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Associations between environmental quality and adult asthma prevalence in medical claims data

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ABSTRACT

As of 2014, approximately 7.4% of U.S. adults had current asthma. The etiology of asthma is complex, involving genetics, behavior, and environmental factors. To explore the association between cumulative environmental quality and asthma prevalence in U.S. adults, we linked the U.S. Environmental Protection Agency's Environmental Quality Index (EQI) to the MarketScan® Commercial Claims and Encounters Database. The EQI is a summary measure of five environmental domains (air, water, land, built, sociodemographic). We defined asthma as having at least 2 claims during the study period, 2003–2013. We used a Bayesian approach with non-informative priors, implementing mixed-effects regression modeling with a Poisson link function. Fixed effects variables were EQI, sex, race, and age. Random effects were counties. We modeled quintiles of the EQI comparing higher quintiles (worse quality) to lowest quintile (best quality) to estimate prevalence ratios (PR) and credible intervals (CIs). We estimated associations using the cumulative EQI and domain-specific EQIs; we assessed U.S. overall (non-stratified) as well as stratified by rural-urban continuum codes (RUCC) to assess rural/urban heterogeneity. Among the 71,577,118 U.S. adults with medical claims who could be geocoded to county of residence, 1,147,564 (1.6%) met the asthma definition. Worse environmental quality was associated with increased asthma prevalence using the non-RUCC-stratified cumulative EQI, comparing the worst to best EQI quintile (PR:1.27; 95% CI: 1.21, 1.34). Patterns varied among different EQI domains, as well as by rural/urban status. Poor environmental quality may increase asthma prevalence, but domain-specific drivers may operate differently depending on rural/urban status.

Abbreviations: CI, confidence interval; EQI, environmental quality index; IRB, institutional review board; MCMC, monte carlo markov chain; PCA, principal component analysis; PR, prevalence ratio; RUCC, rural urban continuum codes; U.S., United States

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1. Introduction

Asthma is a chronic respiratory condition characterized by wheezing, shortness of breath, tightness in the chest, and coughing that results from swollen and narrowed airways (US Department of Health and Human Services, 2016). From 2001–2009, asthma prevalence in the United States (U.S.) increased 12.3% (CDC, 2011), leading to 479,300 hospitalizations and 1.9 million emergency room visits in 2009 (U.S. Centers for Disease Control and Prevention, 2016). The overall cost of asthma, including medical costs and lost productivity due to both morbidity and mortality was $56 billion in 2007 (Barnett and Nurmagambetov, 2011). As of 2014, the prevalence of asthma among U.S. adults was approximately 7.4% (U.S. Centers for Disease Control and Prevention, 2014).

Adults may have been diagnosed with asthma as children or may develop it in adulthood. Family history of asthma and atopy, a genetic predisposition to reaction to environmental allergens, increase the risk of asthma, but are more predictive of early-onset asthma in childhood (U.S. Centers for Disease Control and Prevention, 2014; London et al., 2001). In adults, lower educational attainment and lower household income are associated with increased likelihood of having asthma (U.S. Centers for Disease Control and Prevention, 2016; Bacon et al., 2009). Behavior such as smoking and comorbidities such as obesity and depression are also risk factors for asthma in adults (U.S. Centers for Disease Control and Prevention, 2014; Brunner et al., 2014; Kapadia et al., 2014).

Increasingly, environmental conditions have also been linked to asthma. Ambient air pollution has been associated with incident asthma in U.S. women (Young et al., 2014), asthma-related emergency room visits (Newman et al., 2014) and asthma risk in minorities (Nishimura et al., 2013), and a meta-analysis of six European cohorts indicated air pollution may be associated with adult-onset asthma (Jacquemin et al., 2015). In the early 2000s, the built environment was targeted for policy and research to investigate its role in asthma prevalence (Brisbon et al., 2005; Cummins and Jackson, 2001). Subsequent studies yielded mixed results. For example, proximity of green areas or tree density near homes has been associated with reductions in atopic sensitization or lower asthma prevalence in some studies of children (Ruokolainen et al., 2015; Lovasi et al., 2008), but associated with increased current asthma in others (Dadvand et al., 2014; Andrusaityte et al., 2016). Exposure to land use contaminants such as living near an industrial park or concentrated animal feeding operation has been associated with increased risk of asthma in adults (Al-Wahaibi and Zeka, 2015; Radon et al., 2007). Similarly, water quality provides another potential mechanism for exposure; for example, deposition of nitrates in water has been associated with respiratory tract infections (Gupta et al., 2000).

In short, asthma is a complex condition that is dependent on numerous individual and environmental factors (Holgate, 2011). While exposures from multiple domains of the environment have been separately associated with asthma, no comprehensive measure capturing overall environmental quality, including air, water, land, built environment, and sociodemographics, has been examined in association with asthma. Examining asthma prevalence as a function of the many elements of environmental quality to which humans are simultaneously exposed can facilitate an understanding of how these complex exposures interact to affect asthma.

To explore the association between environmental quality and asthma prevalence, we linked the Environmental Quality Index (EQI) (Lobdell et al., 2014, 2011; Messer et al., 2014), a metric from the U.S. Environmental Protection Agency (US EPA), to the Truven Health MarketScan® Commercial Claims and Encounters Database (hereafter, MarketScan). The EQI integrates information from numerous variables across five environmental domains, enabling a more complete assessment of environmental quality and a better understanding of the role of environmental quality in health outcomes. The EQI has been used in prior studies of health outcomes including cancer incidence, mortality, pediatric multiple sclerosis, and preterm birth, and may also be useful in better understanding asthma (Jian et al., 2016; Rappazzo et al., 2015; Jagai et al., 2017; Lavery et al., 2017). The MarketScan database is a comprehensive source of individual-level, privately-insured medical claims; as such, MarketScan has data on millions more persons than would be covered in a survey, and is not subject to the same recall or non-response bias that occurs with self-reported surveys (Fowles et al., 1997, 1998; Ferver and Burton, 2009). We estimate the association between cumulative environmental quality and asthma among U.S. adults with health insurance plans captured in MarketScan; we further examine the association between individual environmental domains (air, water, land, built and sociodemographic environments) and asthma prevalence. Because health risk profiles differ in general between rural and urban areas in the U.S. Moy et al. (2017), and because asthma studies in particular have indicated mixed results in assessing rural-urban variations (Malik et al., 2012; Roy et al., 2010; Pesek et al., 2010; Son et al., 2015), we additionally explore heterogeneity by county-level rural-urban status.

2. Materials and methods

2.1. Exposure data

The Environmental Quality Index (EQI) is a summary measure constructed by the US EPA which incorporates five environmental domains (air, water, land, built, sociodemographic) into a single index representing the years 2000 – 2005 for all counties in the U.S. Data sources; construction of the EQI has been described elsewhere (Lobdell et al., 2011; Messer et al., 2014), and the data, along with an accompanying technical report, are publicly available (Lobdell et al., 2014). The air, water, and land domains were identified using the EPA's Report on the Environment (EPA, 2008); the built and sociodemographics domains were identified using the literature review and consultation with scientists (Lobdell et al., 2014). Then, 187 data sources across the five domains were evaluated to assess availability at the county level, availability for all 50 states, availability within the 2000–2005 time period, and data quality, which was assessed using reports by data source managers and project investigators, and through research papers that used and critiqued the data sources (Lobdell et al., 2011). Those which were retained for their data quality and availability at the county level for the entire U.S. enabled use of 219 unique variables across each of the five domains: air (87 variables), water (80), land (26), built (14), and sociodemographic (12) (Lobdell et al., 2011). An initial principal components analysis (PCA) produced five domain-specific indices, and a final PCA of the domain-specific indices produced the cumulative EQI.

Because of heterogeneity in environmental quality across the rural-urban continuum, the two-stage PCA process (domain-specific EQIs followed by cumulative EQI) was replicated within each of four rural-urban strata identified using U.S. rural-urban continuum codes (RUCCs) (Messer et al., 2014). RUCCs are a nine-part, county-level classification system defined by the United States Department of Agriculture, Economic Research Service (USDA, 2003; Hines et al., 1970). For the EQI, these nine categories were collapsed into four rural-urban strata: metropolitan-urbanized (original RUCC 1–3), non-metropolitan urbanized (original RUCC 4–5), less urbanized (original RUCC 6–7), and thinly populated (original RUCC 8–9). The use of these four categories is consistent with prior health studies (Luben et al., 2009; Messer et al., 2010; Langlois et al., 2010).

For our main exposure variable, we used quintiles of the EQI to compare higher quintiles (worse quality) to the lowest quintile (best quality). We conducted analyses using the cumulative EQI and the domain-specific indices across the entire U.S, and conducted stratified analyses within each RUCC to examine heterogeneity of effects by rural-urban status. For analyses using the domain-specific indices, all five indices were used in the same model so that associations could be examined in a multi-exposure context.

2.2. Outcome data

The MarketScan health claims database is a compilation of nearly 110 million patient records with information from more than 100 private insurance carriers and large self-insuring companies. Public forms of insurance (i.e., Medicare and Medicaid) are not included, nor are small (< 100 employees) or medium (< 1000 employees) self-insuring companies. For this cross-sectional study, approved claims for the years 2003–2013, which includes 17.5–45.2 million persons annually, are linked across years and geocoded at the county level. The dataset includes both inpatient and outpatient claims, medical procedures and prescription medications. In addition to diagnostic and pharmacy claims, records include patient's age (in years), county of residence, and sex. This dataset defines the population in which we are estimating associations, specifically, U.S. adults aged 18–65 with private health insurance, primarily from large employers (those with > 1000 employees). We excluded the relatively few (n = 6735) individuals over 65 years of age because Medicare is the primary insurance of U.S. adults over 65.

Our final dataset was a person-level dataset that summarized information from the one or more records available on each person to assess whether that person had asthma claims over the study period. Our binary outcome variable, asthma, was defined as adults 18–65 years old with at least two asthma claims over the 2003—2013 period, identified in MarketScan by International Statistical Classification of Diseases and Related Health Problems revision (ICD-9) code 493, including 493.22, 493.20, 493.90, 493.91, 493.12, 493.11, 493.10, 493.00, 493.01, 493.02, 493.92, 493.9, 493.8, 493.81, 493.82, 493.2, 493.1, 493.0, and 493.21 (WHO, 2010). These claims cover inpatient and outpatient visits, procedures, and prescriptions. Given the possibility of misdiagnosis, we required two distinct asthma claims (in this case, not a prescription) be present to count as an asthma diagnosis. We used as many years of outcome data as possible (through 2013), even though the EQI exposure reflects data only through 2005, because we expect the county level EQI rankings to be stable over time. We also conducted parallel analyses requiring only one claim over the study period to assess the extent to which estimates may change based on the two-claim restriction.

2.3. Covariate data

Individual-level demographic data such as sex and age are available in the MarketScan data. Adult asthma risk varies by race and ethnicity (Gorman and Chu, 2009), but individual-level race/ethnicity is not available in MarketScan. However, factors that contribute to asthma may vary by county of residence, and minority composition of a county may partially represent the geographic racial distribution. We included county-level percent racial distributions using 2010 U.S. Census (2017) data[48] to reflect the aspects of social-environmental exposure that are not included in the EQI. Even though the census-based racial distribution does not reflect the profile of the privately-insured study population, it does reflect the racial distribution of the county environment in which the study population lives.

Covariates included individual-level sex, individual-level age category (18–30 (referent), 31–40, 41–50, 51–65), and county-level race-ethnicity percentages for the following groups: American Indian, Asian, Black Hispanic, Black non-Hispanic, Pacific Islander, White Hispanic, and White non-Hispanic (referent).

2.4. Statistical analyses

We used a Bayes approach with non-informative (weak) priors, implementing mixed-effects regression modeling with a Poisson link function (Hedeker and Gibbons, 2006). This approach uses the Poisson distribution to model the distribution of cell counts in a multiway contingency table, and is frequently used to model disease occurrence in insurance claims (Atkin, 1989). This approach enabled us to examine whether environmental quality is associated with prevalence of asthma among individuals in our data.

The unit of our analysis (one row in the data matrix) was a specific sociodemographic group at a specific county, for example, females aged 18–30, in Cook County of Illinois. The Poisson regression response variable was the number of persons with asthma in the demographic group, where the total number of people in the group was the regression offset. The assumptions of the Poisson regression model were as follows. First, we assumed that the data, corresponding to the observed counts of people within each county diagnosed with asthma, were generated by a Poisson process, with rate (λ_{ij}) varying over counties,

$$f(y_{ij}\theta) = \frac{e^{-\lambda_{ij}}\lambda_{ij}^{y_{ij}}}{y_{ij}!},$$

where: $\boldsymbol{\theta}$ is a vector of all model parameters, ($\mathbf{b}$, $\boldsymbol{\Sigma}$). The observed counts of disease incidence (the response variable y_{ij}) was defined as the number of disease cases per county j in the given age and sex stratum i. Second, we assumed that the logarithm of Poisson rate (λ_{ijkl}) was expressed as a linear combination of fixed (age and sex group (k)) and random effects (county (l)).

$$\lambda_{ij} = N_{ij}\exp(\mathbf{X}_i\mathbf{b} + \mathbf{z}\,\mathbf{v})$$

$$= N_{ij}\exp\left(\sum_{m=1}^{M} x_{im}\beta_m + \vartheta_j\right).$$

Here matrix $\mathbf{X}$ is the design matrix for the fixed effects; $\mathbf{b}$ is the corresponding vector of unknown regression weights; $\mathbf{z}$ is a design matrix for random effects; $\mathbf{v}$ is the vector of random effects. The fixed-effect design matrix is a matrix of county-specific zero-centered properties, such as the proportions of ethnic groups. The design matrix $\mathbf{z}$ has a very simple form: entries of 1 for random effects of a given county, and zeros in all other cells. N_{ij} is a county-, and demographic-stratum-specific offset—the total number of people with a specified sex and age living within a given county. Lastly, we accommodated the fact that data were hierarchical;the random term was at the county level in which the county-level model intercepts could vary.

We estimated posterior distribution of parameter of the model using Monte Carlo Markov Chain (MCMC) algorithm, implemented in R package MCMCglmm (Hadfield, 2010). Fixed effects variables were EQI, sex, race, age and weather variables. Random effects were counties. We modeled quintiles of the EQI comparing higher quintiles (worse quality) to the lowest quintile (best quality) to estimate prevalence ratios (PR) and credible intervals (CIs). We estimated associations using the cumulative EQI and domain-specific EQIs, and did so for the U.S. overall (non-stratified) as well as stratified by RUCC.

Statistical analyses were conducted in R version 3.2.3 GUI 1.66 Mavericks build (7060) (R Core Team, 2013).

2.5. Ethical considerations

This study involved de-identified claims data on human subjects. It was reviewed and approved by the Institutional Review Board at the University of Chicago.

3. Results

Among the 71,577,118 U.S. adults with medical claims in MarketScan from 2003–2013 who could be geocoded to county of residence, 1,147,564 (1.6%) met the asthma definition of having at least two asthma claims (Table 1). Approximately half (48%) the total population was male; approximately 31% of those with asthma were male. In the total population, the percentages in each age category were similar for individuals ages 18–65, approximately reflecting the age distribution of the general U.S. population (U.S. Census, 2017). Among

Table 1
Demographics of unique persons in the MarketScan study population, 2003–2013.

Characteristic (N = 71,577,118)	Total N	%	N unique persons with at least 1 asthma claim	%	N unique persons with at least 2 asthma claims	%
Gender						
Male	34,380,820	48%	1,486,408	36%	354,533	31%
Female	37,196,298	52%	2,680,079	64%	793,031	69%
Age						
18–30	20,487,389	29%	918,545	22%	217,570	19%
31–40	15,968,962	22%	892,349	21%	238,337	21%
41–50	16,628,351	23%	1,046,318	25%	299,838	26%
51–65	18,492,416	26%	1,309,275	31%	391,819	34%
Rural-Urban Status						
RUCC1: Metro-urbanized	60,390,968	84%	3,568,689	86%	989,877	86%
RUCC2: Non-metro-urbanized	4,594,342	6%	256,168	6%	68,538	6%
RUCC3: Less urbanized	5,620,691	8%	293,342	7%	76,944	7%
RUCC4: Thinly populated	971,117	1%	48,288	1%	12,205	1%

[a]Excludes records which could not be geocoded to county.

those with asthma, the greatest percentage (34%) was in the older age group (51 – 65).

3.1. Cumulative EQI

We observed an increased prevalence of asthma associated with worse environmental quality using the non-RUCC-stratified cumulative EQI (Table 2, Fig. 1). The worst environmental quality EQI quintile (Q5) had the largest PR (1.27; 95% CI: 1.21, 1.34) relative to the best environmental quality quintile (Q1, referent).

For RUCC-stratified analyses using the cumulative EQI, results varied by stratum (Table 2, Fig. 1). For the metropolitan-urbanized stratum (RUCC 1), the association between environmental quality and asthma prevalence monotonically increased with increasingly worse environments. As with the non-stratified cumulative EQI, the worst EQI quintile in RUCC 1 had the largest PR (1.23; 95% CI: 1.15, 1.31) relative to the best quintile.

In RUCC 2 (non-metropolitan urbanized stratum), RUCC 3 (less urbanized) and RUCC 4 (thinly populated), estimates had a less clear pattern and were mostly null. The exceptions were the worst quality environments in RUCCs 3 and 4, which were inversely associated with asthma prevalence (RUCC 3 PR: 0.89 [95% CI: 0.81, 0.98]; RUCC 4 PR: 0.87 [95% CI: 0.74, 1.02]).

3.2. Domain-specific EQIs

In analyses using each of the individual EQI domains, the most striking results were in the air domain. The non-stratified estimates indicated increased asthma prevalence with worsening air quality; the worst air quality environment had the largest association (PR: 1.54; 95% CI: 1.45, 1.63) (Table 3, Fig. 2). Worse water quality was also positively associated with asthma in all quintiles. In the land, built, and sociodemographic domains, worse quality was somewhat negatively associated with increased asthma, with estimates close to null.

In RUCC-stratified analyses of the domain-specific EQIs, patterns of domain-specific associations varied by RUCC stratum (Table 3). In

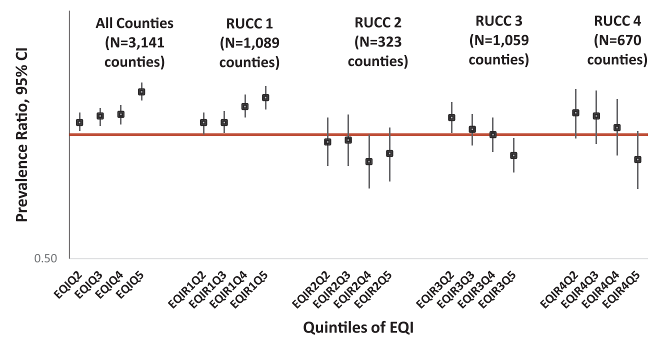

Fig. 1. Associations between Environmental Quality Index and having ≥ 2 asthma claims, all counties and stratified by Rural-Urban Continuum Codes.

RUCC 1 (metropolitan urbanized), worsening air quality was associated with increasing asthma, and poor water quality was somewhat associated with increased asthma. However, land quality was not statistically significantly associated with asthma and estimates had broad credible intervals including zero. In the built and sociodemographic domains, worse quality was not associated or slightly negatively associated with asthma.

The patterns of domain-specific estimates in RUCC 3 (less urbanized) and RUCC 4 (thinly populated) were similar to those of RUCC 1 in the air domain but had more pronounced positive associations in the water domain and slightly positive (but imprecise) associations in the land domain. In RUCC2 (non-metropolitan urbanized) estimates in the air, water, and land domains were close to null. Built environmental quality varied across RUCCs but were mostly null. Sociodemographic environmental qualities also varied across RUCCs but associations were somewhat more pronounced (larger in magnitude), and worsening sociodemographic quality was associated with decreasing asthma prevalence in more rural RUCCs.

Table 2
Associations between cumulative EQI and asthma prevalence using 2 claims, all counties and stratified by RUCC.

EQI Quintile	All Counties (N = 3141 counties) PR (95% CI)	RUCC 1: Metropolitan-urbanized (N = 1089 counties) PR (95% CI)	RUCC 2: Non-metropolitan urbanized (N = 323 counties) PR (95% CI)	RUCC 3: Less urbanized (N = 1059 counties) PR (95% CI)	RUCC 4: Thinly populated (N = 670 counties) PR (95% CI)
Q1 (best)	(referent)	(referent)	(referent)	(referent)	(referent)
Q2	1.07 (1.02,1.13)	1.07 (1.00,1.13)	0.96 (0.84,1.10)	1.10 (1.01,1.20)	1.13 (0.98,1.29)
Q3	1.11 (1.05,1.16)	1.07 (1.01,1.14)	0.97 (0.84,1.12)	1.03 (0.94,1.12)	1.11 (0.95,1.28)
Q4	1.12 (1.06,1.18)	1.17 (1.10,1.25)	0.86 (0.74,1.00)	1.00 (0.91,1.10)	1.04 (0.89,1.22)
Q5 (worst)	1.27 (1.21,1.34)	1.23 (1.15,1.31)	0.90 (0.77,1.04)	0.89 (0.81,0.98)	0.87 (0.74,1.02)

EQI: Environmental Quality Index; RUCC: Rural-Urban Continuum Codes; PR: Prevalence Ratio; CI: Credible Interval.

Table 3
Associations between domain-specific EQIs and asthma prevalence using 2 claims, all counties and stratified by RUCC.

EQI Quintile	All Counties (N = 3141 counties)	RUCC 1: Metropolitan-urbanized (N = 1089 counties)	RUCC 2: Non-metropolitan urbanized (N = 323 counties)	RUCC 3: Less urbanized (N = 1059 counties)	RUCC 4: Thinly populated (N = 670 counties)
	PR (95% CI)	PR (95% CI)	PR (95% CI)	PR (95% CI)	PR (95% CI)
Air Q1 (best)	(referent)	(referent)	(referent)	(referent)	(referent)
Air Q2	1.08 (1.03,1.14)	1.10 (1.03,1.17)	0.91 (0.79,1.05)	1.00(0.91,1.09)	1.04 (0.89,1.21)
Air Q3	1.23 (1.17,1.30)	1.18 (1.11,1.26)	0.95 (0.82,1.10)	1.01(0.92,1.10)	0.92 (0.79,1.09)
Air Q4	1.33 (1.26,1.40)	1.28 (1.19,1.37)	0.96 (0.83,1.13)	1.10(1.01,1.21)	1.09 (0.93,1.28)
Air Q5 (worst)	1.54 (1.45,1.63)	1.25 (1.15,1.35)	1.09 (0.94,1.28)	1.22(1.11,1.34)	1.26 (1.08,1.47)
Water Q1 (best)	(referent)	(referent)	(referent)	(referent)	(referent)
Water Q2	1.06 (1.01,1.11)	1.04 (0.98,1.11)	1.01 (0.88,1.15)	1.11(1.02,1.21)	1.08 (0.94,1.23)
Water Q3	1.06 (1.01,1.11)	1.04 (0.98,1.11)	1.1 (0.95,1.27)	1.08(0.99,1.17)	1.34 (1.16,1.54)
Water Q4	1.21 (1.16,1.27)	1.11 (1.05,1.18)	1.06 (0.93,1.22)	1.30(1.20,1.41)	1.25 (1.08,1.44)
Water Q5 (worst)	1.07 (1.03,1.12)	0.98 (0.92,1.04)	0.98 (0.85,1.13)	1.16(1.06,1.26)	1.20 (1.04,1.38)
Land Q1 (best)	(referent)	(referent)	(referent)	(referent)	(referent)
Land Q2	1.01 (0.97,1.06)	0.98 (0.01,81.35)	1.03 (0.01,81.13)	1.01(0.01,88.85)	1.06 (0.01,84.73)
Land Q3	0.97 (0.93,1.02)	0.97 (0.92,1.02)	0.96 (0.86,1.08)	1.03(0.96,1.11)	1.04 (0.92,1.16)
Land Q4	0.91 (0.86,0.96)	0.93 (0.89,0.98)	0.88 (0.79,1.00)	1.01(0.94,1.09)	1.06 (0.92,1.21)
Land Q5 (worst)	0.90 (0.85,0.94)	0.99 (0.01,77.94)	1.04 (0.01,87.01)	1.04(0.01,87.18)	1.06 (0.01,82.38)
Built Q1 (best)	(referent)	(referent)	(referent)	(referent)	(referent)
Built Q2	0.98 (0.94,1.03)	0.97 (0.91,1.03)	0.96 (0.84,1.10)	0.94(0.86,1.01)	0.93 (0.81,1.06)
Built Q3	0.95 (0.91,1.00)	0.99 (0.92,1.06)	1.05 (0.91,1.20)	0.90(0.83,0.97)	0.95 (0.83,1.09)
Built Q4	0.98 (0.94,1.03)	0.93 (0.87,1.00)	0.93 (0.82,1.07)	0.90(0.83,0.98)	0.98 (0.85,1.12)
Built Q5 (worst)	0.95 (0.91,1.00)	0.97 (0.90,1.04)	0.91 (0.79,1.05)	0.89(0.81,0.97)	1.20 (1.04,1.39)
Socio Q1 (best)	(referent)	(referent)	(referent)	(referent)	(referent)
Socio Q2	1.02 (0.97,1.07)	0.96 (0.91,1.02)	0.91 (0.79,1.06)	1.08(0.99,1.17)	1.17 (1.03,1.33)
Socio Q3	0.99 (0.94,1.04)	0.95 (0.90,1.01)	0.91 (0.77,1.08)	1.08(0.99,1.19)	1.16 (1.00,1.34)
Socio Q4	0.94 (0.89,0.99)	0.96 (0.90,1.02)	0.85 (0.71,1.01)	0.98(0.88,1.09)	0.93 (0.80,1.10)
Socio Q5 (worst)	0.99 (0.93,1.05)	0.88 (0.82,0.95)	0.90 (0.76,1.08)	0.83(0.75,0.93)	0.91 (0.78,1.06)

EQI: Environmental Quality Index; RUCC: Rural-Urban Continuum Codes; PR: Prevalence Ratio; CI: Credible Interval.

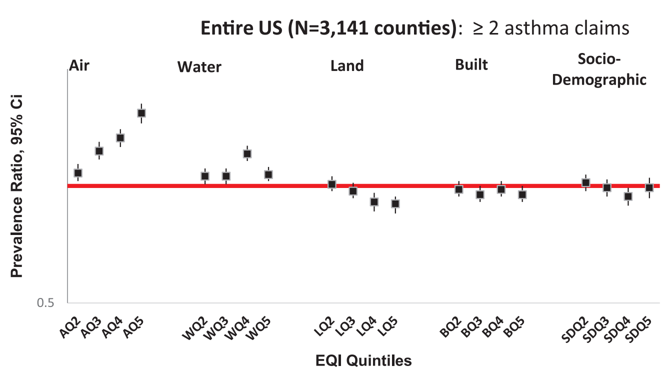

Fig. 2. Associations between domain-specific between Environmental Quality Indices and having ≥ 2 asthma claims, all counties.

3.3. Sensitivity analyses

As previously noted, we employed a conservative asthma definition of having at least two asthma claims during the study period. Defining asthma as requiring only one claim yielded similar effect estimates, which are presented in Supplemental Tables 1 and 2 and Supplemental Figures 1 and 2. We also examined including a third modeling level to cluster counties within states, using a state-specific random effect in addition to county-specific random effects. Estimates were similar to those reported (data not shown). Finally, we considered weather-related variables, but they did not contribute to the associations of interest and were excluded (data not shown).

4. Discussion

We found that worsening cumulative environmental quality is associated with increasing asthma prevalence in U.S. adults captured in MarketScan claims data. Estimates varied, however, across different rural-urban strata, with worsening environmental quality associated with increasing asthma prevalence in the most urban areas (RUCC 1); environmental quality was not associated or inversely associated with asthma in less urban and rural areas (RUCCs 2–4). In domain-specific analyses, decreasing air quality was consistently associated with higher asthma prevalence. Poor water quality was most strongly associated with elevated asthma prevalence in RUCCs 3 and 4, and was still positively associated in the non-RUCC-stratified analysis. Worsening land quality was associated with increasing asthma in stratified analyses for RUCC 3 and 4; however, these associations tended to be small and relatively imprecise with wide credible intervals. Worsening built quality showed inconsistent association with asthma, with some variation in the pattern of association across the stratified analyses, and worsening sociodemographic quality was associated with decreasing asthma in RUCCs 3 and 4.

Our results highlight the complex role of environmental quality in the prevalence of asthma. Prior studies have traditionally focused on single exposures when relating contaminants or environmental features to asthma (Young et al., 2014; Newman et al., 2014; Nishimura et al., 2013; Jacquemin et al., 2015; Ruokolainen et al., 2015; Al-Wahaibi and Zeka, 2015). While studies of single exposures enable specificity, the challenging nature of high dimensional data often prevents accounting for the full context in which those exposures are operating. For example, nitrogen dioxide is thought to increase asthma symptoms (Guarnieri and Balmes, 2014). However, there are multiple pathways of exposure for pollutants such as nitrates, and nitrates in water have been associated with respiratory tract infections in children (Gupta et al., 2000). By only focusing on the concentration of nitrates in the air, we would be missing the nitrates deposited in the water. The EQI captures both routes of exposure with air and water domain nitrate variables.

Our most meaningful results were in the air domain and in the most urban areas (RUCC 1), consistent with studies indicating that air quality is worse in urban areas. For example, a 2017 CDC surveillance study reported differences between rural and urban air quality; the authors found more unhealthy air-quality days in urban areas (Strosnider et al., 2017). This is consistent with the higher density production of pollution from traffic, factories, and human activity in urban areas.

Poor environmental quality was associated with increased asthma in RUCC 1, but patterns were less clear in RUCCs 2–4. Because 84% of the study sample lives in RUCC 1 counties, estimates for RUCC 1 are more precise. This distribution of individuals across RUCCs is consistent with the distribution of the US population across RUCCs (United States Department of Agriculture, 2017). The variations across RUCCs may be due to differences in data availability of EQI variables. While all EQI variables were selected for their availability across the entire US, data were generally more profuse in urban areas, whereas data in suburban and rural areas were more likely to rely on estimation techniques. Variables were evaluated based on their overall contributions to a given domain, a process that occurred prior to stratification by RUCC, and may have resulted in different variable selection had the process occurred after stratification.

We observed some heterogeneity in the domain-specific analyses. Associations between poor air quality and asthma across RUCCs are consistent with prior studies of air pollution and asthma (Young et al., 2014; Newman et al., 2014; Jacquemin et al., 2015). Similar positive associations with water quality across RUCCs suggest potential opportunities for additional research; to our knowledge, no other study has quantified an association between ambient water quality and asthma. Associations in the land domain were difficult to interpret due to the imprecision in the Q2 and Q5 quintiles that likely stems from partitioning of data in those areas. Based on the distribution of the land domain index, the counties in Q2 and Q5 for the land domain may differ from those in other domains in the same RUCC.

Perhaps the most striking variation across RUCCs is in the sociodemographic domain. We would expect that worsening sociodemographic quality would be associated with increased asthma, particularly in urban environments, because the variables contributing to the sociodemographic domain are primarily based on knowledge of sociodemographic deprivation in urban settings; sociodemographic deprivation in suburban and rural settings is not as well understood or defined. Yet, poor sociodemographic quality was counter-intuitively associated with decreased asthma in RUCC 1, and in RUCCs 3 and 4 worsening sociodemographic quality was associated with decreasing asthma prevalence. It is possible that the population represented in this dataset helps explain the unexpected results. We note that the overall prevalence of asthma in this study (1.6%) is substantially lower than that estimated for the U.S (7.4%) (U.S. Centers for Disease Control and Prevention, 2014). The MarketScan claims represent a large portion of the U.S. adult population, and the distributions of the study population by RUCC (Table 1) match that of the U.S. population (United States Department of Agriculture, 2017). However, this data source does not capture those who are uninsured, and the uninsured are known to be differentially affected by poor health outcomes in general (Hadley, 2003) and poor asthma management in particular (Shields, 2007). It also does not capture those on state-based insurance (i.e., Medicaid), which represented approximately 15% of US adults in 2011; Medicaid beneficiaries are lower-income and thus also burdened with worse health outcomes, including respiratory diseases (Kaiser Family Foundation, 2010, 2017). In other words, our study population is more affluent than the general population and is differentially advantaged relative to the sociodemographic environment of their county. For those in the worst sociodemographic quintiles in each RUCC, that individual-level advantage may be particularly stark. It is possible that stark contrast confers a health benefit to an individual of higher sociodemographic class in an area that is classified by the EQI as low sociodemographic quality; biologic benefits of social comparison have been previously demonstrated (Fliessbach et al., 2007) and may manifest in this context as well.

The inferences from this study are limited by the cross-sectional design and ecological nature of the exposure. However, we expect that the variables underlying the EQI are relatively stable over time, and that counties do not shift substantially in their relative ranking of environmental quality. Although the exposure is ecological, it provides a comprehensive representation of the environment, including multiple domains important to understanding asthma. Because the outcome is reliant on claims, persons with asthma who do not have an asthma-related claim during the study period will be misclassified as non-asthmatic. However, claims cover inpatient, outpatient, procedure, and prescription drug claims; routine appointments as well as maintenance and rescue medications are likely accessed even if there is not an acute asthma-related event. Furthermore, we assessed a less restrictive outcome definition that only required one claim, and both overall prevalence and estimates of association were similar. Still, the prevalence of individuals with asthma in this dataset, as measured by claims, is much lower than the prevalence in the U.S. The dataset used in this study is limited to privately insured persons in the U.S. aged 18–65 who work for large (> 999 employees) companies or otherwise have private insurance plans captured by MarketScan. This is a more socioeconomically advantaged population than the U.S. as a whole, likely limiting generalizability.

This study also has several strengths. The EQI offers a novel metric for capturing information from numerous variables across five environmental domains, enabling a more comprehensive assessment of the multitude of simultaneous exposures that may affect asthma prevalence. We controlled for race, but do not expect additional threats from confounding since the EQI is "upstream" of other potentially relevant variables We did examine weather variables as a potential confounder, but did not observe a meaningful change in estimates and excluded the available variables from this analysis. We used MarketScan claims, a rich data source of individual-level data, to estimate the associations between environmental quality and asthma, and leveraged additional information on population demographics and weather by linking additional publicly available data. For parameter estimation, we used a Markov chain Monte Carlo approach. This approach does not rely on assumptions regarding the shape of a likelihood or a posterior distribution surface (as, for example, Laplace approximations do, assuming that the posterior distribution is Gaussian); as a result, the estimated credible intervals are broader than those obtained with a Laplace approximation, but are better estimated. Our study highlights how different aspects of the environment operate together to influence health outcomes. Single exposure studies are limited by the inability to adjust for and directly compare the multitude of environmental exposures to which humans are exposed (Stingone et al., 2017; Carlin et al., 2013; Taylor et al., 2016). The EQI reduces the dimensionality of the vast quantity of data while retaining the information those data offer. It provides useful information on which domains may be particularly important, accounting for the other domains that would be ignored in most studies.

5. Conclusion

We found evidence that worsening environmental quality is associated with increased asthma prevalence, but that domain-specific drivers of this association may operate differently depending on rural-urban status. The EQI offers an upstream summary measure of the cumulative environment over multiple domains. Future U.S. asthma research may be enhanced through consideration of the EQI as a confounder or effect measure modifier.

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Conflicts of interest

The authors declare they have no conflicts of interest.

Appendix A. Supplementary material

Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.envres.2018.06.020.

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