2021

ENVIRONMENTAL RESPIRATORY EXPOSURES AND PULMONARY FUNCTION AMONG RESIDENTS OF RURAL APPALACHIA, KENTUCKY

John C. Flunker
University of Kentucky, johnflunker@uky.edu
Author ORCID Identifier:
https://orcid.org/0000-0003-0715-6254
Digital Object Identifier: https://doi.org/10.13023/etd.2021.142

STUDENT AGREEMENT:

I represent that my thesis or dissertation and abstract are my original work. Proper attribution has been given to all outside sources. I understand that I am solely responsible for obtaining any needed copyright permissions. I have obtained needed written permission statement(s) from the owner(s) of each third-party copyrighted matter to be included in my work, allowing electronic distribution (if such use is not permitted by the fair use doctrine) which will be submitted to UKnowledge as Additional File.

I hereby grant to The University of Kentucky and its agents the irrevocable, non-exclusive, and royalty-free license to archive and make accessible my work in whole or in part in all forms of media, now or hereafter known. I agree that the document mentioned above may be made available immediately for worldwide access unless an embargo applies.

I retain all other ownership rights to the copyright of my work. I also retain the right to use in future works (such as articles or books) all or part of my work. I understand that I am free to register the copyright to my work.

REVIEW, APPROVAL AND ACCEPTANCE

The document mentioned above has been reviewed and accepted by the student's advisor, on behalf of the advisory committee, and by the Director of Graduate Studies (DGS), on behalf of the program; we verify that this is the final, approved version of the student's thesis including all changes required by the advisory committee. The undersigned agree to abide by the statements above.

John C. Flunker, Student

Dr. Wayne Sanderson, Major Professor

Dr. Heather Bush, Director of Graduate Studies

ENVIRONMENTAL RESPIRATORY EXPOSURES AND PULMONARY FUNCTION AMONG RESIDENTS OF RURAL APPALACHIA, KENTUCKY

DISSERTATION

A dissertation submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy in the College of Public Health at the University of Kentucky

By
John C. Flunker
Lexington, Kentucky
Director: Dr. Wayne Sanderson Professor of Biosystems Engineering
Lexington, Kentucky
2021

https://orcid.org/0000-0003-0715-6254

ABSTRACT OF DISSERTATION

ENVIRONMENTAL RESPIRATORY EXPOSURES AND PULMONARY FUNCTION AMONG RESIDENTS OF RURAL APPALACHIA, KENTUCKY

Introduction

Resource extraction exposures are hypothesized to promote adverse respiratory health outcomes among residents of rural Appalachia, yet no studies to date have simultaneously quantified small-scale geographic variation in residential exposure, individual level health factors, and respiratory health outcomes.

Methods

The Mountain Air Project (MAP) is a community engaged cross-sectional study based in Harlan and Letcher counties of Southeastern Kentucky. MAP utilized a novel small-scale method to define residential exposure boundaries: hydrologic unit code (HUC), which represents distinct drainages (AKA "hollows") where residents cluster. We assigned the HUC level density of active and abandoned surface and underground mining, oil/gas wells, coal haul routes, and roadways to each participant. Over a two-year duration, 972 participants with geo-coded addresses and quantified HUC level exposure density were administered a health and exposure survey and a spirometry test by community health workers. In addition, 71 homes received a four-day in-home assessment of gravimetric PM2.5 concentration. Particle sampling with direct reading instruments, measuring particle concentrations from 10-10,000 nanometers (#/cc), was conducted among a convenience sample of roadside locations and participant driveways. Multivariable regression models with robust standard errors were used to validate HUC level exposure and to examine the adjusted associations between HUC level exposures, in-home PM2.5, and pulmonary function.

Results

On average, participants were middle-aged (average = 52.9 years of age), female (59%), under-educated (56% ≤ high school education), and above healthy weight (44% obese), with a high prevalence of smoking (33% current smokers; average of 16.1 pack years) and abnormal pulmonary function (42%). HUC exposure validation models demonstrated that for every one-unit increase in HUC roadway density, the adjusted concentration of particles <100 nm in diameter increased by 0.10 log particles/cc (95% CI: 0.03, 0.16) and particles 100-300 nm in diameter increased by 0.09 log particles/cc (95% CI: 0.01, 0.17). Participants living in HUCs with the highest tertile of roadway density experienced a 4.3% reduction in adjusted FEV_1 percent predicted values (95% CI: -7.44, -1.15) and a 3.8% reduction in adjusted FVC percent predicted values (95% CI: -6.38, -1.21), relative to participants living in the lowest tertile of HUC roadway density. No significant adjusted associations with particle number concentrations or pulmonary function were found among the remaining HUC level environmental exposures. In-home log PM2.5 concentrations were associated with a 24% increase in the adjusted prevalence of abnormal pulmonary function (Prevalence ratio=1.24, 95% CI:1.01-1.51).

Conclusion

Our results suggest roadway and in-home exposures may contribute to adverse respiratory health outcomes among residents of rural Appalachia. Future longitudinal research is needed to further define and quantify HUC level residential environmental exposures and exposure-outcome temporality.

Keywords
Environmental exposure, Appalachia, Pulmonary function, Resource extraction, Particulates

John Flunker
(Name of Student)

05/07/2021
Date

ENVIRONMENTAL RESPIRATORY EXPOSURES AND PULMONARY FUNCTION AMONG RESIDENTS OF RURAL APPALACHIA, KENTUCKY

By
JOHN C. FLUNKER

Wayne Sanderson, PhD
Director of Dissertation

Heather Bush, PhD
Director of Graduate Studies

05/07/2021
Date

ACKNOWLEDGMENTS

The following dissertation, while an individual work, benefited from the insights and direction of several people. First, my Dissertation Chair, Dr. Wayne Sanderson, has provided numerous years of mentorship, support, and insightful guidance into a practical and applied approach to environmental and occupational epidemiology research. In addition, I am grateful for Dr. Steven Browning, who provided mentorship, discussion, and support for creative approaches to exposure assessment and environmental epidemiology. I would also like to thank Dr. David Mannino, whose continual encouragement, timely feedback, and expertise in respiratory health has been essential to this project and many others. With additional gratitude, I thank Dr. Phillip Westgate for his guidance with statistical analyses. I also thank Dr. Michael Sama for his time as an outside examiner. Finally, I thank the participants, field staff, and fellow researchers of the Mountain Air Project for their dedication to our research and for their friendship. I am truly grateful to have the opportunity to continue to collaborate with a diverse and knowledgeable group of colleagues and mentors.

In addition to the technical and instrumental assistance above, I received equally important assistance from family and friends. All provided on-going support throughout the dissertation process, as well as the technical assistance needed for completing the final revisions of the project. I would especially like to thank my parents, Ray and Barb Flunker, my brother, Joe Flunker, in addition to my partner, Kiera Kuepfer, each demonstrating bottomless love, continual curiosity, and limitless enthusiasm for my research endeavors. Thank you as well to James and Joan Schiele for being a constant source of inspiration and for their excellent friendship.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

CHAPTER 1. INTRODUCTION

RURAL APPALACHIAN ENVIRONMENTAL EXPOSURES AND RESPIRATORY HEALTH: SUMMARY OF CURRENT LITERATURE

Past work demonstrates a distinct health disparity between residents of rural and non-rural Appalachia with respect to respiratory disease. Rural Appalachia residents experience a high prevalence of asthma and chronic obstructive pulmonary disease (COPD) in addition to chronic respiratory disease mortality when compared to the general United states population (Dwyer-Lindgren et al., 2017; Hendryx et al, 2015, 2013). The persistent high regional prevalence of smoking, obesity, and low socioeconomic status (Carderelli et al. 2021; Mills et al., 2020; Michimi et al., 2010; Shaw et al., 2004), in addition to poor health outcomes such as heart disease and stroke mortality (Barnette et al., 2000; Halverson et al., 2002) contribute to this disparity. Hegewald and Crapo (2007) reviewed fourteen studies that examine the relationship between socioeconomic status (SES) and pulmonary function, finding an adverse impact of low socioeconomic status on pulmonary function among both adults and children. As $25,000 represents the approximate median household income for the region in 2015 (United States Census Bureau, 2017), low SES may be a contributing factor adverse respiratory health outcomes. Nonetheless, the exact contributing factors to the high regional prevalence of respiratory disease have not been identified to date.

Rural Appalachia is a region with a unique set of environmental exposures that are responsible for particle emissions, including surface and underground mining, oil and gas wells, as well as roadways. For example, past research suggests a link between surface mining and particulate levels in coal extraction regions of rural Appalachia with generally higher levels of particulates in areas with active surface mining, such as course, fine, and ultrafine particulates (Kurth et al., 2015; Kurth et al., 2014; Aneja et al., 2012), as well as higher levels of satellite measured atmospheric particulate matter (Aneja et al., 2017) originating from coal haul operations and rock blasting, respectively. Toxic metals related to coal extraction have also been found in samples taken from mountaintop-removal (MTR) regions (Aneja et al., 2012). Roadway particulates, originating from internal combustion engines, are generally found to be <100 nm (Morawska 2008; Zhang et al., 2004), and are likely associated with the numerous roadways that cover the valleys of rural Appalachia.

Residential exposures from resource extraction activities have long been suspected as contributing factors to regional respiratory disease, with ecological study designs showing an adverse association between residing in mountain top removal regions and respiratory health. For example, Hendryx et al., 2013, 2015, found a higher prevalence of asthma and COPD in mountain top removal mining areas than non-mining areas. This may be due in part to higher levels of particles in regions near mountaintop removal, as links between high levels of course and fine particulates in regions of high mining activity have been noted by ecological studies (Kurth et al., 2015; Kurth et al., 2014; Aneja et al., 2017). Concurrent respiratory exposures from oil and gas wells may also exist (Macey et al., 2014). Despite an association found at the ecological level, a systematic review by Boyes et al (2017) found no conclusive evidence for a clear link between mountain top removal and adverse health effects among local residents due to potential exposure misclassification bias and uncontrolled confounding.

A novel method to define small-scale geographic variation in particle exposures among residents of rural mountainous regions of Appalachia is to delineate distinct boundaries around valleys via the 12-digit Hydrological Unit code (HUC). HUC is classification system, publicly available from the United States Geological Survey (USGS), that creates a series of adjacent watersheds, framing valleys that represent distinct watersheds. As such, the HUC may delineate distinct regions of local exposure with valley walls limiting particle movement. Hypothesized common sources of particles in rural Appalachia include roadways, surface coal mines, underground coal mines, and oil wells. Geocoding of HUC boundaries mixed with publicly available data sets detailing mining permits, oil and gas wells, and roadways allow the estimation of the density of these particle sources per square mile of HUC area. One especially reliable metric for particle exposure at the HUC level is that of roadways density per HUC (roadways miles per HUC square miles), as this exposure source does not tend to vary a dramatically in average intensity and location over time, as opposed to coal mining and oil/gas extraction that vary over a short duration, sometimes only months, in location and intensity of particulate output.

In-home exposures may also influence the regionally high prevalence of poor lung health in rural Appalachia. U.S. citizens spend approximately 87%-90% of their day indoors, with 69% of the day inside a residence, on average (Richardson et al., 2005; Klepeis et al., 2001, EPA 1989). Exposure to particles less than or equal to 2.5 micrometers (μm) in diameter ($PM_{2.5}$) from both outdoor and indoor sources may adversely impact respiratory health (Xing et al., 2016). Particulate levels are especially concentrated indoors (Pope, 2000), often at higher levels than outdoors (EPA, 1987, Chen and Zhao, 2011). Among residents of rural Appalachia, regional rates of smoking suggest environmental tobacco smoke exposure may be a highly prevalent indoor particulate exposure source (Carderelli 2021). Furthermore, among residents of Appalachia, cooking indoors with wood or coal was found to increase the odds of reporting current asthma (Barry et al., 2010). No work to date has examined the impact of in-home particulate exposures on respiratory health among residents of rural Appalachian KY.

In this dissertation, I seek to examine environmental factors, both outdoors and indoors, encountered by residents of rural Appalachia and to explore the relationship between these exposures and pulmonary function. In an effort to identify potential contributing factors to adverse respiratory health outcomes, this research also may help inform interventions to reduce the regional burden of respiratory disease

CHAPTER 2. ROADWAY DENSITY AS AN EXPOSURE METRIC FOR VEHICLE-DERIVED ULTRAFINE PARTICULATES AMONG HYDROLOGIC UNIT CODES ("HOLLOWS") IN RURAL APPALACHIA

ABSTRACT

Background

Rural Appalachia roadways and resource extraction activities may promote regional particulate concentrations and subsequent residential exposures.

Objective

We examined the relationship between commonly encountered environmental residential exposure sources hypothesized to be related to particle emissions in rural Appalachia. Hydrologic unit code (HUC) was used as a small scale metric of exposure area to examine the association between environmental residential exposure metrics and particulate concentrations in two rural Appalachia Kentucky counties.

Methods

Particle concentration (number per cm^3), vehicle density (combustion vehicles/minute), and weather, were measured at 103 randomly selected roadside and driveway sites within 29 HUCs. Multivariable regression was used to model HUC environmental characteristics, namely roadway density, coal haul route density, oil/gas well density, and active surface or underground mining area versus particulate number concentration in the size distributions of <100 nanometers (nm), 100-300 nm, and >300 nm. Multivariable regression models were adjusted for weather, sample location, and sample season.

Results

HUC roadway density predicted roadside/driveway ultrafine particulate concentrations, as well as vehicle density. Adjusted multiple regression models demonstrated that for every one-unit increase in HUC roadway density, particles <100 nm in diameter increased by 0.095 log particles/cc (95% CI: 0.03, 0.16) and by 0.09 log particles/cc (95% CI: 0.01, 0.17) for particles 100-300 nm in diameter, with no association among particles >300 nm. Coal haul route density, underground and surface mining density, and oil/gas well density had no significant associations with particle number concentrations.

Conclusions

HUC roadway density may serve as a proxy exposure metric for vehicle derived ultrafine particulates. Particle measurements did not show an increase in ultrafine concentrations at locations with a high density of mining and oil/gas well operations, suggesting the need for additional exposure quantification.

2.1. INTRODUCTION

Vehicle exhaust, a ubiquitous source of ultra-fine particulates, has been linked to decreased lung function among urban residents who live in close proximity to roadways (McCreanor et al, 2007, Rice et al., 2015). Limited on the ground exposure assessment of roadways and particulate levels has been conducted in rural regions, yet generally lower levels of particulates have been found in rural versus urban regions of the United States on average (Pratt et al., 2018; Morawska et al., 2008). However, in Helsinki Finland rural regions were found to have higher levels of ultrafine particles than urban (Pakkanen et al, 2001). This finding may be due to true differences in particle levels, differences in particle identities in urban versus rural regions, or may represent variation in activity patterns during sampling.

Vehicle exhaust particles are a heterogenous mix of toxic compounds comprised of carbon, sulfur, zinc, phosphorus, and calcium, originating from both fuel combustion and lubricant oils; and are, on average, in the ultrafine particle diameter range (<100 nm). Specifically, many studies to date have mapped the particle size distribution and movement of particles as they disperse from roadway sources, demonstrating the main size distribution of vehicle exhaust is 20–130 nm for diesel engines and 20–60 nm for gasoline engines, with minimal correlation to course particulates (Karjalainen et al., 2014; Zhang et al., 2004; Ristovski et al., 1998; Morawska et al., 2008; Booker 1997). Furthermore, vehicle density, driving conditions, and the spatial distributions of roadways and the vehicles traveling on roadways impact the quantity and distribution of exhaust exposures (Karjalainen et al., 2014; Kozowa, et al., 1994; 2012). For example, Morawska et al. (1999) demonstrated that roadway particles concentrations may be indistinguishable from background levels approximately 200 meters from major roadways in Brisbane Australia. Zou and Levy (2007) concluded a dispersion of 100-300 nm for ultrafine particles from a roadway source. Furthermore, meteorological conditions, such as temperature and humidity may also impact the nucleation and coagulation propensity of small diameter particles, and thus the measured size distribution, of roadway related particulates (Kittelson et al., 2001; Zhu et al., 2002), while wind speed and wind direction may also impact particle concentration (Martins et al., 2010).

Rural Appalachia is a region with a distinct set of environmental exposures that are likely responsible for particle emissions, including surface and underground mining, oil and gas wells, as well as roadways. For example, past research suggests a link between surface mining and particulate levels in coal extraction regions of rural Appalachia, with generally higher levels of particulates in areas with active surface mining (Kurth et al., 2015; Kurth et al., 2014; Aneja et al., 2012), as well as higher levels of satellite measured atmospheric particulate matter (Aneja et al., 2017) originating from coal haul operations and rock blasting. Toxic metals related to coal extraction have also been found in samples taken from mountaintop-removal (MTR) regions (Aneja et al., 2012). Roadway particulates, originating from internal combustion engines, are generally found to be <100 nm (Morawska 2008; Zhang et al., 2004), and are likely associated with the numerous roadways that cover the valleys of rural Appalachia. Thus, each environmental exposure may likely contribute a unique size distribution and type of particles to the air found in close proximity to such emission sources.

Variation in the physical structure of the exposure environment may influence particle concentrations. For example, the most commonly employed metric for estimating traffic related exposures is residence distance via a straight line to a major roadway (Carleson et a., 2015; Kan et al., 2007); however, such a metric may not be applicable to rural settings, especially those that are mountainous. Although flat rural regions may yield roadway particulate dispersion patterns that follow a straight line away from roadways, the tight and precipitous valleys of rural Appalachia, known as “hollows”, may force exhaust particles to remain within small, local areas, promoting significant geographic variation in residential exposures to particulate levels within and between hollows. Therefore, to minimize exposure misclassification, an alternative method that more closely matches particle distributions may help to more accurately define exposure levels.

A novel method to define small-scale geographic variation in particle exposures among residents of rural mountainous regions of Appalachia is to define distinct boundaries around valleys via the 12-digit Hydrological Unit code (HUC). HUC is a classification system, publicly available from the United States Geological Survey (USGS), that creates a series of adjacent watersheds, framing valleys that represent distinct watersheds. As such, the HUC may delineate distinct regions of local exposure with valley walls limiting particle movement. Hypothesized common sources of particles in rural Appalachia include roadways, surface coal mines, underground coal mines, and oil wells. Geocoding of HUC boundaries mixed with publicly available data sets detailing mining permits, oil and gas wells, and roadways allow the estimation of the density of these particle sources per square mile of HUC area. One especially reliable metric for particle exposure at the HUC level is that of roadways density per HUC (roadways miles per HUC square miles), as this exposure source does not tend to vary a dramatically in intensity and location over time, as opposed to coal mining and oil/gas extraction that vary over a short duration, sometimes only months, in location and intensity of particulate output.

In order to determine if HUC roadway density is a viable exposure estimation metric the association between this geographic area metric and physical on the ground particle measurements was conducted. No studies to date address roadway related particulate exposure among residents of rural Appalachia on a small geographic scale.

Thus, we examine the validity of this method of exposure classification that estimates potential vehicle related exposures among residents of rural Appalachia. We also examine the association between common resource extraction exposure sources found in rural Appalachia and particulate concentrations, such as HUC coal haul route density, oil/gas well density, and active surface and underground mining.

2.2. METHODS

This study is a sub-study within the broader Mountain Air Project (MAP) as described in May et al. (2020). Briefly, MAP is a community engaged cross sectional research study examining the impact of environmental exposures on respiratory health among residents of rural Appalachia in Eastern Kentucky. Harlan and Letcher counties, KY were subdivided into distinct Hydrological Unit Codes (HUC) and all homes within randomly selected HUCs were enumerated. MAP participants were recruited from every third enumerated home within a selected HUC. Participants were English speaking adults residing in the enumerated home for a minimum of three years. Participants with pre-existing respiratory disease were preferentially enrolled. One primary resident living in the home was administered a respiratory health and exposure survey, as well as a pulmonary function test by a trained interviewer. A total of 972 participants were sampled over a two-year duration.

This work was funded by the Community-Engaged Research and Action to Reduce Respiratory Disease in Appalachia study through Grant 5R01ES024771 from the National Institute for Environmental Health Sciences (NIEHS).

Hydrologic Unit Code as a respiratory exposure density metric

We defined our exposure region based on the 14-digit HUCs, corresponding to distinct narrow valleys for each of the counties. These 14-digit HUCs are the smallest hydrologic units defined by the United States Geological Survey (USGS) and coincide with residential development patterns and roadways sitting in the base of narrow valleys. Geographic Information Systems (GIS) data for these HUCs, such as roadways density (roadway miles per HUC square miles), coal haulage route density (coal haulage miles per HUC square miles), oil and gas well density (number of wells per HUC square miles), active surface mining density (mine area in square miles per HUC square miles), active underground mining density (mine area in square miles per HUC square miles), were obtained from the Kentucky Geological Survey. HUC boundary polygons were imported into ArcGIS 10.3 (ESRI; Redlands, CA) and HUCs were characterized by their relationship to boundary layers including active coal mining sites from the Kentucky Mine Mapping Information System; point locations of active oil and gas wells from the Kentucky Geologic Survey; roads officially designated as 'coal haul routes' from the Kentucky Transportation Cabinet (KTC), and all streets and roads, also from the KTC. All data sets were the most recent available as of July 2015, immediately prior to participant recruitment for the Mountain Air Project. Oil and gas well density were combined into one variable due to few oil wells in the region (86% of selected HUCs had no oil wells and among those that did, 10% had one well and 5% had two wells). Due to a large percentage of the sampled HUCs lacking surface mine or underground mine activity (63% and 67%, respectively), this variable was collapsed into a dichotomous variable representing presence or absence of each type of mining activity. For this study, we calculated the road miles per square mile for each HUC in the study area using the streets and roads map layer. These exposures were chosen as they are the dominant environmental respiratory exposure sources in region and are of concern to residents. Figure 1 displays the study area counties and the distribution of roadway mile densities per HUC.

Particle sampling

Particles ranging in diameter from 10-10,000 nanometers (nm) were measured by the TSI (Minneapolis MN) Nanoscan and Optical particle sizer. Samples were recorded as the particle number concentration (total particles per cm^3 (cc)). Particle distributions were measured based on factory pre-set bins varying in particle diameter ranges. These bins were summed into larger size distribution groups for analysis to represent likely particle distributions per environmental sources. Particles were grouped into three particle size distributions for analysis: <100 nm in diameter, 100-300 nm, and >300-10,000 nm. The three particle size distribution groupings were selected to capture potential variation in particulate size among the measured environmental exposures. Each device was calibrated by TSI following a yearly established calibration schedule.

Samples were collected over a two-year duration (2016 and 2017) on weekdays from a selection of roadside locations and participant homes in the MAP study. Three samples were collected in HUCs contiguous to selected HUCs. Samples were collected within 2-3 meters of roadways and in the driveways of study participants. Sampling occurred in the absence of nearby idling vehicles or engines and only passing cars were counted. Sampling devices were placed in the roof of the study investigator's vehicle (~2 meters above the ground) prior to sampling and remained on top of the vehicle until sampling was complete. No sampling was conducted until the research vehicle's engine had been turned off for approximately 10 minutes. Care was also taken to collect samples in areas free of extraneous, temporary sources of particulates, such as roadway construction or roadway painting operations. Sampling was conducted on generally warm days (50 to 90 degrees Fahrenheit) without precipitation and with minimal to no wind. Vehicle density (total number of vehicles/total sampling duration in minutes) was recorded during particle sampling by counting every vehicle that passed the sampling location in either direction of travel. Roadside or driveway sampling location was also recorded.

All sampling locations were measured at one time point with the exception of 7 locations for which 2-3 samples were taken over the course of the study. At sampling locations with repeat samples over time the arithmetic average of particle concentration was used in analyses. Analyses with and without these repeated measurement sites were conducted and similar results were found. The researcher had no awareness of HUC roadway density, coal haul density, oil/gas well density, or the presence/absence of surface and underground mining in sampled HUCs. Figure 1 details the location of roadway and driveway sample sites throughout the two study counties among varying levels of HUC roadway density.

To account for the impact of weather on particle concentrations temperature, relative humidity, and wind speed were taken from the nearest weather station reporting all values: the Tucker Guthrie memorial airport and the KY US airport in Harlan KY (36.859°, -83.358°). This data was retrieved from the National Centers for Environmental Information (https://www.ncdc.noaa.gov/cdo-web/confirmation). Sampling time was matched with data recorded at the weather station on a 15 minute cycle. Distance from sampling points to the airport weather station was generally within 20 miles, with a maximum of 40 miles. Sampling month was also recorded to control for seasonal variation in factors that may impact particulate concentrations, such as human activity, plant pollen production, or additional weather conditions not captured by the weather station data. These months were later condensed to four seasons, each three months in duration (i.e. Winter, Spring, Summer, Fall).

Statistical analyses

Differences in particle size distribution among potential confounders were examined via univariate statistics (t-test and Analysis of variance), with follow up pairwise tests. A base adjustment model was applied to all multivariable statistical models in order to adjusted for conditions during sampling (temperature, relative humidity, and wind speed), sample location (driveway or roadside), and sample season (Winter, Spring, Summer, Fall). These adjustments help to control for potential variation in particle levels, irrespective of environmental exposure sources, as well as variation in resource extraction activity by season. Furthermore, as distance from roadway edge differed between roadside and driveway samples location of sampling (i.e. ‘roadside’ or ‘driveway’) was included in all models to account for differences in particle concentrations due to physical location and distance from source and thus variation in concentration of particles due to distance alone.

Multivariable regression models were constructed to examine the HUC level particle number concentration related to the five environmental exposures of interest: roadway density (1), coal haul route density (2), oil/gas well density (3), the area of surface mining (4), and the area of underground mining (5), particulate levels in the three size groups yielding 15 total models. Each exposure was evaluated in a separate adjusted model.

All statistical analyses were conducted with R studio version 1.2.5001 (Boston, MA).

2.3. RESULTS

General sampling descriptive statistics

A total of 103 independent samples were collected at roadside and driveway locations in 29 HUCs distributed throughout Harlan and Letcher counties, KY. Sampling occurred over a wide range of HUC environmental exposure densities (Table 1). This sampling effort provided environmental particulate measurements for 73% (29/40) of the total HUCs selected for inclusion in the Mountain Air Project. The majority of the measurements were taken in participant driveways (67%), while the remainder were taken on roadsides (Table 2). The majority of roadside samples were obtained next to county roads and Kentucky state highways, with few very few samples obtained from city streets, U.S. highways, private, pending, and "other" roads. A total of 39 sampled HUCs had active surface mining permits, while 35 HUCs had active underground mining permits.

Particle sampling was conducted primarily from April through July (60% of samples), with 80% of samples collected from April through October. 14% of samples were collected in The months of December, January, or February (Winter) accounted for 14% of the total samples, while 37% were collected in the months of March, April, and

May, (Spring), 28% were collected in June, July, and August (Summer), and the remaining 21% were collected in September, October, or November (Fall). Table 3.

Particulate concentration differed among seasons and sample location. Via ANOVA with post-hoc Tukey tests, winter was found to be significantly lower in log particle concentration than spring, summer, and fall for 100-300 nm and >300 nm size ranges. There were no differences between seasons at the <100 nm size (Table 3). .Spring, Summer and fall did not significantly differ in particle concertation. A significant difference was found between driveway and roadside samples at <100 nm, with driveway samples roughly 32% lower in concentration than those from a roadside. No other differences existed between roadside and driveway samples at 100-300 and >300 nm. Table 2.

On average, a large proportion of particle sampled (98%) fell into the range of ≤300 nm in diameter with 58% of the total particulates measured ≤100 nm. Among all 103 samples, the average particle concentration of particles <100 nm was 1,675 particles/cc (min=588, max=7,646, std. dev.=1,253), 1,184 particles/cc for particles from 100-300 nm (min=138, max=5,357, std. dev.=882), and 50 particles/cc for particles >300 nm (min=6, max=277, std. dev.=42). Particle concentrations were found to be non-normally distributed and were thus log transformed for multivariable regression analyses.

Multivariable regression models examining three weather components: Temperature, relative humidity, and wind speed versus log transformed particle concentrations demonstrate weather conditions impacted particle concentrations. These models did not contain environmental exposures of interest. Specifically, wind speed, relative humidity, and temperature lowering particle concentrations in the <100 size range, while temperature increased particle concentrations and wind speed and relative humidity lowered the concentration of particles 100-300 nm. At the >300 nm size range wind speed decreased particle concentration while temperature and relative humidity increased particle concentration. Table 4.

Environmental exposure versus particulates

Multivariable linear regression models, adjusting for meteorological conditions while sampling (temperature, relative humidity, and wind speed), sample season (fall, winter, spring, fall), and sample location (roadside or driveway), showed a significant positive association between increasing roadway density and log transformed ultrafine particulate concentrations at both the <100 nm and 100-300 nm size ranges. Specifically, for every one-unit increase in HUC roadway density, particles with a diameter <100 nm increased by 0.095 log particles/cc (95% CI: 0.029, 0.162, P=0.006) and particles 100-300 nm in diameter increased by 0.09 log particles per cc (95% CI: 0.005, 0.17, P=0.041). Among particles in the 300-10,000 nm size range we found no significant association with HUC roadway density, suggesting the major contributors to this exposure metric may be vehicle exhaust particulates in the ≤300 nm range. Figure 2; Figure 3; Table 5.

Results from our vehicle density counts during sampling show a positive association between increasing HUC roadway density and increasing number of vehicles per minute on sampled roadways such that for every one unit increase in roadway density there was a 1.2 unit increase in vehicle density (95% CI = 0.8, 1.5; R^2= 0.27, P<0.0001) via unadjusted univariate regression as well as an multivariable model adjusted for sample season (Beta=1.2, 95% CI = 0.8, 1.5; R^2= 0.27, P<0.0001). Table 5.

We found no significant associations between coal haul route density, nor the presence/absence of active surface or underground mining and particulate concentrations at the HUC level. We found a non-significant, yet positive association between oil/gas well density and the log concentrations of particles <100 nm, such that for every one-unit increase in oil/gas well density we found a 0.027 log particle increase (95% CI = -0.013, 0.067; P=0.019). Figure 2 and table 5.

2.4. CONCLUSION

Our study validates HUC roadway density as a novel method for estimating airborne respiratory particulate concentrations and assigning exposure levels in rural mountainous Appalachia. By using small-scale spatial data based on hydrologic data from the USGS we found that HUC roadway density has a strong positive associated with ultrafine particle concentrations, both <100 nm and 100-300 nm size distributions. This size range has been reported to be associated with diesel and unleaded gasoline exhaust (Morawska 2008; Zhang et al., 2004; Kittelson, 1998). Furthermore, we found a significant relationship between both increasing HUC roadway density and vehicle density, as well as a positive association between vehicle density and ultrafine particles. When condensed, the above findings suggest the primary particulates association with HUC roadway density are likely due to vehicles with combustion engines and that ultrafine particulate levels within an HUC may fluctuate due to both roadway density and the number of vehicles commonly found traveling on such roadways. Thus, roadway density per HUC is likely a valid vehicle derived particulate exposure proxy useful for modeling particulate exposure in small geographic areas of rural mountainous Appalachia where on the ground measurements are not feasible. Although traditionally high levels of roadway related particulates have been associated with urban regions, our study demonstrates that in rural regions, specifically rural HUCs, the concentrations of roadway particulates may also be high.

Our models may allow for the extrapolation of particulate concentrations in HUCs that have not physically been visited for particle measurements. For example, based on our regression equation one can estimate expected levels of particulates in relation to HUC roadway density. This approach provides a smaller scale estimate of exposure than zip code or county level EPA PM2.5 data, likely reducing exposure misclassification found in larger ecological study designs. Thus, our method of HUC level exposure classification, may help to limit exposure misclassification, especially in the case of roadway respiratory exposures, by using a small-scale unit of area, representing the tight precipitous "hollows" of Eastern Kentucky, and rural Appalachia as a whole. This method of HUC level exposure estimation may also be applicable to other mountainous regions where roadways and residential areas are often in close proximity at the base of deep valleys.

Environmental exposure sources and subsequent exposure may be highly variable within a county such that county level exposure classification may ignore variability, thereby washing out any exposure estimate variability. For example, Kioumourtzoglou et al. (2014) found a weak correlation between PM 2.5 levels measured by personal exposure monitors versus EPA county level exposure, suggesting personal activity patterns and scale of measurement may impact exposure estimates. Furthermore, as micro-climate variation and topology between valleys may change the movement of particles, HUC level measurements may help to control for microclimate variations and subsequent effects on particulate levels among HUCs. In addition, residents do not have the same activity patterns, nor do they live the same distance from the exposure source, so an HUC level exposure classification approach may help to control for such variability in functional exposure. This may be especially true for roadway based particulate exposures as traffic density may vary between roads and time of day. Thus, establishing a method of exposure classification on a small geographic scale is crucial to estimate exposure accurately, as well as to correctly examine associations with health outcomes, such as respiratory disease.

Counter to past studies that detected heightened levels of particulates in MTR regions (Kurth et al., 2014; Aneja et al., 2012), we did not find a similar positive association. A number of plausible explanations for this difference exist. The above mentioned studies have relied either on larger-scale exposure classification methods than that of the HUC, such as satellite imagery and ecological levels of exposure boundary, or measurements directly at surface mining sites, yet none have taken measurements in residential areas. Spatial heterogeneity in particulate levels may impact the accuracy of assigned exposure levels, depending on the scale at which the exposure boundary is applied. For example, larger scale boundaries may overestimate the level of particulates in a region, ignoring small scale heterogeneity, while finer scale measurements obtained directly at the exposure source may be limited in generalizability to larger areas. Thus, our scale of exposure differs from past studies and may account for small-scale geographic variation in residential exposure.

Heterogeneity in the temporality of extraction activities within a region may also contribute to a lack of agreement between past studies and our results. For example, due to the constantly changing nature of mining permits and production of coal-based resources, a wide range of spatiotemporal fluctuations in particle emissions may occur within a time period and geographic region. Coal mining activity has steadily been declining in rural Appalachia and it may be possible that despite active mining permits in the HUCs we measured, active extraction may not have been occurring at the time we measured particles. As such, future research should examine variation in temporal patterns of extraction activity, via repeated measures, activity to more precisely define exposure

Oil and gas extraction related exposures among residents of rural Appalachia are of particular concern given the recent shift from coal to natural gas among resource extraction companies and global markets. Although we found a positive association between oil and gas well density with particles <100 nm, this association was not statistically significant. Past studies have found an association between the presence of oil and gas wells and heightened levels of volatile organic compounds (Macey et al, 2014) as well as heightened hazardous air pollutants, as defined by the U.S. Environmental Protection Agency, in regions with ongoing oil/gas extraction (Garcia-Gonzales et al., 2019). Future studies may seek to elucidate the exposures from oil and gas extraction in Appalachia with respect to sampling over a greater range in oil and gas well density, temporal fluctuations in activity and particle concentrations, as well as examining the identity of emitted particles.

Strengths and limitations

This is the first study in rural Appalachia to examine on-the-ground associations between a method of exposure classification to account for small-scale variation in exposure and particle number concentration. This study validates HUC roadway density as a valid metric of particle exposures, especially among particles ≤100 nm. Despite the strengths and novel nature of the HUC approach to classifying roadway exposure our methods do have limitations. We did not sample equally among each level of roadway density, thus a few of our HUCS with only one measure of particulates and car density may be prone to misclassification error. We also used convenience sampling on roadways used for frequent travel in each HUC and in areas close to where many study participants resided. Although this is a strength in exposure assessment, as we measured particulate exposure in populated areas, it is also possible that we may have not sampled as great of a variety of HUCs. Although, we did not see a statistically significant difference in roadway density per driveway versus roadside samples, differences in particle types and sources may exist between the two, yet this seems unlikely since the majority of our sampled particulates fell within the size range known to be associated with vehicle exhaust. Furthermore, our estimate of mining activity and oil/gas extraction has limitations, as we have little information on the exact details of when mining activity, specifically coal extraction and blasting occurs. Finally, although we included active mining permits at the start of the study to define the presence of exposure, whether active mining occurred during that permit period and while we were conducting particle sampling is unknown.

Summary

Our study employed a novel small-scale estimate of geographic variation in exposure sources encountered in rural Appalachia, linking HUC level environmental exposures with distinct particle number concentrations ranging from 10-10,000 nm, finding a strong positive relationship between HUC roadway density and ultra-fine particles. This work represents the first step in quantifying roadway and resource extraction related respiratory exposures and sets the stage for beginning to disentangle the complex web of exposures and factors influencing the respiratory health of rural Appalachia residents.

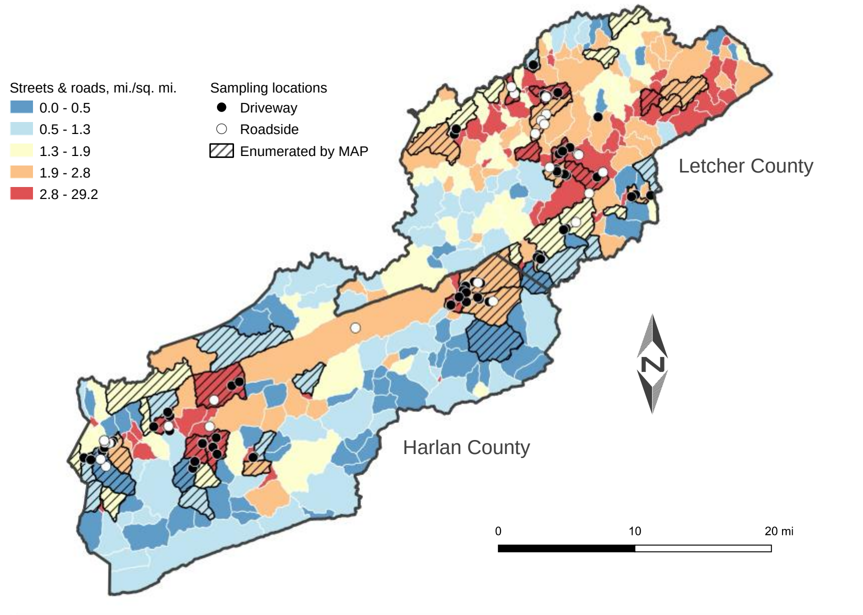
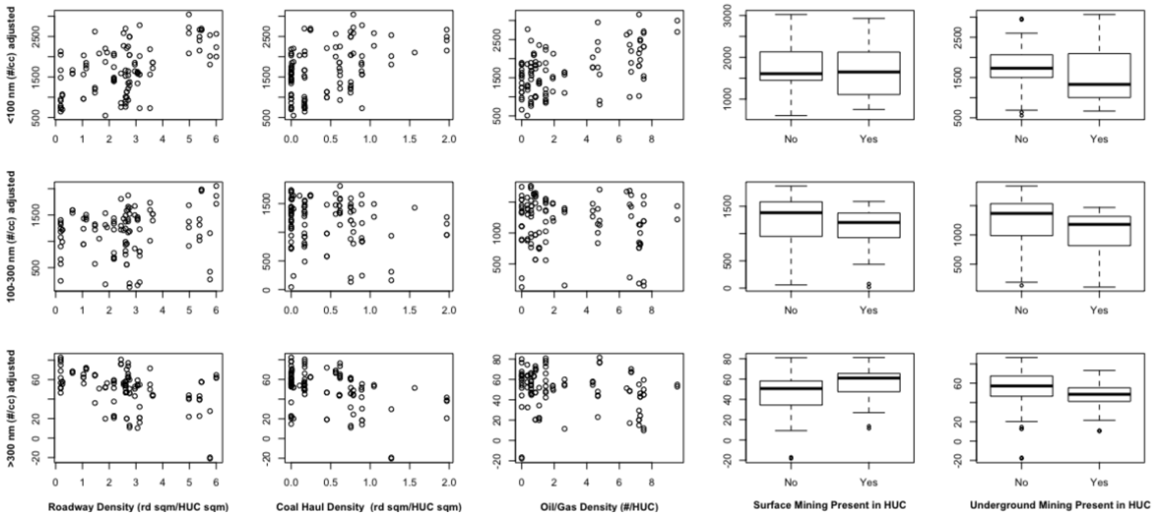


Figure 2.1. MAP study area denoting HUC roadway density levels, selected HUCs, and particle sampling locations

Figure 2.2. Scatter plots and box plots demonstrating adjusted* associations between environmental exposure sources and non-log transformed particle concentrations



*Adjusted for weather, location, and season during sampling

Figure 2.3. Adjusted particle concentration for particles <100 nm versus roadway density

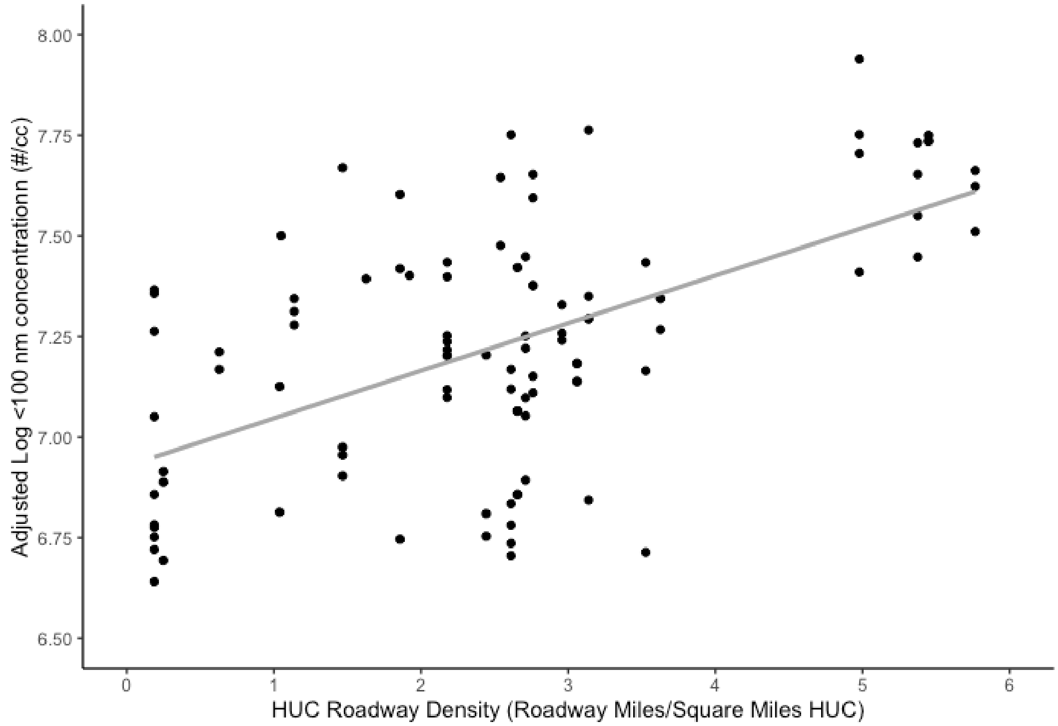


Table 2.1. HUC exposure metric details

HUC metric (Exposure/HUC mile^2)	Mean (std. dev)	Min	Max
Roadway density*	2.62 (1.59)	0.19	6.00
Oil/gas well density$^+$	1.61 (2.28)	0.00	8.44
Surface mine density^	0.29 (0.90)	0.00	0.30
Underground mine density^	0.03 (0.80)	0.00	0.31
Coal Haul route density*	0.44 (0.49)	0.00	1.97
Vehicle density$^\#$	2.22 (3.60)	0.00	20.00

*Road miles per HUC mile^2; +Number of oil and gas wells per HUC mile^2; ^ Mining surface area mile^2 per HUC mile^2
Number of vehicles per minute on roadway

Table 2.2. Sample location versus particle concentrations (non-transformed)

Location		<100 nm (#/cc)	100-300 nm (#/cc)	>300 nm (#/cc)
Driveway N=69	Mean (Std. dev)	1468.70* (954.54)	1229.90 (1011.33)	51.58 (46.91)
	Range	588.37 - 6261.76	137.59 - 5356.72	6.06 - 276.75
	Geometric Mean	1269.35	899.68	34.93
Roadside N=34	Mean (Std. dev)	2124.87* (1659.01)	1063.18 (539.16)	44.37 (27.03)
	Range	587.66 - 7646.43	460.86 - 2237.09	9.91 - 127.28
	Geometric Mean	1689.06	940.89	36.54

Table 2.2. Seasonal factors versus particle concentrations (non-transformed)

Season		<100 nm (#/cc)	100-300 nm (#/cc)	>300 nm (#/cc)
Winter	Mean (Std. Dev.)	1344.19 (303.78)	469.86 (128.26)	13.22 (2.91)
N = 15	Range	957.67-1868.06	181.95-618.13	9.18-18.17
	Geometric Mean (GSD)	1313.18	446.56	12.92
Spring	Mean (Std. Dev.)	2112.54 (1651.56)	1330.97 (657.39)	52.64 (34.87)
N = 37	Range	616.12-7646.43	460.86-2907.61	9.91-127.82
	Geometric Mean GSD)	1674.13	1163.78	41.39
Summer	Mean (Std Dev)	1462.12 (1181.53)	1119.87 (564.92)	49.07 (21.98)
N = 29	Range	587.66-6261.76	137.59-2117.45	6.06—86.19
	Geometric Mean (GSD)	1197.41	927.72	41.92
Fall	Mean (Std. Dev.)	1493.53 (794.72)	1465.50 (1459.75)	68.13 (65.38)
N = 22	Range	636.20-2981.91	196.15-5356.72	7.18-276.75
	Geometric Mean (GSD)	1307.67	968.26	43.62

Table 2.3. Log transformed particle concentrations (number of particles per cubic centimeter) regressed on weather factors.

	Log <100 nm (#/cc) ß adj. (95% CI)	Log 100-300 nm (#/cc) ß adj. (95% CI)	Log >300-10,000 nm (#/cc) ß adj. (95% CI)
Temperature	-0.009* (-0.016, -0.001)	0.018* (0.010, 0.026)	0.031* (0.022, 0.040)
Relative Humidity	-0.003 (-0.011, 0.004)	-0.004 (-0.013, 0.004)	0.004 (-0.006, 0.014)
Wind Speed	-0.047* (-0.086, -0.009))	-0.059* (-0.103, -0.015)	-0.002 (-0.051, 0.047)
Adjusted R^2	0.02	0.10	0.11
Observations per model	103	103	103

*P<0.05

Note: each column is a separate model containing the listed covariates

Table 2.4. HUC Exposures and particle association models: Adjusted Airborne Particle Concentrations (Particle Diameter Size Groups) by One-Unit Change in HUC Exposure Variables

	Log <100 nm (#/cc) ß (95% CI) Adj. R2	Log 100-300 nm (#/cc) ß (95% CI) Adj. R2	Log >300-10,000 nm (#/cc) ß (95% CI) Adj. R2
Roadway Density	0.095** (0.029, 0.162) 0.23	0.09* (0.005, 0.17) 0.29	-0.02 (-0.11, 0.08) 0.30
Coal Haul Density	0.133 (-0.118, 0.384) 0.18	0.14 (-0.17, 0.44) 0.27	-0.06 (-0.40, 0.28) 0.30
Oil/gas Well Density	0.027 (-0.013, 0.067) 0.19	-0.003 (-0.05, 0.04) 0.26	-0.01 (-0.06, 0.05) 0.30
Active Surface Mining (Present)	-0.229 (-0.482, 0.023) 0.20	-0.20 (-0.50, 0.11) 0.27	-0.02 (-0.36, 0.33) 0.30
Active Underground Mining (Present)	0.022 (-0.247, 0.203) 0.17	-0.26 (-0.53, 0.001) 0.29	-0.31* (-0.60, -0.01) 0.33
Vehicle Density+	0.019 (-0.013, 0.050) 0.18	0.054** (0.017, 0.091) 0.32	0.040 (-0.002, 0.082) 0.32
Observations per model	103	103	103

Note: ** P<0.001, *p<0.05, ^p<0.1; Each ß value, 95% CI, and adjusted R2 (Adj. R2) represents a separate model adjusted for weather, season, and sample location; +Vehicle density model adjusted for weather, season, and sample location. Number of observations are the same within each particle diameter size grouping (i.e. N=103

CHAPTER 3. ENVIRONMENTAL EXPOSURES AND PULMONARY FUNCTION AMONG RESIDENTS OF RURAL APPALACHIA, KENTUCKY

ABSTRACT

Background

Environmental resource extraction exposures are hypothesized to be associated with reduced respiratory health among residents of rural Appalachia, yet a conclusive link has remained unclear.

Methods

As part of the community based cross-sectional study, the Mountain Air Project, we examined the association between the density of active and abandoned surface and underground mining, oil/gas wells, coal haul routes, and roadways versus pulmonary function among residents of two southeastern Kentucky counties. We utilized a novel small-scale method of exposure classification, hydrologic unit code (HUC), representing exposure boundaries of mountainous valleys (AKA “hollows”) to define levels of exposure. Homes were randomly selected from enumerated hollows and participants were administered questionnaires about health and respiratory exposures as well as pulmonary function tests over a two-year duration.

Results

On average, participants were 52.9 years of age (21.1 - 96.8 range; 15.5 std dev), 59% female, 56% had a high school education or less, 33% were current smokers with a mean of 16 pack years, and 44% were obese. Pulmonary function was poor, with 42% abnormal tests (872 interpretable tests with 183 (21%) restricted and 187 (21%)

obstructed spirometry). While the range of HUC mining and oil/gas well density was limited among sampled HUCs, roadways were common and varying in density among all HUCs. Via multivariable regression models with robust standard errors, adjusted for individual level health covariates, occupational mining exposure, and in-home exposures, we found those participants living in HUCs with the highest level of roadway density experienced a significant 4.3% (-7.44, -1.15 95% CI) reduction in FEV_1 percent predicted and a 3.8% (-6.38, -1.21: 95% CI) reduction in FVC percent predicted, relative to the lowest level of HUC roadway density. We also found that living in a higher coal haul density HUC was marginally associated with a 2.05 % (95% CI: -4.59, 0.49) reduction in FVC % predicted, relative to those living in the lowest density HUCs (P=0.12). No clear associations between past/present surface mining, past/present underground mining, or oil/gas well density and pulmonary function were detected.

Significance

Rural Appalachian roadways, transmitting passenger and heavy vehicles, represent a ubiquitous yet overlooked residential respiratory exposure that may contribute to the high prevalence of respiratory disease among residents of rural mountainous Appalachia. Additional research is needed to examine spatial and temporal variation over time in roadway and resource extraction exposures and associations with pulmonary function.

3.1. INTRODUCTION

Rural Appalachia residents experience a high prevalence of asthma and chronic obstructive pulmonary disease (COPD) in addition to chronic respiratory disease mortality when compared to the general United states population (Dwyer-Lindgren et al., 2017). This burden of disease may be especially pronounced in mining regions of rural Appalachia (Hendryx et al, 2015, 2013). The persistent high regional prevalence of smoking, obesity, and low socioeconomic status (Carderelli et al. 2021; Mills et al., 2020; Michimi et al., 2010; Shaw et al., 2004) may contribute to the observed prevalence of respiratory disease, yet the exact contributing factors have not been identified to date.

Residential exposures from resource extraction activities have long been suspected as contributing factors to the regional respiratory disease, with ecological study designs showing an adverse association between residing in mountain top removal regions and respiratory health. For example, Hendryx et al. (2013, 2015) found a higher prevalence of asthma and COPD in mountaintop removal mining areas than non-mining areas. This may be due in part to higher levels of particles in regions near mountaintop removal, as links between high levels of course and fine particulates in regions of high mining activity have been noted by ecological studies (Kurth et al., 2015; Kurth et al., 2014; Aneja et al., 2017). Concurrent respiratory exposures from oil and gas wells may also exist (Macey et al., 2014). However, Flunker et al. (Dissertation Chapter 2) found no association between mining activity (active surface or underground) or oil and gas well density versus outdoor particle number count concentrations, both in the ultrafine and fine particle size distribution ranges, when exposures were evaluated at a small geographic scale within resource extraction regions. Furthermore, despite an association found at the ecological level, a systematic review by Boyes et al (2017) found no conclusive evidence for a clear link between mountain top removal and adverse health effects among local residents due to potential exposure misclassification bias and uncontrolled confounding.

Roadways may be perceived as a ubiquitous and mundane source of particulate emissions, yet the close proximity of many homes to roadways in rural Appalachia may promote residential exposure to vehicle combustion engine derived particulates. For example, ultrafine particles are associated with high levels of roadway density in Southeastern KY Appalachian valleys (Flunker et al., Dissertation Chapter 2), suggesting roadway density may be a viable proxy of vehicle related particle exposures in the region. Indeed, particulates originating from internal combustion engines, are generally found to be ultrafine size range (Morawska 2008; Zhang et al., 2004) and may be inhaled by residents living close to roadways, especially busy roadways.

Although an adverse association between roadways and reduced pulmonary function has been noted in urban areas among adults and children (Rice et al., 2015; Kan et al., 2007, Carleson et al., 2015; Rice et al., 2015; Balmes et al., 2009; Kan et al., 2007; Heinrich et al., 2005), such an example is missing for rural regions, and in particular rural Appalachia. The high regional rates of respiratory disease in Appalachia and often close proximity between roadways and residential areas, suggest residents may have heightened risk for exposure and adverse health impacts. This may be especially true among those with respiratory disease, as asthmatics may be pre-disposed to a reduction in lung function following roadway related exposures (McCreanor et al, 2007; Penttinen et al., 2001).

Straight line distance from residences to roadways with various car densities has been a common exposure classification method employed by past studies (Carleson et a., 2015; Kan et al., 2007), and most, if not all, have been conducted in urban settings (Lipfert et al., 2008). However, such a method may not be the best approach in rural settings with precipitous valleys that may prevent roadway particles from moving in a straight line to nearby residences. As the scale of exposure must relate to the activity patterns of residents and the scale of exposure classification must match the variability of the exposure itself, smaller-scale more individualized approaches to assigning exposure levels than ecological studies that use zip code or county level metrics to apply exposure may better capture geographic heterogeneity in exposure.

Here we apply a small-scale geographic unit of exposure classification, HUC density, that is particularly germane to the type of geographic variation in residential Appalachian environmental exposures, to explore associations between common environmental exposures and pulmonary function among residents of two rural Appalachia Kentucky counties.

3.2. METHODS

Hydrologic unit code method of exposure classification

We examined the relationship between the density of commonly encountered environmental exposures, namely roadways, active surface and underground mining, abandoned surface and underground mining, and oil/gas wells versus pulmonary function among residents living in two rural counties in Eastern Kentucky. Exposures were classified on a small geographic scale via the land use regression metric: 14-digit hydrologic unit code (HUC), which is a set of adjacent USGS designated geographic polygons that roughly outline portions of watersheds. These polygon outlines roughly follow the ridge-lines of Eastern Kentucky and frame the deep valleys that residents primarily live within. These geographic units make the HUC a reasonable boundary circumscribing the density of environmental exposures within small scale geographic regions. The valley walls likely buffer wind and restrict air flow of airborne particulates. Mining exposure was classified based on the boundaries of active underground and surface coal mining sites, as well as inactive underground and surface coal mining sites obtained from the Kentucky Mine Mapping Information Systems. Roadway related exposures were obtained from the Kentucky Transportation Cabinet, which included all streets, roads, and those roads defined as coal haul routes. The point locations of active oil and gas wells were obtained from the Kentucky Geologic Survey. All data sets were based on the most recently available information as of July 2015, just prior to the study's start date. To estimate the level of environmental exposure for each participant living in a given HUC, we used the proportion of the HUC area covered by the exposure (square miles exposure per square miles in HUC) to estimate exposure density. This method was applied to all examined exposures, aside from oil/gas well density that was classified based on the number of oil/gas wells per HUC square mile. Our metric of classifying exposures has not been used previously, yet likely approximates respiratory particulate exposure, especially for roadways, as exemplified by a significant association between increasing roadway density per HUC and ultra-fine particle concentrations (Flunker et al., Dissertation Chapter 2).

Participant selection

Methods are described in detail elsewhere (Carderelli et al., 2021; May et al., 2019), but briefly, selected HUCs for study inclusion were randomly selected from all Harlan and Letcher county HUCS with a random number generator. Each HUC was given a three level score (low, medium, or high) that was a summary of all environmental exposures present. In selected HUCS all homes were enumerated on foot and every third home was approached for study inclusion for a total of at least 10 homes per HUC. Acceptance rate of inclusion in study was 82% with written informed consent obtained. Participants with existing lung disease were preferentially enrolled, with a maximum of two adult participants per household selected. Adults with pre-existing lung disease were preferentially enrolled to increase statistical power, as these cases may otherwise be missed with random sampling. We sampled adult male and female participants, obtaining 872 reliable spirometry results, one test per participant, that were combined with survey and land use exposure metrics to include in our statistical models. The study was approved by the University of Kentucky Institutional Review board. and was conducted between the months of November 2015 and August 2017.

Questionnaire description

Participants were administered a detailed environmental exposure questionnaire regarding in-home respiratory exposures, individual level risk factors for disease such as smoking, exercise, BMI, comorbidities, occupation, as well as a suite of additional health conditions. Questionnaires were administered by trained community health workers at the same time participants were also given a pulmonary function test.

Pulmonary function

An Easy One® spirometer was used by trained community health interviewers to administer pulmonary function tests to all participants. Training was provided to community health workers by DM. One pulmonary function test was given to each participant and no post-test bronchodilators were used, as a physician could not be present for each test and clinic access was not feasible. Tests with three reliable spirograms were considered ‘interpretable’. Pulmonary function tests were interpreted and graded for quality by a board-certified physician pulmonologist (DM). Percent predicted values of forced expiratory volume in 1 second (FEV_1) and forced vital capacity (FVC) were determined following the methods of Hankinson et al (1999) which calculates percent predicted values based on age, height, race, and gender. Only pulmonary function tests graded as ‘interpretable’ were included in analyses.

Multiple imputation of in-home PM2.5 levels

A convenience subsample of participants were selected for a detailed four-day in-home air quality assessment. The details of this sub-study are described elsewhere (Flunker et al., Dissertation Chapter 4). Briefly, in-home gravimetric PM2.5 was measured over a four-day period, with 70 samples obtained over the two year study duration. In-home tests spaced evenly throughout the two-year duration or the MAP study. We used the PM2.5 concentrations in micrograms per cubic meter ($\mu g/m^3$) from the 70 homes to estimate in-home PM2.5 for all study participants. This 70-home data set was used to impute PM2.5 values for the remainder of the study population who did not receive in-home air quality assessments (902 homes) based on six questions in the overall 972 MAP survey. These questions showed a high level of association with measured in home PM2.5 values in the 70 homes examined or are known to be positively associated with in-home particulate levels. The imputation regression equation used to predict PM2.5 in non-measured homes was as follows:

Imputed PM2.5 $\mu g/m^3$ *= water incursion past year (y/n) + mold damage past year (y/n) + dogs/cats in home (y/n) + pest problem in past year (y/n) + current smoker in home (y/n) + burn candles (y/n).*

Specifically, to impute estimated PM2.5 fully conditional specification (FCS) multiple imputation was conducted via SAS Proc MI FCS with 40 burn in iterations, 93 imputations, and no maximum or minimum values set. The average of the 93 imputed values were assigned to each participant, yielding a complete data set with PM2.5 values for all 972 participants. The imputation process yielded an average imputed value of in-home PM2.5= 38.3 $\mu g/m^3$, a standard deviation of 29.09, a minimum of 1.4, and a maximum of 280.9. These imputed values closely matched the mean, minimum/maximum values, and to a lesser degree, the standard deviation of the actual measurements in the original source N=70 in-home data set (Mean=35.6 $\mu g/m^3$, Standard deviation =55.48, minimum=1.6, maximum=280.9).

Covariates

Covariates were grouped into three categories to control for factors that may impact pulmonary function and potentially confound evaluation of the association with levels of environmental exposures. These include individual level health factors (smoking status/pack years, education, body mass index (BMI), physical activity in the last month), occupational exposures such as work in mines (any mining employment, current or past), and in-home exposures (hours at home per day, years in current home, and in-home PM2.5 imputed). Pack years per participant were calculated by dividing the number of cigarettes smoked per day by 20 and multiplying that by the number of years smoked for both current and former smokers. Those who had smoked less than 100 cigarettes in their lifetime were classified as non-smokers and given a pack year score of 0. BMIs were calculated as the ratio of weight in kilograms to height in centimeter squared and were then categorized as: normal/underweight BMI (<25.0), overweight BMI (≥25.0 -

29.9), and obese BMI (≥30.0). The small number of participants (n=18) who were in the underweight BMI category were grouped with the normal BMI category to ensure adequate group size for analysis. Education level was determined as the highest level obtained by the participant and categorized <high school, high school graduate, or >high school.

Statistical analyses

Univariate t-tests and analysis of variance tests were conducted followed by post-hoc Tukey multiple comparison tests to examine univariate associations between environmental exposures, personal and demographic characteristics, and pulmonary function, namely percent predicted FEV_1 and FVC as continuous outcome variables. A base adjustment model was selected to be applied to all multivariable models. Univariate analyses on confounders that were statistically significant with the outcome variables, percent predicted FEV_1 and FVC, as well as known or suspected confounders were included in the base adjustment model. The selected base model for adjustment controlled for personal health indicators, occupational mining exposures, and in-home exposures that all may co-vary with environmental exposures and are known to be associated with pulmonary function. This base model was then applied to each environmental exposure model as a standard set of adjustments.

Multivariable linear regression with robust standard errors was used to examine the association between HUC level exposures and pulmonary function. Seven HUC level exposures, each evaluated in a separate model to avoid multicollinearity, were examined as predictors of FEV_1 and FVC percent predicted. The HUC level environmental exposures of interest included: roadway density, coal haul route density, oil/gas well density, active surface mining, active underground mining, inactive surface mining, and inactive underground mining density; yielding a total of 14 adjusted models.

All analyses were conducted with R studio version 1.2.5001 (2021).

3.3. RESULTS

Participant characteristics

On average, participants were 52.9 years of age (standard deviation=15.5; range=21.1 - 96.8), 59% were female, 25% has less than a high school education, 31% had a high school education, and 44% with greater than a high school education. Obesity was fairly prevalent among participants with 44% categorized as having an 'obese' BMI. Among participants, 33% were current smokers, 24% were former smokers, 43% were never smokers, with an average pack-years smoking of 16.1 (standard deviation=24.5; range=0 – 276 range). Regarding respiratory health, 20% (n=195) of participants self-reported a medical diagnosis of asthma, 21% (128) reported a medical diagnosis of COPD, and 9.6% (n=84) reported a medical diagnosis of black lung. Participants were generally sedentary, spending on average 19.7 (standard deviation=3.9; range=8.0-24.0) hours at home per day, only about half (54%) had exercised in the last month. Average duration of years in the current home was 17 years (standard deviation=15.5; range=1-94). The use of gas, coal or wood for indoor heating or cooking was infrequent, with 4% (n=32) reporting a gas furnace in the home, 6% (n=51) reporting a wood furnace, 4% (n=37) reporting a coal stove, and 8% (n=71) reporting a wood burning stove in the home. Occupational mining exposures were present, as 18% were current or past surface miners, while 21% were current or past underground miners, with an average mining employment duration of 22.3 years (standard deviation=13.1; 1.5 – 60.0 range;) regardless of mining type.

HUC exposure classification

All participants living in selected HUCs experienced some form of environmental exposure, with roadways representing the exposure with the greatest amount of variability (Mean =2.69 road miles per HUC square miles, standard deviation=1.44, range=0.19-6.0). Active resource extraction exposures were much more minimal in variation, with a mean of 0.015 square miles per HUC square miles (standard deviation=0.05 range: 0-0.30) for active surface mining and a mean of 0.05 square miles per HUC square miles (standard deviation=0.11, range =0-0.48) for active underground mining. Only 21% of participants lived in HUCs with active surface mining and 39% lived in HUCs with active underground mining. The mean density of abandoned surface mining was 0.04 square miles per HUC square miles (standard deviation=0.07, range=0.00-0.43) and the mean density of abandoned underground mines was 0.37 square miles per HUC square miles (standard deviation=0.40, range=0.00-1.53). Past mining was much more prevalent than current mining, as 61% of participants lived in HUCs with past surface mining and 93% lived in HUCs with past underground mining. Few selected HUCs lacked current and/or past mining activity, with only 7% of participants residing in HUCs lacking any type of current or past mining activity. Coal haul route density was variable in density among HUCs, with a mean of 0.34 road miles per HUC square miles (standard deviation=0.36, range=0-1.27). Oil/gas well density was variable in exposure density among selected HUCs, with a mean of 1.62 wells per square mile HUC area (standard deviation=2.29, range=0-8.44). Oil wells were frequent among selected HUCs

(68% of participants exposed), while gas wells were generally absent (5% of participants exposed).

Pulmonary function

A total of 972 pulmonary function tests were administered to study participants. Only tests graded as interpretable by the study physician pulmonologist (DM), resulting in 872 tests included in analyses. Abnormal pulmonary function was prevalent in the population (42%), among which 183 tests (20.9%) were classified as restricted and 187 tests (21.4%) of tests were classified as obstructed. The average percent predicted FEV_1 value was 83.2% (15%-151% range) while the average percent predicted FVC value was 86.1% (19%-150% range).

Univariate associations

Significant associations were found between pulmonary function and age, pack-years, smoking status, education, BMI, physical activity, underground mining employment, hours at home, years in the current residence, and imputed in-home PM2.5 levels. Specifically, pulmonary function declined with increasing age, increasing pack-year tertile, former or current smoking status (relative to never smokers), lower levels of educational attainment (≤ high school versus >high school), higher levels of BMI (reduced FVC with higher levels of BMI), reduced level of physical activity (relative to lower), a lack of underground mining employment, increased hours at home (relative to less), increased years at home (relative to less), and exposure to imputed in-home PM2.5 levels above the EPA action level (versus below the EPA action level). Gender, surface mining employment, any mining employment, and years of mining employment (tertile coding) were not significantly associated with measures of pulmonary function. Table 1**.**

All unadjusted univariate associations between environmental exposures and pulmonary function, aside from roadway density, showed minimal change in pulmonary function with increasing density of exposure at the HUC level. With each increasing tertile of roadway density percent predicted FEV_1 decreased (85%, 83%, and 81%, respectively) and FVC decreased (88%, 87%, and 84%, respectively). Coal haul route density also showed a marginal 1% decline in FEV_1 and a 2% decline in FVC, when comparing the highest tertile to the lowest. The remainder of environmental exposures were generally equal between levels in percent predicted FEV_1 and FVC. In some cases, such as active underground mining and abandoned underground/surface mining, FEV_1 and FVC slightly increased when comparing the lowest tertile to the highest, yet this was not statistically significant. Table 2.

Multivariable modeling - environmental exposures and pulmonary function

Modeling strategy

To minimize confounding in the modeled relationship between exposures of interest and pulmonary function, a base model was constructed and applied to each model. This base model adjusted for pack years (tertile), BMI categories, physical activity in the last month (yes /no), any mining employment current or past (yes/no), hours at home per day (median cut), in-home imputed PM2.5 (EPA action level cut point). Continuous and categorical model covariate forms of base model covariates were examined to best model the exposure-outcome of interest. Ultimately, categorical coding of the above covariates was included in the base model for ease of interpretation and to maximize model fit. In all cases, the model AIC value was not different by more than a few points for the continuous versus categorical coding of each covariate. Continuous versus categorical coding was also evaluated for each environmental exposures of interest, with no significant difference between either coding option versus pulmonary function outcomes. Active underground and surface mining were assessed as ‘any activity (>0 square miles/HUC square miles)’ or ‘no activity’ (>0 square miles/HUC square miles) due to a large number of selected HUCs without active underground or surface mining, and thus limited variation in exposure, preventing tertile coding.

Multivariable model results

Results from adjusted multivariable linear regression models demonstrate a statistically significant reduction in pulmonary function with increasing HUC roadway density quartiles. Specifically, those participants living in HUCs with a high level of roadway density have a 4.3% (-7.44, -1.15 95% CI) reduction in FEV_1 percent predicted and a 3.8% (-6.38, -1.21: 95% CI) in FVC when compared to the lowest quartile of roadway density (Tables 2 and 3). A reduction in pulmonary function was also found when comparing the lowest level of roadway density to the middle tertile, such that those participants in the middle tertile level had a 2.330 % (-5.224, 0.563) reduction in FEV_1 percent predicted and a 1.0 % (-3.645, 1.496) reduction in FVC percent predicted, yet neither were statistically significant. These results suggest a dose-response relationship may exist between increasing roadway density levels of exposure and decreasing pulmonary function among study participants. We found no statistically significant adverse association between surface or underground mining activity, nor oil/gas well density, and pulmonary function, after adjusting for potential confounders. Coal haul density per HUC showed an adverse impact on FVC percent predicted, such that relative to the lowest tertile, participants living in the HUCs with highest density of coal haul routes had a 2.050 % (95% CI: -4.593, 0.492) reduction in FVC percent predicted, although this was not statistically significant (P=0.12), while coal haul route density had no perceivable impact on FEV_1 percent predicted. All model variance inflation factor values were below 1.7 with residuals normally distributed and no significant outliers. Table 3.

Sensitivity analyses

Continuous and categorical forms of environmental exposures of interest were examined to evaluate how functional form may impact outcome measures of FEV_1 and FVC, significance, and R^2 values. We found no significant difference in results when comparing continuous to categorical forms in adjusted models. For example, when roadway density was examined as a continuous form, and adjusted for the base model, for every one-unit increase in roadway density there was a 0.91% (95% CI: -1.81, -0.008; P=0.04; Adjusted R^2=0.14) decrease in percent predicted FEV_1 and a 1.2% (95% CI: -1.74, -0.30; P= 0.008; Adjusted R^2=0.09) decrease in percent predicted FVC.

To investigate how those with pre-existing respiratory disease, namely those with asthma, COPD, and/or black lung, impacted our modeled associations between environmental exposures and pulmonary function, we repeated the above multivariable analyses with robust standard errors on only those participants lacking pre-existing lung disease (N=494). We found little change from this exclusion, as living in an HUC with highest tertile of HUC roadway density was associated with a 4.4 % (95% CI: -7.8, -1.0) decline in FEV_1 percent predicted and a 4.0% 95% CI: -7.2, -0.9) decrease in FVC percent predicted, relative to participants in the lowest tertile of HUC roadway density. However, for HUC coal haul density, removal of those with pre-existing respiratory disease strengthened the association between exposure and outcome, such that relative to the lowest HUC coal haul route density tertile, those participants in the highest density tertile experienced a 3.4% (95% CI: -6.7, -0.2) reduction in FEV_1 percent predicted and -4.0% (95% CI: -6.9, -1.0) reduction in FVC percent predicted. No other environmental exposures showed any change in significance, magnitude, or direction of the relationship between exposure and pulmonary function.

3.4. CONCLUSION

We examined the association between common environmental respiratory exposures and pulmonary function encountered by residents of rural Appalachia, finding a significant adverse relationship between higher levels of HUC roadway density and a reduction in pulmonary function (FEV_1 and FVC percent predicted). Although an adverse association between roadways and residential respiratory health has been documented in urban environments (Carleson et al., 2015; Rice et al., 2015; Kan et al., 2007; Heinrich et al., 2005; Venn et al., 2005), as well as in occupational settings (Hart et al., 2012), this is the first study to show a similar relationship in a rural setting, particularly among residents of rural Appalachia.

Previous exposure assessment in rural Appalachia Kentucky suggests nanoparticles emitted from vehicles may be a significant component of roadway exposures experienced by residents. For example, Flunker et al. (Dissertation Chapter 2) found the particle number concentration of ultrafine particles <100 nanometers were higher in those hollows with a greater HUC roadway density, while increasing car density was also significantly associated with increasing HUC roadway density. Ultrafine vehicle exhaust particles exposures are associated with increased daily mortality among exposed

German residents (Stolzel et al., 2007). Residents with pre-existing respiratory conditions, such as asthma or COPD, may be especially vulnerable to effects from vehicle exhaust exposure (Nitschke et al., 2016; Penttinen et al 2001). Thus, a plausible link between vehicle emissions related to roadways and respiratory health may exist among residents of rural Appalachia. Future work examining vehicle density on roadways, vehicle composition, as well as exhaust particle constituents may help to further elucidate the relationship between roadways and adverse health among residents.

Counter to past ecological studies that found an adverse association between mining regions and respiratory health outcomes among nearby residents, such as asthma and COPD (Hendrix 2014, 2015), we did not find that current or historic mining activity were associated with a reduction in pulmonary function. Resource extraction activity and exposures vary frequently in time and space, making the quantification and measurement of outcomes difficult, thus it is possible that current mining permit areas were not actively being mined during our study period. However, our study also included estimates of past mining activity per HUC, yet an adverse association was not detected between historic mining and pulmonary function. Finally, coal mining activity may be declining in the region and previously higher levels of residential exposure may no longer be present.

Contrasting results between our study and those previously conducted may also be due to study design. The majority of past studies are ecological designs, relying on regional measures of exposure classification and thereby applying the same level of exposure to large geographic areas with likely underlying variation in exposure. Indeed, Boyes et al (2017) found no conclusive evidence for a clear link between mountain top removal and adverse health effects among local residents due to potential exposure misclassification bias and uncontrolled confounding. Measurement of individual level health factors may reduce such confounding. For example, socioeconomic status, has been demonstrated to co-vary with environmental exposures (Evans et al 2002), while higher BMI has been linked to roadway related exposures (Li et al., 2016). Such covariance between exposure and indicators of personal health may be especially prevalent in rural mountainous Appalachia where undesirable or inexpensive land and housing near to coal mines or along valley floors near busy roads may place residents in higher exposure areas than those with higher socioeconomic status.

Our results suggest high levels of HUC coal haul route density may also reduce pulmonary function. We found a marginally significant decrease in FVC percent predicted among participants living in the highest coal haul route density HUCs, relative to those in the lowest. Furthermore, this relationship was intensified when those with asthma, COPD, and black lung were removed for multivariable analyses, suggesting this group may attenuate the modeled exposure-response relationship, perhaps via differing behaviors from those without respiratory disease, such as the avoidance of perceived environmental respiratory exposures or asthma triggers. However, these results should be interpreted with caution, as coal haul routes are also major roadways, and separating the effect of coal trucks from that of residential vehicles is not possible in our analyses. As such, our measure of roadway density may reflect coal haul exposure while our measure of coal haul density may also be linked to overall roadway density. Furthermore, we do not know what exhaust constituents or coal particulates may drive the adverse association between coal haul route density and pulmonary function. Future research to quantify the intensity and duration of such coal haul route exposures, as well as the identity of associated particles, is crucial to better understand the nature and health effects of this exposure.

The link between respiratory exposure sources and health effects must be based respirable particle exposures. Thus, for the case of environmental resource extraction, higher levels of respirable particulates or differing particle identities must be detected in mining regions. To date, the evidence for such a link is somewhat mixed regarding Appalachian mining exposures due to variation in distance from exposure source and method of quantification. For example, Kurth et al (2015) found a high concentration of crustal elements in mountain top mining samples obtained directly at mining sites. Furthermore, Aneja et al (2017) found higher levels of atmospheric PM2.5 in mining regions of Appalachia and hypothesized this may be due to coal transportation. Conversely, Flunker et al (Dissertation Chapter 2) found no significant association between current mining activity and particle number concentrations among samples collected in residential locations of Kentucky coal mining counties. Measurements taken during verified active periods of mining and at a distance from emission sources that matches residential activity patterns are needed to elucidate the true nature of this exposure.

We found no association between oil and gas well density and pulmonary function. However, this may not be surprising since these wells are often on private land and in remote regions with limited population density that were not sampled by researchers. Nonetheless, it is possible that volatile organic compound levels may be high near oil/gas and wells (Macey et al., 2014), resulting in potential respiratory exposures among those living in areas with a higher density of oil and gas wells. Future work examining particulate emissions from oil and gas wells, specifically variability in the type of particles and their concentrations may prove beneficial in characterizing the nature and concentration of exposures.

Our work represents a unique method of quantifying and classifying small scale geographic variation in environmental exposures. Such a method may be especially beneficial in mountainous regions where variation between valleys in terms of exposure a residential density patterns may be highly variable, making county level or zip code level methods of applying exposure level prone to misclassification, especially in the case of particulate exposures that may follow mountain valleys, settling in the deepest areas. This may be especially true for roadway density, as smog build up in mountainous valleys has long been a concerning phenomenon for respiratory health. Furthermore, for the case of roadway exposure classification in mountainous regions, especially rural Appalachia, distance to roadway may not be appropriate as an exposure classification metric, as steep mountains and valleys may separate residences from roadways, making roadway density per valley or hollow, likely less prone to exposure misclassification.

Strengths and limitations

Our study has numerous strengths. Specifically, we are the first study to examine small-scale geographic variation in environmental exposures versus pulmonary function measures among residents of rural Appalachia. Our level of exposure classification represents a functional geographic classification of exposure such that an HUC represents the tight valley, or hollow, in which residents live and spend much of their time (e.g. participants spent an average of 19.7 hours at home per day). Furthermore, unlike researchers employing ecologic analyses, we adjusted for individual level health factors, thereby controlling for confounders that may impact pulmonary function and co-vary with environmental exposures among HUCs, such as level of education, smoking, and obesity. Thus, our approach allows for considerable variation in exposure and outcome to be present among our participants and within the study region while controlling for numerous potential individual level confounders. The ability to assign levels of exposure over small geographic areas, as well as control for individual level co-variates, may have increased exposure classification and reduced confounding in comparison to ecological studies that found an adverse association between coal mining and residential respiratory health.

Variation in the continuity of exposure particle emissions in both time and space my impact our ability to detect an association between exposure and respiratory health. For example, while mining permits may change over time, as well as associated coal haul routes, major roadways are likely more of consistent exposure. Thus, we may have been were more likely to detect an association between pulmonary function and roadway density than mining activity. In fact, the majority of the population centers of the region are found in HUCs with higher roadway density, yet low densities of resource extraction. However, it is certainly possible that there may be a small portion of the regional population that lives near to active mines or other forms of resource extraction and may suffer adverse effects from such exposures.

Worthy of discussion is the timing of our outcome measure, pulmonary function, with respect to our HUC level measures of exposures. We only measured pulmonary function on one occasion, so we were not able to detect changes in pulmonary function over time, nor were we able to ascertain the appropriate lag time for a pulmonary function response following exposure. However, additional results from this population show a lack of association between mining exposures and asthma (W.J. Christian, Personal communication), perhaps a respiratory health indicator of more long term and chronic exposure than a single pulmonary function test. It is also possible that by preferentially enrolling those with pre-existing respiratory disease (and potentially higher exposure levels), that we may have over-estimated the strength of the association between environmental exposures and respiratory health in the general Appalachian population. Although this bias in the strength of the measured association is possible, sensitivity analyses eliminating those with self-reported pre-existing respiratory disease yielded similar results for roadway density and pulmonary function and, in fact, strengthened the association between coal haul route density and reduced pulmonary function. Furthermore, among sampled individuals, the prevalence of asthma and COPD is 20% and 21%, respectively, and although this does not represent the true regional prevalence due to preferentially sampling those with pre-existing lung disease, generally these percentages match that of adults in rural mountaintop removal regions of Eastern Kentucky (KY) (18% and 26%, respectively; Hendryx, 2013). This similarity in prevalence suggests our sample of participants may be representative of regional prevalence of respiratory disease, and thus the associations we modeled may be generalizable to the exposed population of rural Appalachia.

Summary

Among residents of rural Appalachia Kentucky, we found that living in an HUC with a high level of roadway density was associated with reduced pulmonary function, while living in an HUC with a high density of coal haul routes was also associated with reduced pulmonary function. However, counter to past ecological studies we found no associations between active or inactive mining and measures of pulmonary function. Our findings point to the potential benefit of implementing vehicle emission testing standards in the state of Kentucky. As generally all regions of rural Appalachia no dot require period vehicle emissions testing, roadway related exposures are likely prevalent and potentially harmful to resident's health. Future exposure assessment studies and cohort with repeated measures of pulmonary function may help to elucidate the relationship between common Appalachian environmental exposures and respiratory health among residents of rural mountainous Appalachia.

Table 3.1. Pulmonary function per MAP participant characteristics-Univariate associations

Characteristic	**N**	**Mean FEV$_1$ % predicted (95% CI)**	**Mean FVC % predicted (95% CI)**
Age (Years)*			
≤ 21 - 45.9	292	89.6 (88.0, 91.2)^{A}	92.7 (91.1, 94.2)^{A}
≥ 46.0 - 60.9	290	80.9 (78.7, 83.2)^{B}	84.0 (82.3, 85.8)^{B}
≥ 61	290	79.1 (76.5, 81.7)^{B}	81.6 (79.5, 83.6)^{B}
Gender ^{NS}			
Male	356	82.9 (80.8, 85.0)	86.1 (84.4, 87.8)
Female	516	83.4 (81.8, 85.1)	86.1 (84.7, 87.5)
Pack years (Years)*			
0/Never smoked	381	88.5 (86.8, 90.1)^{A}	87.9 (86.3, 89.4)^{A}
1 - 18.39	202	86.7 (84.3, 89.1)^{A}	90.0 (87.8, 92.1)^{A}
>18.39	287	74.1 (71.7, 76.6)^{B}	81.3 (79.4, 83.2)^{B}
Smoking status*			
Never	379	88.5 (86.8, 90.2)^{A}	87.8 (86.3, 89.4)^{A}
Former	205	81.5 (78.7, 84.3)^{B}	84.4 (82.0, 86.8)^{B}
Current	288	77.5 (75.1, 79.9)^{B}	85.1 (83.2, 87.0)^{A,B}
Education*			
< High School	218	79.1 (76.1, 82.1)^{A}	83.2 (80.7, 85.7)^{A}
High School	273	82.7 (80.5, 85.0)^{A,B}	85.7 (83.8, 87.6)^{A,B}
> High School	380	85.9 (84.1, 87.7)^{B}	88.0 (86.5, 89.5)^{B}
BMI*			
Normal/underweight (< 25.0)	206 / 18	80.9 (77.9, 83.9)^{A}	88.3 (85.9, 90.7)^{A}
Overweight (≥ 25.0 - 29.9)	253	85.0 (82.4, 87.6)^{A}	87.8 (85.8, 89.8)^{A}
Obese (≥ 30.0)	373	82.9 (81.2, 84.7)^{A}	83.7 (82.1, 85.3)^{B}
Physical activity in last month*			
No	400	80.4 (78.2, 82.5)^{B}	83.5 (81.8, 85.3)^{B}
Yes	472	85.6 (84.1, 87.2)^{A}	88.3 (86.9, 89.6)^{A}
Surface mining employment ^{NS}			
No	713	83.3 (81.9, 84.7)	86.2 (85.0, 87.4)
Yes	159	82.9 (79.7, 86.3)	85.7 (83.1, 88.3)
Underground mining employment*			
No	687	84.0 (82.6, 85.4)^{B}	86.5 (85.3, 87.7)^{A}
Yes	185	80.4 (77.3, 83.5)^{A}	84.6 (82.1, 87.2)^{A}
Any mining employment ^{NS}			
No	614	83.7 (82.2, 85.2)	86.4 (85.1, 87.7)
Yes	258	82.1 (79.5, 84.6)	85.3 (83.3, 87.4)
Years of any mining (among miners) ^{NS}			
none	614	83.7 (82.2, 85.2)	86.4 (85.1, 87.7)
<16.0	126	83.3 (79.9, 86.7)	86.8 (84.1, 89.6)
≥16.0	132	80.8 (76.9, 84.7)	83.9 (80.9, 87.0)
Hours at home (Hour)*			
<21	419	87.3 (85.8, 88.8)^{A}	88.9 (87.6, 90.2)^{A}
≥21	452	79.4 (77.4, 81.4)^{B}	83.5 (81.9, 85.2)^{B}
Years in current home (Year)*			
<12	406	83.3 (81.4, 85.1)^{A}	87.5 (85.9, 88.0)^{A}
≥12	464	82.8 (81.0, 84.7)^{A}	84.9 (83.4, 86.4)^{B}
PM2.5 in-home – imputed^*			
≤ 35 µg/m^3	582	85.8 (84.3, 87.3)^{A}	86.5 (85.1, 87.8)^{A}
>35 µg/m^3	290	78.1 (75.7, 80.4)^{B}	85.4 (83.5, 87.3)^{A}

^ Imputed via multiple imputation fully conditional specification (FCS) with 100 iterations of data from a subsample of 71 MAP participant homes. See text for imputation equation.
*P≤0.05 via t-test/ANOVA with significant Tukey pair-wise groups denoted by ^{A,B}
NS = P>0.05 via t-test/ANOVA
Note: 18 participants in underweight BMI category, therefore lumped in with normal

Table 3.2. Pulmonary function per MAP HUC level environmental exposures- Univariate associations

Exposure	N	Mean FEV_1 % predicted (95% CI)	Mean FVC % predicted (95% CI)
HUC roadway density (Road miles/HUC mile^2)*			
Tertile 1 (0 - 2.18)	295	85.0 (82.6, 87.3) [A]	87.6 (85.7, 89.5) [A]
Tertile 2 (2.19 - 2.96)	309	83.1 (81.1, 85.1) [A]	86.7 (84.9, 88.6) [A, B]
Tertile 3 (> 2.96)	268	81.4 (79.0, 83.8) [A]	83.8 (81.9, 85.7) [B]
HUC coal haul route density (Road miles/HUC mile^2) [NS]			
Tertile 1 (0 -0.007)	314	83.4 (81.1, 85.7)	86.6 (84.8, 88.5)
Tertile 2 (0.008 – 0.44)	275	83.9 (81.7, 86.1)	87.0 (85.1, 89.0)
Tertile 3 (>0.44)	283	82.4 (80.2, 84.5)	84.6 (82.8, 86.5)
HUC oil gas well density [NS]			
Tertile 1 (0 – 0.50)	290	81.8 (79.5, 84.1)	85.4 (83.6, 87.2)
Tertile 2 (0.51 – 0.83)	296	83.2 (81.1, 85.4)	86.3 (84.4, 88.2)
Tertile 3 (> 0.83)	286	84.6 (82.3, 87.0)	86.6 (84.8, 88.5)
Active surface mining in HUC [NS]			
No	686	83.1 (81.6, 84.5)	86.1 (84.9, 87.4)
Yes	186	83.8 (81.0, 86.6)	86.1 (83.8, 88.3)
Active underground mining in HUC [NS]			
No	528	82.8 (81.1, 84.5)	85.4 (84.0, 86.8)
Yes	344	83.9 (81.8, 85.9)	87.2 (85.5, 88.9)
Abandoned surface mining in HUC [NS]			
Tertile 1 (0)	340	83.1 (81.0, 85.2)	85.8 (84.1, 87.6)
Tertile 2 (> 0 - 0.02)	247	82.9 (80.6, 85.2)	85.7 (83.7, 87.6)
Tertile 3 (> 0.02)	285	83.7 (81.3, 86.0)	86.8 (84.9, 88.8)
Abandoned underground mining in HUC [NS]			
Tertile 1 (0 – 0.068)	299	83.0 (80.9, 85.1)	85.3 (83.5, 87.0)
Tertile 2 (0.069 – 0.37)	285	83.4 (81.2, 85.7)	86.7 (84.8, 88.9)
Tertile 3 (> 0.38)	288	83.2 (80.8, 85.6)	86.4 (84.4, 88.4)

*$P \leq 0.05$ via t-test/ANOVA with significant Tukey pair-wise groups denoted by [A,B]
NS = $P > 0.05$ via t-test/ANOVA

Table 3.3. Environmental exposures versus FEV_1 PP and FVC PP adjusted$^+$ multivariable models with robust standard errors

HUC Environmental exposure	FEV_1 PP	FVC PP
	Estimate (95% CI)	**Estimate (95% CI)**
HUC roadway density (Road miles/HUC mile^2)		
Tertile 1 (0 - 2.18)	Ref	Ref
Tertile 2 (2.19 - 2.96)	-2.33 (-5.22, 0.56)	-1.07 (-3.65, 1.50)
Tertile 3 (> 2.96)	-4.30 (-7.44, -1.15)*	-3.80 (-6.38, -1.21)$^+$
Adj. R^2	0.14	0.09
HUC coal haul route density (Road miles/HUC mile^2)		
Tertile 1 (0 -0.007)	Ref	Ref
Tertile 2 (0.008 – 0.44)	0.15 (-2.87, 3.16)	-0.32 (-2.91, 2.27)
Tertile 3 (>0.44)	-0.87 (-3.92, 2.19)	-2.05 (-4.59, 0.49)$^\#$
Adj. R^2	0.13	0.09
HUC oil and gas well density		
Tertile 1 (0 – 0.50)	Ref	Ref
Tertile 2 (0.51 – 0.83)	0.16 (-2.87, 3.20)	-0.04 (-2.70, 2.62)
Tertile 3 (> 0.83)	1.20 (-1.92, 4.33)	0.08 (-2.47, 2.64)
Adj. R^2	0.13	0.08
Active surface mining in HUC		
No	Ref	Ref
Yes	0.96 (-2.06, 3.98)	0.29 (-2.30, 2.87)
Adj. R^2	0.14	0.09
Active underground mining in HUC		
No	Ref	Ref
Yes	0.86 (-1.72, 3.45)	1.25 (-0.97, 3.48)
Adj. R^2	0.14	0.09
Abandoned surface mining in HUC		
Tertile 1 (0)	Ref	Ref
Tertile 2 (> 0 - 0.02)	0.01 (-2.92, 2.94)	0.12 (-2.42, 2.66)
Tertile 3 (> 0.02)	-0.28 (-3.37, 2.82)	0.26 (-2.31, 2.83)
Adj. R^2	0.13	0.08
Abandoned underground mining in HUC		
Tertile 1 (0 – 0.068)	Ref	Ref
Tertile 2 (0.069 – 0.37)	-0.41 (-3.59, 2.77)	0.43 (-2.26, 3.11)
Tertile 3 (> 0.38)	0.27 (-2.92, 3.46)	0.88 (-1.76, 3.52)
Adj. R^2	0.13	0.09

Adjusted via base model that includes the covariates: BMI, physical activity, pack years, education, mining employment, hours at home, and in-home PM 2.5^
* p = 0.007; + p = 0.005; # p=0.12
^ Imputed via multiple imputation fully conditional specification (FCS) with 100 iterations from a subsample of 71 MAP participant homes.

CHAPTER 4. IN-HOME RESPIRABLE PARTICLUATE SOURCES, PM2.5, AND THE RISK OF ABNORMAL PULMONARY FUNCTION AMONG RESIDENTS OF RURAL APPALACHIA, KENTUCKY

ABSTRACT

Introduction

Residents of rural Appalachia experience exposure to outdoor environmental exposures, subsequently reducing lung function, yet no studies to date have examined the influence of the in-home environment on lung function.

Methods

The Mountain Air Project (MAP) is a community-based research study examining residential environmental exposures related to respiratory disease among residents of rural Appalachia living in Eastern Kentucky (Harlan and Letcher counties).
MAP participants (N=972) were recruited by door to door enumeration. Each participant received a respiratory exposure and symptomatology survey as well as a pulmonary function test. In a convenience subset of this study population (N=61), we performed an in-home air quality assessment consisting of a 4-day gravimetric air quality test for particulate matter ≤2.5 micrometers(μm) in diameter (PM2.5). We modeled the adjusted association between in-home PM2.5 concentrations and the prevalence of abnormal pulmonary function via modified Poisson regression with robust standard errors.

Results

On average, participants were 55 years of age, spent 20 hours (+/- 3.5 std. dev.) in their residence per day, 53% were current smokers with an average of 23 pack years, and 63% had ≤ high school education. The prevalence of abnormal pulmonary function was

46% (31% restrictive and 15% obstructive) with a mean exposure level to PM2.5 of 35.7 ug/m^3 (+/- 55.5 std. dev.). We found in-home PM2.5 concentrations were most strongly associated with being a current smoker and having indoor pest problems in the last year. Multivariable Poisson regression models with robust standard errors demonstrate that for every one-unit increase in log PM2.5 µg/m^3 concentrations there is a 24% increase in the risk of abnormal pulmonary function (Prevalence ratio=1.24, 95% CI:1.01-1.51), adjusting for age, gender, hours in the home per day, education, and pack-years. Furthermore, relative to individuals exposed to PM2.5 levels below the Environmental Protection Agency (EPA) action level, those individuals exposed to levels of PM2.5 higher than the EPA action level experienced a 62% increase in the risk of abnormal pulmonary function (Prevalence ratio=1.62, 95% CI:1.00-2.64), adjusting for age, gender, hours in the home per day, education, and pack-years.

Conclusion

Our results underscore the potential role of in-home particulate exposures in contributing to the risk of abnormal pulmonary function among residents of rural Appalachia, Kentucky.

4.1. INTRODUCTION

U.S. citizens spend approximately 87%-90% of their day indoors, with 69% of the day inside a residence, on average (Richardson et al., 2005; Klepeis et al., 2001, EPA 1989). Exposure to particles less than or equal to 2.5 micrometers (µm) in diameter (PM2.5) from both outdoor and indoor sources may adversely impact respiratory health (Xing et al., 2016). Particulate levels are especially concentrated indoors (Pope, 2000), often at higher levels than outdoors (EPA, 1987, Chen and Zhao, 2011), suggesting the in-home environment may adversely impact respiratory health.

Common indoor activities with a high level of daily repetition generate particulates inside the home, promoting re-occurring respiratory exposures. Environmental tobacco smoke (ETS) may be one of the most prevalent indoor particulate exposures due to frequent and daily smoking by indoor smokers. ETS has significant impacts on the levels of indoor respirable particulate matter as homes with smokers may have 10-50 times the concentration of particles less than 2.5 μm in diameter (PM2.5) compared to non-smoking homes (Fernandez et al., 2015; Van Deusen et al., 2009). Further, a significant proportion of the cigarette combustion particulate output is particulate matter ≤ 1.0 μm in diameter (Kant et al., 2016), which may penetrate deeper in the lungs than larger particulates. Subsequently, exposure to ETS, an exposure with high frequency and repetition, is associated with reduced lung function (Hersoug et al., 2010; Chan-Yeung and Dimich-Ward, 2003) as well as increased asthma related hospital and emergency room visits among asthmatic adults (Eisner et al., 2002). Cooking, another high frequency and repetitious activity, has generally been found to be a strong source of indoor particulates (Abdullahi et al., 2013, Buonnano et al., 2009, Afshari et al., 2005), with wood combusting stoves and fireplaces promoting high concentrations of particulates (Heringa et al., 2011), with an adverse association between coal use indoors and reduced pulmonary function noted among inner city residents of China (Jie et al., 2014). Finally, the presence of indoor pets may lead to higher levels of particulates (Hulin et al., 2012) and may increase respiratory allergic reactions (Chan and Leung, 2018).

Less frequently present in-home respiratory exposures may also be associated with elevated particulate levels and adverse health outcomes. For example, water damage and mold are associated with elevated in-home particulate concentrations, and may exacerbate allergic reactions (Hulin et al., 2012), while indoor mold exposure may reduce lung function among non-asthmatic adults (Hernberg et al., 2014). Furthermore, exposure to fine and ultrafine particulate matter (10-300 nm) in the home, and endotoxins are also associated with reduced lung function (Karotti et al., 2014). Insect and rodent pests may also promote the presence of dust mites and respiratory allergens, leading to lower respiratory symptoms and allergic diseases (Hulin et al., 2012). Seemingly mundane, less frequent exposures may also elevate particulates, such as burning scented candles (Karotti et al., 2014); Afshari et al., 2005), which may promote adverse respiratory effects (Wolkoff and Nielson, 2017).

Past work demonstrates a distinct health disparity between residents of rural and non-rural regions of Appalachia, especially in terms of respiratory disease. For example, the prevalence of smoking, obesity, and low socioeconomic status (Carderelli et al. 2021; Mills et al., 2020; Michimi et al., 2010; Shaw et al., 2004), in addition to poor health outcomes such as heart disease and stroke mortality (Barnette et al., 2000; Halverson et al., 2002) are common in the region. Hegewald and Crapo (2007) reviewed fourteen studies that examine the relationship between socioeconomic status (SES) and pulmonary function, finding an adverse impact of low socioeconomic status on pulmonary function among both adults and children. As $25,000 representing the approximate median household income for the region, according to the 2015 U.S. census (United States

Census Bureau, 2017), low SES may be a contributing factor to the regional burden of disease.

Past ecological studies suggest environmental exposures may also promote adverse health in the region, as within rural mountain top mining regions higher rates of kidney, heart, and respiratory disease mortality are found than in non-mountaintop removal mining areas (Hendryx, 2009). Environmental respiratory exposures may indeed be higher in the region, as the prevalence of asthma among adults in rural mountaintop removal regions of eastern Kentucky (KY) was 18%, with a 26% prevalence of chronic obstructive pulmonary disease (Hendryx, 2013). These prevalence are much higher than that of the general U.S. population in the same time period, 8% and 7%, respectively (Akinbami et al., 2012; Ford et al., 2013). Among residents of rural Appalachia Kentucky, Flunker et al. (Dissertation Chapter 3) found an adverse association between lung function and living in a valley (AKA "hollow") with a high level of roadway density, yet, counter to past ecological results, no association was detected between respiratory health and resource extraction.

In-home exposures may also influence the regionally high prevalence of poor lung health in rural Appalachia. For example, regional rates of smoking suggest environmental tobacco smoke exposure may be a highly prevalent indoor particulate exposure source (Carderelli 2021). Furthermore, among residents of Appalachia, cooking indoors with wood or coal was found to increase the odds of reporting current asthma (Barry et al., 2010). These in-home exposures may be commonly encountered on a frequent basis by regional residents, especially among those who spend a great deal of time indoors.

No work to date has examined the impact of in-home particulate exposures on respiratory health among residents of rural Appalachian KY. Here we present analyses examining the relationship between in-home particulate exposures, specifically PM2.5 and abnormal pulmonary function among residents of Harlan and Letcher counties in southeastern KY. We quantify associations between common exposures and levels of PM2.5 in the home and then model the association between in-home PM2.5 and the risk of abnormal pulmonary function.

4.2. METHODS

This study is derived from a sub-sample of participants from the Mountain Air Project (MAP), the methodological details of MAP are described elsewhere (May et al., 2019). Briefly, MAP is a community based research project geared towards assessing the environmental and individual contributions to respiratory health among residents of two Appalachian counties in eastern Kentucky-Harlan and Letcher. MAP participants were identified for recruitment from within randomly selected hydrologic unit codes (HUC) from all HUCs in Harlan and Letcher counties. All homes within the selected HUCs were enumerated by the researchers and every third numbered home was selected for potential inclusion in the study. Participants were age 21 years or older, English speaking, and residing in the home in for at least three years. Residents with pre-existing lung disease were preferentially enrolled to ensure enough cases for analyses examining associations between environmental exposures and respiratory health outcomes. A maximum of two adults per household were selected for interviews, with one primary informant participating in a respiratory health and exposure survey administered by community health workers. Participants were also administered pulmonary function tests by the community health workers during the same meeting when the questionnaire was administered. Participants with recent chest surgery were excluded from pulmonary function testing. Participants were reimbursed $25.00 for their time. A total of 972 participants were enrolled with complete survey and pulmonary function data.

A convenience sample of participants who had completed the overall MAP study survey and spirometry participated in an in-home assessment of air quality and respiratory exposures. The interviewer who conducted the original interview telephoned participants to obtain consent for the in-home assessment. Inclusion criteria included a complete survey and pulmonary function data. No other exclusion criteria was used to maximize sample size. Participants were reimbursed $50 for their participant in the in-home assessment.

All study procedures were approved by the University of Kentucky Institutional Review Board, and all participants provided informed consent.

Environmental Survey (Survey administered to 972 MAP participants)

All MAP participants completed an interviewer-administered environmental exposure survey, which examined potential sources of environmental exposures to particulates, chemicals, characteristics of the housing related to home heating, environmental tobacco smoke exposure, and home construction. Details about the home, such as home type (single family, mobile home with foundation, mobile home without foundation, and apartment), year the home was built, and years in current home were also recorded. We assessed length of time indoors per day by asking participants: "How many hours do you spend in your primary residence per day?" This was recorded on a continuous scale but was then dichotomously coded at the median. Current smoking status was assessed by the question “Have you smoked any cigarettes in the last 30 days (current smoker)?”, while former smoker status was ascertained by the question “Have you smoked more than 100 cigarettes in your lifetime (former smoker)?”. Current and former smokers were asked how many cigarettes they smoked on average per day and the duration of smoking was determined based on age one started smoking and stopped smoking. This information was used to calculate “Pack-years”, which was defined as the number of cigarettes smoked per day divided by 20, the quotient of this was then multiplied by the number of years smoking.

This survey also gathered information on respiratory health, comorbidities, general health, and occupational history. Participants were asked whether they had an MD diagnosis of Chronic Obstructive Respiratory Disease (COPD) as well as an MD diagnosis of Asthma. Participant physical activity was assessed with the question “Have you engaged in any physical activity in the last month?” Height (in inches) and weight (in pounds) were ascertained and recorded as continuous variables. Body Mass Index (BMI) was calculated as weight in kilograms divided by height in meters squared. Participants were also asked their current job title, which was used to code workers into dusty versus non-dusty occupations. Past occupational history of mining was also inquired about.

Participant socioeconomic status was ascertained by education level. Education level was recorded as 1^{st}-5^{th} grade, 6^{th}-8^{th} grade, or 9^{th}-11^{th} grade, completed high school or GED, some college but no degree, associate degree, bachelor’s degree, or graduate/professional school. This was collapsed to > high school and ≤ high school education.

Pulmonary function testing (Methods for 972 MAP participants)

Participants were administered pulmonary function tests (PFT) by trained interviewers with the TrueFlow spirometer (ndd Medical Technologies, Zurich, Switzerland) at the time of the first survey administration. Spirometry training was conducted by a pulmonary physician at the University of Kentucky (DM), who also reviewed spirometry tests on a weekly basis for quality. Post bronchodilator tests were not performed due to cost, lack of training, and the inability of participants to travel to a pulmonary clinic. PFTs were examined and classified by a physician pulmonologist (DM) and reproducible spirograms were used for pulmonary function classification. 'Normal' pulmonary function was defined as FEV1/FVC ≥0.70 and FEV1 ≥80% predicted, while 'abnormal' pulmonary function was defined as a PFT showing restrictive (FEV1/FVC ≥0.70 and FVC<80% predicted) and/or obstructive (FEV1/FVC<0.70) lung function. Due to small sample size with reliable pulmonary function tests (n=60) restrictive and obstructive cases were collapsed into the "abnormal" category and compared to the characteristics and exposures of normal cases.

Indoor sampling methods (Subsample of MAP participants)

Indoor air was sampled in the same homes selected for the in-home exposure survey using an occupational sampling protocol adapted for indoor air (Pavilonis et al., 2013). The BGI OMNI 400 sampling pumps (BGI Waltham, MA) and SKC PM2.5 samplers (SKC, Eighty Four, PA) were used to sample respirable dust (PM2.5) over the four-day sampling period at a rate of 4 liters per minute. The sampler and pump were positioned in the room in the home where the family reported spending the most time. The sampler and pump were at least 1 meter above the floor and in an area of the room away from vents and doors. Temperature and relative humidity were also recorded during sampling with the TSI Q-trak. The samples were collected on 37 mm polytetrafluoroethylene (PTFE) filters with a 0.8 µm pore size (Pall Corp, Ann Arbor, MI). Filters were pre-and post-weighed with an electrical microbalance (Mettler MTS, Columbus, OH) with a sensitivity of 2 µg. Before weighing, filters were stored in a temperature- and humidity-controlled room for 48-hours to allow for acclimatization to a standard temperature (68^{o} F) and relative humidity (50%). Sampling pumps were calibrated at the start and the end of sampling, with the average of these measurements used as the airflow rate over the sampling period. The microbalance was calibrated at the start and end of every weighing session. Field blanks were collected for each sampling period and differences between pre- and post-weight were used to adjust PM2.5 weight. To estimate PM2.5 concentration over the four-day sampling period, the difference between pre- and post-sampling filter weight was divided by average flow rate and then multiplied by the number of sampling minutes. PM2.5 measurements were log-transformed to minimize the influence of outliers. PM2.5 samples were also coded as above or below the Environmental Protection Agency (EPA) action level cut point of 35 $\mu g/m^3$. Approximately four weeks after testing, study participants were mailed a results letter that detailed the results of their in-home testing

In-home exposure sources versus PM2.5 (Subsample of MAP participants)

We examined common types of in-home exposures for association with PM2.5 levels. Specifically, we examined whether a current smoker lived in the home, if the participant had a current dusty job, if water or mold problems had occurred in the past year, if a pest problem had occurred in the last year, and if so, whether that pest was cockroaches or rodents. We also examined if pesticides had been applied inside the home in the last year. Participants were asked if they burned candles or use scented deodorizers in the home. Finally, the type of heating and cooking methods were ascertained, and specifically if those involved wood, gas, or coal.

Statistical analyses

The association between demographic and exposure categories with continuous PM2.5 concentrations variables were analyzed via t-test, while associations between exposure categories with the dichotomized version of PM2.5 were analyzed with Chi-square. Chi-square was also used to examine associations between in-home smoking and additional exposure categories. All continuous covariates included in analyses were coded into two groups based on median value cut-points. As the high prevalence of our outcome of interest made the odds ratio an inaccurate estimate of prevalence or risk ratio, negating the use of logistic regression, we first examined adjusted associations between in-home PM2.5 and pulmonary function via a log-binomial model with robust standard errors, yet this model failed to converge. Thus, a modified Poisson with robust empirical standard errors was used to examine the adjusted association between in-home PM2.5 and the risk of abnormal pulmonary function (Spiegelman and Hertzmark, 2005).

All statistical analyses for this paper were conducted using SAS Version 9.4 (Copyright © 2013, SAS Institute Inc., Cary, NC, USA).

Covariates

Due to small sample size, covariates were dichotomized at the median values to allow for an adequate number of observations per cell. As such, factors used to adjust the relationship between in-home PM2.5 and the risk of pulmonary function included: age (≤58.7 vs. >58.7 years), gender (male vs. female), level of education (≤high school or

>High school), hours at home (≥22 vs. <22 hours home/day), and pack-years (≤6.7 vs. >6.7).

Modeling

A modified Poisson regression model was constructed to evaluate the relationship between the in-home concentrations of PM2.5 that were above or below the EPA action level (≥35 µg/m^3 versus <35 µg/m^3) and the risk of abnormal pulmonary function, controlling for age (≤58.7 vs. >58.7), pack years (≤6.7 vs. >6.7), gender, time indoors at residence per day (≥22 hours home/day vs. <22), and level of education (≤ high school versus >high school). An additional model was constructed with PM2.5 log-transformed in a continuous form with the same covariate adjustments as were used in the adjusted model with PM2.5 coded as above or below the EPA cut-point.

4.3. RESULTS

Home Sample details

We performed an in-home assessment on the homes of 70 participants with 61 interpretable pulmonary function tests. There was a 64% participation rate among those selected and eligible homes that were contacted by interviewers (70/110 homes). Approximately, 55% of the selected MAP HUCs were included in the in-home assessment portion of the study (22/40). There were no significant differences between participants characteristics that were not included in the in-home assessment versus those that were included in terms of single family home (63% vs. 68%, respectively), age (52 vs 55 years, respectively,), nor any differences in terms of ever smoker (56% vs. 55%, respectively), male gender (42% vs. 33%, respectively), Caucasian race (98% vs. 96%, respectively), less than or equal to a high school education (56% vs. 63%, respectively), and household income<$25,000 (61% vs. 67%, respectively).

Among the 61 residences of participants with interpretable pulmonary function tests, 41 (67%) were single family homes, 12 (20%) were mobile home or trailer, and two (3%) were an apartment, with an average home size of 1,900 ft^2.

Environmental exposure: In-home particulate sources

Among surveyed homes included in analyses 23% (14) of sampled homes were above the EPA air quality standard of 35 $\mu g/m^3$, while the arithmetic mean PM2.5 exposure level was 37.8 $\mu g/m^3$(std. dev.=57.8, min=1.6, max=280.9). Participant exposure to in-home PM2.5 sources were relatively common. Homes with a current smoker (26% of all homes) and those homes with a reported a pest problem in the last year (61%) had significantly elevated log PM2.5 $\mu g/m^3$ concentrations and a significant proportion of homes above the EPA action level for PM2.5. Homes reporting a cockroach problem (6%) and those reporting a rodent problem (13%) in the past year also demonstrated significantly elevated log PM2.5 $\mu g/m^3$ concentrations, while pesticide application in the last year was marginally associated with elevate PM2.5. Table 1. Specifically, we found that homes with a current smoker had a greater log concentration of PM2.5 (2.63 vs 3.86 $\mu g/m^3$, respectively) in comparison to non-smoker homes, as well as a greater proportion of homes ≥EPA action level (56% versus 11%, respectively). We also found those with pest problems in the last year tended to have higher levels of log PM2.5 and statistically significant higher proportion of homes above the EPA action level than homes without a pest problem in the past year. Furthermore, this pattern seemed to have been driven by cockroaches and rodents, as the presence of each was associated with elevated log PM2.5 levels and a greater proportion of homes with ≥EPA action level. Pesticide application in the last year was also associated with higher, yet non-significant levels of log PM2.5, and marginally significantly associated (P=0.08) with a higher proportion of homes ≥EPA action level. Cooking with wood and/or coal was infrequent (7% and 3%, respectively) and showed no association with PM2.5. Heating with a wood or gas furnace was also infrequent (7% and 8%, respectively), with each exposure source exhibiting elevated log PM2.5 μg/m^3 levels, yet this was not statistically significant. Although a mold problem in the last year (10% of homes) was associated with higher levels of log PM2.5 this was not statistically significant. Water problems in the past year (13% of homes) showed no association with PM2.5. No distinct associations with PM2.5 were detected from dogs and/or cats in the home (48% of homes), burning of candles in the home (66% of homes), or the use of scented deodorizer (56% of homes). Table 1.

We found the presence of current smoker living in the home co-occurred with our exposure source categories. A current smoker in the home was significantly associated with a pest problem in the last year (37.5% of homes with pests had a current smoker versus 9.7% of homes without pests had a current smoker; Chi-Square=5.91, P=0.033), having a gas furnace in the home (66.7% of homes with a gas furnace had current smokers versus 21.5% of homes without a gas furnace had a current smoker; Chi-Square=7.14, P=0.007), and marginally associated with indoor pesticide application in the last year (39.1% of homes with pesticide application had current smokers versus 18.8% of homes without pesticide application had a current smoker; Chi-Square=3.41, P=0.062). All other in-home exposure sources were not significantly associated with the presence of a current smoker living in the home.

Participant characteristics

Among 61 participants with reliable and interpretable pulmonary function tests, the average age was 55 years (Std. dev.=14.8, min=24.5, max=81.3), 67% were female, 95% were White, with generally low levels of socioeconomic status (59% ≤High school education) and high rates of current smoking (26%). Participants spent an average of 19.9 hours (Std. dev.= 3.5, min=9, max=24) indoors per day. Twenty six percent (n=16) were past miners, while there were not any current miners. Among participants, 35.5% (n=16 participants) had a medical diagnosis of COPD, 12 of which were classified as abnormal pulmonary function, while 13% (n=8) had a medical diagnosis of asthma, five of which were classified as abnormal pulmonary function. Table 2.

Respiratory disease and symptoms

We found few statistically significant associations between self-reported respiratory disease or respiratory symptoms and in-home PM2.5. Among those with COPD, mean exposure levels to in-home PM2.5 were slightly higher than those without COPD, with respect to both the geometric mean of PM2.5 (2.88 versus 3.16 log $\mu g/m^3$, respectively) and the proportion of participants exposed to levels above the EPA action level (31.3% versus 20.0%, respectively. In contrast, those participants with a medical diagnosis of asthma experienced lower levels of mean in-home PM2.5 than those without asthma, both in terms of the log PM2.5 (2.42 versus 3.03 $\mu g/m^3$, respectively) as well as the proportion exposed to PM2.5 levels above the EPA action level (0% versus 26.4%, respectively). Neither associations were statistically significant. Table 3.

With respect to self-reported respiratory symptoms, among participants reporting phlegm production most days for ≥ three months per year there was a significant association with both higher mean log concentration of in-home log PM2.5 (3.71 vs 2.79 μg/m^3, respectively) and a higher proportion exposure to in-home PM2.5 above the EPA action level (45.5% vs 18.0%, respectively) than those without phlegm production most days. Although, participants reporting wheezing in the past month and shortness of breath in the last month experienced higher in-home log μg/m^3 PM2.5 levels and a higher proportion of individuals with PM2.5 exposure above EPA action level, these associations were not statistically significant. No other clear patterns emerged when examining the association between the remainder of respiratory symptoms and PM2.5. Table 3.

Pulmonary function

We detected an overall abnormal pulmonary function prevalence of 46% (n=28/61) in our sample of participants with interpretable pulmonary function tests (19 restricted, 9 obstructed, 33 normal). Eight pulmonary function tests were not used due to being coded as uninterpretable by the pulmonologist (DM) for poor reproducibility and/or spirogram quality. One pulmonary function test was not used for analyses as the participants had not resided in the home for more than one month.

Among those participants with abnormal pulmonary function, the number of participants exposed to PM2.5 levels ≥ EPA action level was twice that of those participants with normal pulmonary function (32% versus 15%, respectively). The level of log mean PM2.5 concentration was also greater among those with abnormal pulmonary function, but this was not statistically significant (2.78 versus 3.16, respectively). Table 3.

Univariate associations demonstrate a larger proportion of abnormal pulmonary function cases among those who spend over 22 hours indoors versus those who spend less than 22 hours indoors (67.9% versus 27.3%, respectively). We also found a larger proportion of abnormal pulmonary function cases among older participants in comparison to younger participants (58.6% versus 34.4%, respectively). No other significant associations were noted. Table 1.

Multivariable Poisson regression modeling association between in-home PM2.5 and prevalence of abnormal pulmonary function

We modeled the association between in-home PM2.5 and the prevalence of abnormal pulmonary function based on 61 reliable pulmonary function tests and exposure surveys. Pearson correlation analyses to assess multicollinearity indicated a general lack of correlation among covariates in the multivariable models. Multivariable Poisson regression models using robust standard errors demonstrate that for every one-unit increase in log PM2.5 concentrations in the home there is a 24% increase in the risk of abnormal pulmonary function (prevalence ratio=1.24, 95% CI:1.01-1.51), adjusting for age, gender, hours in the home per day, education, and pack years. Furthermore, relative to individuals exposed to PM2.5 concentrations below the EPA action level, those individuals exposed to PM2.5 concentrations higher than the EPA action level experienced a 62% increase in the risk of abnormal pulmonary function (prevalence ratio=1.62, 95% CI:1.00-2.64), adjusting for age, gender, hours in the home per day, education, and pack-years. Tables 4 and 5.

4.4. DISCUSSION

We sought to examine the relationship between in-home respiratory exposure sources, in-home PM2.5, and pulmonary function among residents of rural Appalachia in Eastern KY. We found those participants exposed to higher levels of in-home PM2.5 experienced an increased risk of abnormal pulmonary function, relative to those exposed to lower PM2.5 levels, both with respect to log PM2.5 concentrations and with respect to the EPA action level of 35.0 µg/m3. Such an adverse association between in-home PM2.5 exposure and reduced pulmonary function has previously been noted in urban settings (Xing et al., 2016; Karotti et al., 2014), yet this has not been examined among a rural Appalachian residential population. As the prevalence of cancers and respiratory disease in rural Appalachian KY counties is higher than both the overall state of Kentucky and the U.S. as a whole (CDC, 2008; 2012), our findings suggest in-home particulate exposures may potentially contribute to the burden of disease among regional residents.

Our results suggest one of the dominant contributors to in-home PM2.5 concentrations among Appalachia homes may be environmental tobacco smoke (ETS). Among the 16 homes in our study with current smokers, we found significantly higher in-home mean log PM2.5 concentrations than non-smoking homes, as well as a larger proportion (62%) of homes above the EPA action level for PM2.5 than non-smoker homes. Furthermore, current smoking rates are high in rural Appalachia (Cardarelli et al., 2021) and smoking is a frequent and re-occurring daily source of particulates, making ETS a common exposure with a potentially high dose among the exposed. ETS exposures have previously been found to be associated with reduced pulmonary function, specifically percent predicted FEV1 among healthy individuals (Hersoug et al., 2010;

Chan-Yeung and Dimich-Ward, 2003), in addition to respiratory symptoms, such as the frequent phlegm production we detected, as well as lung cancer (Davis, 1998; Environmental Protection Agency, 1997; National Research Council, 1986). Thus, our results suggest in-home ETS exposure and active smoking may contribute to regional adverse respiratory health outcomes.

The presence of in-home pests may also potentially contribute to the observed regional prevalence of adverse respiratory health outcomes among rural Appalachia residents. Our results denote a potential link between exposure and PM2.5 emissions, with heightened PM2.5 levels, both log concentrations and the proportion of home above the EPA actions level, associated with pest problems in the last year and pesticide application in homes. In conjunction with the relatively high prevalence of this exposure and the previously documented adverse association between respiratory health and in-home pests (Sheehan et al., 2010), our results suggest these exposures may be linked to a reduction in pulmonary function among regional residents. However, as we found homes with reported pests or pesticide application also tended to have more current smokers than homes without pests or pesticide application, substantial conclusions about singular emission sources cannot be made. We also were not able to ascertain the duration of time from when these exposures occurred to the timing of our PM2.5 measurements, nor were we able to determine exposure dose or frequency. Future research with repeated exposure measures may help to determine the role of multiple co-occurring in-home exposures on particulate concentrations.

Despite the potential adverse impact of in-home exposures on lung function, the in-home environment is highly modifiable, giving residents direct control over potential exposures. Exposures can be minimized or eliminated by behavior changes, as in-home particulate levels may decrease when differing in-home practices are instilled. For example, cleaning dust and dirt inside the home, reducing indoor clutter, using an exhaust fan when cooking, eliminating moisture sources in the home, and the use of high efficiency HVAC systems, portable filter devices, or central air cleaning systems with filters have all been demonstrated to reduce in-home particulate levels (Azim et al., 2016; Laumbach et al., 2015; CDC, 2010). Such simple interventions are easily adapted and may promote residential respiratory health by controlling emissions from multiple exposure sources.

We also found that the risk of abnormal pulmonary function was heightened among those participants that spend a greater number of hours indoors per day, suggesting time spent indoors may be associated with exposure to higher doses of in-home particulates. As such, the individual dose of in-home PM2.5 exposure is likely higher among those who spend more time indoors than those who spend less time indoors, especially in homes with current smokers or pest problems,. This increased time in the home with higher PM2.5 exposure doses may lead to in reduced pulmonary function. Conversely, it is also plausible that having poorer health may also cause people to spend more time in their home, making the directionality of the association difficult to disentangle with a cross-sectional design. Future longitudinal research is needed to ascertain whether a greater amount of time in one's home more leads to disease, or if poorer health causes people to spend more time in the home.

The respiratory effects of in-home particulate exposures may be exacerbated by low socioeconomic status (SES) among residents of rural Appalachia. For example, in

2015, Harlan and Letcher counties had average household incomes of $25,814 and $30,333, respectively, far below the U.S. national average of $57,000 and for the state of KY ($45,000; U.S. Census 2015). Furthermore, the same disparity holds true for educational attainment, with 65% and 62% of Harlan and Letcher county residents with ≤ high school education, in comparison to 42% with ≤ high school education in the US, and 52% with ≤ high school education in the state of KY (CEDIK 2013; U.S. Census 2013). Indeed, a review of 14 studies, by Hegewald and Crapo (2007), found an adverse association between low SES and reduced pulmonary function. Thus, among residents of rural Appalachia, issues surrounding low SES, such as poor health, reduced income, reduced education, and limited access to both health insurance and healthcare may promote the adverse respiratory health effects from common in-home exposures.

Strengths and limitations

This is the first study to quantify in-home PM2.5 and to examine the association between in-home PM2.5 and the risk of abnormal pulmonary function among residents of rural Appalachia. Our results also help to elaborate in-home factors that may contribute to the regionally high prevalence of respiratory disease. However, our study also has limitations. Given that we conducted a cross-sectional study we were unable to infer the directionality of causation between in-home particulate exposures and pulmonary function for some variables such as time spent in the home, thus, we cannot determine whether these current PM2.5 directly contributed to the observed risk of abnormal pulmonary function. However, based on two exposure metrics, log PM2.5 $\mu g/m^3$ and PM2.5 levels above or below the EPA action level, we see a consistent adverse relationship between higher levels of exposure and increased risk of abnormal pulmonary function. Furthermore, out assessment of particulate exposure was based on a four-day sampling period and this may not have been representative of exposures at other non-sampled times. In addition, the four-day PM2.5 sample may not overlap with in-home exposures participants may have experienced in previous years, such as a water or mold problems or pest infestations in the past, and the presence of co-occurring exposures, such as in-home smoking during our four-day sampling period, may skew particle concentrations estimated to be associated with specific exposure sources. As our assessment of sources of PM2.5 exposure and respiratory symptoms are self-reported, recall or response bias is also a concern, especially if such bias if differential among levels of exposure. To minimize these potential issues, we constructed an adjusted modified Poisson regression model to look at in-home PM2.5 exposure and a physiological outcome, spirometry, both lacking the recall bias potential.

Due to the difficulty associated with residents allowing researchers in their homes, as well as the cost of such testing, we had a relatively small sample size of 61 homes with complete in-home exposure data and pulmonary function tests. This small sample size made it impossible to include all possible factors in our model and prevented us from estimating interactions among covariates. This sample size also made stratified analyses difficult due to very low cell counts and low power. Finally, those participants with less clean homes may have been less prone to participate in our exposure assessment.

Summary

Our results suggest in-home PM2.5 exposures, likely originating from tobacco smoke and pests, may increase the risk of abnormal pulmonary function among residents of rural Appalachia. These risks may be compounded by co-occurring outdoor environmental exposures. Fortunately, the in-home environment is modifiable. Thus, we suggest improving home cleanliness, reducing in-home smoking, and improving home ventilation to lower the level of in-home particulate exposures and the subsequent risk of abnormal pulmonary function. Future research should speciate particulates and examine greater variation in exposure over time, perhaps from both indoor and outdoor respiratory exposures.

Table 4.1. Sources of PM2.5 among 61 MAP homes – Univariate associations

Exposure^	level	% (N) per exposure level	PM2.5 μg/m^3 Geometric mean (Std. dev.)	% ≥ PM2.5 EPA action level
Current smoker living in home	No	45	2.63 (0.89)*	11.1*
	Yes	16	3.86 (1.12)	56.3
Water problem in past year	No	52	2.98 (1.01)	23.1
	Yes	8	2.97 (1.54)	25.0
Mold problem in past year	No	55	2.90 (1.08)	21.8
	Yes	6	3.42 (1.14)	33.3
Pest problem in past year	No	24	2.72 (0.83)	8.3*
	Yes	37	3.11 (1.22)	32.4
Cockroach problem in past year	No	55	2.86 (1.08)*	18.2*
	Yes	6	3.84 (0.87)	66.7
Mice/ rodents problem in past year	No	53	2.87 (1.07)	18.9*
	Yes	8	3.52 (1.13)	50.0
Dog(s) and/or cat(s) in home	No	32	2.95 (1.03)	21.9
	Yes	29	2.95 (1.18)	24.1
Pesticides applied in home in past year	No	42	2.86 (1.06)	16.7+
	Yes	19	3.17 (1.15)	36.8
Burn candles in home	No	21	2.98 (1.14)	19.0
	Yes	40	2.93 (1.08)	25.0
Scented deodorizers	No	27	2.84 (1.04)	18.5
	Yes	34	3.04 (1.14)	26.5
Wood furnace	No	57	2.91 (1.11)	22.8
	Yes	4	3.54 (0.64)	25.0
Gas furnace	No	56	2.89 (1.03)	21.4
	Yes	5	3.71 (1.54)	20.0
Wood stove	No	57	2.98 (1.12)	24.6
	Yes	4	2.60 (0.51)	0.0
Coal stove	No	58	2.97 (1.11)	24.1
	Yes	2	2.56 (0.86)	0

* P≤0.05 t-test or Chi-square
+ P=0.08
^ N=972 survey questions

Table 4.2. Demographic characteristics versus pulmonary function

MAP participant characteristic^	Level	N	% Abnormal pulmonary function
Gender	Male	20	55.0
	Female	41	41.5
Age	≤58.7	32	34.4*
	>58.7	29	58.6
Education	≤ High School	36	55.6[1]
	> High School	25	32.0
BMI^^	Underweight	3	100[+]
	Normal	8	12.5
	Overweight	15	46.7
	Obese	31	45.2
Current smoker	No	45	40.0[+]
	Yes	16	62.5
Pack years	Low (≤6.7)	31	41.9
	High (>6.7)	30	50.0
Physical exercise in last month	No	30	56.7[+]
	Yes	31	35.5
Hours at home per day	Low (<22)	33	27.3*
	High (≥22)	28	67.9
Years in home	Low (≤14)	30	53.3
	High (>14)	31	38.7
Ever dusty job	No	43	44.2
	Yes	18	50.0
Ever coal miner	No	45	40.0
	Yes	16	62.5

*p≤0.05 via chi-square
1 p=0.06 via chi-square
+P≤0.10
^^N=57
^N=972 survey questions

Table 4.3. Respiratory health versus in-home PM2.5 exposure among MAP participants

MAP participant respiratory health characteristic^	Level	N^+	In-home PM2.5 $\mu g/m^3$ Geometric mean (Std. dev)	% ≥ PM2.5 EPA Action Level
Abnormal pulmonary function	No	33	2.78 (1.02)	15.2
	Yes	28	3.16 (1.15)	32.1
Asthma	No	53	3.03 (1.13)	26.4
	Yes	8	2.42 (0.65)	0
COPD	No	45	2.88 (1.09)	20.0
	Yes	16	3.16 (1.11)	31.3
Cough most days ≥3 months/year	No	48	2.97 (1.08)	22.9
	Yes	13	2.88 (1.16)	23.1
Persistent cough in past month	No	43	2.93 (1.08)	23.3
	Yes	18	3.02 (1.15)	22.2
Wheezing in past month	No	42	2.87 (1.10)	19.0
	Yes	19	3.14 (1.07)	31.6
Phlegm most days ≥3 months/year	No	50	2.79 (1.02)*	18.0*
	Yes	11	3.71 (1.12)	45.5
Shortness of breath in past month	No	35	2.82 (1.09)	20.0
	Yes	26	3.13 (1.09)	26.9
Sinus infection past two weeks	No	43	2.94 (1.18)	27.9
	Yes	18	2.97 (0.87)	11.1
Seasonal allergy past two weeks	No	26	3.04 (0.99)	26.9
	Yes	35	2.89 (1.09)	20.0

^ N=972 survey questions
* P≤0.05 t-test or Chi-square
+ N=61 participants with reliable spirometry

Table 4.4. Modified Poisson model* with robust standard errors - Adjusted prevalence ratio of abnormal pulmonary function per one-unit increase in Log PM2.5 μg/m^3

Exposure/MAP participant characteristic	**Level of exposure**	**Adjusted Prevalence Ratio**	**95% Confidence Limits**		**P value**
			Lower	**Upper**	
Log PM2.5 (μg/m^3)		1.24	1.01	1.51	0.039
Education	≤ High School	Reference			
	> High School	0.56	0.32	0.99	0.045
Hours at home per day	Low (<22)	Reference			
	High (≥22)	2.27	1.24	4.17	0.008
Age	≤58.7	Reference			
	>58.7	1.37	0.82	2.31	0.231
Gender	Male	Reference			
	Female	0.82	0.52	1.29	0.390
Pack years	Low (≤6.7)	Reference			
	High (>6.7)	0.79	0.49	1.27	0.322

*Model based on 61 participants with reliable pulmonary function tests

Table 4.5. Modified Poisson model* with robust standard errors - Adjusted prevalence ratio of abnormal pulmonary function per exposure to in-home PM2.5 above or below EPA action level

Exposure/MAP participant characteristic	**Level of exposure**	**Adjusted Prevalence Ratio**	**95% Confidence Limits**		**P value**
			Lower	**Upper**	
PM2.5	<EPA action level	Reference			
	≥EPA action level	1.62	1.00	2.64	0.052
Education	≤High School	Reference			
	>High School	0.60	0.34	1.06	0.076
Hours at home per day	Low (<22)	Reference			
	High (≥22)	2.25	1.21	4.18	0.010
Age	≤58.7	Reference			
	>58.7	1.36	0.80	2.32	0.260
Gender	Male	Reference			
	Female	0.79	0.50	1.24	0.307
Pack years	Low (≤6.7)	Reference			
	High (>6.7)	0.82	0.51	1.32	0.420

*Model based on 61 participants with reliable pulmonary function tests

CHAPTER 5. OVERALL DISSERTATION CONCLUSIONS

This dissertation seeks to examine environmental respiratory exposures encountered by residents of rural Appalachia, modeling their relationship with associated pulmonary function outcomes. Through a combined exposure assessment approach of both small-scale geographic variation and field measurements, we quantified particle concentrations associated with resource extraction exposures and well as indoor exposures in a region previously lacking this detail of exposure assessment. Our study also included detailed information on individual level health factors and direct physiological measures of respiratory health, namely 'forced expiratory volume in one second' (FEV_1) and 'forced vital capacity' (FVC). Our exposure assessment and outcome measures greatly improve the resolution of the exposure outcome relationship beyond that of previous ecological studies.

Our study employed a unique estimate of small-scale geographic variation in exposure sources encountered in rural Appalachia, linking HUC level environmental exposures with distinct particle number concentrations ranging from 10-10,000 nm, finding a strong positive relationship between HUC roadway density and ultra-fine particles. This work represents the first step in quantifying roadway and resource extraction related respiratory exposures and sets the stage for beginning to disentangle the complex web of exposures and factors influencing the respiratory health of rural Appalachia residents.

Among residents of rural Appalachia Kentucky, we found that living in an HUC with a high level of roadway density was associated with reduced pulmonary function, while living in an HUC with a high density of coal haul routes was also associated with reduced pulmonary function. However, counter to past ecological studies we found no associations between active or inactive mining and measures of pulmonary function. Our results suggest population centers may have limited current exposure to such particle sources and that accounting for both small-scale geographic variation in exposure and individual level health factors may impact the measured association between exposure and outcome. Our findings point to the potential benefit of implementing vehicle emission testing standards in the state of Kentucky. As approximately 19 states do not require periodic vehicle emissions, and generally all regions of rural Appalachia no dot require period vehicle emissions testing, roadway related exposures are likely prevalent and potentially harmful to resident's health.

In addition to residential respiratory exposures from outdoor emission sources, our results suggest in-home PM2.5 exposures from ETS and pests may increase the risk of abnormal pulmonary function among residents of rural Appalachia. The risk of reduced pulmonary function may be compounded by co-occurring outdoor environmental exposures. Fortunately, the in-home environment is modifiable. Thus, we suggest improving home cleanliness, reducing in-home smoking, and improving home ventilation to lower the level of in-home particulate exposures and the subsequent risk of abnormal pulmonary function.

Future research should continue to refine exposure assessment of roadways and in-home exposure to PM2.5, examining how these common exposures promote adverse respiratory health among residents or rural Appalachia. Quantifying variation in the temporal and spatial patterns of resource extraction and roadway exposures as well as in-home exposures over time, speciating particulates from varying exposure sources, and measuring temporal variation in pulmonary function among residents is crucial to reducing the burden of respiratory disease in rural Appalachia.

REFERENCES

Abdullahi K.L. , J.M. Delgado-Saborit, R.M. Harrison. Emissions and indoor concentrations of particulate matter and its specific chemical components from cooking: a review. *Atmos Environ*. 2013; 71:260-294b.

Afshari A, Matson U, Ekberg LE. Characterization of indoor sources of fine and ultrafine particles: a study conducted in a full-scale chamber. Indoor Air. 2005; 15(2):141-50.

Akinbami LJ, Moorman JE, Bailey C, et al. Trends in asthma prevalence, health care use, and mortality in the United States, 2001–2010. NCHS data brief, no 94. Hyattsville, MD: National Center for Health Statistics. 2012.

Aneja, A. P., Pillai, P. R., Isherwood, A., Morgan, P., and Aneja, S. P.: Particulate matter pollution in the coal-producing regions of the Appalachian Mountains: Integrated ground-based measurements and satellite analysis, *J. Air Waste Manage. Assoc.* 2017; 67:421–430.

Aneja, V.P., A. Isherwood, and P. Morgan. Characterization of particulate matter (PM10) related to surface coal mining operations in Appalachia. *Atmos. Environ*. 2012;54:496–501.

Azimi, P., D. Zhao, and B. Stephens. Modeling the impact of residential HVAC filtration on indoor particles of outdoor origin (RP-1691). *Science and Technology for the Built Environment*. 2016; 22:431–62.

Balmes JR, Earnest G, Katz PP, et al. Exposure to traffic: lung function and health status in adults with asthma. *J Allergy Clin Immunol*. 2009;123(3):626-631.

Barry, A.C., Maninno, D.M., Hopenhayn, C., Bush, H. Exposure to indoor biomass fuel pollutants and asthma prevalence in Southeastern Kentucky: results from the Burden of Lung Disease (BOLD) study. *J Asthma*. 2010; 47(7):735-41.

Boyles AL, Blain RB, Rochester JR, et al. Systematic review of community health impacts of mountaintop removal mining. *Environ Int*. 2017;107:163-172.

Buonanno, G., Morawska, L. and Stabile, L. Particle Emission Factors During Cooking Activities. *Atmos. Environ.* 2009; 43:3235–3242.

California Environmental Protection Agency. Health effects of exposure to environmental tobacco smoke. Office of Environmental Health Hazard Assessment, Sacramento, CA, 1997.

Cardarelli, K., Westneat, S., Dunfee, M. *et al.* Persistent disparities in smoking among rural Appalachians: evidence from the Mountain Air Project. *BMC Public Health.* 2021; 21:270-2021.

Carlsen HK, Modig L, Levinsson A, et al. Exposure to traffic and lung function in adults: a general population cohort study. *BMJ Open*. 2015;5(6):e007624. Published 2015 Jun 24.

Centers for Disease Control and Prevention. Asthma in Kentucky. 2008. https://www.cdc.gov/asthma/stateprofiles/Asthma_in_KY.pdf

Centers for disease control and prevention. COPD among adults in Kentucky. 2010. https://www.cdc.gov/nceh/lead/publications/final_companion_piece.pdf

Centers for disease control and prevention. Kentucky COPD fact sheet. 2012. https://www.cdc.gov/copd/maps/docs/pdf/ky_copdfactsheet.pdf

Chan SK, Leung DYM. Dog and Cat Allergies: Current State of Diagnostic Approaches and Challenges. *Allergy Asthma Immunol Res*. 2018;10(2):97-105.
Chan-Yeung M, Dimich-Ward H. Respiratory health effects of exposure to environmental tobacco smoke. *Respirology*. 2003; 8(2):131-9.
Chen, C., and Zhao, B. Review of relationship between indoor and outdoor particles: I/O ratio, infiltration factor and penetration factor. *Atmos. Environ*. 2011; 45, 275–288.
Community & Economic Development Initiative of Kentucky. County education data profiles. 2013. https://cedik.ca.uky.edu/data_profiles/education
Davis, M. Exposure to Environmental Tobacco Smoke. Identifying and Protecting Those At Risk. *JAMA*. 1998; 280(22):1947-1949
Dwyer-Lindgren L, Bertozzi-Villa A, Stubbs RW, et al. Trends and Patterns of Differences in Chronic Respiratory Disease Mortality Among US Counties, 1980-2014. *JAMA*. 2017;318(12):1136-1149.
Eisner M, Yelin E, Katz P, Earnest G, Blanc P. Exposure to indoor combustion and adult asthma outcomes: environmental tobacco smoke, gas stoves, and wood smoke. *Thorax*. 2002; 57(11):973-978.
Evans GW, Kantrowitz E. Socioeconomic status and health: the potential role of environmental risk exposure. *Annu Rev Public Health*. 2002;23:303-331.
Fernández, E., Ballbè, M., Sureda, X. et al.Particulate Matter from Electronic Cigarettes and Conventional Cigarettes: a Systematic Review and Observational Study. *Curr Envir Health*. 2015; 2:423-429.
Ford ES, Croft JB, Mannino DM, Wheaton AG, Zhang X, Giles WH. COPD Surveillance—United States, 1999-2011. *Chest*. 2013;144(1):284-305.
Garcia-Gonzales D.A., Seth B.C. Shonkoff, Jake Hays, Michael Jerrett. Hazardous Air Pollutants Associated with Upstream Oil and Natural Gas Development: A Critical Synthesis of Current Peer-Reviewed Literature. *Annual Review of Public Health.* 2019;40(1):283-304.
Hankinson JL, Odencrantz JR, Fedan KB. Spirometric reference values from a sample of the general U.S. population. *Am J Respir Crit Care Med*. 1999;159(1):179-87.
Hart JE, Eisen EA, Laden F. Occupational diesel exhaust exposure as a risk factor for chronic obstructive pulmonary disease. *Curr Opin Pulm Med*. 2012;18(2):151-4.
Hegewald, MJ, and Crapo, RO. Socioeconomic Status and Lung Function. *CHEST*. 2007;132(5):1608 –1614.
Heinrich J**,** Topp R, Gehring U, *et al.* Traffic at residential address, respiratory health, and atopy in adults: the National German Health Survey 1998. *Environ Res*.2005;98:240–9.
Hendryx M, Luo J. An examination of the effects of mountaintop removal coal mining on respiratory symptoms and COPD using propensity scores. *International journal of environmental health research*. 2015;25:265–276.
Hendryx, M. Personal and Family Health in Rural Areas of Kentucky with and without Mountaintop Coal Mining *The Journal of Rural Health*, 2013; 29 Suppl 1:s79-88.
Hendryx M. Mortality from heart, respiratory, and kidney disease in coal mining areas of Appalachia. *Int Arch Occup Environ Health* 2009; 82:243–249.
Heringa, M. F., P. F. DeCarlo, R. Chirico, T. Tritscher, J. Dommen, E. Weingartner, R. Richter, et al. Investigations of primary and secondary particulate matter of

different wood combustion appliances with a high-resolution time-of-flight aerosol mass spectrometer. *Atmos. Chem. Phys*. 2011;11(12):5945-5957.
Hernberg, S., Sripaiboonkij, P., Quansah, R., Jaakkola, J. J. K. & Jaakkola, M. S. Indoor molds and lung function in healthy adults. *Respiratory Medicine*. 2014; 108(5), 677–684.
Hersoug LG, Husemoen LL, Sigsgaard T, Madsen F, Linneberg A. Indoor exposure to environmental cigarette smoke, but not other inhaled particulates associates with respiratory symptoms and diminished lung function in adults. *Respirology*. 2010; 15(6):993-1000.
Hulin M, Simoni M, Viegi G, Annesi-Maesano, I. Respiratory health and indoor air pollutants based on quantitative exposure assessments. *European Respiratory Journal.* 2012; 40:1033-1045.
Jie Y., Houjin H., Xun M., Kebin L., Xuesong Y., Jie X. Relationship between pulmonary function and indoor air pollution from coal combustion among adult residents in an inner-city area of southwest China. *Brazilian Journal of Medical and Biological Research*. 2014; 47(11):982-989.
Kan H, Heiss G, Rose KM, et al. Traffic exposure and lung function in adults: the Atherosclerosis Risk in Communities study Thorax. 2007;62:873-879.
Kant N, Müller R, Braun M, Gerber A, Groneberg D. Particulate Matter in Second-Hand Smoke Emitted from Different Cigarette Sizes and Types of the Brand Vogue Mainly Smoked by Women. Tchounwou PB, ed. International Journal of Environmental Research and Public Health. 2016; 13(8):799.
Karjalainen P, Rönkkö T, Pirjola L, Heikkilä J, Happonen M, Arnold F, Rothe D, Bielaczyc P, Keskinen J. Sulfur driven nucleation mode formation in diesel exhaust under transient driving conditions. Environ Sci Tech. 2014; 48:2336–2343.
Karottki D.G., Beko G, Clausen G, Madsen AM, Andersen ZJ, Massling A, Ketzel M, Ellermann T, Lund R, Sigsgaard T, et al. Cardiovascular and lung function in relation to outdoor and indoor exposure to fine and ultrafine particulate matter in middle-aged subjects. Environ Int. 2014; 73:372–81
Kioumourtzoglou, M., Spiegelman, D., Szpiro, A.A. et al. Exposure measurement error in PM2.5 health effects studies: A pooled analysis of eight personal exposure validation studies. Environ Health.2014;13:2.
Kittelson, B.D. Engines and nanoparticles: a review. Journal of Aerosol Science. 1998;29(5):575–588.
Klepeis NE, Nelson WC, Ott WR, Robinson JP, Tsang AM, Switzer JV, Behar JV, Hern SC, Engelmann WH. The National Human Activity Pattern Survey (NHAPS): a resource for assessing exposure to environmental pollutants Journal of Exposure Analysis and Environmental Epidemiology. 2001; 11:231–252.
Kurth L, Kolker A, Engle M, Geboy N, Hendryx M, Orem W, et al. Atmospheric particulate matter in proximity to mountaintop coal mines: Sources and potential environmental and human health impacts. Environmental geochemistry and health. 2015;37:529–544. [
Kurth LM, McCawley M, Hendryx M, Lusk S. Atmospheric particulate matter size distribution and concentration in west Virginia coal mining and non-mining areas. Journal of exposure science & environmental epidemiology. 2014; 24:405–411.

Kurth, L., A. Kolker, M. Engle, N. Geboy, M. Hendryx, W. Orem, M. McCawley, L. Crosby, C. Tatu, M. Varonka, and C. DeVera. Atmospheric particulate matter in proximity to mountaintop coal mines: sources and potential environmental and human health impacts. Environ. Geochem. Health. 2015; 37(3):529–44.

Li W, Dorans KS, Wilker EH, et al. Residential proximity to major roadways, fine particulate matter, and adiposity: The framingham heart study. Obesity. 2016;24(12):2593-2599.

Liu S-K, Cai S, Chen Y, Xiao B, Chen P, Xiang X-D. The effect of pollutional haze on pulmonary function. Journal of Thoracic Disease. 2016; 8(1):E41-E56.

Macey GP, Breech R, Chernaik M, et al. Air concentrations of volatile compounds near oil and gas production: a community-based exploratory study. Environ Health. 2014;13:82.

Martins LD, Martins JA, Freitas ED, et al. Potential health impact of ultrafine particles under clean and polluted urban atmospheric conditions: a model-based study. *Air Qual Atmos Health*.2010;3(1):29–39.

May, B.A., Cardarelli, K.M., Silver, R., Christian, W.J., Schoenberg, N.E., & Browning, S.R. Hollows as Sampling Units for Community-Based Participatory Research in Appalachia: The Mountain Air Project. *Progress in Community Health Partnerships: Research, Education, and Action*. 2019; 13(4), 401-410.

Michimi A, Wimberly MC. Spatial patterns of obesity and associated risk factors in the conterminous U.S. *Am J Prev Med*. 2010; 39(2):e1-12.

Mills CW, Johnson G, Huang TTK, Balk D, Wyka K. Use of Small-Area Estimates to Describe County-Level Geographic Variation in Prevalence of Extreme Obesity Among US Adults. *JAMA Netw Open*. 2020; 3(5):e204-289.

Morawska, L., Ristovski, Z., Jayaratne, E.R., Keogh, D.U., Ling, X. Ambient nano and ultrafine particles from motor vehicle emissions: Characteristics, ambient processing and implications on human exposure. *Atmospheric Environment.* 2008;42:8113–8138.

National Research Council (US) Committee on Passive Smoking. Environmental Tobacco Smoke: Measuring Exposures and Assessing Health Effects. Washington (DC): National Academies Press (US); 1986. 11, Effects of Exposure To Environmental Tobacco Smoke On Lung Function and Respiratory Symptoms.

Nitschke, M., Appleton, S.L., Li, Q. *et al.* Lung function reductions associated with motor vehicle density in chronic obstructive pulmonary disease: a cross-sectional study. *Respir Res*. 2016; 17:138.

Pakkanen TA, Kerminen V, Korhonen CH, Hillamo RE, Aarnio P, Koskentalo ea. Urban and rural ultrafine (PM0.1) particles in the Helsinki area. *Atmos Environ.* 2001;35:4593–4607.

Paulin L, Hansel N. Particulate air pollution and impaired lung function. *F1000Research*. 2016; 5:F1000 Faculty Rev-201.

Pavilonis B.T., Anthony TR, O'Shaughnessy PT, Humann MJ, Merchant JA, Moore G, Thorne PS, Weisel CP, Sanderson WT. Indoor and outdoor particulate matter and endotoxin concentrations in an intensely agricultural county. *J Expo Sci Environ Epidemiol.* 2013; 23:299–305.

Penttinen P, Timonen KL, Tiittanen P, Mirme A, Ruuskanen J, Pekkanen J: Number concentration and size of particles in urban air: effects on spirometric lung function in adult asthmatic subjects. *Environ Health Perspect* 2001, 109: 319–323.

Pope, C.A. Review: Epidemiological Basis for Particulate Air Pollution Health Standards; *Aerosol Sci. Technol.* 2000; 32: 4-14.

Pratt GC, Herbrandson C, Krause MJ, Schmitt C, Lippert CJ, McMahon CR, Ellickson KM. Measurements of gas and particle polycyclic aromatic hydrocarbons (PAHs) in air at urban, rural and near-roadway sites. *Atmos Environ*. 2018;179:268–278.

Prescott E., Lange P, Vestbo J and the Copenhagen City Heart Study Group. Socioeconomic status, lung function, and admission to hospital for COPD. Results from the Copenhagen City Heart Study. *Eur Respir J*. 1999; 13: 1109–1114.

Rice MB, Ljungman PL, Wilker EH, et al. Long-term exposure to traffic emissions and fine particulate matter and lung function decline in the Framingham heart study. *Am J Respir Crit Care Med*. 2015;191(6):656-664.

Rice MB, Rifas-Shiman SL, Litonjua AA, Oken E, Gillman MW, Kloog I, Luttmann-Gibson H, Zanobetti A, Coull BA, Schwartz J, *et al*. Lifetime exposure to ambient pollution and lung function in children. *Am J Respir Crit Care Med.* 2016;193:881–888.

Richardson G, Eick S, Jones R. How is the indoor environment related to asthma?, literature review. *J. Adv. Nurs*. 2005; 52:328e39.

RStudio Team (2020). RStudio: Integrated Development for R. RStudio, PBC, Boston, MA. URL http://www.rstudio.com/.

SAS Institute Inc. SAS® 9.4. Cary, NC. 2013.

Shaw T, A DeYoung, and E W. Rademacher Educational Attainment in Appalachia: Growing with the Nation, But Challenges Remain. Journal of Appalachian Studies Vol. 10, No. 3, Appalachia Counts: The Region in the 2000 Census. 2004;

Sheehan, W. J., Rangsithienchai, P. A., Wood, R. A., Rivard, D., Chinratanapisit, S., Perzanowski, M. S., Chew, G. L., Seltzer, J. M., Matsui, E. C., & Phipatanakul, W. Pest and allergen exposure and abatement in inner-city asthma: a work group report of the American Academy of Allergy, Asthma & Immunology Indoor Allergy/Air Pollution Committee. *The Journal of allergy and clinical immunology*. 2010; *125*(3): 575–581.

Spiegelman D., and Hertzmark E., Easy SAS Calculations for Risk or Prevalence Ratios and Differences. *American Journal of Epidemiology*. 2005; 162(3):199–200.

U.S. Environmental Protection Agency. Report to Congress on indoor air quality: Volume 2. 1989. EPA/400/1-89/001C. Washington, DC.

U.S. Environmental Protection Agency. The total exposure assessment methodology (TEAM) study: Summary and analysis. 1987; EPA/600/6-87/002a. Washington, DC.

U.S. Environmental Protection Agency. What is Mountaintop mining? Mid Atlantic Mountaintop Mining. 2013. http://www.epa.gov/region3/mtntop/.

Van Deusen, A, Hyland A, Travers MJ, Wang , Higbee, King, BA, Alford T, Cummings, KM; Secondhand smoke and particulate matter exposure in the home. *Nicotine & Tobacco Research*. 2009; 11(6):635–641.

Venn A, Yemaneberhan H, Lewis S, Parry E, Britton J. Proximity of the home to roads and the risk of wheeze in an Ethiopian population. *Occup Environ Med*. 2005;62(6):376-380.

Wolkoff P, Nielsen GD. Effects by inhalation of abundant fragrances in indoor air - An overview. *Environ Int*. 2017; 101:96-107.

Xing Y-F, Xu Y-H, Shi M-H, Lian Y-X. The impact of PM2.5 on the human respiratory system. *Journal of Thoracic Disease*. 2016; 8(1):E69-E74.

Zhang QI, Charles O. Stanier, Manjula R. Canagaratna, John T. Jayne, Douglas R. Worsnop, Spyros N. Pandis, and Jose L. Jimenez. Insights into the Chemistry of New Particle Formation and Growth Events in Pittsburgh Based on Aerosol Mass Spectrometry *Environmental Science & Technology* 2004;*38*(18):4797-4809.

Zhou Y, Levy JI. Factors influencing the spatial extent of mobile source air pollution impacts: a meta-analysis. *BMC Public Health*. 2007;7:89.

Zhu Y, Hinds WC, Kim S, Sioutas C. Concentration and size distribution of ultrafine particles near a major highway. *J Air Waste Manag Assoc*. 2002;52(9):1032-42.

VITA

John C. Flunker, MS, MPH

EDUCATION

2015 Master of Public Health (MPH)-Environmental health
University of Kentucky. Lexington, KY

2011 Master of Science (MS)-Ecology
University of Missouri-St. Louis. St. Louis, MO

2005 Bachelor of Science (BS)-Biology
University of Missouri-St. Louis. St. Louis, MO

PROFESSIONAL POSITIONS

2015-2020 Research Analyst. Mountain Air Project University of Kentucky. College of Public Health. Department of Epidemiology. Lexington, KY

2019-2020 Research Consultant. University of Kentucky Center for Appalachian Research in Environmental Sciences
University of Kentucky. College of Medicine. Lexington, KY

2018 Research Consultant. Maryland Casino Worker Occupational Health and Safety Feasibility Study
University of Maryland. School of Social Work. Baltimore, MD

2014-2017 Research Associate. Thoroughbred Worker Health and Safety Study
University of Kentucky. College of Public Health. Department of Health behavior. Lexington, KY

2014-2021 Guest Lecturer. Occupational Health Studies: Physical agents, respiratory exposures, and controls.
University of Kentucky. College of Public Health. Department pf Environmental and occupational health. Lexington, KY

2011-2013 Health Examiner. Beaver Dam Offspring Study
University of Wisconsin–Madison. School of Medicine and Public Health. Department of Epidemiology. Madison, WI

TEACHING EXPERIENCE

2014-2015 Graduate Teaching Assistant. Animal physiology laboratory. Department of Biology University of Kentucky. Lexington, KY

2010 Substitute Science Teacher. Monona Grove and Mt. Horeb School Districts. Madison, WI

2009-2010 Lead instructor-Biology. Adjunct faculty. Introductory biology lecture and laboratory. St. Louis Community College-Wildwood. St. Louis, MO

2006-2009 Graduate Teaching Assistant-Biology. Department of Biology. University of Missouri–St. Louis. St. Louis, MO

2007 Biology instructor-Tenth grade. National Science Foundation GK-12 Graduate Fellow. Jennings High School. Jennings, MO

FUNDED RESEARCH GRANTS

2018-2019 Principal Investigator. Thoroughbred horse barns particulate distribution and exposure levels among varying work tasks.
University of Kentucky. College of Public Health. Lexington, KY
Educational Research Center Pilot Grant (NIOSH/CDC funded).
$10,000.00 awarded.

2016-2017 Principal Investigator. Geographic Variation in the distribution and concentration of fine particulate matter exposure among rural regions of the Southeastern United States.
University of Kentucky. College of Public Health. Lexington, KY
Educational Research Center Pilot Grant (NIOSH/CDC funded).
$9,880.00 awarded.

ACADEMIC AWARDS

2015 University of Kentucky. College of Public Health. Promising Researcher

2015 University of Kentucky. Graduate Research Day: First Place- College of Public Health Oral Presentation. Pulmonary function among Latino thoroughbred workers

PUBLICATIONS

---

1. **Flunker, J. C.,** Clouser, J. M., and Swanberg, J. (2020). Analysis of Thoroughbred horse farm workers' compensation insurance claims in Kentucky: Injury frequency, cost, lost time, and associated occupational factors. Am J Ind Med. 63(10): 936-948.

2. Clouser, J. M*., **Flunker, J. C*.,** Swanberg, J., Betz, G., Baidwan, S., and Tracy, K. (2018). Occupational exposures and associated risk factors among U.S. casino workers: A narrative review. AIMS Public Health. 5(4):378-393. *equal contribution to authorship

3. **Flunker, J. C.,** Clouser, J. M., Mannino, D. and Swanberg, J. (2016). Pulmonary function among Latino thoroughbred horse farmworkers. Am J Ind Med. 60(1):35-44.

4. Swanberg, J., Clouser, J. M., Gahn, W., **Flunker, J.C.,** Westneat, S., and Browning, S. (2016). Poor safety climate, long work hours, and musculoskeletal discomfort among Latino horse farmworkers. Arch Environ Occup Health. Aug 11:1-8.

5. Swanberg, J., Clouser, J.M., Mannino, D., Gahn, W. and **Flunker, J.C.** (2015). Individual and occupational characteristics associated with respiratory symptoms among Latino horse farm workers. Am J Ind Med. 58(6):679-87.

6. R. Rios, R.J. Marquis, and **Flunker, J.C.** (2008). Population variation in traits associated with ant attraction in Chamaecrista fasciculata. Oecologia. 156(3):577-88.

CONFERENCE PRESENTATIONS

2019 **Flunker, J. C.** Nanoparticle exposure among Thoroughbred workers (ORAL–Presented by **JCF**). At: Southeastern States Occupational Network (SouthON) Annual Meeting. Tampa, FLA.

2018 **Flunker, J. C.,** In-home particulate exposure and pulmonary function among residents of southeastern Appalachia. (ORAL– Presented by **JCF**). At: Southeastern States Occupational Network (SouthON) Annual Meeting. Charleston, SC.

2016 Swanberg, J., Clouser, J. M., Gahn, W., **Flunker, J.C,** and Westneat, S. Poor safety climate, long work hours, and musculoskeletal discomfort among Latino horse farmworkers (ORAL–Presented by **JCF**). At: Southeastern States Occupational Network (SouthON) Annual Meeting. New Orleans, LA.

2015 **Flunker, J. C.,** Clouser, J. M., Mannino, D. and Swanberg, J. Pulmonary function among Latino thoroughbred horse farmworkers (ORAL–Presented by **JCF**). At: University of Kentucky Research Symposium. Lexington, KY.

2015 Swanberg, J., Clouser, J.M., Mannino, D., Gahn, W. and **Flunker, J.C.** Individual and occupational characteristics associated with respiratory symptoms among Latino horse farm workers (POSTER–Presented by **JCF**). At: American Public Health Association Annual Meeting. Chicago, IL.

2015 **Flunker, J. C.,** Clouser, J. M., Mannino, D. and Swanberg, J. Pulmonary function among Latino thoroughbred horse farmworkers (POSTER–Presented by **JCF**). At: COPD 9. Chicago, IL

2015 Swanberg, J., Clouser, J.M., Mannino, D., Gahn, W. and **Flunker, J.C.** Individual and occupational characteristics associated with respiratory symptoms among Latino horse farm workers (POSTER–Presented by **JCF**). At: International Society for Agricultural Safety and Health Annual Meeting. Normal, IL.

2008 **Flunker, J. C.** and R.J. Marquis. Soil Moisture and Tri-trophic interactions (ORAL–Presented by **JCF**). At: University of Missouri – St. Louis. Bio-Lunch Seminar. St. Louis, MO.

2006 **Flunker, J. C.** and R.J. Marquis. Do ant exclusion treatments differ in fitness effects and efficacy? (ORAL–Presented by **JCF**). At: Midwest Ecology and Evolution Conference. St. Louis, MO.

2006 **Flunker, J. C.** and R.J. Marquis. Do ant exclusion treatments differ in fitness effects and efficacy? (ORAL-–Presented by **JCF**). At: University of Missouri-St. Louis Undergraduate Research Symposium. St. Louis, MO.