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ORIGINAL CONTRIBUTION

Exacerbation of Renal, Cardiovascular, and Respiratory Outcomes Associated with Changes in Climate

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Exposure to environmental variables including declining air quality and increasing temperatures can exert detrimental effects on human health including acute exacerbations of chronic diseases. We aim to investigate the association between these exposures and acute health outcomes in a rural community in Colorado. Meteorological and adult emergency department visit data were retrospectively collected (2013-2017); for asthma outcomes, additional data were available (2003-2017). Daily environmental exposure data included PM_{10}, maximum daily temperature (MDT), and mean humidity and precipitation. Total daily counts of emergency department (ED) diagnoses for myocardial infarction, congestive heart failure, urolithiasis, and exacerbation of chronic obstructive pulmonary disease (COPD) and asthma, were calculated during the study period. Time series models using generalized estimating equations were fit for each disease and included all four environmental factors. Between 2013 and 2017, asthma and COPD exacerbation accounted for 30.8% and 25.4% of all ED visits (n=5,113), respectively. We found that for every 5˚C increase in MDT, the rate of urolithiasis visits increased by 13% (95% CI: 2%, 26%) and for every 10μg/m^3 increase in 3-day moving average PM_{10}, the rate of urolithiasis visits increased by 7% (95% CI: 1%, 13%). The magnitude of association between 3-day moving average PM_{10} and rate of urolithiasis visits increased with increasing MDT. The rate of asthma exacerbation significantly increased as 3-day, 7-day, and 21-day moving average PM_{10} increased. This retrospective study on ED visits is one of the first to investigate the impact of several environmental exposures on adverse health outcomes in a rural community. Research into mitigating the negative impacts of these environmental exposures on health outcomes is needed.

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Abbreviations: PM, Particulate matter; MDT, maximum daily temperature; ED, emergency department; COPD, chronic obstructive pulmonary disease; CHF, congestive heart failure; SLV, San Luis Valley; CVD, cardiovascular disease; MI, myocardial infarction; ICD, International Classification of Diseases; RR, risk ration; CI, confidence intervals; GEE, Generalized Estimating Equations.

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INTRODUCTION

The negative health impacts of climate-related exposures such as heat and air pollution are well established [1]. A large proportion of existing studies on the effects of climate-related exposures on cardiovascular, pulmonary, and renal outcomes have been conducted on urban populations [2]. More research on relationships between human health and environmental exposures in rural areas is needed. Rural areas are especially vulnerable to these effects due to an aging population, a higher prevalence of outdoor workers and laborers, exposure to wildfires, and several other social determinants of health including access to medical care and healthy food [3,4]. One such rural community is the San Luis Valley (SLV), a high-altitude community located in south central Colorado covering approximately 8,000 square miles of the Colorado Plateau. The SLV is the highest mountain plain desert in North America located between the Sangre De Cristo and San Juan mountain ranges. It is approximately the size of Connecticut with an average elevation of 7,500 feet. This bi-ethnic community is home to approximately 46,000 residents and experiences the highest poverty level in Colorado [5,6]. The community experiences high rates of chronic diseases including diabetes, chronic kidney disease, and asthma in an aging population with 19.9% of people being 65 years of age or older [5,7,8].

Concurrently, the SLV is experiencing the impacts of climate change including an increase in the annual temperature by 3.2°F since 1962, leading to declining snowpack in the past 20 years [9]. This has created environmental conditions supporting sustained drought which decreases the availability of water resources. Reduced ground water and surface water can be associated with a moisture deprived vadose zone, which prevents the growth of ground vegetation playing a key role in preventing the uptake of particulate matter by the wind [10,11]. Concurrent increase in wildfires contributes to increase in airborne particulate matter (PM) and PM deposits on snowpack and create a cycle of cumulative effects. Particulate deposits on snowpack reduces albedo, which accelerates seasonal snowmelt and further exacerbates the annual decrease in ground moisture [12,13] – further increasing the impacts of regional climate change.

Increasing ambient temperatures have been linked to higher incidence of heat-related illness and may entail numerous secondary consequences for healthcare systems [2,14-17]. Increases in the exacerbation of acute-on-chronic illnesses such as cardiovascular disease (CVD), atherosclerosis, and congestive heart failure (CHF) have also shown to be of concern during heat waves [17-19]. Furthermore, decreased air quality can trigger acute-on-chronic cardiovascular and respiratory episodes as well. Particularly concerning is the effect of increasing amounts of particulate matter on individuals with chronic respiratory disease and pre-existing CVD [20-26]. Additionally, acute diseases such as urolithiasis have also been associated with environmental factors such as heat and humidity; stone formation in the renal collecting system may arise from heat-related decreases in urine volume and increases in the concentration of lithogenic substrate in the urine, although the mechanism is likely multifactorial [27-29]. Moreover, pulmonary diseases such as asthma and COPD have been associated with heat events and air quality [30-36].

In terms of secondary consequences for healthcare systems, surges in demand for emergency medical services due to acute illness or exacerbation of chronic illness can result in numerous adverse healthcare worker and patient-oriented outcomes including worker fatigue, prolonged boarding times, staffing shortages, and poor patient outcomes [37].

Presently, there exists a knowledge gap in understanding the effects of environmental exposures related to climate and air quality on acute and acute-on-chronic diseases in rural populations. With research identifying multiple factors such as PM and other pollutants contributing to air quality and directly impacting health [22], we can anticipate decreased air quality due to higher ambient temperatures and increased aridity induced by climate change that will allow for additional mobilization of surface dust and other course particulates. We proposed this study to clarify the knowledge gap by looking at ED and environmental data from the SLV region.

METHODS AND PROCEDURES

Study Design

This study consists of investigating retrospectively collected time series data on environmental exposures (temperature, humidity, precipitation, air quality) and adult emergency department visits for acute and acute-on-chronic health outcomes in the SLV of Colorado between January 2013 and December 2017. Data from two EDs were used, the first located in Alamosa, which has the largest population density in the SLV, with the second ED located 15 miles south in La Jara (which is nearly identical in climate).

Meteorological Data

Publicly available meteorological data from the National Center for Atmospheric Research (NCAR) and the National Oceanic Atmospheric Association (NOAA) was used for this study. Air quality monitors for particulate matter ≤10 μm in diameter (PM_{10}) located in Alamosa City are maintained by the Colorado Air Pollution Control Division (CAPCD) within the Colorado Department of Public Health and Environment (CDPHE). Daily measurements of PM_{10} (µg/m^3), maximum daily temperature (˚C), mean humidity (percent), and mean precipitation (mm) were considered. PM_{10} was measured by two separate monitors within the study area (one at Adams State University and one at a local Municipal Building), therefore, the average between the two monitors was used to assess PM_{10} exposure. All other environmental exposures were measured from the meteorological station located at the SLV Regional Airport 2 miles south of Alamosa. Each environmental variable was incorporated into statistical models as a continuous measure.

Health Data

Following approval from the Colorado Multiple Institutional Review Board (COMIRB), data on emergency room visits were obtained from SLV Health which manages both EDs in the study area. International Classification of Diseases (ICD) version 9 and 10 were used to identify outcomes of interest, which included myocardial infarction (MI) (ICD-9 410 series, ICD-10 I21-I22 series), stroke (ICD-9 430-437, ICD-10 I60-I63 series), exacerbation of CHF (ICD-9 428 series, ICD-10 I50 series and I11.0), asthma exacerbation (ICD-9 493 series, ICD-10 J45 series), COPD exacerbation (ICD-9 491, 492, and 496 series, ICD-10 J41-J44 series), and urolithiasis (ICD-9 599.6, 599.69, 592.0-1, 592.9, 593.89, 274.11, 753.2, 788.0, ICD-10 N20-N23 series). Patient-level data were obtained from January 1st, 2013 to December 31st, 2017 for subjects over 18 years of age. Variables included date of visit, ED facility (Alamosa or Conejos County), sex, age, and diagnosis for the underlying cause of visit. Total daily counts of each diagnosis of interest were calculated over the study period and used as the outcome in subsequent models. Additional data on asthma exacerbation were available from January 1st, 2003 to December 31st, 2012 and included in this analysis to identify any potential trends spanning beyond the available climate data.

Statistical Analysis

Each outcome of interest consisted of daily total counts during the study period, thus, Poisson models were used to fit each time series, using generalized estimating equations (GEE) and a first-order autoregressive covariance structure to account for serial correlation; a scale parameter was included to account for over-/under-dispersion. Model-based standard errors were used for all estimates. All four environmental factors, PM_{10}, maximum daily temperature, humidity (albeit low), and precipitation were included in each model. Also in each model, seasonal health trends (eg, influenza) were accounted for by including month, while weekly trends in ED visits were accounted for by including day of the week (both as class variables). Cubic splines for year were employed to give the model flexibility and account for any time trends not associated with environmental exposure or those accounted for by month or day of week. Knots were placed at one-year intervals starting at 6 months to account for approximate 2-year cycles in ED visits. Each outcome was modeled using PM_{10} with a specific lag structure: same-day air pollution (lag 0), 1-day lagged, 2-day lagged, 3-day moving average, or 7-day moving average. Models were also fit for threshold based PM_{10} (≥50 µg/m^3 vs <50 µg/m^3 and ≥100 µg/m^3 vs <100 µg/m^3) for all lag structures. It should be noted that 3-day and 7-day moving averages included the current day and days leading up to the current day. Finally, temperature was further examined by including 1-day lagged MDT in models with PM_{10} at various lag structures, as well as models that included the PM_{10}-by-MDT interaction (lag 0 MDT with various PM_{10} lags). Note, the primary follow-up period for this study was January 1st, 2013 to December 31st, 2017 since ED data for all outcomes of interest were available during this period. For asthma exacerbations, ED data was available starting January 1st, 2003 which allowed for a 15-year period analysis for this specific outcome. As a sensitivity analysis and given the extended study period, 14-day, 21-day, and 28-day moving averages for PM_{10} were used for modeling asthma exacerbations over 15 years. Observations for 14-day, 21-day, and 28-day moving averages were weighted by the number of PM_{10} measurements used for each moving average. Statistical significance was considered at α=0.05 significance level. Analysis was carried out using SAS version 9.4 (Cary, NC: SAS Institute Inc, 2013) and R version 4.1.1 (R Foundation for Statistical Computing, Vienna, Austria, 2021).

RESULTS

From January 2013 to December 2017, there were 2,240 patients who visited EDs in the SLV with a total of 5,113 disease diagnoses of interest. Table 1 shows the demographic characteristics for all asthma exacerbations (n=1,574), CHF (n=653), COPD (n=1,299), MI (n=388), stroke (n=270), and urolithiasis (n=929) diagnoses during the study period. Average patient age differed across diagnoses where asthma exacerbations had the youngest mean age at 38.2 years (SD=22.1) and congestive heart failure had the oldest mean age at 75.6 years (SD=15.2). The distribution of sex across diseases also differed such that myocardial infarction had the largest disparity between male and female patients (63.1% male) and stroke had the smallest disparity between male and female patients (53% male). Across all diseases, the primary emergency room was Alamosa Regional Medical Center.

Table 2 shows the mean (5th-95th percentile) PM_{10},

Table 1. Population Characteristics by Disease Classification

Characteristic	Asthma	CHF	COPD	MI	Stroke	Urolithiasis
Total count, n	1,574	653	1,299	388	270	929
Age in years, mean (SD)	38.2 (22.1)	75.6 (15.2)	70.2 (12.3)	70.7 (12.6)	72.1 (17.2)	49.1 (16.7)
Sex, n (%)						
Female	900 (57.2)	294 (45)	533 (41)	143 (36.9)	143 (53)	431 (46.4)
Male	674 (42.8)	359 (55)	766 (59)	245 (63.1)	127 (47)	498 (53.6)
Hospital, n (%)						
Conejos County Hosp. ED	366 (23.3)	151 (23.1)	274 (21.1)	41 (10.6)	38 (14.1)	112 (12.1)
Alamosa Regional Med. ED	1,162 (73.8)	391 (59.9)	883 (68)	311 (80.2)	216 (80)	815 (87.7)
Admission to Hospital	46 (2.9)	111 (17)	142 (10.9)	36 (9.3)	16 (5.9)	2 (0.2)

Note: CHF = Congestive Heart Failure; COPD = Chronic Obstructive Pulmonary Disease; MI = Myocardial Infarction; SD = Standard Deviation; ED = Emergency Department.

Table 2. Mean (5th, 95th percentile) for Environmental Variables by Season

	Season^			
Variable	Winter	Spring	Summer	Fall
PM_{10} (μg/m^3)	20.5 (6.5, 42.5)	24.4 (7.0, 59.0)	22.2 (11.0, 42.5)	18.8 (8.0, 34.0)
MDT (°C)	2.7 (-5.9, 11.9)	14.7 (5.3, 22.6)	26.3 (22.0, 30.0)	17.0 (5.1, 26.4)
Humidity (%)	40.5 (21.0, 59.9)	23.8 (16.7, 42.6)	30.4 (17.7, 49.3)	44.1 (27.2, 63.8)
Precipitation (mm)	0.4 (0.0, 2.7)	0.7 (0.0, 4.7)	1.1 (0.0, 5.9)	0.7 (0.0, 4.3)

Note: MDT = Maximum Daily Temperature; ^Seasons were categorized as Winter (Dec., Jan., Feb.), Spring (Mar., Apr., May), Summer (Jun., Jul., Aug.), and Fall (Sep., Oct., Nov.)

MDT, humidity, and precipitation across the four different seasons during the study period. Mean daily PM_{10} peaked during the spring months with an average 24.4 μg/m^3 while max daily temperature peaked during the summer months at an average 26.3˚C. Daily humidity was highest during the fall months at an average 44.1% whereas daily precipitation was highest during summer at an average 1.1 mm/day.

Associations between each environmental variable and incidence rates for diseases of interest are shown in Table 3 based on GEE models. In most cases, increases in environmental factors were associated with an increase in disease diagnosis rates although in almost every case this relationship was not statistically significant. Interestingly, each 5˚C increase in maximum daily temperature was associated with a 13% increase in the mean rate of urolithiasis diagnoses (RR=1.13; 95% CI: 1.02, 1.26).

Table 4 shows the association between 1-day lagged, 2-day lagged, 3-day moving average, and 7-day moving average PM_{10} values and disease diagnosis rates. An increase in 10 μg/m^3 of PM_{10} was associated with a 4% increase in the rate of urolithiasis diagnoses the following day (RR=1.04; 95% CI: 1.00, 1.07). Additionally, a 10 μg/m^3 increase in the 3-day moving average of PM_{10} was associated with a 7% increase in the rate of urolithiasis diagnoses (RR=1.07; 95% CI: 1.01, 1.13). Extending the study period to include asthma exacerbation diagnoses from January 1st, 2003 to December 31st, 2012, we observed an increased rate of asthma exacerbations with increasing PM_{10} (Figure 1). Each 10 μg/m^3 increase of 1-day lagged and 2-day lagged PM_{10} was associated with a 1% (95% CI: 0.02%, 2%) and 1% (95% CI: -0.4%, 2%) increased rate of asthma exacerbation diagnoses, respectively. In terms of moving averages, PM_{10}, each 10 μg/m^3 increase was associated with increased rate of asthma exacerbation diagnoses, respectively, at 2% (95% CI: 1%, 4%) for 3-day, 3% (95% CI: 0.4%, 6%) for 7-day, 2% (95% CI: -2%, 6%) for 14-day, and 5% (95% CI: 0.4%, 10%) for 21-day. The 28-day moving average produced a similar RR compared to the 21-day moving average. However, the RR for 28-day moving average PM_{10} was not statistically significant ($p = 0.07$).

Given the relationship between MDT, PM_{10}, and incidence of urolithiasis diagnoses, we examined the interaction between PM_{10} and MDT when modeling urolithiasis diagnosis counts. While the PM_{10}*MDT interaction was negligible for 1-day-lagged PM_{10} ($p=0.43$), a significant positive interaction existed for the 3-day moving average of PM_{10} ($p=0.04$). For the latter, a 5% increase in rate of urolithiasis occurred for each 10 μg/m^3 increase of PM_{10} for MDT at its minimum, whereas it increased to 9% at the maximum MDT (Appendix A: Table S1).

Table 3. Relationship Between Number of Emergency Room Visits and Environmental Variables by Disease Classification, Expressed as Rate Ratio (RR) with 95% Confidence Intervals

Outcome	PM_{10}		MDT		Humidity		Precipitation	
	RR (95% CI)	p-val.	RR (95% CI)	p-val.	RR (95% CI)	p-val.	RR (95% CI)	p-val.
Asthma	0.99 (0.95, 1.03)	0.55	1.07 (0.98, 1.17)	0.11	1.03 (0.95, 1.12)	0.48	0.98 (0.95, 1.02)	0.36
COPD	1.00 (0.97, 1.03)	1.00	1.02 (0.93, 1.11)	0.72	1.05 (0.97, 1.14)	0.23	0.99 (0.95, 1.02)	0.49
CHF	0.99 (0.94, 1.04)	0.74	1.01 (0.9, 1.14)	0.88	1.04 (0.93, 1.17)	0.48	1.00 (0.96, 1.05)	0.94
MI	0.96 (0.88, 1.04)	0.32	1.00 (0.86, 1.17)	0.99	1.13 (0.98, 1.31)	0.08	0.94 (0.88, 1.00)	0.07
Stroke	0.95 (0.85, 1.05)	0.30	0.97 (0.79, 1.19)	0.76	1.01 (0.83, 1.22)	0.95	0.96 (0.88, 1.04)	0.35
Urolithiasis	1.02 (0.99, 1.06)	0.21	1.13 (1.02, 1.26)	0.02	1.04 (0.94, 1.14)	0.45	1.00 (0.96, 1.04)	0.93

Notes: Rate ratio (RR) for PM_{10} are increases of 10 μg/m^3. RR for Max Daily Temperature (MDT) are increases of 5˚C. RR humidity are increases of 10%. RR for precipitation are increases of 1 mm. RR (95% CI) estimated from multivariable Poisson models as described in Methods. p-values are reported to the second decimal place. COPD = Chronic Obstructive Pulmonary Disease; CHF = Congestive Heart Failure; MI = Myocardial Infarction.

Table 4. Relationship Between Number of Emergency Room Visits and PM_{10} by Disease Classification, Expressed as Rate Ratio (RR), with 95% Confidence Intervals. Various lag structures are considered for PM_{10}

Outcome	1-Day Lag		2-Day Lag		3-Day MA		7-Day MA	
	RR (95% CI)	p-val.	RR (95% CI)	p-val.	RR (95% CI)	p-val.	RR (95% CI)	p-val.
Asthma	1.01 (0.98, 1.04)	0.46	1.00 (0.96, 1.03)	0.87	1.00 (0.95, 1.05)	0.98	1.01 (0.94, 1.09)	0.71
COPD	1.00 (0.96, 1.03)	0.86	1.02 (0.99, 1.05)	0.21	1.02 (0.97, 1.07)	0.56	1.02 (0.95, 1.10)	0.59
CHF	1.02 (0.99, 1.06)	0.21	0.98 (0.94, 1.04)	0.55	1.00 (0.93, 1.07)	0.97	0.96 (0.86, 1.06)	0.40
MI	0.97 (0.90, 1.05)	0.42	1.02 (0.96, 1.07)	0.58	0.97 (0.87, 1.07)	0.55	0.94 (0.82, 1.08)	0.41
Stroke	1.04 (0.99, 1.09)	0.15	1.01 (0.95, 1.08)	0.72	1.02 (0.92, 1.14)	0.69	0.96 (0.81, 1.13)	0.62
Urolithiasis	1.04 (1.00, 1.07)	0.03	1.02 (0.99, 1.06)	0.23	1.07 (1.01, 1.13)	0.03	1.08 (0.99, 1.17)	0.10

Notes: This table describes rate ratio (RR) for incidence of primary health outcomes with varying PM_{10} lag structures. RR are for increases in PM_{10} of 10 μg/m^3. RR (95% CI) estimated from multivariable Poisson models as described in Methods. p-values are reported to the second decimal place. COPD = Chronic Obstructive Pulmonary Disease; CHF = Congestive Heart Failure; MI = Myocardial Infarction.

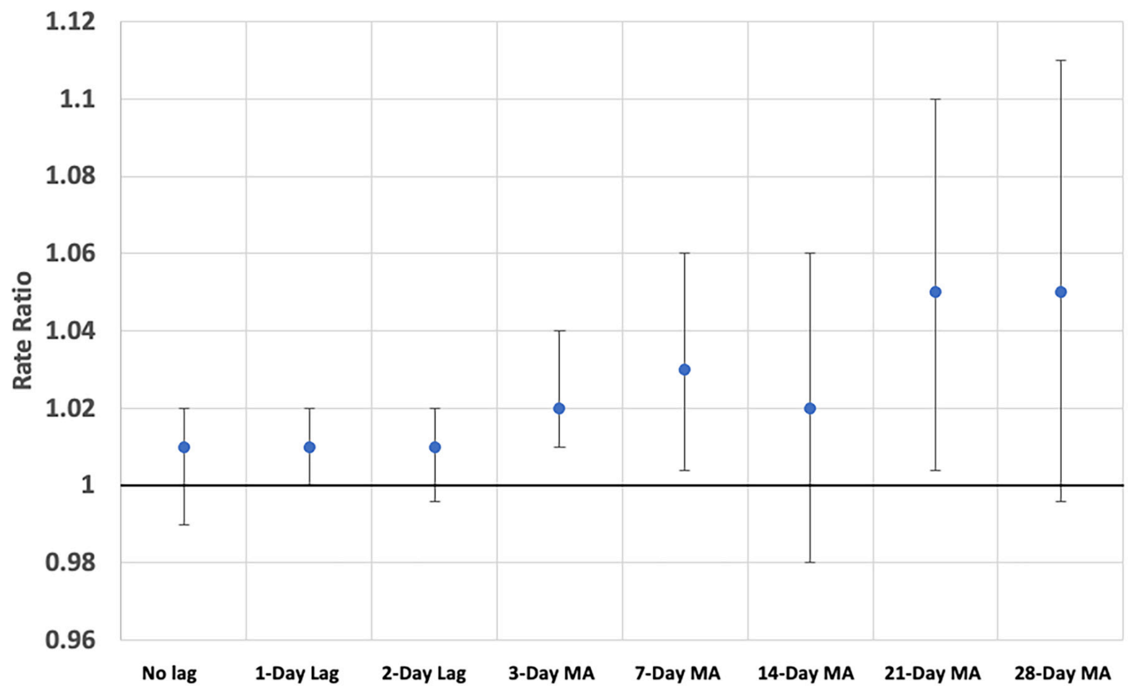

Figure 1. The relationship between number of emergency room visits for asthma exacerbations and PM_{10} (expressed as rate ratio (RR) with error bars representing 95% Confidence Intervals) across lag structures and moving averages (MA), during the 15-year study period.

We also examined the effect of 1-day lagged MDT in conjunction with 1-day lagged PM_{10} on the mean rate of ED diagnoses for each outcome, shown in Appendix A: Table S2. Controlling for humidity, precipitation, and 1-day lagged PM_{10}, each 5˚C increase in MDT was associated with a 15% increase in the mean rate of urolithiasis diagnoses the following day (RR=1.15; 95% CI: 1.04, 1.27). In terms of precipitation, a 1 mm increase in daily precipitation was associated with a 7% decrease in the mean rate of MI (RR=0.93; 95% CI: 0.87, 1.00). Additionally, we observed a marginally significant relationship between mean daily humidity and MI diagnoses such that a 10% increase in mean daily humidity was associated with a 14% increase in the mean rate of MI diagnoses (RR=1.14; 95% CI: 0.99, 1.30).

DISCUSSION

With respect to maximum daily temperature, we found that each 5˚C increase in MDT was associated with a 13% increase in the mean rate of ED urolithiasis diagnoses. Additionally, we found that higher MDT the previous day was also associated with increased mean rates of urolithiasis diagnoses. Physiologically, it is difficult to explain the short time lag between exposure to elevated MDT and the increased rate of urolithiasis diagnosis, as stone formation is typically a complex process taking weeks to months [38]. That said, previous epidemiologic studies of stone disease in relation to high ambient temperature have noted that the maximum risk of emergency department presentation for urolithiasis occurs within 3 days of exposure [39,40], which likely relates to concentration of lithogenic solute in the renal collecting system (due to dehydration) and rapid progression of stone growth. Though our finding is best explained by this mechanism, it is also possible that our models may not capture additional factors that may contribute to an individual's proclivity for stone disease. For example, dietary habits – such as frequent ingestion of foods enriched in sodium or dietary oxalate – can increase risk for urolithiasis in certain individuals [41]. If dietary habits changed seasonally (eg, consumption of potatoes, an oxalate-rich food harvested in the SLV), it is conceivable that there could be additional seasonal variation in risk of stone formation that could compound with the risk conferred by high temperature exposure.

Of note, prolonged temperature exposure above 33-35˚C for several days is considered extreme heat [42]. However, during summer, maximum daily temperatures in the SLV averaged 26.4˚C with few values exceeding 30˚C. This suggests that heat and climate acclimatization may be playing a role and heat exposure is less about an absolute threshold and more of a relative one, which is consistent with some previous literature [43]. Across the

US, some regions may be more likely to see a shift in this relative threshold in response to changes in climate [27]. Prior studies have further shown that morbidity and all-cause mortality as well as heat-related hospitalizations start to occur at moderate heat index values which are usually well below the alert thresholds used by early warning systems [44]. Therefore, our data support a more nuanced approach to heat alert criteria and highlight the opportunity to refine early warning systems to best support local epidemiological conditions. It should be noted that a 5˚C increase of the MDT is distinct from a 5˚C increase in the average daily temperature. A difference in MDT should not be interpreted in the same way as hourly changes during the day (eg, morning to afternoon) as it represents the hottest temperature of the entire day and should be interpreted as additional risk of warmer days and not within an individual day. Additionally, there could be other variables that play a role in this exposure that were not considered, such as high radiant heat exposure.

In terms of air quality, we found that 1-day lagged and 3-day moving average PM_{10} measurements were associated with increased mean rates of urolithiasis. Given that same day PM_{10} was not significantly associated with increased rates of urolithiasis diagnoses, our findings suggest a delayed effect on the mechanism of urolithiasis in the context of PM_{10} exposure. While PM $\leq 10\,\mu$m can reach the alveoli, PM smaller than $1\,\mu$m can penetrate deeper, accessing the renal tubules through the bloodstream, and potentially altering urine metabolite profiles. Increased membranous nephropathy and reduced renal function has been demonstrated in association with $PM_{2.5}$ exposure [45,46]. These findings could suggest the association with PM_{10} is due to the correlation of occurrence of $PM_{2.5}$ and PM_{10} [47]. It has also been suggested that the vascular damage from oxidative stress caused by PM can lead to inflammatory changes that could precipitate urolithiasis [46,48,49]. Additionally, we observed an increased rate of urolithiasis with higher PM_{10} exposure as MDT increased. The effects of decreased hydration status at higher maximum daily temperatures on stone formation appear to compound with the effects of poor air quality exposure (see Appendix A: Table S2).

Although we did not observe statistically significant relationships between same day, 1-day lagged, 2-day lagged, 3-day moving average, and 7-day moving average PM_{10} values and cardiovascular outcomes, we found that thresholding daily PM_{10} values provided enough signal to detect increased rates of stroke. We found that days with $PM_{10} \geq 50\ \mu g/m^3$ have > 2-fold increase in the mean rate of ED stroke diagnoses the following day compared to days with $PM_{10} < 50\ \mu g/m^3$ (RR=2.06; 95% CI: 1.12, 3.79) (Appendix A: Table S3). Interestingly, we did not observe any statistically significant relationships between pulmonary outcomes and air quality during the 5-year study period of January 1st, 2013 to December 31st, 2017. However, utilizing asthma exacerbation and climate data spanning January 1st, 2003 to December 31st, 2017 we observed a statistically significant increase in the rate of asthma exacerbations with increasing 1-day lagged, 3-day moving average, 7-day moving average, and 21-day moving average PM_{10}. Thus, a longer study period was needed to observe the effects of air quality on some pulmonary outcomes.

Limitations, Strengths, and Generalizability

As with all observational studies, these results should be evaluated alongside other similar bodies of work. Our estimates control for several factors, which is the standard approach in air pollution modeling. For example, PM_{10} effect estimates adjust for meteorological variables and time trends. Raw monitor data was used for this study with some days missing meteorological values and therefore were excluded from analysis. For the PM_{10} data, days where a measurement was available for only one monitor might over-represent that site; however, this is likely to be a negligible issue due to the high correlation between monitors (r=0.93). Beyond this, we assumed an equal exposure among the entire population of the SLV from centrally located monitors, which may not accurately reflect the entire SLV. Aside from anecdotal evidence, no data is available that would indicate behavioral change (ie, staying indoors) in response to days with extreme PM exposure. Occupational data was also not available for integration into our analysis. Events such as MI and stroke are rare in a general population and even sparser in the rural population we analyzed in this study, which may make it more difficult to estimate effects accurately in these disease subpopulations. Lastly, a small percentage of health data may have been coded in error where the data reflects a condition that was not the underlying cause of the ED visit – but is anticipated to be non-differential and any bias would reduce associations towards the null hypothesis.

The unique geographic location of this population makes this study a strong addition to the existing body of research on climate associated hazards and health outcomes. Rural populations are often overlooked when considering large environmental studies, which can result in most research focusing on densely populated urban areas. This study is generalizable to aging populations, perhaps with a higher burden of chronic disease, as well as an agriculturally employed workforce. The temperature associations reported in this study are also important because they reflect an idea of relative rather than absolute heat exposure and a population's acclimatization.

Implications and Next Steps

This study setting and population were chosen because it is rural with a high prevalence of climate-vulnerable people. However there were a small number of events over the study period; thus, limiting evaluation of individual diagnostic codes within major diagnoses. Previous work has suggested differing mechanisms for temperature and exacerbation of ischemic and hemorrhagic stroke; however, evaluating each diagnosis individually was not feasible given the sample size (n=95 and n=152 respectively) [50]. Similarly, evaluating individual sub-diagnoses of myocardial infarction was limited by sample size as previous research in highly population urban areas have done [51].

Elderly individuals and those in the agricultural industry are more vulnerable to climate effects because of a decreased ability to adapt to increased stressors as well as a higher level of exposure. Rural populations are additionally at increased risk of cardiovascular events such as MI and stroke because of the access to care (less intensive care, less cardiac catheterization capability, and higher cardiac cause-mortality) and transport distance to higher level care centers [52,53]. Due to this, the environmental factors that are associated with these outcomes are of even higher concern in this population. Despite the described limitations, we believe our findings still hold significant impact for the community as they face significant drought, rising ambient temperatures, and increased exposure to wildfire smoke on top of structural disparities.

Findings from this study provide evidence of the need for immediate and long-term medical care planning and environmental exposure mitigation for the future of rural health especially in the Western US.

CONCLUSION

Our study is one of the first to address relationships between several environmental variables and adverse health outcomes in a rural Colorado population. Analysis of the environmental exposures unique to this region, the downstream health outcomes they precipitate, and the strain placed on healthcare systems as a result is essential for a population that is uniquely vulnerable from both an environmental perspective as well as a health equity perspective. This body of work supports recommendations calling for education and preventative interventions to be tailored to this unique area to decrease morbidity and mortality from climate-related factors. Further studies need to elicit health trends from environmental variables not analyzed here such as radiant heat exposure, wind speed, and $PM_{2.5}$. Importantly, this study highlights the need for added research attention to under-studied and vulnerable rural populations and provides further impetus for resilience planning that addresses the unique environmental exposures and health outcomes experienced by these populations.

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Appendix A

Table S1. Relationship between number of emergency visits for urolithiasis and PM_{10}, modified by maximum daily temperature (MDT), expressed as ratio ratios (RR) with 95% confidence intervals.

PM_{10}*	Temp = -12.6		Temp = 8.2		Temp = 16.2		Temp = 24.2		Temp = 32.2	
	RR (95% CI)	p-value	RR (95% CI)	p-value	RR (95% CI)	p-value	RR (95% CI)	p-value	RR (95% CI)	p-value
0-Day Lag	1.01 (0.97, 1.05)	0.78	1.02 (0.98, 1.05)	0.37	1.02 (0.99, 1.06)	0.25	1.02 (0.99, 1.06)	0.17	1.03 (0.99, 1.07)	0.11
1-Day Lag	1.03 (0.99, 1.07)	0.13	1.04 (1.00, 1.07)	0.04	1.04 (1.00, 1.07)	0.02	1.04 (1.01, 1.07)	0.02	1.04 (1.01, 1.08)	0.02
2-Day Lag	1.01 (0.98, 1.05)	0.54	1.02 (0.99, 1.06)	0.16	1.03 (0.99, 1.06)	0.10	1.03 (1.00, 1.07)	0.06	1.04 (1.00, 1.08)	0.04
3-Day MA	1.05 (0.99, 1.12)	0.09	1.07 (1.01, 1.13)	0.02	1.08 (1.02, 1.14)	0.01	1.08 (1.02, 1.15)	0.01	1.09 (1.03, 1.16)	0.01
7-Day MA	1.07 (0.98, 1.17)	0.11	1.08 (0.99, 1.18)	0.08	1.08 (0.99, 1.18)	0.08	1.09 (0.99, 1.19)	0.08	1.09 (0.99, 1.20)	0.08

*Estimates shown in the table are for increases of 10 $\mu g/m^3$ in PM_{10}.
Note: From left to right, min, Q1, Q2, Q3, and maximum daily temperature over study period. RR (95% CI) estimated from multivariable Poisson models as described in Methods. p-values are reported to the second decimal place. MA = moving average.

Table S2. Relationship between number of emergency room visits and PM_{10} by disease classification.

Outcome	1-Day Lagged PM_{10}		1-Day Lagged MDT		Humidity		Precipitation	
	RR (95% CI)	p-value	RR (95% CI)	p-value	RR (95% CI)	p-value	RR (95% CI)	p-value
Asthma	1.01 (0.98, 1.04)	0.49	1.04 (0.96, 1.13)	0.35	1.02 (0.94, 1.11)	0.65	0.98 (0.95, 1.02)	0.34
COPD	1.00 (0.96, 1.03)	0.84	1.01 (0.93, 1.10)	0.76	1.04 (0.96, 1.13)	0.34	0.99 (0.96, 1.02)	0.57
CHF	1.02 (0.98, 1.06)	0.23	1.00 (0.90, 1.12)	0.99	1.04 (0.93, 1.16)	0.47	1.00 (0.96, 1.04)	0.93
MI	0.97 (0.90, 1.05)	0.45	0.99 (0.86, 1.14)	0.86	1.14 (0.99, 1.30)	0.06	0.93 (0.87, 1.00)	0.05
Stroke	1.04 (0.98, 1.09)	0.19	1.04 (0.86, 1.26)	0.68	1.07 (0.89, 1.29)	0.47	0.95 (0.87, 1.04)	0.27
Urolithiasis	1.03 (1.00, 1.07)	0.07	1.15 (1.04, 1.27)	0.01	1.03 (0.94, 1.13)	0.57	0.99 (0.95, 1.03)	0.71

Note: This table describes rate ratio (RR) for incidence of primary health outcomes. RR for PM_{10} are increases of 10 $\mu g/m^3$. RR for Max Daily Temperature (MDT) is considered at increases of 5°C. RR for humidity are increases of 10%. RR for precipitation are increases of 1 mm. RR (95% CI) estimated from multivariable Poisson models as described in Methods. p-values are reported to the second decimal place. COPD = Chronic Obstructive Pulmonary Disease; CHF = Congestive Heart Failure; MI = Myocardial Infarction.

Table S3. Relationship between number of emergency room visits and threshold based PM_{10} (≥ 50 vs. <50 $\mu g/m^3$).

Outcome	0-Day Lag		1-Day Lag		2-Day Lag		3-Day MA		7-Day MA	
	RR (95% CI)	p-value	RR (95% CI)	p-value	RR (95% CI)	p-value	RR (95% CI)	p-value	RR (95% CI)	p-value
Asthma	0.67 (0.43, 1.06)	0.08	0.92 (0.62, 1.37)	0.69	0.9 (0.6, 1.35)	0.62	1.03 (0.69, 1.54)	0.88	1.03 (0.65, 1.63)	0.91
COPD	0.78 (0.51, 1.18)	0.23	0.81 (0.54, 1.22)	0.32	1.28 (0.91, 1.8)	0.16	1.17 (0.8, 1.71)	0.41	1.17 (0.76, 1.8)	0.49
CHF	0.51 (0.25, 1.02)	0.06	0.84 (0.48, 1.49)	0.56	1.13 (0.69, 1.86)	0.63	1.01 (0.58, 1.74)	0.98	0.75 (0.37, 1.51)	0.42
MI	0.7 (0.31, 1.61)	0.40	0.72 (0.31, 1.65)	0.43	1.36 (0.72, 2.56)	0.34	0.91 (0.42, 2.01)	0.82	0.33 (0.08, 1.37)	0.13
Stroke	0.83 (0.34, 1.98)	0.67	2.06 (1.12, 3.79)	0.02	1.19 (0.56, 2.52)	0.64	1.7 (0.86, 3.37)	0.13	0.73 (0.25, 2.11)	0.56
Urolithiasis	0.93 (0.58, 1.5)	0.77	1.34 (0.89, 2.04)	0.17	1.15 (0.73, 1.81)	0.55	1.26 (0.8, 1.98)	0.32	1.42 (0.81, 2.46)	0.22

Note: Results are expressed as rate ratios (RR) with 95% confidence intervals. Various lag structures are considered for PM_{10}. RR (95% CI) estimated from multivariable Poisson models as described in Methods. p-values are reported to the second decimal place. COPD = Chronic Obstructive Pulmonary Disease; CHF = Congestive Heart Failure; MI = Myocardial Infarction.