13] The European Paper on Rhinosinusitis and Nasal Polyps and the American Academy of Otolaryngology and Neck Surgery (AAO-HNS) recommend a consensus definition for the clinical diagnosis of chronic rhinosinusitis, which includes

What this study adds

We found robust associations of greater urbanization, higher greenness, higher cumulative growing degree days, and lower precipitation with increased odds of radiologic sinus inflammation. No prior studies have evaluated associations of surrogates for aeroallergens with objective findings of chronic rhinosinusitis. Our approach builds on literature showing the impact of climate change-driven variations in temperature and precipitation on the timing, duration, and distribution of aeroallergens across urban and rural geographies. Findings suggest that aeroallergens and air pollutants play a role in radiologic sinus inflammation and highlight the trends we might expect with the continued influence of climate change in the region.

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Data are not publicly available because they are protected health information. Persons interested in the data should contact the corresponding author. Data use would require IRB approval, data use agreement, and appropriate safeguards.

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Figure 1. Coronal section of sinus computed tomography scan showing normal (left) and partial opacification of the maxillary and ethmoid sinuses (right) in two individuals from the Geisinger Health System.

symptoms (discharge or drainage, obstruction, smell loss, and facial pain or pressure) for 12 weeks or more, along with objective evidence of inflammation based on clinical endoscopy or sinus computed tomography (CT) scan.[1,14] Epidemiological studies often do not include objective evidence of disease in their case definition. This use of self-reported symptoms and diagnosis may lead to misclassification due to symptom overlap with other upper respiratory diseases, such as allergic and nonallergic rhinitis.[2,15] Objective findings, including radiologic sinus inflammation based on sinus CT scans, may decrease the risk of misclassification.[16]

There is growing interest in how climate change-driven meteorological variation in temperature and precipitation are impacting respiratory diseases through increased exposure to risk factors such as aeroallergens (pollens from weeds, trees, and grasses).[17,18] Seasonal and perennial aeroallergens are important contributors to adverse respiratory and dermatologic health conditions, including asthma exacerbation, allergic rhinitis, atopic dermatitis, and allergic conjunctivitis.[19,20] The role of aeroallergens in the onset and exacerbation of chronic rhinosinusitis is inconclusive, in part due to subjective and self-reported outcomes in epidemiologic studies, as well as limitations of sample size and exposure assessment. Current literature evaluating the role of aeroallergens in chronic rhinosinusitis has primarily focused on individual allergy testing and self-reported allergies.[21–23] No prior studies have evaluated associations of environmental and community features as surrogates for aeroallergens with objective findings of chronic rhinosinusitis.

We evaluated associations of land cover, greenness, weather metrics associated with plant growth (precipitation, cumulative growing degree days [CGDDs]), community type, and season with radiologic sinus inflammation using electronic health records data from the Geisinger Health System in 38 counties of Pennsylvania. Without direct aeroallergen measurements at the spatial and temporal scale necessary for our study, we utilized the listed variables as surrogates for aeroallergens. This approach builds on literature evaluating the impact of climate change-driven variations in temperature and precipitation on the timing and duration of aeroallergen growing seasons, geographic distribution of pollen production, changes in land use, and increase in concentration and allergenicity of tree, grass, and weed pollens across urban and rural geographies.[24–27]

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Methods

Study population and design

We completed a nested case–control analysis with electronic health record data from the Geisinger Health System, a regional healthcare provider serving over 3 million individuals across a 45-county service region in central, south-central, and northeastern Pennsylvania.[28] We selected cases and controls from 2008 to 2018 using electronic health records data from ~1.5 million individuals, including individuals who had a minimum of two encounters within 4 years before their index date (date of sinus CT scan or control encounter date), were aged 18–80 years, and had a residential address within a 38-county study region that included the majority of individuals (some counties have very few Geisinger Health System patients). We retrospectively identified individuals with radiologic sinus inflammation based on outpatient sinus CT scan radiology reports, excluding individuals with a sinus CT scan from an inpatient or emergency room setting, a prior diagnosis of sinus tumor (benign or malignant), Mounier-Kuhn syndrome, primary ciliary dyskinesia, and cystic fibrosis. Controls with no chronic rhinosinusitis diagnosis were randomly selected with replacement and frequency matched 5:1 on sex, age category, and year of encounter. The Institutional Review Board of the Geisinger Health System approved this study (IRB# 2019-0547) with a waiver of consent and a Reliance Agreement with the Johns Hopkins Bloomberg School of Public Health (BSPH IRB No: 23211).

Identification of radiologic sinus inflammation

We identified cases with radiologic sinus inflammation (Figure 1) using an electronic health records-based free text algorithm applied to sinus CT radiology reports. We used a previously published list of terms[13] excluding the sinus surgery terms in addition to the listed exclusions of minimal disease, odontogenic sinusitis, facial trauma, and tumors/masses. This approach was validated using chart review and had a positive predictive value of 0.90. Though our case definition for radiologic sinus inflammation did not include self-reported symptoms of chronic rhinosinusitis, we made the assumption that individuals who underwent a sinus CT scan had a symptomatic reason for an imaging study.

Confounding variables

We used electronic health record data from demographics and social history, vital signs, diagnoses and procedures free text and codes (electronic diagnosis group, an EPIC-based system, current procedural terminology, and International Classification of Disease [ICD-9, ICD-10]), laboratory data, digital imaging, and encounter notes. We identified potential confounding variables including age, sex (male and female), race (White, Black, Asian, American Indian or Alaska Native, Native Hawaiian or Pacific Islander, other, and missing), ethnicity (Hispanic or Latino, not Hispanic or Latino), Medical Assistance status (anytime, no time; Pennsylvania Medicaid program and surrogate for family socioeconomic status),[29] smoking status (current, former, never, and missing), body mass index (kg/m^2), count of outpatient encounters (all time), contact time (years) with the Geisinger Health System, and distance (miles) to the nearest Geisinger Health System imaging facility.

We identified co-occurring conditions as potential confounders and mediators, diagnosed before the index date, using previously published criteria.[12,13] We included asthma (one diagnosis), chronic obstructive pulmonary disease (one diagnosis), pneumonia (two diagnoses), obstructive sleep apnea (two diagnoses), allergic rhinitis (two diagnoses), gastroesophageal reflux disease (two diagnoses), eosinophilia (>500 cells/L, ever vs. never), and acute sinusitis (two diagnoses).

Exposure variables

We obtained residential addresses from most recent contact with the Geisinger Health System (at the time of the 2020 data pull) and geocoded addresses to latitude and longitude with ArcGIS Desktop 10.8 and StreetMap Premium 2021 using previously published methods.[30] We evaluated time-dependent and nontime-dependent variables with varying sources and spatial and temporal scales (Table 1). We assigned time-dependent exposures, including normalized difference vegetation index (NDVI), CGDD, and cumulative precipitation, within two *a priori* specified latency and duration windows (3-month latency/3-month duration and 3-month latency/6-month duration). We based decisions about latency and duration on the natural history of chronic rhinosinusitis, namely that a diagnosis requires 3 months of symptoms and clinical objective evidence. Latency refers to the time between the end of the exposure window and the date of the sinus CT scan. Exposures within the latency period were not included because we hypothesized that they could not have contributed to the outcome. Duration refers to the length of the exposure. Nontime-dependent metrics, including percent agricultural land cover, percent forested land cover, modified rural-urban commuting area (mRUCA) community type, and season were assigned using the closest available data to the index date.

We downloaded NDVI from the United States Geological Survey Landsat[32] and generated a mean NDVI value within each latency and duration window. using a 1250 × 1250 m^2 residential buffer. We accessed weather data through the PRISM Climate Group at Oregon State University,[33] including daily (24-hour) precipitation and temperature (mean, minimum, and maximum) at a spatial resolution of 30 arc seconds (approximately 3.4 km [longitude] × 4.6 km [latitude]). Weather metrics of cumulative precipitation (inches) and CGDDs were utilized as predictors of plant growth.[34,35] We calculated cumulative precipitation as the sum of precipitation within the duration window and CGDDs as the sum of growing degree days within the duration window. A growing degree day is the difference between the mean daily temperature and a base temperature, or the lowest temperature at which plant growth begins. We selected a base temperature of 50°F (10°C) as it is commonly used to evaluate plant growth in Pennsylvania.[36,37] We hypothesized that higher greenness and higher CGDDs would indicate plant growth and be associated with increased odds of radiologic sinus inflammation. Though we hypothesized that higher precipitation may be associated with plant growth, increasing aeroallergens, the literature suggested that higher precipitation may also remove aeroallergens from the air.[38,39] We hypothesized that lower precipitation may contribute to higher concentrations of atmospheric aeroallergens and would be associated with increased odds of radiologic sinus inflammation.

Nontime-dependent exposures were assigned based on residential address, the spatial scale of available data, and the closest available data to the index date. Land cover data were accessed through the United States Geological Survey National Land Cover Dataset.[40,41] We used 2008 and 2018 data to aggregate land classes into percent agricultural (grassland, pasture, and cultivated crops) and percent forested (deciduous forest, evergreen forest, and mixed forest). We assigned percent agricultural and percent forested values within a 1250 × 1250 m^2 residential buffer. Index dates before 1 January 2014 were assigned 2008 data, and index dates on or after 1 January 2014 were assigned 2018 data. The mRUCA community type variable was based on previously published methods that modified existing Department of Agriculture Rural-Urban Commuting Area designations. The mRUCA community type applies a four-level categorization (higher density urban, lower density urban, suburban/small-town, and rural) at the census tract level for clearer geographic delineations between urban and suburban areas.[31] A categorical season variable (fall [September, October, and November], winter [December, January, and February], spring [March, April, and May], summer [June, July, and August]) was assigned based on the index date. We hypothesized that higher percent agriculture, higher percent forested, rural communities, and spring and summer seasons would reflect higher concentrations of aeroallergens and be associated with increased odds of radiologic sinus inflammation. In sensitivity analyses, we evaluated a community socioeconomic deprivation variable, created from American Community Survey indicators,[42,43] and assigned to cases and controls based on the year of encounter.

Statistical analysis

The overarching goal of the analysis was to estimate associations of land cover, greenness, weather metrics associated with

Table 1.

Summary of key environmental and community exposures and spatial and temporal scales at which they were assigned

Variable	Source	Spatial scale	Latency	Duration
Percent forested	National Land Cover Database	1250 × 1250 m^2 residential buffer	Not time-varying (2008 or 2018)	
Percent agricultural	National Land Cover Database	1250 × 1250 m^2 residential buffer	Not time-varying (2008 or 2018)	
Normalized difference vegetation index (mean)	United States Geologic Survey Landsat	1250 × 1250 m^2 residential buffer	3 months	3 months, 6 months
mRUCA community type	Location, Environmental Attributes, and Disparities Network[31]	Census Tract	Not time-varying	
Precipitation (cumulative inches)	PRISM Climate Group	4 km residential buffer	3 months	3 months, 6 months
CGDD	PRSIM Climate Group	4 km residential buffer	3 months	3 months, 6 months

CGDD indicates cumulative growing degree day; mRUCA, modified rural-urban commuting area.

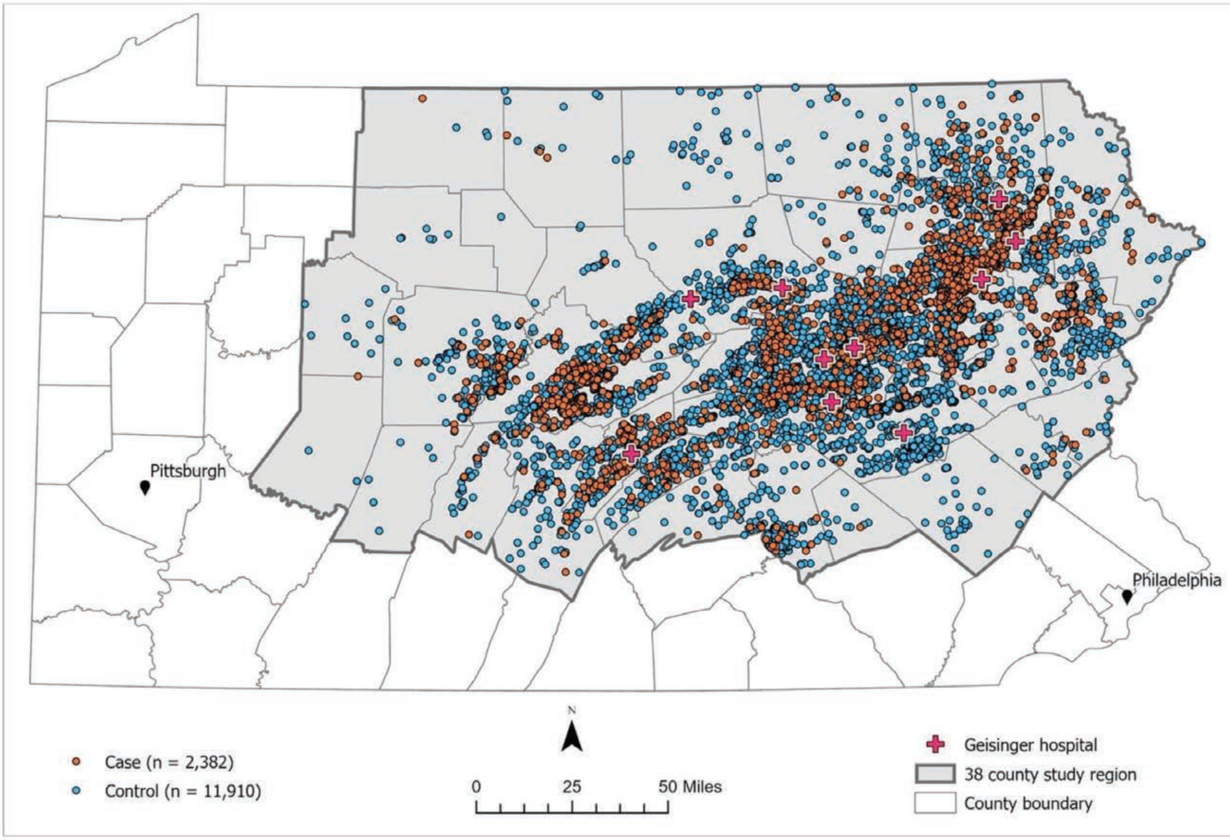

Figure 2. Distribution of cases and controls in the 38-county study region in Pennsylvania.

plant growth (precipitation, CGDDs), mRUCA community type, and season as surrogates for aeroallergens with radiologic sinus inflammation while adjusting for confounding variables. We used logistic regression with robust standard errors clustered on community to estimate associations (odds ratio, 95% confidence intervals). Analyses were completed using Stata/MP V.14 (College Station, TX).

We characterized our study population and exposure variables with descriptive statistics, distributions, and correlations before modeling. We ran separate models for each of the key exposure variables using prespecified latency and duration windows. In the base model, we adjusted for age (years; centered linear, quadratic terms to allow for nonlinearity), sex, race, ethnicity, Medical Assistance status, and smoking status. In sensitivity analyses, we evaluated potential confounders and mediators, including body mass index (centered linear and quadratic terms, and categorical), outpatient encounters (z-transformed linear and quadratic terms), duration of contact time with the Geisinger Health System (years, centered linear and quadratic terms), distance to the nearest Geisinger Health System imaging facility (miles, centered linear and quadratic terms), community socioeconomic deprivation, and common co-occurring conditions (ever vs. never before the index date for eosinophilia, asthma, chronic obstructive pulmonary disease, allergic rhinitis, acute sinusitis, pneumonia, obstructive sleep apnea, and gastroesophageal reflux disease). We retained base model variables, outpatient encounters, and selected co-occurring conditions (eosinophilia, asthma, chronic obstructive pulmonary disease, allergic rhinitis, acute sinusitis, and outpatient encounters) in the final model. We excluded the others because associations did not meaningfully change with or without the variable in the model. Because of concern that some of the co-occurring conditions might be mediators between our exposure variables and radiologic sinus inflammation, we repeated models with and without the co-occurring conditions that we considered to be potential mediators (eosinophilia, allergic rhinitis, and acute sinusitis) and found that associations stayed the same or strengthened. We evaluated all exposure pairs in separate models to determine the independence of associations and adjust for potential confounding by our identified exposure variables. We evaluated stratified models for exposure pairs with nonpositivity (nonoverlapping distributions). Global tests were evaluated to determine the significance of each set of exposure terms.

We completed a post hoc analysis to evaluate the utilization of imaging studies among individuals with and without Medical Assistance (any time and no time) in the Geisinger Health System from 2016 to 2019. We included 984,979 individuals aged 18–80 years and evaluated the utilization of sinus CT, chest CT, and brain magnetic resonance imaging studies by Medical Assistance status, age category (18–45, 46–65, and 66–80 years), and sex (male and female).

Results

Characteristics of study participants

The study sample included 2382 individuals with evidence of radiologic sinus inflammation and 11,910 controls across 38 counties in Pennsylvania (Figure 2). Cases and controls had a mean (SD) age of 49.5 (15.3) years and were predominately non-Hispanic White. Cases had a higher number of outpatient encounters, were more likely to be former smokers, had a residential address closer to a Geisinger Health System imaging facility, and were more likely to have a history of co-occurring conditions. Controls were more likely to have received Medical Assistance and be current or never smokers (Table 2).

Table 2.

Selected characteristics of cases with radiologic sinus inflammation and frequency-matched (age, sex, and year of encounter) controls

Variable	Cases with RSI	Controls without RSI	*P* value
Number	2,382	11,910	
Age, years, mean (SD)	49.6 (15.1)	49.5 (15.3)	0.92
Sex, female, n (%)	1,232 (51.7)	6,162 (51.7)	0.99
Race, n (%)			
White	2,311 (97)	11,495 (96.5)	0.44
Black, Asian, American Indian or Alaska Native, Native Hawaiian or Pacific Islander, Other	65 (2.7)	385 (3.2)	
Missing	6 (0.3)	30 (0.3)	
Ethnicity, n (%)			
Hispanic or Latino	40 (1.7)	250 (2.1)	0.005
Non-Hispanic or Latino	2,311 (97)	11,393 (95.7)	
Missing	31 (1.3)	267 (2.2)	
Medial assistance, ever, n (%)	329 (13.8)	1,860 (15.6)	0.003
Smoking status, n (%)			
Current	427 (17.9)	2,304 (19.3)	<0.001
Former	696 (29.2)	3,247 (27.3)	
Never	1,094 (45.9)	5,837 (49)	
Missing	165 (6.9)	522 (4.4)	
Body mass index, kg/m^2, mean (SD)	30.4 (6.9)	30.5 (7.5)	0.67
Contact time with the Geisinger Health System, years, mean (SD)	5.82 (3.2)	5.89 (3.3)	0.34
Outpatient encounters, all, mean (SD)	26.7 (30)	20.4 (23.0)	<0.001
Distance to Geisinger Health System imaging facility, miles, mean (SD)	7.46 (8.63)	8.17 (9.79)	<0.001
mRUCA community type, n (%)			
Higher density urban	199 (8.4)	810 (6.8)	<0.001
Lower density urban	371 (15.6)	1599 (13.4)	
Suburban/small-town	783 (32.9)	3612 (30.3)	
Rural	1029 (43.2)	5889 (49.4)	
CRS, 2 diagnoses ever, n (%)	613 (25.7)	0 (0)	
CRS, 2 diagnoses in prior 12 months, n (%)	414 (17.4)	0 (0)	
Eosinophilia, ever >500 cells/μl, n (%)	453 (19)	1,270 (10.7)	<0.001
Asthma, 1 diagnosis, n (%)	416 (17.5)	847 (7.1)	<0.001
COPD, 1 diagnosis, n (%)	194 (9.0)	627 (5.8)	<0.001
Allergic rhinitis, 2 diagnoses, n (%)	702 (29.5)	1,208 (10.1)	<0.001
Acute sinusitis, 2 diagnoses, n (%)	1,084 (45.5)	2,169 (18.2)	<0.001

COPD indicates chronic obstructive pulmonary disease; CRS, chronic rhinosinusitis; mRUCA, modified rural-urban commuting area.

Adjusted associations of final model variables and key exposure variables

In the final model, age, sex, race, ethnicity, and smoking status were not associated with radiologic sinus inflammation. Individuals who had received Medical Assistance (any time) had decreased odds of radiologic sinus inflammation. A number of outpatient encounters and selected co-occurring conditions (eosinophilia, asthma, chronic obstructive pulmonary disease, allergic rhinitis, and acute sinusitis) were associated with increased odds of radiologic sinus inflammation (Table 3).

We evaluated time-varying exposures using prespecified latency and duration windows, finding stronger associations with 3-month latency and 6-month duration (reported) variables than with 3-month latency and 3-month duration (results not shown). After full adjustment in separate models (Table 4), we found that the lowest quartiles of percent agriculture, percent forested, and precipitation, and highest quartiles of CGDDs were associated with increased odds of radiologic sinus inflammation. Residence in higher density urban, lower density urban, and suburban/small-town communities (compared with rural) was associated with increased odds of radiologic sinus inflammation. We found increased odds of radiologic sinus inflammation in the winter and spring seasons (compared with summer).

Table 3.

Associations of final model variables, including the base model, outpatient encounters, and selected co-occurring conditions, with radiologic sinus inflammation

Variable	Odds ratio (95% confidence interval)
Age	
Centered	1.00 (0.99–1.00)
Centered squared	1.00 (0.99–1.00)
Sex	
Female	0.92 (0.83–1.02)
Male	1.0
Race	
White	1.0
Black, Asian, American Indian or Alaska Native, Native Hawaiian or Pacific Islander, other	1.07 (0.79–1.44)
Missing	1.24 (0.49–3.12)
Ethnicity	
Hispanic—Latino	0.84 (0.57–1.23)
Not Hispanic—Latino	1.0
Missing	0.55 (0.38–0.81)
Medical assistance status	
Any time	0.79 (0.68–0.91)
No time	1.0
Smoking status	
Current	1.04 (0.92–1.18)
Former	1.09 (0.97–1.23)
Never	1.0
Missing	2.67 (2.16–3.29)
Outpatient encounters	
Z-transformed	0.84 (0.77–0.92)
Z-transformed squared	1.03 (1.01–1.05)
Asthma (ever, one diagnosis)	1.68 (1.44–1.98)
Eosinophil (ever, >500 cells/μl)	1.81 (1.57–2.08)
Chronic obstructive pulmonary disease (one diagnosis)	1.41 (1.15–1.75)
Acute sinusitis (2 diagnoses)	3.29 (2.89–3.75)
Allergic rhinitis (2 diagnoses)	2.36 (2.05–3.75)

Sensitivity analyses

Body mass index, duration of contact time, distance to the nearest imaging facility, and several co-occurring conditions showed no association with radiologic sinus inflammation and did not meaningfully change associations of key exposure variables. We found independent associations between the lower quartiles of community socioeconomic deprivation (less deprived areas) and increased odds of radiologic sinus inflammation. In combined models, community socioeconomic deprivation did not meaningfully change associations of key exposure variables.

Combined and stratified models

We evaluated separate models with each exposure pair to address whether the primary exposure variables confounded one another. Adjusting for percent forested and percent agricultural strengthened the NDVI association, with the highest quartiles of mean NDVI associated with increased odds of radiologic sinus inflammation (Table 5). When stratified by mRUCA community type, the percent agriculture and percent forested associations became null, suggesting that these associations were confounded (results not shown). Associations of CGDDs, precipitation, and mRUCA community type were robust and independent with no confounding by other exposure variables. We evaluated season as a potential confounding variable in combined models, finding that neither associations nor inferences substantively changed.

Table 4.

Adjusted associations[a] of key exposure variables with radiologic sinus inflammation

Variable	Quartile 1	Quartile 2	Quartile 3	Quartile 4	Global test *P*-value
Percent agricultural	1.35 (1.12–1.65)	1.33 (1.13–1.56)	1.10 (0.96–1.27)	Reference	0.003
Percent forested	1.22 (1.02–1.46)	0.97 (0.82–1.15)	0.89 (0.78–1.03)	Reference	0.009
NDVI, L3D6	Reference	0.98 (0.85–1.14)	1.10 (0.94–1.29)	1.12 (0.94–1.33)	0.20
CGDD, L3D6	Reference	1.14 (0.99–1.30)	1.35 (1.19–1.54)	1.29 (1.14–1.46)	<0.001
Precipitation	1.18 (1.03–1.36)	1.21 (1.05–1.38)	1.09 (0.96–1.25)	Reference	0.03
	Higher density urban	Lower density urban	Suburban/small-town	Rural	
mRUCA community type	1.70 (1.31–2.21)	1.43 (1.12–1.83)	1.27 (1.07–1.51)	Reference	<0.001
	Fall	Winter	Spring	Summer	
Season	1.07 (0.94–1.23)	1.26 (1.10–1.43)	1.42 (1.25–1.61)	Reference	

[a]Models (separate regressions) adjusted for age, sex, race, ethnicity, Medical Assistance, smoking status, outpatient encounters, eosinophilia, asthma, chronic obstructive pulmonary disease, allergic rhinitis, and acute sinusitis.

CGDD indicates cumulative growing degree day; D6, duration 6 months; L3, latency 3 months; mRUCA, modified rural-urban commuting area; NDVI, normalized difference vegetation index.

Table 5.

Associations[a] of mean NDVI with radiologic sinus inflammation, adjusted for percent agriculture and percent forested land cover

Variable	Adjusted for	Quartile 1	Quartile 2	Quartile 3	Quartile 4	Global test *P*-value
NDVI, L3D6	Percent agriculture	Reference	1.05 (0.92–1.22)	1.23 (1.06–1.42)	1.26 (1.07–1.48)	0.008
NDVI, L3D6	Percent forested	Reference	1.06 (0.93–1.22)	1.23 (1.07–1.42)	1.31 (1.12–1.54)	0.002

[a]Models (separate regressions) adjusted for age, sex, race, ethnicity, Medical Assistance, smoking status, outpatient encounters, eosinophilia, asthma, chronic obstructive pulmonary disease, allergic rhinitis, and acute sinusitis.

D6 indicates duration 6 months; L3, latency 3 months; NDVI, normalized difference vegetation index.

Discussion

In a case-control analysis, we evaluated associations of land cover, greenness, weather metrics associated with plant growth, community type, and season as surrogates for aeroallergens with radiologic sinus inflammation, an objective finding of chronic rhinosinusitis. We found strong and consistent associations of higher greenness, lower precipitation, higher CGDDs, and greater urbanization with increased odds of radiologic sinus inflammation.

After adjusting for percent agriculture and percent forested, we found an independent association of higher NDVI with increased odds of radiologic sinus inflammation. This finding is consistent with existing studies showing that exposure to greenness is associated with increased odds of wheezing, asthma, allergic rhinitis, and aeroallergen sensitization.[44,45] Our findings suggest that aeroallergens from cultivated green spaces and landscapes rather than agricultural and forested lands may play a role in radiologic sinus inflammation.

We found that lower quartiles of precipitation were associated with increased odds of radiologic sinus inflammation. Our findings are consistent with studies showing that higher precipitation and relative humidity are negatively associated with pollen and aeroallergen concentrations.[39] Studies have shown that atmospheric pollen concentrations decreased with high-intensity rainfall and remain unchanged with lower intensity rainfall.[38] While there is evidence of thunderstorm-related increases in ground-level pollen concentrations immediately before rainfall events,[38,46,47] our findings suggest that lower precipitation and drier air are associated with radiologic sinus inflammation. Lower precipitation and drier air may also contribute to higher concentrations of air pollutants. Previous studies have found that precipitation can improve air quality through wet deposition, reducing the concentration of air pollutants, including $PM_{2.5}$.[48,49]

Higher CGDDs were independently associated with increased odds of radiologic sinus inflammation. Higher CGDDs happen later in the growing season, suggesting that aeroallergens common in the late summer and fall, including ragweed, may play a role in radiologic sinus inflammation.[27,50] We found higher CGDDs in higher density urban and lower density urban areas (compared with rural and suburban/small-town areas), reflective of an urban heat island effect, and longer growing seasons in urban areas.[51] These findings are supported by literature showing that ragweed grew faster, flowered earlier, and produced more pollen in urban locations than in rural and suburban communities.[51,52]

We found a strong and independent association of mRUCA community type with increased odds of radiologic sinus inflammation. The association increased in strength from suburban/small-town to lower density urban to higher density urban areas (compared with rural). The association with higher density urban and lower density urban areas supports our CGDD association findings and also suggests that air pollutants may play a role in radiologic sinus inflammation. While previous studies have reported inconsistent associations of air pollutants with the development and progression of chronic rhinosinusitis,[53,54] there is evidence that allergic rhinitis differs across urban and rural communities. Individuals living in urban areas may be more affected by pollen-induced respiratory allergy due to a combination of airway sensitization and mucosal damage from exposure to air pollutants.[55,56]

Winter and spring seasons were associated with increased odds of radiologic sinus inflammation, compared with summer. The spring association supports our hypothesis and suggests that exposure to aeroallergens may increase radiologic sinus inflammation. The winter association may be explained by seasonal peaks in certain air pollutants ($PM_{2.5}$ and NO_2), indoor aeroallergens, and seasonal viral or bacterial infections.

We found an independent association between the lower quartiles of community socioeconomic deprivation (less deprived areas) and increased odds of radiologic sinus inflammation. These findings are in contrast to literature that suggests socioeconomic and neighborhood deprivation are associated with respiratory disease symptoms and exacerbation, sinus surgery, and chronic rhinosinusitis disease severity.[57–59] The observed association with lower community socioeconomic deprivation quartiles may be related to other environmental and community features in the region that are associated with respiratory diseases and symptoms that were not included in this analysis.[60,61]

While our primary motivation and aim were to address the role of aeroallergens in radiologic sinus inflammation, we acknowledge that our findings capture a more complex and broad set of environmental and community risk factors. The exposures that we evaluated may act through more than one pathway, both directly and indirectly, on radiologic sinus inflammation.[62]

We completed several post hoc descriptive analyses (results not shown) to address potential concerns that associations may have been reflective of differential access to care. We found no important differences across community socioeconomic deprivation quartile in Medical Assistance status, number of outpatient encounters, or contact years with the Geisinger Health System. We found that higher density urban and lower density urban areas had more community socioeconomic deprivation. The contrasting independent associations of higher density urban and lower density urban areas and less community socioeconomic deprivation with radiologic sinus inflammation suggests that differential access to care was not driving our associations. We found no important differences across mRUCA community type by distance to a Geisinger Health System imaging facility, contact years with the Geisinger Health System, or the number of outpatient encounters. We stratified cases and controls by Medical Assistance (any time and no time), finding that individuals with any history of Medical Assistance had more outpatient encounters and longer duration of contact with the Geisinger Health System. In addition, we evaluated the utilization of sinus CT, chest CT, and brain magnetic resonance imaging by Medical Assistance status among 984,979 individuals aged 18–80 years during the years 2016–2019. We found that the proportion of persons who received imaging studies was larger among those who received Medical Assistance at any time compared with those who never received it, regardless of age category (18–45, 46–65, and 66–80 years) or sex (male and female). This suggests that Medical Assistance status did not limit access to the imaging studies that defined our outcome and that our associations were unlikely to be due to ascertainment bias.

This study had several strengths including the use of electronic health records data with longitudinal data collection, a large sample size that is representative of the region's general population, the use of objective findings for our case definition, and the power to detect small associations.[63] There were also limitations. The lack of racial and ethnic diversity in our study population presents limitations of generalizability. Although we did not use symptoms in our case definition, we held the assumption that people who had a sinus CT scan were likely to have symptoms. The reliance on a positive CT scan may result in the inclusion of more severe cases. Many factors influence the ability to get a sinus CT scan. While we evaluated Medical Assistance status and community socioeconomic deprivation as surrogates for selection bias, this could still be present. The text algorithm used to identify radiologic sinus inflammation from sinus CT scan radiology reports could not identify phenotype variations (e.g., polypoid disease) or inflammatory endotypes.[64] Though we assigned community variables based on residential addresses, actual exposure to aeroallergens could be affected by unmeasured variables such as occupation, travel, and time spent outdoors. Without a direct measure of aeroallergens at the spatial or temporal scale necessary for our study, it was not possible to validate our exposure surrogates with aeroallergen data. We believe that our selected surrogates have face validity relevance to aeroallergens, including land use and weather metrics that contribute to vegetation growth and distribution and prior scientific evidence of their validity for this use.[45,65,66] While associations with mRUCA community type suggest that air pollutants may play a role in radiologic sinus inflammation we did not include air pollutants in this analysis.

We prespecified our primary analyses, evaluated potential confounders, and interpreted our findings with an eye to the issue of multiple comparisons. The totality of our findings was more than what would be expected due to chance alone.

Conclusion

In this case–control analysis, we evaluated associations of land cover, greenness, weather metrics associated with plant growth, community type, and season as surrogates for aeroallergens with radiologic sinus inflammation, an objective finding of chronic rhinosinusitis, in a regionally representative sample from 38 counties in Pennsylvania. Independent associations of higher CGDDs, greater urbanization, lower precipitation, and higher greenness with radiologic sinus inflammation suggest that drier and longer growing seasons in urban areas may play a role in radiologic sinus inflammation. These findings support our hypothesis that aeroallergens play a role in radiologic sinus inflammation and highlight the trends we might expect with the continued influence of climate change-driven variation in weather and land use in this region. Our findings reflect the complexity of direct and indirect impacts of environmental, weather, and community features variables in sinus inflammation and make a strong call for more evidence on how these factors impact chronic rhinosinusitis, alone and in combination.

Conflicts of interest statement

The authors declare that they have no conflicts of interest with regard to the content of this report.

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