

ARTICLE



Environmental exposures and pulmonary function among adult residents of rural Appalachian Kentucky

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BACKGROUND: Estimated residential exposures of adults to roadway density and several metrics of resource extraction, including coal mining and oil and gas drilling, were hypothesized to contribute to the prevalence of respiratory disease in rural Appalachia.

OBJECTIVE: Determine how small-area geographic variation in residential environmental exposures impacts measures of pulmonary function among adults in a community-based study.

METHODS: We examined associations between residential environmental respiratory exposures and pulmonary function among 827 adult participants of the “The Mountain Air Project”, a community-based, cross-sectional study in Southeastern Kentucky during 2016–2018. Exposures characterized the density of roadways, oil/gas wells, or current/past surface and underground coal mining at the level of 14-digit hydrologic unit code (HUC), or valley “hollow” where participants resided. Each participant completed an in-person interview to obtain extensive background data on risk factors, health history, and occupational and environmental exposures, as well as a spirometry test administered by experienced study staff at their place of residence. Multivariable linear regression was used to model the adjusted association between each environmental exposure and percent predicted forced expiratory volume in one second (FEV₁PP) and forced vital capacity (FVCPP).

RESULTS: Adjusted regression models indicate persons living in HUCs with the highest level of roadway density experienced a reduction in both FEV₁PP (−4.3; 95% CI: −7.44 –1.15;) and FVCPP (−3.8; 95% CI: −6.38, −1.21) versus persons in HUCs with the lowest roadway density. No associations were detected between the metrics associated with mining and oil and gas operations and individual pulmonary function.

IMPACT STATEMENT:

- Our work demonstrates the potential adverse impact of roadway-related exposures on the respiratory health of rural Appalachia residents. We employed a novel method of small-area exposure classification based on the hydrologic unit code (HUC), representing potential exposure levels per hollow occurring in proximity to the residence, and controlled for individual-level risk factors for reduced respiratory health. We highlight an overlooked yet ubiquitous source of residential exposure from motor vehicles that may contribute to the regionally high prevalence of respiratory disease in rural Appalachia.

Keywords: Roadway exposure; Respiratory; Hydrologic unit code; Pulmonary function; Resource extraction

Journal of Exposure Science & Environmental Epidemiology (2024) 34:981–989; <https://doi.org/10.1038/s41370-023-00584-4>

INTRODUCTION

Asthma, chronic obstructive pulmonary disease (COPD), and subsequent mortality rates are unusually high throughout rural Appalachia compared to the overall United States population [1]. This burden of respiratory disease is especially high in mining regions of rural Appalachia [2, 3]. Residential exposures from resource extraction activities, such as coal mining and oil and gas drilling, have long been suspected as contributing factors to regional respiratory disease, with ecological study designs

documenting adverse associations between residing in mountain top removal regions and respiratory health outcomes. For example, Hendryx et al. [2, 3] found a higher prevalence of asthma and COPD in mountaintop removal mining areas compared to non-mining areas. This relationship has been hypothesized to be due to high levels of dust particles in regions near mountaintop removal, as associations between high levels of coarse and fine particulates in regions of high mining activity have been noted [4, 5]. Concurrent respiratory exposures from oil and gas wells may also exist [6].

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Received: 17 June 2022 Revised: 8 July 2023 Accepted: 18 July 2023
Published online: 29 August 2023

However, a systematic review by Boyles et al. [7] found no conclusive evidence for a clear link between mountain top removal and adverse health effects among local residents due to potential exposure misclassification and uncontrolled confounding. The persistent high prevalence of risk factors for respiratory health among residents of rural Appalachia, such as current or past smoking, obesity, and low socioeconomic status [8–11], may further confound estimates of association between environmental respiratory exposures and respiratory health outcomes.

Exposures from roadway traffic may be especially prevalent among rural Appalachian residents, as many homes are situated in deep valleys positioned close to roadways. Particulates originating from internal combustion engines are generally in the ultrafine size range [12, 13] and may be inhaled by residents living close to roadways, especially busy roadways. Although proximity to roadways, namely linear residential distance to roadways, and associated reduced pulmonary function has been noted in urban areas among adults and children [14–19], such an example is absent for rural Appalachia. The high regional rates of respiratory disease in Appalachia and often close proximity between roadways and residential areas, suggest residents may experience a heightened risk for roadway-related exposures, with subsequent impacts on respiratory health. This may be especially true among those residents with respiratory disease, as asthmatics may be predisposed to a reduction in lung function following roadway-related exposures [20, 21].

Straight-line distance from a home to a roadway is a commonly employed method to estimate residential roadway-related exposures [15, 19], and has often been applied to urban settings [22]. However, in rural settings with precipitous mountain valleys that meander, a straight line from roadway to nearby residences may not represent true particle distribution patterns. As such, a valley

(“hollow”) level estimate of exposure may more accurately capture geographic heterogeneity and potential residential exposure patterns in rural mountainous Appalachia. This small-area estimate of spatial variation in exposure can be captured by delineating valleys based on the United States Geological Survey Hydrologic Unit Code (HUC), which outlines water drainages within a region. Here we apply a novel method of exposure classification, HUC density, to explore associations between common environmental exposures and pulmonary function among residents of two rural Appalachia Kentucky counties, adjusting for individual level health factors, such as smoking and socioeconomic status.

MATERIALS/SUBJECTS AND METHODS

Environmental exposures (via hydrologic unit code)

Environmental respiratory exposures in two rural counties in Eastern Kentucky were quantified on a small-area geographic scale as the density of exposure per 14-digit hydrologic unit code (HUC). Exposures of interest included roadways, coal haul routes, active surface and underground mining, abandoned surface and underground mining, and oil/gas wells. HUC is a set of adjacent United States Geological Survey designated geographic polygons that outline watersheds. These polygon outlines roughly follow the ridge-lines of Eastern Kentucky and frame the deep valleys where residents primarily live. These geographic units make the HUC a reasonable boundary to circumscribe environmental exposures within small-areas of rural mountainous Appalachia, as valley walls likely buffer wind and restrict air flow of airborne particulates. Figure 1 details the distribution of exposures among HUCs throughout the study region.

Generally, we defined the density of environmental exposure per HUC as the unit of exposure divided by the area of the HUC.

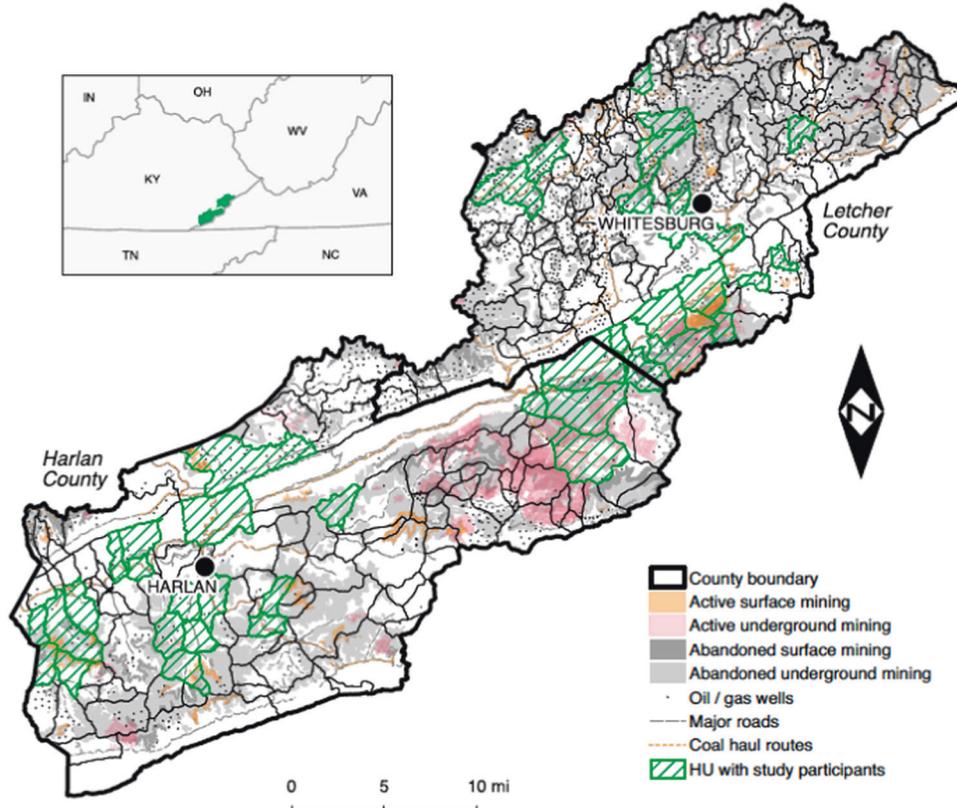


Fig. 1 Mountain Air Project (MAP) study area. The distribution of environmental exposures per 14-digit hydrologic unit code (HUC) among Harlan and Letcher counties, KY, are detailed for each HUC in the study area (outlined in black). HUCs containing MAP study participants are outlined in green.

Roadway and coal haul route density per HUC were defined as the number of linear miles of roadway per square mile of HUC area. The density of current and past surface and underground mining was calculated as the proportion of the HUC area utilized by surface or underground mining (square miles exposure area per square miles HUC area). Oil/gas well density was defined as the number of oil/gas wells per HUC square mile area. Ultimately, for ease of interpretation, tertile cut points were applied to the HUC density of roadways, coal haul routes, abandoned surface and underground mining, and oil/gas wells, while dichotomous coding was applied to active surface and underground mining due to limited variability in exposure presence and density per HUC. The distribution of these HUC-level exposures within the MAP study area are shown in Fig. 1. Information on potential exposure sources were obtained from publicly available data, and exposure outlines were overlaid onto one map with HUC boundaries in ArcGIS desktop version 10 [23]. Mining exposures were estimated 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 exposure data were obtained from the Kentucky Transportation Cabinet, which included all streets, roads, and those roads defined as coal haul routes. State primary system roadways, defined by the Kentucky Transportation Cabinet as high-volume intrastate routes and rural principal and minor arterioles and rural major collectors, are the main regional transportation routes, often located in tight valleys near to residences. 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, immediately prior to the study's start date. Full details on the exposure estimation metrics and methods can be found in May et al. [24].

Participant selection

Methods for selection of participants are described in detail elsewhere [11, 24]. Briefly, each HUC in Harlan and Letcher counties was given a three-level index score (low, medium, or high), summarizing the intensity of all environmental exposures combined within an HUC. Ten HUCs (i.e., hollows) per each index level were then randomly selected for a total of 30 HUCs distributed among Harlan and Letcher counties were included in the study. In selected HUCs all homes were enumerated by in-person visits of field staff 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% for the full study sample of 972 persons with written informed consent obtained. Adults (≥ 18 years of age) with pre-existing lung disease were preferentially enrolled and up to two adults per household were enrolled when one of the adult's reported pre-existing lung disease. Of the 972 persons enrolled in the full study, 10 persons (2 each from five homes) shared the same home environment. One spirometry test and exposure survey were administered per participant. These were combined with the land use exposure metrics for statistical analyses. The study was approved by the University of Kentucky Institutional Review Board and was conducted between November 2015 and August 2017.

Questionnaire description

Trained community health workers administered to each participant a detailed environmental exposure questionnaire regarding in-home respiratory exposures, living conditions, socioeconomic status, work-related exposures, and individual health risk factors for disease such as smoking, exercise, height, and weight. Questionnaires were administered at the same time that participants were given a pulmonary function test.

Spirometry tests

Spirometry tests were administered via the Easy One[®] spirometer to participants by the community health workers. Spirometry testing training was provided to community health workers by the study MD pulmonologist (DM) and study manager (BM). One spirometry 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 reproducible spirograms were considered "interpretable". Spirometry results were interpreted and graded for quality by a board-certified physician pulmonologist (DM). Percent predicted values of forced expiratory volume in 1 s (FEV₁) and forced vital capacity (FVC) were determined following the methods of Hankinson et al. [25] which calculates percent predicted values based on age, height, race, and sex. Only spirometry tests graded as 'interpretable' were included in the analyses.

Covariates

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 and years in current home) were examined as potential covariates. 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 zero. BMI per participant was calculated as the ratio of weight in kilograms to height in centimeter squared and were then categorized as: underweight (<18.5) normal (<25.0), overweight (≥ 25.0 – 29.9), and obese (≥ 30.0). The small number of participants ($n = 18$) who were in the underweight BMI category (<18.5) were grouped with the normal BMI category to ensure adequate sample size and reliable confidence intervals and estimates per BMI group in adjusted analyses. Those participants in the underweight BMI category fell in the upper end of the underweight range for BMI (Mean = 17.2, 95% CI = 16.6, 17.7). Education level was coded as the highest level obtained by the participant and was categorized as <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 (current roadway, coal haul route, oil/gas, and surface/underground mining and past surface/underground mining), personal and demographic characteristics, and pulmonary function outcomes (percent predicted FEV₁ and FVC as continuous outcome variables). Covariates were evaluated as potential confounders by examining their relationship with both exposure and pulmonary function outcomes. Suspected and known confounders were used to create a base adjustment model, which was then applied to each multivariable environmental exposure model.

Multivariable linear regression models with robust standard errors were used to examine the adjusted association between HUC level exposures and pulmonary function. Seven HUC level exposures (roadway density, coal haul route density, oil/gas well density, active surface mining, active underground mining, inactive surface mining, and inactive underground mining density) were examined as predictors of FEV₁ and FVC percent predicted, with each association of interest modeled and adjusted for BMI (Underweight/normal, overweight/obese), physical activity (no/yes in last month), pack years (tertiles), education (>high school, high school, <high school), past/current mining employment (no/yes), and hours at home (below/above median cut-point). A total of 14 adjusted models were created, with seven models examining the

relationship between environmental exposures and FEV₁ percent predicted and seven models examining the same exposures versus FVC percent predicted. Only those participants with complete cases of exposure, outcome, individual level health factors, and confounders were used in modeling analyses. All statistical analyses were conducted using R, version 4.2.0 [26].

RESULTS

Participant characteristics

The study included 872 participants with interpretable spirometry tests and complete data for analyses. On average, participants were 52.9 years of age (standard deviation = 15.5; range = 21.1–96.8), 59% female, 44% were categorized as having an “obese” BMI, and 25% had less than a high school education, 31% had a high school education, and 44% had greater than a high school education (Table 1). Thirty-three percent of participants were current smokers and 24% were former smokers, with an average of 16.1 pack-years (standard deviation = 24.5; range = 0.0–276 range), while 43% of the population were never smokers.

Participants self-reported medical diagnoses of respiratory diseases with the following prevalence: asthma 22% ($n = 195$); COPD 15% ($n = 128$); and black lung 10% ($n = 84$). Participants were generally sedentary, spending on average 19.7 hours at home per day (standard deviation = 3.9; range = 8.0–24.0) and only about half (54%) had exercised in the last month. Participant’s average duration 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 among participants, 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. Several participants had occupational mining exposures, with 18% reporting current or past surface mining employment and 21% reporting current or past underground mining employment. The average duration of any mining employment was 22.3 years (standard deviation = 13.1; 1.5–60.0 range).

Spirometry tests

A total of 972 spirometry tests were administered to residents recruited into the study; however, only 872 of those tests were graded as interpretable by the study physician pulmonologist. Among these tests, 183 (20.9%) were classified as restricted and 187 (21.4%) were classified as obstructed. The average percent predicted FEV₁ value was 83.2% (15–151% range) and the average percent predicted FVC value was 86.1% (19–150% range).

HUC exposure classification

Roadway density per HUC area had the highest density of exposure among the selected HUCs, with a mean of 2.69 road miles per HUC square miles (standard deviation = 1.44, range = 0.19–6.0). Active resource extraction exposure metrics showed minimal variation in the exposure levels, with a mean of 0.015 (standard deviation = 0.05 range: 0–0.30) square miles per HUC square miles for active surface mining and a mean of 0.05 (standard deviation = 0.11, range = 0.0–0.48) square miles per HUC square miles for active underground mining. Active surface or underground mining were present among less than one-third of HUCs, at 21 and 39%, respectively. The mean density of abandoned surface mining was 0.04 (standard deviation = 0.07, range = 0.0–0.43) square miles per HUC square miles and the mean density of abandoned underground mines was 0.37 square miles per HUC square miles (standard deviation = 0.40, range = 0.0–1.53). Past mining was much more common 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 generally low among HUCs, with a mean of 0.34 road miles per HUC square miles (standard deviation = 0.36, range = 0.0–1.27). Oil and/or gas well density was highly variable among selected HUCs, with a mean of 1.62 wells per square mile HUC area (standard deviation = 2.29, range = 0.0–8.44). Oil wells were frequent in selected HUCs (68% of participants with oil wells in HUC of residence), while gas wells were generally absent (5% of participants exposed).

Univariate associations

Significant associations were found between the mean FEV₁ percent predicted and mean FVC percent predicted versus age, pack-years, smoking status, education, BMI, physical activity, underground mining employment, hours at home, and years in the current residence, (Table 1). Specifically, the percent predicted values declined with increasing age, increasing pack-year tertiles, former or current smoking status (relative to never smokers), lower levels of educational attainment (\leq 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), and a higher number of years living in the home (relative to fewer). Gender, surface mining employment, any mining employment, and years of mining employment (tertile coding) were not significantly associated with measures of pulmonary function.

HUC environmental exposures, as coded in final multivariable models, versus average percent predicted FEV₁ and FVC are presented in Table 2. 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 FEV₁ 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 FEV₁ 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 FEV₁ and FVC. In some cases, such as active underground mining and abandoned underground/surface mining, FEV₁ and FVC slightly increased when comparing the lowest tertile to the highest, yet this was not statistically significant.

Multivariable modeling—environmental exposures and pulmonary function

Modeling strategy. To adjust for potential confounding in the relationship between HUC environmental exposures of interest and pulmonary function, a base model was constructed and applied to each HUC exposure variable. This base model included covariates to adjust for pack-years (tertile coding), BMI (underweight/normal versus overweight/obese), physical activity in the last month (yes/no), any current or past mining employment (yes/no), and hours at home per day (median cut). Continuous and categorical forms of base model covariates were examined in univariate analyses (and later, adjusted models) with no difference in significance of association detected. Ultimately, categorically coded covariates were included in the final 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, including pack years, BMI, and hours at home per day. Due to limited variability in the presence of mining among HUCs (i.e., numerous HUCs without active mining), active underground and surface mining were classified as ‘any activity ($>$ 0 square miles/HUC square miles)’ or ‘no activity’ ($>$ 0 square miles/HUC square miles).

Table 1. Pulmonary function per MAP participant characteristics - Univariate associations.

Characteristic	N	Mean FEV ₁ % predicted (95% confidence interval)	Mean FVC % predicted (95% confidence interval)
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	379	88.5 (86.8, 90.2) ^A	87.9 (86.2, 89.4) ^A
1–18.39	206	86.2 (83.7, 88.6) ^A	89.6 (87.4, 91.8) ^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*			
Underweight (<18.5)	18	80.3 (70.7, 89.9) ^A	87.2 (80.1, 94.3) ^A
Normal (≥18.5–25.0)	188	80.9 (77.7, 84.1) ^A	88.4 (85.9, 90.9) ^A
Overweight (≥25.0–29.9)	253	85.0 (82.4, 87.6) ^A	87.8 (85.8, 89.8) ^A
Obese (≥30.0)	372	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 (miners only)^{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

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

Table 2. MAP HUC level environmental exposures versus pulmonary function-univariate associations.

Exposure	N	Mean FEV ₁ % predicted (95% confidence interval)	Mean FVC % predicted (95% confidence interval)
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 (Total wells/HUC mile ²) ^{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 (Mining mile ² /HUC mile ²) ^{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 (Mining mile ² /HUC mile ²) ^{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 (Mining mile ² /HUC mile ²) ^{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 (Mining mile ² /HUC mile ²) ^{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.

95% CI = 95% Confidence interval.

Adjustment for correlated exposures among the five pairs of participants (10 total participants) was not controlled for in statistical models due to limited variability in such exposure clustering among the MAP population.

Multivariable model results. Results from adjusted multivariable linear regression models based on complete data for 827 participants demonstrate a statistically significant reduction in pulmonary function associated with increasing HUC roadway density tertiles. Specifically, those participants living in HUCs with the highest level of roadway density have a 4.3% (95% confidence interval [CI]: –7.5, –1.1) reduction in FEV₁ percent predicted and a 3.8% (95% CI: –6.4, –1.2) reduction in FVC when compared to the lowest tertile 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 2.3% (95% CI: –5.3, 0.6) reduction in FEV₁ percent predicted and a 1.1% (95% CI: –3.7, 1.5) 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, yet non-significant ($p = 0.12$), impact on FVC percent predicted, such

that participants living in the HUCs with highest density of coal haul routes had a 2.1% (95% CI: –4.6, 0.5) reduction in FVC percent predicted relative to the lowest tertile of exposure. Coal haul route density had no detected impact on FEV₁ percent predicted. For all models, variance inflation factor values were below 1.7 with residuals normally distributed and no detected significant outliers.

Sensitivity analyses

We examined the impact of coding HUC roadway density as a continuous variable in adjusted models, finding similar model conclusions as per above-presented categorically coded models. For example, for each one-unit increase in HUC roadway density participants experienced a 0.94% reduction in FEV₁ percent predicted (95% CI: –1.85, –0.03) and a 1.0% reduction in FVC percent predicted (95% CI: –1.7, –0.29). We also examined continuous versions of coal haul routes, current or past mining, and oil/gas well density per HUC in adjusted models, finding no difference in model conclusions versus categorically coded models.

We hypothesized that participants with pre-existing respiratory disease may have differing risk-reduction behaviors than those without, which may impact potential exposure and exposure-outcome relationships. We excluded those with pre-existing self-reported respiratory disease, namely those with asthma, COPD, and/or black lung ($N = 494$), repeating the same adjusted multivariable analyses with robust standard errors as above. We found

Table 3. Environmental exposures versus FEV₁ percent predicted and FVC percent predicted (PP) adjusted^a multivariable models with robust standard errors.

HUC environmental exposure	FEV ₁ PP Estimate (95% confidence interval)	FVC PP Estimate (95% confidence interval)
HUC roadway density (Road miles/HUC mile ²)		
Tertile 1 (0–2.18)	Ref	Ref
Tertile 2 (2.19–2.96)	–2.34 (–5.25, 0.58)	–1.07 (–3.65, 1.50)
Tertile 3 (>2.96)	–4.30 (–7.45, –1.14)*	–3.80 (–6.38, –1.20) ⁺
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)	0.17 (–2.85, 3.20)	–0.33 (–2.92, 2.27)
Tertile 3 (>0.44)	–0.85 (–3.90, 2.21)	–2.05 (–4.60, 0.49) [#]
Adj. R ²	0.13	0.09
HUC oil and gas well density (Total wells/HUC mile ²)		
Tertile 1 (0–0.50)	Ref	Ref
Tertile 2 (0.51–0.83)	0.22 (–2.83, 3.27)	–0.06 (–2.72, 2.61)
Tertile 3 (>0.83)	1.35 (–1.80, 4.50)	0.05 (–2.53, 2.62)
Adj. R ²	0.13	0.09
Active surface mining in HUC (Mining mile ² /HUC mile ²)		
No	Ref	Ref
Yes	1.04 (–1.98, 4.07)	0.26 (–2.31, 2.84)
Adj. R ²	0.13	0.09
Active underground mining in HUC (Mining mile ² /HUC mile ²)		
No	Ref	Ref
Yes	0.86 (–1.72, 3.45)	1.24 (–0.98, 3.48)
Adj. R ²	0.14	0.09
Abandoned surface mining in HUC (Mining mile ² /HUC mile ²)		
Tertile 1 (0)	Ref	Ref
Tertile 2 (>0–0.02)	0.16 (–2.78, 3.09)	0.09 (–2.45, 2.63)
Tertile 3 (>0.02)	–0.18 (–3.28, 2.93)	0.24 (–2.34, 2.82)
Adj. R ²	0.13	0.09
Abandoned underground mining in HUC (Mining mile ² /HUC mile ²)		
Tertile 1 (0–0.068)	Ref	Ref
Tertile 2 (0.069–0.37)	–0.44 (–3.62, 2.75)	0.43 (–2.26, 3.12)
Tertile 3 (>0.38)	0.47 (–2.73, 3.68)	0.82 (–1.82, 3.47)
Adj. R ²	0.13	0.09

^aBase model plus adjustment for the covariates: BMI (underweight/normal versus overweight/obese), physical activity (no/yes in last month), pack years (tertiles, lowest to highest), education (>high school, high school, <high school), mining employment (ever no/yes), and hours at home (median cut-point).

N = 827 for FEV₁ and FVC models.

*p = 0.007; +p = 0.005; #p = 0.12.

little change in model results from this exclusion, as, among those lacking self-reported respiratory disease, 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 FEV₁ 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 FEV₁ 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.

DISCUSSION

This study is the first to report that a ubiquitous source of environmental respiratory exposure, roadways, estimated as the density of roadway miles per HUC square mile, is associated with a reduction in lung function among residents of rural Appalachia Kentucky. Specifically, both FEV₁ and FVC percent predicted values decreased in similar magnitude with increasing levels of HUC roadway density among MAP participants, suggesting roadway exposures in the region may have the potential to impact pre-clinical changes in both restrictive and obstructive lung function patterns. Although roadways have been linked to adverse respiratory health outcomes in urban environments [14, 15, 17, 19, 27], as well as in occupational settings [28], this is the first study to report pre-clinical changes in lung function resulting from roadway-related exposure among residents of rural Appalachia. Rural residents, especially those with asthma or COPD, may experience an increased risk of negative health effects related to vehicle exhaust exposure [20, 29], while higher levels of roadway density within a small area have been linked to an increased prevalence of Asthma among rural Appalachia residents [30]. Thus, our results support the conclusion that a plausible link may exist between vehicle emissions, a surrogate exposure of which may be HUC roadway density, and observed patterns of regional lung health among rural Appalachia residents.

Past epidemiologic studies employing an ecological study design have found that residents of regions with active mining experience a high prevalence of respiratory health issues, such as asthma and COPD [2, 3]. However, we did not find such an association when exposure and personal level risk factors were estimated over a small area and at the individual level, respectively. This difference in findings may be due in part to spatial and temporal variation in mining activity. Coal mining activity and exposures vary in time and space, making the quantification and measurement of these exposures and their impact on respiratory health difficult, especially with a cross-sectional study design. For example, it is possible that current mining permit areas were not actively being mined during our study period, subsequently limiting. Furthermore, coal-mining activity has been declining in the study region in recent years and previously higher levels of residential exposure to mining-related particulates may have subsided to much lower levels during our study period. However, we did not detect a reduction in pulmonary function among participants with past mining activity in their HUC, ultimately suggesting that residential mining exposures may have little measurable impact on respiratory health among our sample of rural Appalachia residents.

Our results highlight the importance of estimating both individual-level exposure and risk factors when examining associations between residential exposures and respiratory health outcomes, as each may co-vary at a small spatial scale within a geographic area. We detected considerable variation in HUC exposure metrics and personal health/risk factors for respiratory disease within two KY counties, noting no effect of current or past mining on respiratory health when controlling for small-scale spatial variation in exposure and individual-level risk factors. Indeed, in a review of studies that define mountain top removal (MTR) mining exposure at the county-level, Boyles et al. [7] found no conclusive evidence for a link between MTR mining and adverse health effects among residents due to potential aggregation bias, exposure misclassification, and uncontrolled confounding. This uncontrolled confounding may be reduced by measuring individual factors that may co-vary with environmental exposures, such as socioeconomic status [31] and BMI [32].

HUC coal haul route density may be associated with reduced pulmonary function among residents of rural Appalachia. 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 density HUCs. Furthermore,

this relationship was intensified when those with self-reported asthma, COPD, and black lung were removed for multivariable analyses, suggesting this at-risk group may attenuate the modeled exposure-outcome relationship, perhaps via differing behaviors from those without respiratory diseases, such as the avoidance of perceived environmental respiratory exposures or asthma triggers. However, these results should be interpreted carefully, as coal haul routes are often major roadways, and separating the effect of coal truck exposure from that of residential vehicles (i.e., HUC coal haul density versus roadway density) is not possible in our analyses. In fact, researcher conducted vehicle counts on major roadways into and out of regional population centers suggest state roads and highways often carry both passenger and transportation trucks, many of which are coal hauling trucks. 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.

Strengths and limitations

Our study is the first to examine small-area geographic variation in environmental exposures versus pulmonary function measures among residents of rural Appalachia, while controlling for individual-level health factors. Our geographic exposure classification method estimates HUC-level respiratory exposures found in the tight valleys, or hollows, in which residents live and spend much of their time (e.g., participants spent an average of 19.7 h at home per day). This method is especially beneficial for this mountainous region where exposures may be highly variable among the narrow valleys (hollows). In this topology, air flow patterns and particulate concentrations that may follow the mountain valleys leading to greater exposures for some residences. We also adjusted for individual-level risk factors, thereby controlling for confounders that may affect pulmonary function and may 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 estimated while controlling for potential individual-level confounders. This yields more accurate exposure classification and reduced potential confounding in comparison to previous ecological studies that found adverse associations between coal mining exposures and residential respiratory health.

Spatial and temporal variation in particulate emission patterns may have influenced our ability to detect an association between environmental exposures and respiratory health. For example, while areas with active mining permits and designated coal haul roads may change over time, major roadways are likely to provide more uniform exposures to particulates over time. Thus, we may have been more likely to detect an association between pulmonary function and roadway density than to observe an association with exposures from mining activity. In fact, many of the population centers of the region are found in HUCs with higher levels of roadway density, yet low densities of active or abandoned mines. It is also possible that, by chance, our sampling methods (i.e., random sampling of all HUCs in Harlan and Letcher counties) may have missed residents in HUCs with higher levels of resource extraction exposure, such as mining or oil and gas well density. Finally, our method of exposure classification for roadways, density of roads per square mile, may also lead to potential misclassification, as roadways may vary in vehicle type and usage patterns in time and space, such that particulate exposure patterns may differ among similar levels of HUC roadway density.

Summary

Among residents of rural Appalachia Kentucky, we found that living in an HUC with a high level of roadway density was associated with a reduction in both FEV₁ and FVC percent predicted. Similar reductions in lung function may result from living in an HUC with a high density of coal haul routes. Counter to

past epidemiologic studies using an ecological study design, we found no associations between active or inactive mining and measures of pulmonary function. As the confines and airflow patterns of hollows may serve to concentrate vehicle exhausts, roadway-related exposures in regions of rural Appalachia may be prevalent and potentially harmful to residents' health. Improved exposure assessment studies and cohorts with repeated measures of pulmonary function could be employed to better understand the relationship between common environmental exposures and respiratory health among residents of rural mountainous Appalachia. Future work examining vehicle density on roadways, vehicle composition, as well as exhaust particle constituents may help to better elucidate the relationship between roadways and adverse respiratory health outcomes.

DATA AVAILABILITY

The datasets used during the current study are available from the corresponding author upon reasonable request.

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ACKNOWLEDGEMENTS

We gratefully acknowledge the leadership and contributions of Nancy Schoenberg, PhD, as a co-investigator of the study, Beverly May, DrPH, and Nell Fields of the Mountain Air Project staff, and the contributions of the Mountain Air Project Community Advisory Board. Susan Westneat, MA, provided data management and statistical and analytic support on the study. We recognize the editorial and technical support of Steve Claas of the Office of Scientific Writing at the University of Kentucky. We also acknowledge the tireless efforts of the community health workers including

Darlene Warf, Betty Keith, Denise Baird, Libby Honeycutt, and Penny Lee who recruited participants and administered surveys and spirometry tests. Finally, we acknowledge the time and efforts of the participants in the Mountain Air Project and are grateful for their participation.

AUTHOR CONTRIBUTIONS

JCF conducted the environmental field survey for exposure evaluation, created databases, analyzed and interpreted data, and was the lead author on this paper. WTS was involved in study design and data collection, editing, analyzing, and interpreting data, and editing the manuscript. WJC was involved in study design, data analysis and interpretation, and editing the manuscript. DMM was involved in study design, evaluation of pulmonary spirometry, interpreting data analysis, and editing the manuscript. SRB was the overall principal investigator of the study and was the lead in study design, data collection, and writing editing the manuscript.

FUNDING

The authors received support for this work from three federal grants: NIEHS R01 ES024771; NIEHS P30 ES026529; and CDC/NIOSH T42 OH010278 This work was supported by NIEHS R01ES024771-01, CDC/NIOSH T42OH010278, and NIH/NIEHS T32ES015459.

COMPETING INTERESTS

The authors report no competing interests.

ETHICAL APPROVAL

The protocol, study procedures, and consent forms were approved by the Institutional Review Board of the University of Kentucky, Lexington, Kentucky (UK IRB number 48792). Written informed consent was obtained from all participants.

ADDITIONAL INFORMATION

Supplementary information The online version contains supplementary material available at <https://doi.org/10.1038/s41370-023-00584-4>.

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