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A Retrospective, Time-Stratified, Case-Crossover Study of the Effect of $PM_{2.5}$ on Asthma Exacerbations in Rural Counties in Wisconsin

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Abstract **Air pollution is a pervasive environmental health hazard with the potential to worsen respiratory health outcomes, including asthma exacerbations. The impact of $PM_{2.5}$ on asthma exacerbations among rural populations is not well understood. Our analysis used a retrospective, time-stratified, case-crossover study design to examine the relationship between $PM_{2.5}$ and asthma exacerbations. We included asthma exacerbations that occurred January 1, 2019–June 30, 2022, among residents of seven rural counties in Wisconsin with a $PM_{2.5}$ air monitor. We also used $PM_{2.5}$ data collected by the Wisconsin Department of Natural Resources and weather data available from the National Oceanic and Atmospheric Administration (NOAA). Further, we used conditional logistic regression to assess the association between asthma exacerbations and lagged $PM_{2.5}$ levels, adjusting for maximum daily temperature. We found $PM_{2.5}$ levels (μg/m^3) 2 days prior to exacerbation were significantly associated with asthma exacerbations (hazard ratio 1.184; 95% confidence interval [1.051, 1.344]). Our study demonstrated an increased hazard of asthma exacerbations with higher levels of $PM_{2.5}$ in rural populations. These findings highlight the need for further research and efforts to mitigate the effects of air pollution in rural areas.**

Keywords: **asthma, respiratory health, air pollution, $PM_{2.5}$, rural health**

Introduction

Asthma is a prevalent chronic lung disease that affects approximately 1 in 10 children (Centers for Disease Control and Prevention [CDC], 2023a) and 1 in 7 adults in Wisconsin (CDC, 2023b). Asthma symptoms can be triggered by tobacco smoke, dust mites, pests, mold, pets, and outdoor air pollution (CDC, 2024). Outdoor air pollution varies by geography (Strosnider et al., 2017) and is influenced by seasonal weather patterns (Winquist et al., 2014). $PM_{2.5}$ is one of the most ubiquitous pollutants and has been shown to exacerbate asthma symptoms. Multiple epidemiological studies have demonstrated that $PM_{2.5}$ levels are positively correlated with asthma symptoms (Berhane et al., 2016), emergency department visits (Romieu et al., 1996), hospitalizations (Zheng et al., 2015), and mortality (Atkinson et al., 2014).

Our study's aim was to investigate the association between $PM_{2.5}$ and asthma exacerbations in rural areas of Wisconsin because most previous studies have focused on urban centers. Assessing time-varying pollutant exposures on asthma exacerbations can be challenging, however, particularly when working with administrative data sets that only include cases. To overcome this challenge, we employed the case-crossover study design, which uses cases and self-matched referent periods to effectively control for confounding characteristics (Maclure, 1991).

In recent years through public health surveillance, we have observed that some rural counties in Wisconsin have experienced increasing rates of asthma-related emergency department visits and hospitalizations, and we hypothesized that poor air quality could be a contributing factor. Given the important role of agriculture in Wisconsin's rural economy, agricultural practices such as prescribed burning, soil tilling, livestock operations emissions, and farm equipment use could generate substantial amounts of $PM_{2.5}$ (Domingo et al., 2021; U.S. Environmental Protection Agency, 2024). Additionally, wildfires occurring in other U.S. states and Canada can lead to high levels of particulate matter that adversely affect the air quality in Wisconsin. Our study examined the relationship between $PM_{2.5}$ and asthma exacerbations in seven rural counties in Wisconsin. Although one study that spanned both rural and urban populations examined the impact of $PM_{2.5}$ on asthma exacerbations (Bozigar et al., 2021), our study is the first to specifically focus on rural populations, contributing to the understanding of the impact of air pollution on asthma exacerbations in rural areas.

TABLE **1**

Main Characteristics of Asthma Exacerbations Among Residents From Ashland, Dodge, Forest, Grant, Sauk, Taylor, and Vilas Counties in Wisconsin

Characteristic	# (%) or Mean ± *SD*
Exacerbations	1,424 (100)
Type of exacerbation	
Emergency department visit	1,267 (89.0)
Hospitalization	80 (5.6)
Observation stay	77 (5.4)
$PM_{2.5}$ (μg/m^3)	
Mean: All possible days	6.7 ± 4.7
Mean: Exacerbation days	7.5 ± 4.8
Mean age at time of exacerbation (years)	35 ± 21.7
Age group (years)	
0–4	103 (7.2)
5–17	231 (16.2)
18–34	406 (28.5)
35–64	525 (36.9)
≥65	159 (11.2)
Race and ethnicity	
Asian	5 (0.4)
Black	57 (4.1)
Hispanic	77 (5.5)
Native American	74 (5.3)
White	1,179 (84.7)
Not provided	32

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Methods

Case Definition of Asthma Exacerbation

To identify asthma exacerbations, we used hospital discharge data collected by the Wisconsin Hospital Association that had been shared with the Wisconsin Department of Health Services. We defined an asthma exacerbation as any emergency department visit, hospitalization, or observation stay with an ICD-10 (International Classification of Disease, 10th revision) code of J45 that occurred during January 1, 2019–June 30, 2022. We restricted our analysis to Wisconsin residents of seven rural counties (Ashland, Dodge, Forest, Grant, Sauk, Taylor, and Vilas) with $PM_{2.5}$ air monitors operated by the Wisconsin Department of Natural Resources. Rural county classifications were based on the Federal Office of Rural Health Policy data files (Health Resources and Services Administration, 2024). Second encounters for cases occurring within 7 days of a prior exacerbation and exacerbations with missing $PM_{2.5}$ data were excluded from the analysis.

$PM_{2.5}$ Exposure

We used $PM_{2.5}$ data collected by the Wisconsin Department of Natural Resources from all rural counties with air monitors (n = 7). Throughout Wisconsin, the Wisconsin Department of Natural Resources operates a network of air monitors that use federally approved methods for measuring air quality (Wisconsin Department of Natural Resources, n.d.-a). We used the daily average of $PM_{2.5}$ in our analyses as both a continuous variable and categorical variable using Air Quality Index (AQI) categories (Wisconsin Department of Natural Resources, n.d.-b). To handle the small number of random missing $PM_{2.5}$ values, we imputed missing values with the mean of nearby daily values (1 day before and 1 day after), as done by Chi et al. (2019). Gaps of more than 1 day were not imputed.

Meteorological Exposures

We downloaded weather data from the National Oceanic and Atmospheric Administration (NOAA) for the dates December 18, 2018–July 14, 2022, for the seven rural counties included in this analysis. We included an additional 2 weeks before and after the case date range as potential control dates. We used only the maximum daily temperature from this data set. To handle the small number of missing values, we imputed missing values with the mean of nearby daily values (1 day before and 1 day after). As temperature data for Forest County were unavailable, we used temperatures from the adjacent Vilas County for Forest County measurements.

Statistical Analysis

We used a retrospective, time-stratified, case-crossover study design to test for associations between $PM_{2.5}$ exposures and asthma exacerbations. We applied conditional logistic regression for multivariate analyses to produce hazard ratios (HR) and 95% confidence intervals (CI) (SAS PHREG with TIES=BRESLOW; Wang et al., 2011). We combined clinical encounter data with daily $PM_{2.5}$ measurements and daily maximum temperature from each county. Control exposure periods were selected by matching the day of the week for 1–2 weeks prior to and 1–2 weeks after the exposure date for each exacerbation (n = 3–4). We created lag days for $PM_{2.5}$ exposures on the day of the exacerbation (lag0) and 1–6 days prior to the exacerbation (lag1–6). We also included a 7-day $PM_{2.5}$ average to represent the total exposure to $PM_{2.5}$ in the 7-day period prior to the exacerbation.

All models were adjusted for daily maximum temperature (°F). In secondary analyses, we assessed potential effect modification by sex, race and ethnicity, age, season, and county of residence. Race and ethnicity were evaluated as potential effect modifiers given the substantial asthma disparities observed among Black and Native American populations compared with Asian and White populations in Wisconsin (Wisconsin Department of Health Services, 2020). All analyses were conducted using SAS version 9.4.

Results

Characteristics of Asthma Exacerbations

A total of 1,424 asthma exacerbations were identified during the study period among residents of seven Wisconsin rural counties, including 1,267 (89%) emergency department visits, 80 (6%) hospitalizations, and 77 (5%) observation stays (Table 1). The mean age at the time of exacerbation was 35 years, and 820 (58%) of the cases were female patients. Most of the patients were White (85%), and 5% were Native American, 5% were Hispanic, 4% were Black, and <1% were Asian. A relatively even distribution of exacerbations was observed across the seasons, with spring (32%) having the highest proportion, followed by fall (26%), winter (22%), and summer (21%). The mean $PM_{2.5}$ level for all possible days in the study period was 6.7 µg/m^3 (±4.7), and the mean level on exacerbation days was 7.5 µg/m^3 (±4.8).

TABLE **1** continued

Main Characteristics of Asthma Exacerbations Among Residents From Ashland, Dodge, Forest, Grant, Sauk, Taylor, and Vilas Counties in Wisconsin

Characteristic	# (%) or Mean ± *SD*
Sex	
Male	604 (42.4)
Female	820 (57.6)
County	
Ashland	139 (9.8)
Dodge	449 (31.5)
Forest	31 (2.2)
Grant	264 (18.5)
Sauk	336 (23.6)
Taylor	97 (6.8)
Vilas	108 (7.6)
Unique days (total/possible)	811/1,277 (63.5)
Median exacerbations/day (range)	1 (1–8)
Mean exacerbations/day	1.8 ± 0.96
Exacerbations by season	
Winter (December–February)	309 (21.7)
Spring (March–May)	454 (31.9)
Summer (June–August)	295 (20.7)
Fall (September–November)	366 (25.7)
Mean daily maximum temperature (°F)	57.3 ± 21.2

Association Between $PM_{2.5}$ and Asthma Exacerbations

The number of exacerbations per AQI category of lag0–6 was compared with all days in the study period, which revealed significant differences in lag0–5 ($p < .05$; Table 2). There were higher percentages of moderate to unhealthy AQI levels in lag0–5 compared with the whole study period, with lag2 (2 days prior to exacerbation) having the greatest difference ($p = .0001$). After controlling for maximum daily temperature, conditional logistic regression analysis showed that $PM_{2.5}$ levels on lag2 were significantly associated with increased hazard of asthma exacerbations (HR 1.184; 95% CI [1.051, 1.344]; Table 3).

Stratified analysis found no effect modification by sex, race and ethnicity, age, season, or county of residence on lag2 (all *p*-values >.05; Figure 1). Associations between $PM_{2.5}$ and asthma exacerbations, however, were highest among female patients (HR 1.219; 95% CI [1.041, 1.438]); White individuals (HR 1.195; 95% CI [1.041, 1.370]); people ≥65 years (HR 1.524; 95% CI [1.105, 2.119]); exacerbations occurring in spring (HR 1.268; 95% CI [1.020, 1.568]); and residents of Ashland County (HR 1.424; 95% CI [1.062, 1.931]) and Sauk County (HR, 1.331; 95% CI [1.010, 1.757]).

Discussion

Our case-crossover study aimed to assess the relationship between $PM_{2.5}$ and asthma exacerbations in rural Wisconsin. We identified cases with asthma exacerbations using hospital discharge data from the Wisconsin Hospital Association among residents of seven rural counties with a $PM_{2.5}$ air monitor. We used $PM_{2.5}$ data collected by the Wisconsin Department of Natural Resources as the exposure variable, and we included daily maximum temperature data from NOAA in the analysis.

When the number of exacerbations per AQI category of lag0–6 was compared with all days in the study period, significant differences were revealed in lag0–5, as the percentage of exacerbations in the moderate to unhealthy AQI levels was significantly higher than the whole study period. After controlling for maximum daily temperature, $PM_{2.5}$ levels on lag2 were significantly associated with an increased hazard of an asthma exacerbation occurring. The stratified analysis on lag2 found elevated associations among female cases, White individuals, people ≥65 years, exacerbations occurring in spring, and residents of Ashland and Sauk counties.

Our findings are consistent with previous studies conducted in urban areas and demonstrate that asthma exacerbations are more likely to occur in the days following higher $PM_{2.5}$ levels. For instance, a study by Rosser et al. (2022) found a significant association between $PM_{2.5}$ and asthma exacerbations on lag days 2 and 3. Similarly, Glad et al. (2012)

TABLE 2

Number of Exacerbations per Air Quality Index (AQI) Category in Rural Counties in Wisconsin From January 1, 2019–June 30, 2022

AQI Levels of Health Concern for 24-hr $PM_{2.5}$ (µg/m³)	All Days in Study Period # (%)	Lag0 # (%)	Lag1 # (%)	Lag2 # (%)	Lag3 # (%)	Lag4 # (%)	Lag5 # (%)	Lag6 # (%)
Good (0–12.0)	7,847 (89.3)	1,239 (87.0)	1,222 (86.1)	1,209 (85.5)	1,214 (86.2)	1,224 (86.9)	1,218 (86.4)	1,238 (87.9)
Moderate (12.1–35.4)	928 (10.6)	184 (12.9)	194 (13.7)	199 (14.1)	191 (13.6)	184 (13.7)	190 (13.5)	168 (11.9)
Unhealthy for sensitive groups (35.5–55.4)	12 (0.1)	1 (0.1)	2 (0.1)	3 (0.2)	4 (0.3)	0	1 (0.1)	1 (0.1)
Unhealthy (55.5–140.4)	4 (0.05)	0	1 (0.1)	3 (0.2)	0	0	1 (0.1)	2 (0.1)
Very unhealthy (140.5–210.4)	0	0	0	0	0	0	0	0
Hazardous (>210.4)	0	0	0	0	0	0	0	0
Missing	148	0	5	10	15	16	14	15
Total	8,939	1,424	1,424	1,424	1,424	1,424	1,424	1,424
p-value	–	.0191	.0064	.0001	.0026	.0096	.0109	.1945

TABLE 3

Multivariate Analysis of the Relationship Between 10-Unit Increases of $PM_{2.5}$ and Asthma Exacerbations by Lag Day

Lag Day	Hazard Ratio	95% CI	*p*-Value
Main model: 10-unit increases			
Lag0	1.072	[0.942, 1.219]	.3127
Lag1	1.083	[0.951, 1.231]	.2303
Lag2	**1.207**	**[1.072, 1.370]**	**.0024**
Lag3	1.072	[0.942, 1.219]	.2725
Lag4	0.932	[0.817, 1.062]	.2772
Lag5	0.980	[0.860, 1.116]	.7585
Lag6	0.980	[0.860, 1.116]	.7307
Average: Lag0–6	1.127	[0.904, 1.397]	.2959
Main model: 10-unit increases controlling for maximum temperature			
Lag0	1.041	[0.914, 1.195]	.5434
Lag1	1.041	[0.914, 1.195]	.5352
Lag2	**1.184**	**[1.051, 1.344]**	**.0069**
Lag3	1.062	[0.932, 1.207]	.3810
Lag4	0.914	[0.801, 1.041]	.1918
Lag5	0.970	[0.851, 1.105]	.6534
Lag6	0.970	[0.851, 1.116]	.7007
Average: Lag0–6	1.072	[0.860, 1.344]	.5542

Note. The bolded values indicate significant results as $p < .05$. CI = confidence interval.

reported an effect on the total population on lag day 1 and lag days 1–3 for Black individuals in their study. Moreover, Chi et al. (2019) found an association between $PM_{2.5}$ and multiple respiratory diseases on lag days 3–5.

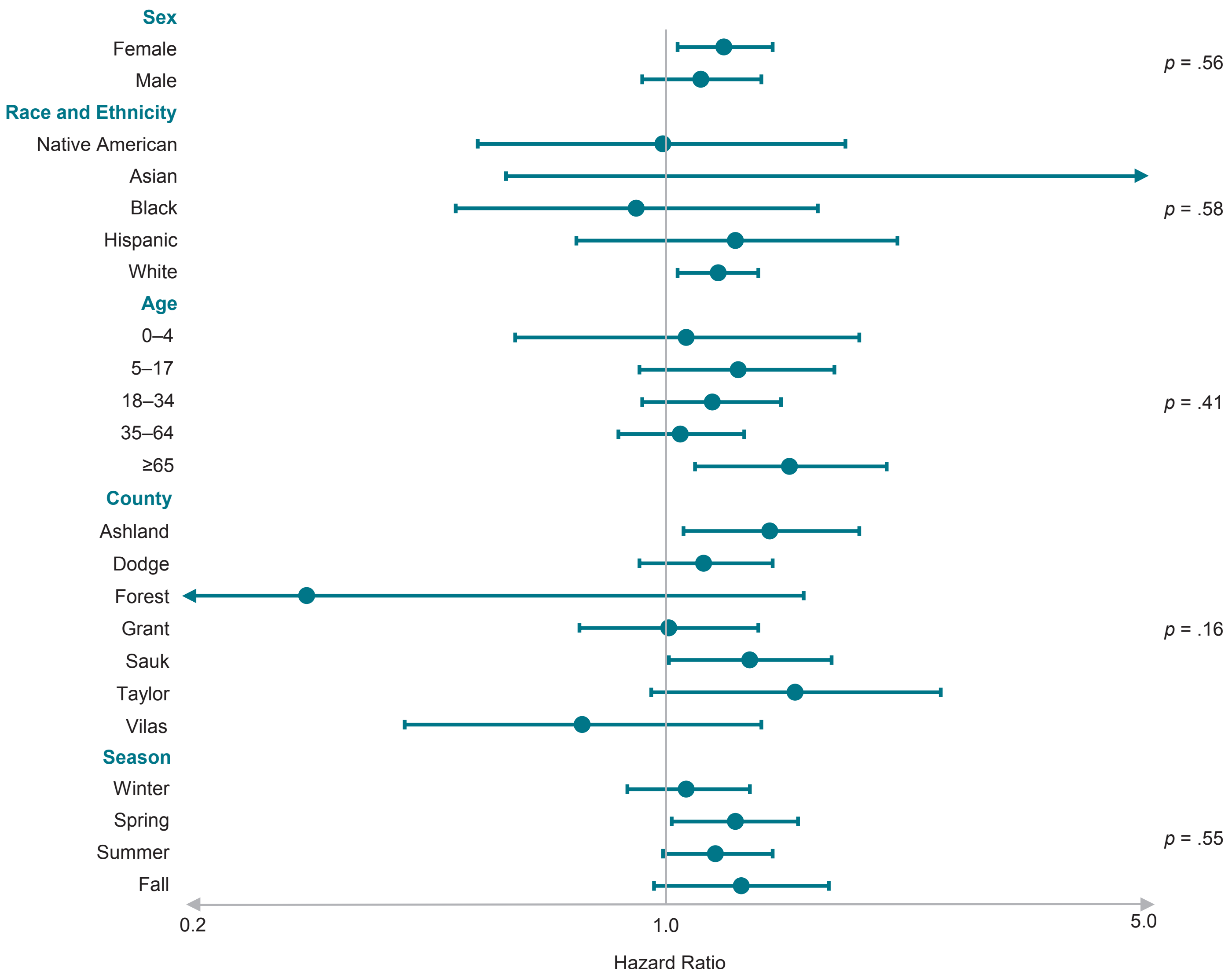
Our study, however, was notable in that we found an elevated hazard of asthma exacerbations with $PM_{2.5}$ levels for people ≥65 years. Some studies have reported inconsistent findings—for example, a study by Bozigar et al. (2021) found no association between $PM_{2.5}$ and asthma exacerbations. These discrepancies might be due to differences in study design, study populations, or exposure assessments.

The strengths of our study include the use of a case-crossover study design, which is an effective method for assessing time-varying exposures in administrative data sets with only case data included. This study design is advantageous because it uses self-matched referent periods, which naturally control for confounding factors. Another strength is the inclusion of data from multiple rural counties, expanding our knowledge base on the relationship between $PM_{2.5}$ and asthma exacerbations in rural areas.

Our study was limited by the following factors. We included data only from seven rural counties in Wisconsin, thus limiting the generalizability of our results to other rural areas of the state. Additionally, we were unable to include wind speed data due to missing observations or humidity data because they

FIGURE **1**

Hazard Ratios and 95% Confidence Intervals for Potential Effect Modifiers on the Relationship Between 10-Unit Increases of $PM_{2.5}$ and Asthma Exacerbations on Lag2



were not available for the selected rural counties. Furthermore, we lacked information on individual-level covariates, such as smoking status and comorbidities, which could modify the relationship between $PM_{2.5}$ and asthma exacerbations.

Conclusion

Our study provides valuable insight into the characteristics of asthma exacerbations in rural areas. It also highlights the importance of looking beyond urban centers with the highest levels of $PM_{2.5}$ when developing interventions and policies to prevent asthma exacerbations. Our findings support the need for efforts to improve a) air quality in rural areas to reduce the burden of asthma exacerbations in these communities and b) communications within rural areas regarding air quality and associations with poor asthma outcomes. Further research is needed to confirm our results in other rural areas and to identify individual-level risk factors that could modify the relationship between $PM_{2.5}$ and asthma exacerbations.

The implications of this research are important, and our findings could enhance targeted interventions in rural areas to improve asthma management and reduce poor outcomes associated with air pollution.

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Did You Know?

The U.S. Environmental Protection Agency has designated January as National Radon Action Month. Radon is the leading cause of lung cancer deaths among nonsmokers in the U.S. Learn more about the effort to take action against radon at www.epa.gov/radon/national-radon-action-month-information.