Environment International 130 (2019) 104911

Contents lists available at ScienceDirect

Environment International

journal homepage: www.elsevier.com/locate/envint

Residential proximity to concentrated animal feeding operations and allergic and respiratory disease

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ARTICLE INFO

Handling Editor: Olga-Ioanna Kalantzi

Keywords:
Air pollution
Concentrated animal feeding operation
Lung function
Allergies
Asthma

ABSTRACT

Background: Air emissions from concentrated animal feeding operations (CAFO) have been associated with respiratory and allergic symptoms among farm workers, primarily on swine farms. Despite the increasing prevalence of CAFOs, few studies have assessed respiratory health implications among residents living near CAFOs and few have looked at the health impacts of dairy CAFOs.

Objectives: The goal of this study was to examine objective and subjective measures of respiratory and allergic health among rural residents living near dairy CAFOs in a general population living in the Upper Midwest of the United States.

Methods: Data were from the 2008–2016 Survey of the Health of Wisconsin (SHOW) cohort ($n = 5338$), a representative, population based sample of rural adults (age 18+). The association between distance to the nearest CAFO and the prevalence of self-reported physician-diagnosed allergies, asthma, episodes of asthma in the last 12 months, and asthma medication use was examined using logistic regression, adjusting for covariates and sampling design. Similarly, the association between distance to the nearest CAFO and lung function, measured using spirometry, was examined using multivariate linear regression. Restricted cubic splines accounted for nonlinear relationships between distance to the nearest CAFO and the aforementioned outcomes.

Results: Living 1.5 miles from a CAFO was associated with increased odds of self-reported nasal allergies (OR = 2.08; 95% CI: 1.38, 3.14), lung allergies (OR = 2.72; 95% CI: 1.59, 4.66), asthma (OR = 2.67; 95% CI: 1.39, 5.13), asthma medication (OR = 3.31; 95% CI: 1.65 6.62), and uncontrolled asthma, reported as an asthma episode in last 12 months (OR = 2.34; 95% CI: 1.11, 4.92) when compared to living 5 miles from a CAFO. Predicted FEV1 was 7.72% (95% CI: −14.63, −0.81) lower at a residential distance 1.5 miles from a CAFO when compared with a residence distance of 3 miles from a CAFO.

Conclusions: Results suggest CAFOs may be an important source of adverse air quality associated with reduced respiratory and allergic health among rural residents living in close proximity to a CAFO.

1. Introduction

Over the last several decades, large livestock farms, including concentrated animal feeding operations (CAFOs), have increasingly replaced small farms across the globe. The change in normative agricultural practices from smaller farms to large-scale farming productions, while more efficient for meat production, may also increase risk of adverse respiratory health or other outcomes among communities living in rural communities. CAFOs increase both the quantity and concentration of airborne particulates, gases, and vapors associated with farming (Schiffman et al., 2001). More than 400 compounds have been found in and around CAFO facilities, including volatile organic compounds (VOCs), endotoxins, ammonia, and hydrogen sulfide (Schiffman et al., 2001). While respiratory health effects among CAFO farm workers are well documented (Douglas et al., 2018; Kirkhorn and Garry, 2000; Radon, 2006), less is known about the extent to which CAFO air emissions affect the health of nearby residents.

Beyond increasing air emissions, potential for increased exposure to emerging antibiotic resistance microorganisms and outbreaks of zoonotic viral and bacterial pathogens have drawn attention to potential health risks among residents living near CAFOs (Gilchrist et al., 2007; Li et al., 2015; Rogers and Haines, 2005). Several agents, such as ammonia, hydrogen sulfide, endotoxins, and viral and bacterial pathogens from animal manure can be absorbed by dust particles and stay

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Abbreviations: OR, Odds ratio; CI, Confidence interval; FEV1, Forced expiratory volume in one second

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https://doi.org/10.1016/j.envint.2019.104911
Received 28 September 2018; Received in revised form 7 June 2019; Accepted 8 June 2019

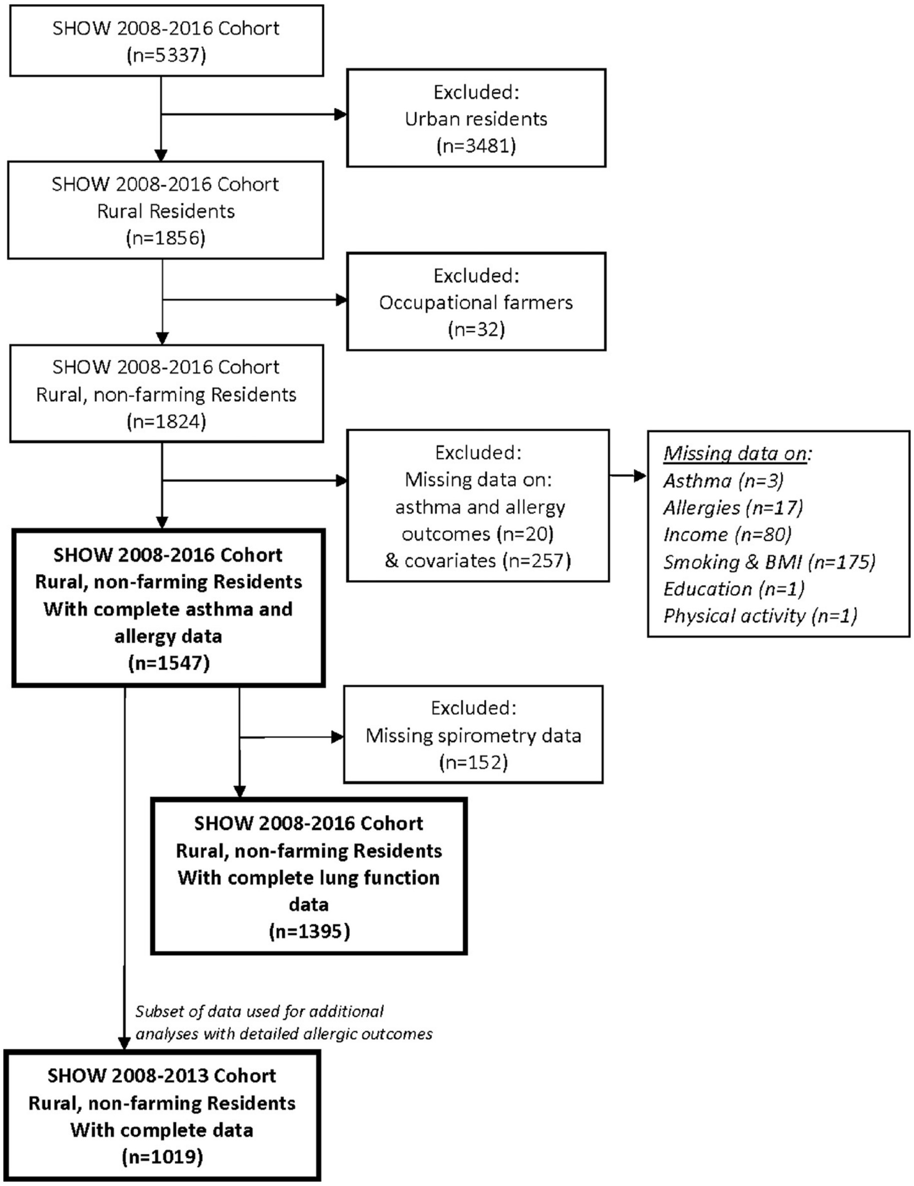

Fig. 1. Flow chart of the study sample, depicting exclusion criteria and sample size.

airborne for long periods and travel several miles, potentially exposing nearby residents to elevated levels of livestock-related agents (Cole et al., 2000; Omland, 2002; Dungan, 2010).

Three studies in the United States (U.S.) found the prevalence of asthma to be higher among children and adolescents attending schools (Mirabelli et al., 2006; Sigurdarson and Kline, 2006), and living (Pavilonis et al., 2013), near swine CAFOs. Studies among adults have found more mixed results. Two ecological studies among adults in the Netherlands (Hooiveld et al., 2016) and Greece (Michalopoulos et al., 2016) found null results when assessing residential proximity to livestock farms with allergy and asthma outcomes. Yet, an ecological study in North Carolina, U.S. found the prevalence of wheezing to be higher among adults living near swine CAFOs (Wing and Wolf, 2000). Two studies in rural Germany found the number of animal houses near a residence and measured ammonia levels to be associated with decreased lung function in adults (Radon et al., 2007a; Schulze et al., 2011). However, only measured ammonia levels were associated with sensitization of allergies (Schulze et al., 2011).

Three Netherlands studies found mixed results using general practice electronic medical records (EMR) to identify cases and controls of asthma and allergies. Inverse associations were found between distance to the nearest farm and asthma, allergies, and COPD (Borlée et al., 2015; Smit et al., 2014) and negative associations between the numbers of livestock farms within 1000 m of residence and lung function (Borlée et al., 2017). Yet living within 1000 m of > 11 farms had increased odds of wheezing and COPD (Borlée et al., 2015), and measured ammonia was associated with decreased lung function (Borlée et al., 2017). The only adult study in the U.S. to use EMR found living near a CAFO was associated with increased odds of asthma medication use and asthma-related hospitalizations (Rasmussen et al., 2017).

Several of the aforementioned studies (Sigurdarson and Kline, 2006; Wing and Wolf, 2000; Michalopoulos et al., 2016) consisted of people living near 2–3 identified livestock operations, small regions consisting of a few rural towns in Germany (Radon et al., 2007a; Schulze et al., 2011) or a rural county in the U.S. (Pavilonis et al., 2013). While studies in the Netherlands (Borlée et al., 2015, 2017; Smit et al., 2014) have used population-based study samples using electronic medical records from general practices, only one study in the United States has attempted to done so by using asthma hospitalization, emergency, and medication data from Geisinger Clinic in Pennsylvania (Rasmussen et al., 2017). Generating generalizable results from clinic data in the United States can be challenging as those who do not seek medical care due to inconvenience, cost, or lack of insurance go unreported.

The number of studies on the effect of CAFO air emissions exposure on respiratory health among nearby residents is limited and results are inconsistent. Furthermore, many prior studies have grouped exposure to CAFOs, removing individually variability. This study advances understanding of public health implications of CAFOS by using cubic spline regression to examine the association between residential proximity to CAFOs and respiratory health effects in order to account for non-linearity and retain individual levels of exposure. This study uses a well-characterized, rural sample of Wisconsin residents. Wisconsin ranks second after California as the state with the largest number of dairy cows (USDA, 2017); over 90% of its CAFOs being dairy CAFOs (WDNR, 2016). To our knowledge, no studies to date have looked at respiratory effects among residents living near dairy CAFOs.

2. Materials and methods

2.1. Study sample

Data came from the 2008–2016 Survey of the Health of Wisconsin (SHOW) state-wide sample of adults ages 18 and older ($n = 5338$). SHOW participants are randomly selected using a probability sampling proportion to size with replacement (PPSWR) approach (Nieto and Peppard, 2010). Between 2008 and 2013, a two-stage probability-based cluster sampling was used to randomly select census block groups (stage 1) and household addresses (stage 2) annually within strata of region and poverty level (Nieto and Peppard, 2010). SHOW 2014–2016 cohort was designed as a three-year sample instead of an annual sample as in prior years. A three stage cluster-sampling approach was employed. One county per strata was randomly selected within strata of county mortality rates, followed by random selection of census block groups by poverty status strata. Then 30–35 residential households were randomly selected via US postal service listings.

SHOW recruits 400–1000 participants every year. Across all years of the study, on average 67% of individuals who screen eligible complete each study component (interview and exam). However, participation rates vary from 47% in some urban communities to > 80% in some rural communities.

Fig. 1 describes the analytic sample selected for this study which includes a subset of 1856 (35%) rural participants among the 5338 SHOW subjects. Participants were considered rural if their residence was located in rural census block group defined by the U.S. Census Bureau as having fewer than 2500 people (U.S. Census Bureau, 2015). Additionally, 32 subjects who reported farming as their current occupation were excluded due to increased likelihood of occupational contact with livestock. While livestock contact could be assessed as a surrogate of a higher level of exposure to CAFOs, the number of individuals with occupational exposure was too small to examine this sub-population separately. Since those with livestock contact may or may not live near a CAFO, they were excluded to reduce confounding. Subjects with missing data on any of the respiratory outcomes or confounders of interest were also excluded from analyses, resulting in a final sample size of 1547 for asthma and allergy outcomes, and 1395 for objectively measured lung function outcomes. Detailed allergy data was only collected for 2008–2013 SHOW cohort, resulting in $n = 1019$ for detailed allergy analyses. All residential household addresses were geocoded using CENTRUS software (Pitney Bowes Inc., Stamford, CT) and linked to the nearest CAFO using ArcGIS v10.3 software (ESRI, Redlands, CA).

2.2. Concentrated animal feeding operations (CAFOs)

Data on CAFO location, type (dairy cow, hog, chicken, or turkey), years of operation and total animal units are maintained by the Wisconsin Department of Natural Resources' (WDNR) and Department of Agriculture, Trade and Consumer Protection (DATCP) under the Wisconsin Pollutant Discharge Elimination System (WPDES) program. WPDES falls under the Clean Water Act (CWA) National Pollutant Discharge Elimination System (NPDES) which requires states to regulate point source pollution to waters of the entire United States. CAFOs are defined by the CWA [Section 502(14)] as point sources, thus requiring a discharge permit and monitoring by WPDES.

CAFOs are defined as an animal feeding operation (AFO) where the following conditions are met: 1) animals are confined for a total of 45 days or more in any 12-month period and 2) animals do not have access to crops, vegetation or forage growth in the normal growing season. AFOs that have 1000 or more animal units (1 animal unit = 1000 pounds of live animal weight) are considered a large CAFO (1000+ cattle, 700+ dairy cows, 2500+ swine, 55,000+ turkeys). Medium CAFOs (300–999 cattle, 200–699 dairy cows, 750–2499 swine, 16,500–54,999) are additionally regulated under WPDES if the facility has a manmade ditch or pipe that carries manure or wastewater to surface water or if the animals come into contact with surface water that passes through the area where they are confined (40 CFR § 122.23 (b), 2012).

According to publicly available data downloaded from WDNR WPDES program there were a total of 284 CAFOs operating in Wisconsin in 2016. Ninety percent (244 large, 2 medium) were dairy CAFOs, followed by swine (5 large, 9 medium), beef (10 large, 3 medium), poultry (1 medium, 10 small). Publicly available data were limited, therefore additional data including the location, start date, and end date of all permitted CAFOs established between 2007 and 2015 was obtained via an open records request to the Wisconsin DATCP. The DATCP data was used to ensure CAFOs were in existence during SHOW participants' year of participation in the study (when residential address and health data were collected). Supplementary Fig. 1 from the WDNR shows the proportion of CAFOs by animal type has remained stable over the last decade, with over 90% of the CAFOs in Wisconsin being dairy.

Residential proximity to the nearest CAFO was used as a proxy to estimate potential exposure to air emissions from CAFOs. Distance from a participant's residence to the nearest CAFO was calculated using the "Near" tool in ArcGIS (ESRI, Redlands, CA). Participants were linked by cohort year to the nearest CAFO, only including CAFOs that were in existence during both the year they participated AND the year prior.

2.3. Allergy, asthma, and lung function

Self-report history of respiratory allergies and asthma was collected during in-home interviews. Current allergies were defined as having reported "yes" to the survey question "Do you still have allergies or hay fever?" as a follow-up to the question "Has a doctor or other health professional ever told you that you had allergies or hay fever?" Allergy type was defined based on response to the question "Where do allergy symptoms occur?" For this analysis individual with nasal, sinus, lung, eye, and skin as sites of allergies most likely to be triggered by CAFO air emissions were included. Those reporting digestion, food, or insect allergies were unlikely to be related to proximity to CAFOs and were defined as not having respiratory allergies.

Participants were defined as having current asthma if they responded yes to the survey question "Do you still have asthma?" which is a follow-up to the question "Has a doctor or other health professional ever told you that you had asthma?" Those who report having current asthma are also asked "During the last 12 months, have you had an episode of asthma or an asthma attack?" and if they have taken prescription medication to prevent or stop asthma attacks within the last 30 days.

Forced expiratory volume in 1 s (FEV1) and forced vital capacity (FVC) were measured via spirometry using an electronic peak flow meter (Jaeger AM, Yorba Linda, CA), and validated protocol (Richter et al., 1998). Trained technicians gave study participants explicit directions on how to breathe into the spirometry device. Measurements were considered valid if two FEV1 and FVC readings were within 10% of the highest value measured. FEV1 to FVC ratio (Tiffeneau index) and percent predicted FEV1 (FEV1 divided by predicted FEV1) were also assessed to account for inter-individual variability in lung function measurement. Predicted FEV1 was calculated using sex, race, age, and height as defined by the NHANES general U.S. population (Hankinson et al., 1999).

2.4. Covariates and confounding

Self-reported demographic data including age (years), gender (male vs. female), education (high school or less, some college, and bachelor's degree or higher) and household income were gathered via personal interviews. Poverty to income ratios were calculated using U.S. Department of Health and Human Services poverty guidelines and the midpoint of the household income range identified by the participant. Body mass index (BMI) was calculated from measured weight and height as kg/m^2. Physical activity was defined as Metabolic Equivalent of Task (MET)-minutes/week of moderate or vigorous activity using self-report data from a modified International Physical Activity Questionnaire - IPAQ (Craig et al., 2003). Income, BMI and MET-minutes/week were used as continuous variables in all statistical models, but log transformed to adjust for skewness. Additional self-reported questionnaire items assessed as potential confounders include: home smoking policy, household pets, smell of mildew or mold inside, and the use of any pesticides inside the home in the last 12 months. Sensitivity analyses were also run to test for potential confounding by previously identified environmental sources of allergies and respiratory health in the population (Schultz et al., 2017) residential proximity to the nearest primary or secondary roadway and industry were also examined.

2.5. Statistical analysis

Restricted cubic splines functions were applied to the residential distance in order to account for nonlinear relationships between distance to the nearest CAFO and respiratory health. Knots were placed at the minimum, maximum, and 25th, 50th, 75th percentiles of the distance variable (0.24, 6.17, 9.07, 17.9, 69.9 miles). Univariate as well adjusted multiple linear (lung function outcomes) and logistic (allergic and asthma outcomes) regression models were used to examine associations between residential proximity to a CAFO and respiratory health. Potential confounders selected a priori from the literature. Covariates that did not change the main effect estimate by > 10% were excluded from the multivariate models. An adjusted odds ratio (OR) or an adjusted beta-coefficient value with two-sided p-value < 0.05 was regarded as statistically significant. To acquire estimates from the spline regression, comparisons were made between different residential distances, while holding confounders constant. Residential distances of interest were chosen a priori from literature estimating air pollution and distance from CAFOs (Schinasi et al., 2011; Williams et al., 2011; Wilson and Serre, 2007; Wing et al., 2013; Michalopoulos et al., 2016), and from univariate spline regression trends between distance to nearest CAFO and each outcome. SAS version 9.4 (SAS Institute Inc. Cary, NC) was used for all statistical analyses. All adjusted analyses included sampling weights to account for sampling design, response rates and spatial clustering.

3. Results

Descriptive characteristics of the study population by residential proximity to the nearest CAFO are presented in Table 1. The majority of the study population (72%) lived > 5 miles from a CAFO, 4% (n = 65) lived < 1.5 miles of a CAFO and 23% (n = 361) lived 1.5–5 miles from a CAFO. Those living near a CAFO (< 1.5 miles) were more likely to be males, never-smokers, younger, less educated and diagnosed with asthma when compared with those living middle-distance (1.5–5 miles) and far (> 5 miles) from a CAFO. Those living near a CAFO were also less likely to live near a major roadway and have allergies when compared to the populations living middle-distance and far from a CAFO (Table 1). Unadjusted cubic spline plots revealed the log odds of asthma and allergy outcomes decreased, and lung function increased, as distance from a CAFO increased, leveling off at around 5 miles (Supplementary Fig. 2). Therefore, results include comparisons between distances of 1–3 miles compared with 5 miles from a CAFO.

Close residential proximity to a CAFO (living within 1–3 miles) remained positively associated with reporting any allergy symptoms even after controlling for gender, age, BMI, smoking status, education, income, pet ownership (Fig. 2). Mold in the home, smoking policy in the home, indoor chemical use, and residential proximity to an industrial site and roadway did not change the main effects and were not included in final models. Odds of allergies was > 2-fold when comparing living 1 and 1.5 miles from a CAFO to 5 miles from a CAFO (OR = 2.55; 95% CI: 1.49, 4.36 and OR = 2.02; 95% CI: 1.33, 3.08) and decreased as distance from a CAFO increased. Similar associations were seen among those with nasal- and lung-specific allergies, with the strongest associations seen with lung allergies. The adjusted odds of lung allergies was consistently > 2-fold higher among those living 1–3 miles from a CAFO when compared to those living 5 miles from a CAFO. Supplementary Tables 1 and 2 show results of all distance comparisons made for the previously mentioned allergy outcomes, along with current allergies assessed with the entire 2008–2016 cohort. While results indicate residential proximity is associated with eye and dermal allergies, none of the results were statistically significant (Supplemental Table 2).

Residential proximity to a CAFO was similarly associated with asthma and asthma control measures, including one or more asthma attacks in the last 12 months or taking asthma medication. Reporting current asthma was consistently about 1.8–1.9 times greater among those living 1–3 miles versus 5 miles from a CAFO (Fig. 3). The odds of ever being diagnosed with asthma was 3.11 (95% CI: 1.49, 4.36) and 2.67 (95% CI: 1.33, 3.08) when comparing 1 and 1.5 miles from a CAFO to 5 miles from a CAFO. Similar to the associations seen with current and nasal-specific allergies, the odds of doctor diagnosed asthma and asthma medication use decreased as distance from a CAFO increased. Those living 1, 1.5, 2, 2.5 miles from a CAFO, asthma medication was 4, 3, 2.5, and 2 times greater, respectively, when compared to those living 5 miles from a CAFO; all associations statistically significant. Odds of an asthma attack were consistently 2-fold higher at 1–3 miles versus 5 miles from a CAFO, with the odds being 2.34 (95% CI: 1.11, 4.92) times higher at 1.5 miles versus 5 miles from a CAFO.

Among the SHOW 2008–2013 cohort, the odds of reporting both allergies of nose or lungs and current asthma was 2.67 (95% CI: 0.97, 6.38) times greater and 2.14 times greater among those living 1 and 1.5 miles from a CAFO when compared to those living 5 miles from a CAFO (Fig. 2). Associations were lower at 2 and 2.5 miles but increased again to 2.74 (95% CI: 1.43, 5.23) when comparing 3 miles to 5 miles from a CAFO. This finding suggests that those in this study population with the presence of asthma or allergies may have allergic asthma. Results of all distance comparisons made with the aforementioned asthma outcomes can be seen in Supplementary Table 3. Similar directional associations are seen when distances of 1–3 miles are compared with 3, 4, and 6 miles as a reference value instead of 5 miles.

FEV1 percent predicted and FEV1/FVC were significantly lower among individuals living 1–3 miles from a CAFO when compared to those living5 miles from CAFO (Fig. 3).While not statistically significant, Fig. 4 shows FEV1 percent predicted was 11.31 L/s (95% CI: 0.51, 23.14) lower at 1 mile, and 7.00 L/s (95% CI: 2.26, 16.26) lower at 1.5 miles, when compared with 5 miles from a CAFO. The difference in FEV1 percent predicted decreased at 2 and 2.5 miles versus 5 miles until it reached 0 when comparing 3 miles versus 5 miles from a CAFO. FEV1/FVC was 0.039 (95% CI: 0.008, 0.07) lower at 1 mile, and 0.027

Table 1
Characteristics of the study population.

	Residential distance from nearest CAFO				
	Total study sample (*n* = 1547)	≤ 1.5 miles 2.4 km (*n* = 65)	1.5–5 miles 2.4–8 km (*n* = 361)	≥ 5 miles 8 km (*n* = 1121)	
	N	%	%	%	p-trend
Gender					0.82
Male	682	47.7	44.3	43.8	
Female	865	52.3	55.7	56.2	
Age (in years)					0.48
18–39	320	23.1	18.8	21.1	
40–59	711	44.6	50.1	44.7	
60–94	516	32.3	31.0	34.2	
Race					0.12
White (non-Hispanic)	485	98.5	93.9	92.3	
Non-white	42	1.5	6.1	7.7	
Education					0.67
H.S./GED or less	475	38.5	31.0	30.2	
Some college	606	36.9	38.2	39.6	
Bachelors or higher	466	24.6	30.7	30.2	
Income					0.0001
< $25,000	246	6.2	11.6	17.8	
$25,000–$49,999	401	43.1	23.8	25.6	
$50,000–$99,999	590	35.4	45.7	35.9	
> $99,999	310	15.4	18.8	20.7	
Smoking status					0.84
Current	247	13.8	15.0	16.4	
Former	488	27.7	32.1	31.6	
Never	812	58.5	52.9	52.0	0.39
BMI					
< 25	381	20.0	28.0	23.8	
25–30	501	38.5	29.9	32.8	
> 30	665	41.5	42.1	43.4	
Physical activity					
< 600 met min/wk	392	24.6	27.7	24.6	0.50
≥600 met min/wk	1155	75.4	72.3	75.4	
Proximity to major roadway					0.02
< 300 m	493	20.0	28.5	33.6	
≥300 m	1054	80.0	71.5	66.4	

CAFO: concentrated animal feeding operation; km: kilometer; N: number; H.S.: high school; GED: General Education Development test; BMI: body mass index; wk.: week
p-trend: statistical significance by Chi-square test.

(95% CI: 0.003, 0.051) lower at 1.5 miles, when compared with 5 miles from a CAFO. Results of all distance comparisons, including FEV1 and FVC outcomes, can be found in Supplementary Table 4.

4. Discussion

These findings add to the emerging body of literature regarding public health impacts of concentrated animal feeding operations among rural populations. Much of the existing research has been conducted in Europe. This one of the first studies to examine how rural respiratory health is potentially influenced by farming practices in a general population based sample of adults in the United States. Among this well-characterized population-based sample, household proximity to a CAFO was associated with numerous respiratory outcomes including increased odds of self-reported allergies and asthma, and decreased lung function.

The use of cubic splines to explore nonlinear relationships between proximity to a CAFO and respiratory health outcomes was a strength of this study. Associations between residential proximity within 3 miles of a CAFO and increased prevalence of allergies, asthma, and decreased lung function were observed. Each of the respiratory outcomes followed a similar nonlinear relationship with distance from CAFOs and a 5 mile reference cut point was determined based on visual plots of the cubic spline functions of distance to the nearest CAFO regressed by each respiratory outcome separately. The non-linearity relationship seen in respiratory outcomes is not surprising as levels of constituents from air emissions from point sources (i.e. airports, roadways, industries, livestock facilities) tend follow a similar exponential decay as distances from the sources increase (Batterman et al., 2014; Dungan, 2010; Hadlocon et al., 2015; Maantay et al., 2009; Moreira et al., 2005; O'Shaughnessy and Altmaier, 2011; Polidori et al., 2010; Zhou and Levy, 2007).

Study findings are consistent with, and add strength to other U.S.-based studies of asthma and allergy symptoms among people living near AFOs or CAFOs. Pavilonis et al. (2013) found cumulative exposure to AFOs < 3 miles from residence was associated with an increased odds of asthma (1.51 $p = 0.014$) and asthma medication or wheeze (1.38 $p = 0.023$) among school age children. Similarly, Rasmussen et al. (2017) found adult asthmatics recruited from a clinic based sample and living within 3 miles of a CAFO compared > 3 miles had increased odds of ordering asthma medications (OR = 1.11 (95% CI: 1.04, 1.19)) and asthma hospitalizations (OR = 1.29; 95% CI: 1.15, 1.46). The smaller farm sizes may have contributed to the smaller effect sizes seen in Pavilonis et al. (2013) study. Not to mention, diagnosis of pediatric asthma is based on symptoms, which vary throughout a child's life, and also day to day (Asher et al., 2012; Jacob et al., 2017; Yang et al., 2017). The focus on hospitalizations and emergency department visits (Rasmussen et al., 2017) may have underestimated asthma events by excluding those who live near CAFOs but do not seek medical care due to being uninsured, financially insecure, or far from services.

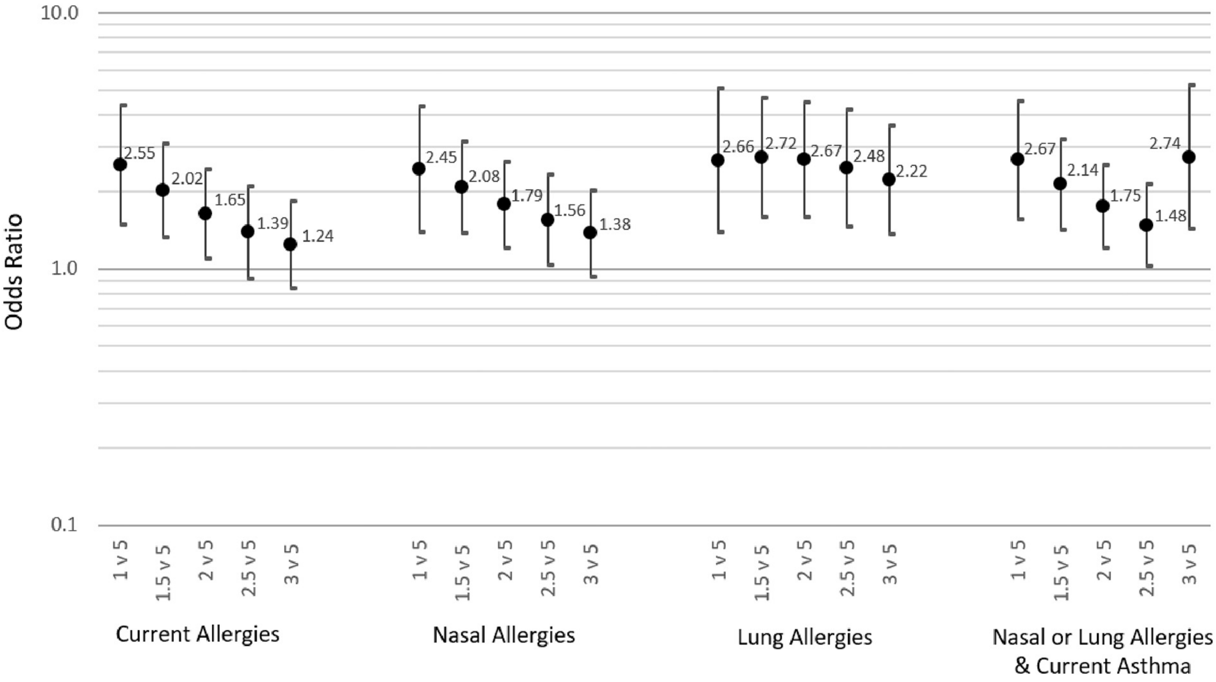

Fig. 2. Results of logistic regression assessing allergic outcomes by restricted cubic spline of residential distance to the nearest CAFO. Residential distances of 1, 1.5, 2, 2.5 and 3 miles (1.6, 2.4, 3.4, 4.0, 4.8 km) from a CAFO were compared with a residential distances of 5 miles (8.0 km) from a CAFO. Models are adjusted for gender, age, poverty to income ratio, education, BMI, smoking status, pet ownership and proximity to major roadways.

Results showed stronger associations with doctor diagnosed asthma than with current asthma. Discrepancies could be due to several factors, including a lack of clarity regarding the survey question assessing current asthma. Cross-tab frequencies on current asthma and asthma medication in the last 12 months revealed several participants reported not having current asthma because it is under control from taking asthma medication. Discrepancies between current asthma and doctor diagnosed asthma are not uncommon and can be due to several other factors including misdiagnosis, remission and relapse of asthma (Aaron et al., 2017).

Current allergies of any type and nasal allergies were 2.5 times higher at 1 mile from a CAFO, and decreased to 1.3 times higher at 3 miles from a CAFO when compared to 5 miles from a CAFO. Lung allergies remained 2.2–2.6 times higher at distances 1–3 miles from a CAFO when compared to 5 miles. The ability to assess allergy by type is a unique contribution, and something few studies have been able to do. Our study confirms findings from a few U.S. studies that have looked at proximity to CAFOs and allergies or allergy-like symptoms. Wing and Wolf (2000) found those living within 2 miles of a CAFO had increased prevalence of running nose, coughing, headache, itchy eyes, running nose, and sore throat. Mirabelli et al. (2006) found stronger associations with adolescents attending schools within 3 miles of a CAFO and asthma when stratified by those with allergies.

Findings in the U.S, are largely in contrast to those found in Europe,

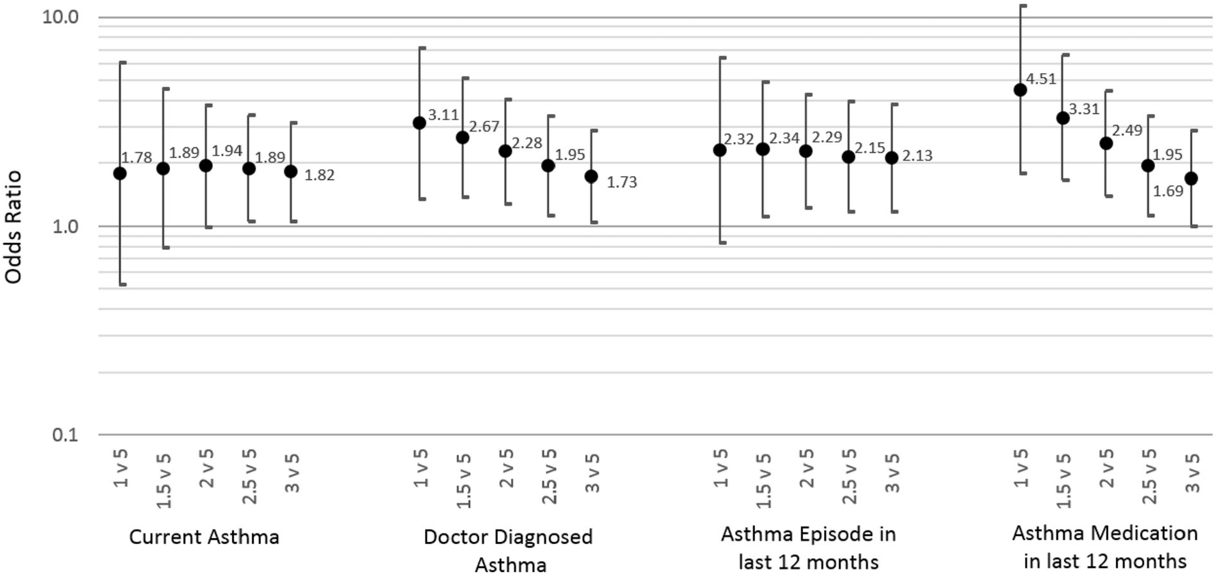

Fig. 3. Results of logistic regression assessing asthmatic outcomes by restricted cubic spline of residential distance to the nearest CAFO. Residential distances of 1, 1.5, 2, 2.5 and 3 miles (1.6, 2.4, 3.4, 4.0, 4.8 km) from a CAFO were compared with a residential distances of 5 miles (8.0 km) from a CAFO. Models are adjusted for gender, age, poverty to income ratio, education, BMI, smoking status, pet ownership and proximity to major roadways.

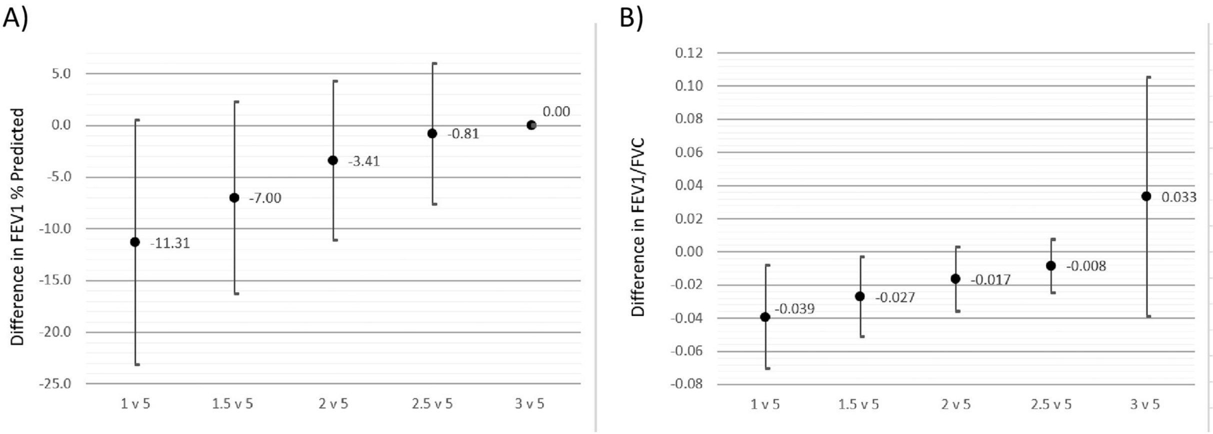

Fig. 4. Results of linear regression assessing (A) FEV1% predicted and (B) FEV1/FVC ratio by restricted cubic spline of residential distance to the nearest CAFO. Residential distances of 1, 1.5, 2, 2.5 and 3 miles (1.6, 2.4, 3.4, 4.0, 4.8 km) from a CAFO were compared with a residential distances of 5 miles (8.0 km) from a CAFO. Models are adjusted for gender, age, poverty to income ratio, education, BMI, smoking status, pet ownership, height, and physical activity.

particularly in Germany and Netherlands, where proximity cut points are typically at 500 m (0.31 miles) or 1000 m (0.62 miles). Several factors may contribute to this. For example, European confined livestock farms are generally smaller than in the U.S., densely clustered, and located in areas of higher population density. Thus, shorter distance cut points and livestock farm counts within 500 or 1000 m are more appropriate. Borlée et al. (2015, 2017) is one of the few studies to assess nonlinear associations using cubic splines of CAFO proximity and nasal allergies, finding inverse results to those seen in this study. Borlée et al. (2015) and Smit et al. (2014) both found inverse associations with doctor diagnosed asthma and allergies using EMR data in the Netherlands. Hooiveld et al. (2016), another Netherlands study which used EMR data found null results, but did not use individually measured exposure data as seen in the other two Netherlands studies. (Radon et al., 2007a) found self-reported asthma and nasal allergies were associated with increased livestock farm odor in Germany, but the number of animal houses near the home was not a predictor of allergies or specific sensitization. (Schulze et al., 2011) is one of the few European studies to find those exposed to higher ammonia levels from livestock farms to be 4.2 times more likely to be sensitized against ubiquitous allergens.

Findings from European studies largely suggest livestock farms provide a protective effect, if any, and support the hygiene hypothesis, specifically with allergy endpoints. The most comprehensive studies dedicated to disentangling the various factors of the protection against allergy provided by farming, such as ALEX, GABRIEL Advanced Surveys, and PASTURE, have been performed in European regions where dairy production is the main activity and where farming is not industrialized; (Alfvén et al., 2006; Genuneit et al., 2011; Riedler et al., 2001) rather in mid-mountain-altitude and among small cheese farms in areas like the Alps (Lis et al., 2008; Roque et al., 2016). In the ALEX and GABRIEL studies, the overall farm effect has been explained by specific and diverse exposure to types of livestock, crops, straw, fodder storage, manure, and unpasteurized milk (Vuitton et al., 2014; Vuitton and Dalphin, 2017). However, the industrialization of farming is thought to have decreased the microbial diversity and increased the abundance of specific bacterial genera which may induce inflammatory response (Kong et al., 2012; Powers et al., 2015; Schaeffer et al., 2017). This is further supported by studies showing household dust and the nasal microbiota from farm children to have higher alpha and beta diversity than those found from nonfarm children, and lower nasal microbiota diversity to be associated with asthma prevalence (Depner et al., 2015; Pekkanen et al., 2018).

However, protective or null effects have also been seen among adults living near non-traditional, industrialized confined livestock operations in Europe, which are generally smaller in size than CAFOs seen in the United States. (Borlée et al., 2015, 2017; Hooiveld et al., 2016; Radon et al., 2007b; Smit et al., 2014; Michalopoulos et al., 2016) This suggests that the dose of exposure to microbes, in combination with particulate matter, gases, and vapors emitted from livestock operations, may also play a role in the respiratory health effects seen among nearby residents. While it appears both the dose and type of exposure to microbial agents from livestock farms may be of importance, additional research is needed with attempts to identify etiological agents from livestock agents. Differences in the size and management practices of the livestock farms themselves, the microbial diversity emitted, the regulations imposed on them or the populations living near them are all factors which may have contributed to the different results seen in the European studies when compared to the U.S.

Discrepancy in findings across studies in Europe and the U.S. could also be due to varying ways in which asthma and allergies are diagnosed, or defined. Asthma diagnoses are often made based on symptoms and treatment based on severity of symptoms. However, asthma is a heterogeneous disease that manifests differently in different people, symptoms can vary over time and change day to day within the same person, and therefore diagnoses may vary by individual, doctor, or region. (Jacob et al., 2017) Previous studies have showed the challenges to accurately diagnosing asthma have resulted in over- or under-diagnosis of asthma. (Jacob et al., 2017) Furthermore, distinctions between allergic and non-allergic asthma can often not be made without a serological test. All these factors may also contribute to discrepancies in results across the literature.

Lung function was positively associated with proximity to a CAFO, with lung function improving as distance from a CAFO increased. The effect sizes, although most non-significant, were similar to results from European studies of adults in Germany and the Netherlands (Schulze et al., 2011; Radon et al., 2007a, 2007b). A distance of 1.5 miles was associated with −7.0% predicted FEV1 when compared with a distance of 5 miles from a CAFO. Schulze et al. (2011) found a −8.19% predicted FEV1 among those with average ammonia concentration greater than or equal to 19.71 $\mu g/m^3$ when compared to those with levels below. Similarly Radon et al. (2007a, 2007b) reported a −7.4% predicted FEV1 among those more than twelve animals houses within 500 m of home. While definitions of exposure to CAFO varied, the fact that all three studies found very similar results suggests residential proximity to a CAFO, or many AFOs, is likely associated with decreased lung function.

As one of the first studies in the U.S. to use a randomly selected statewide, population-based sample of rural adult residents to assess multiple respiratory health effects among people living in proximity to CAFOs, this study has numerous strengths. Prior U.S. studies have tended to rely on grouped exposures, removing individually variability among the exposure (Mirabelli et al., 2006; Rasmussen et al., 2017; Sigurdarson and Kline, 2006; Wing and Wolf, 2000). Our study was able to report on the nonlinear association between proximity to the nearest CAFO and respiratory health outcomes in the U.S., providing an important link between dispersion modeling of CAFO emissions and human health effects.

While utilizing a randomly selected statewide sample is a strength of this study, it is also a limitation. Rare exposures, such as living near a CAFO in the U.S., can result in low power and are best studied with cohort studies where subjects are selected by exposure status. Low power may have resulted in our inability to detect interaction with proximity to a CAFO and smoking status. Though we carefully controlled for multiple confounding factors, residual confounding or confounding by other unmeasured factors may affect estimated associations including individuals with potential higher livestock exposures via occupation. However, the number of subjects reporting livestock exposure was small and not sufficient to examine as a separate subpopulation. Similarly, residents in urban areas were not included to reduce bias and reduce potential unmeasured confounding introduced by air pollution sources unique to urban areas. The cross sectional nature of this study also limits conclusions regarding the temporal association between exposure and respiratory outcomes, particularly self-reported asthma prevalence. Self-report is not ideal and can lead to recall bias, however asthmatic and allergic symptoms may go clinically underreported in rural areas, where people may be less likely to seek medical care due to inconvenience, cost, or lack of insurance. While objective and self-report data on asthma was available, this study relied on self-report of allergies. Therefore, results cannot definitively tease out allergic and non-allergic asthma, something that would have strengthened the study and increased comparability with other studies. Furthermore, the lack of allergic sensitization data limits comparisons with other studies.

We were able to acquire retrospective CAFO data and ensure CAFOs linked to participant residences were in existence prior and during their study participation. However, the farm size and type could not be validated from this data. Additionally, we were unable to account for proximity to non-CAFO livestock farms. The assumption being made here is that the distribution of smaller farms is random throughout the study sample, resulting in non-differential misclassification bias. This assumption results in estimates biased towards the null.

5. Conclusion

In summary, residential proximity to a CAFO among individuals from a randomly sampled general population health survey was positively associated with self-reported nasal and lung allergies, asthmatic outcomes, and objectively measured lung function. This study provides evidence for respiratory health effects among residents living near dairy CAFOs. CAFOs may be an important source to regulate as current evidence suggests that large livestock farms may contribute to health disparities among rural residents. Building on findings from this observational study, future research should consider longitudinal study designs, more refined estimates of exposure source-apportioned air constituents in nearby homes, and more systematic tracking and validation of outcomes. More research is also needed to understand the mixtures of airborne agents from nearby livestock facilities in order to identify any etiological agents which may be associated with asthma, allergies, or lung function in residents living near large livestock facilities. Passive air pollution monitoring using filters or dust collection in homes would be useful to collect in order to better understand composition of air particles and how they may change over time. A cohort study which selects study participants by residential proximity and monitors respiratory health symptoms across multiple seasons should also be considered. Alternatively, a case-control study that recruits from hospitals and clinics in areas with a large concentration of CAFOs and could follow-up self-reported symptomology overtime could overcome some existing limitations of this work.

Sources of funding

Funding for SHOW comes from the Wisconsin Partnership Program (PERC) Award (223 PRJ 25DJ). This project was also supported by funding from the National Heart Lung and Blood Institute (1 RC2 HL101468) the National Institutes of Health's Clinical and Translational Science Award (5UL 1RR025011). Authors also acknowledge support from a core grant to the Center for Demography and Ecology at the University of Wisconsin-Madison (P2C HD047873), the National Institutes of Health, National Center for Advancing Translational Sciences CTSA award (UL1TR000427), and National Institute for Minority Health and Health Disparities award (1P60MD0003428).

Declaration of Competing Interest

None.

Acknowledgements

The authors thank the staff and graduate students at the Survey of the Health of Wisconsin (SHOW) for assistance in data processing and analysis. We would also like to thank the Wisconsin Partnership Program for continued funding of this work. We would also like to thank the SHOW participants for their time and contribution to this work.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envint.2019.104911.

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