



# Relative exposure to swine animal feeding operations and childhood asthma prevalence in an agricultural cohort

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## ABSTRACT

Large swine animal feeding operations (AFOs) have become the model of livestock production throughout the United States. Epidemiological studies have consistently shown an increase in adverse respiratory symptoms among workers at AFOs. However, the impact on communities surrounding these facilities is still being investigated. We evaluated the association between relative environmental exposure to AFOs and the prevalence of prescribed medication for wheeze and/or childhood asthma in rural Iowa.

Demographic and health information on 565 children aged 0–17 was obtained from a previous population-based cohort study while data on the AFOs were collected from publically available tax records. We created a metric of each child's relative environmental exposure to swine CAFOs which incorporated the size of the AFO as well as distance and wind direction. We determined the association between self-reported prescription medication for wheeze and/or self-reported physician diagnosed asthma and relative exposure while controlling for recognized risk factors using correlated logistic regression.

The prevalence of childhood asthma in the cohort was 11.0% while 22.7% of children had been previously prescribed medication for wheeze or had a lifetime asthma diagnosis. Children with a larger relative environmental exposure to AFOs had a significantly increased odds of both outcomes ( $OR=1.51$ ,  $p=0.014$  asthma;  $OR=1.38$ ,  $p=0.023$  asthma or medication for wheeze). When stratified into exposure quartiles a linear trend was observed with asthma or medication for wheeze as the dependent variable but not with asthma alone. This study is the first to investigate children's cumulative relative exposure to smaller AFOs and adds to the growing volume of literature supporting a link between proximity to swine AFOs and adverse respiratory health.

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## 1. Introduction

The rural landscape in the US has undergone a marked change over the last two decades. During this time, the number of hogs raised in the US has remained relatively constant while the number of swine producers has decreased dramatically (Donham et al., 2007; Merchant et al., 2005). In just over 20 years, swine producers have decreased by more than 70% and it is now estimated that nearly 80% of hog operations have 2000 head or more (Key and McBride, 2007). This movement toward animal feeding operations (AFOs) has led to increased efficiency and decreased costs, but has not been without adverse consequences. The large amount of animal waste generated by these facilities

has negatively impacted the environment, the health of AFO workers, and possibly nearby residents (Iowa State University and The University of Iowa Study Group, 2002; Cole et al., 2000; Radon et al., 2007; Schenker et al., 1998; Wing and Wolf, 2000).

A fundamental difference between animal production a half century ago and now is the substantial accumulation of animal waste in a single location. One fully-grown hog is capable of producing upwards 6.8 kg of waste a day. Therefore, a 2000 head operation can produce approximately 5000 metric tons of waste annually. Consequently, a single swine AFO can generate as much waste annually as a small city (USEPA, 2004). Manure management strategies at hog operations can vary and are dependent on numerous factors including climate, land topography, and size. Facilities in the Midwest typically use deep pits to store waste; while anaerobic lagoons are more prevalent in the Southeastern US. Generally, liquid waste is disposed by either applying it to the adjacent fields as fertilizer and/or hauled away (National Research Council's Committee on Animal Nutrition, 2003). While in the pit

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or lagoon, this slurry undergoes anaerobic fermentation which can produce large concentrations of noxious gasses including ammonia, hydrogen sulfide, and volatile organic compounds. In addition to gasses, manure also contains large quantities of endotoxin, a component of the external membrane of gram negative bacteria, which is a potent inflammagen (Cole et al., 2000; Von Essen and Auvermann, 2005). Epidemiological studies conducted on swine workers show increased prevalence of asthma, asthma-like symptoms, and chronic bronchitis (Donham et al., 2007; Iversen et al., 1988; Schenker et al., 1998; Zejda et al., 1993). Researchers are now investigating whether similar health effects are experienced by populations surrounding swine AFOs. Recent community-based studies have found a positive association between living or going to school near swine AFOs and a variety of adverse respiratory health outcomes, including increased asthma prevalence (Merchant et al., 2005; Mirabelli et al., 2006; Radon et al., 2007; Sigurdarson and Kline, 2006; Wing and Wolf, 2000).

Asthma is a chronic respiratory disease characterized by reversible airflow obstruction and airway hyper-responsiveness (Moorman et al., 2007). About half of all asthma cases are diagnosed before the age of three and 80% of cases by age six (Slavin, 2002). The etiology of the disease is not fully understood, but it is believed to involve a complex interaction between genetic factors and environmental stimuli with atopy playing a major role (Maddox and Schwartz, 2002; Mochizuki et al., 1999). Multiple air pollutants have been associated with the pathogenesis and exacerbation of asthma, including exposure to PM<sub>2.5</sub>, NO and NO<sub>2</sub>, ozone, environmental tobacco smoke, and allergens (Clark et al., 2010; Eder et al., 2006; Islam et al., 2007; McConnell et al., 2002; von Mutius, 2009).

Over the past 30 years, the prevalence of childhood asthma has more than doubled in the United States and other western countries (Eder et al., 2006). Asthma is now currently the most common chronic disease among children, and recent morbidity statistics estimate that 6.7 million children are affected by asthma in the US (Akinbami et al., 2009). Exposure to environmental pollutants and the inability to adapt to the changing environment are two hypotheses that have emerged to explain the dramatic increase in the prevalence of asthma (von Mutius, 2009).

The aim of this study was to evaluate the association between residential proximity to swine AFOs and the prevalence of two respiratory health outcomes: self-reported physician-diagnosed asthma; and self-reported prescription medication for wheeze or self-reported physician-diagnosed asthma. Extensive data on potential confounders were available among an established cohort of rural children living in intensely agricultural county. We constructed a metric to estimate children's relative exposure to swine AFOs which took into account the distance and direction of the AFOs to the child's home as well as the size of the operation.

## 2. Methods

### 2.1. Study population, recruitment, and data collection.

Medical, demographic and environmental information were obtained from Round 2 (1999–2004) of the Keokuk County Rural Health Study (KCRHS). The KCRHS is a population-based, prospective cohort study that began in 1994 primarily to study the prevalence and incidence of injury and respiratory disease in an intensely agricultural-rural population. Keokuk County is entirely rural with no towns that exceed a population greater than 2500 residents. Of the 370,688 acres the county spans, 86% is used for farmland (Iowa State University, 2009). Round 2 of the study included 565 children who ranged in age from birth through 17 years.

Recruitment methodology for the KCRHS has been previously published (Merchant et al., 2002; Stromquist et al., 2009). Briefly, children were selected

into the cohort by a stratified random sampling method with farms and rural non-farming households being overly sampled compared to those individuals who lived in town. Participants in Round Two of the KCRHS included 62 children who were diagnosed with asthma in their lifetime. Asthma status was determined from the question, "Has a doctor ever diagnosed the child with asthma?". Data on children that have been prescribed medication for wheeze ( $n=120$ ) was also assessed through the question, "Has the child ever been prescribed medication for wheezing?".

Demographic and health data on the children were collected using a standardized questionnaire at a research facility in a centrally located town within the county. Trained interviewers collected all data using a computer-prompted questionnaire. Previously published national surveys were used to develop questionnaires for this study, including the National Health Interview Survey, the American Thoracic Survey, and the Third National Health and Nutrition Examination Survey. The majority of health information about the child was provided by the child's biologic mother or female legal guardian. Children above the age of 12 were eligible to complete an adolescent questionnaire regarding agricultural tasks the child may have performed.

Following the medical questionnaire and tests, an industrial hygienist visited each household to conduct an environmental assessment of the property and home. This assessment included a questionnaire that was completed on site, usually by the male head of household. Questionnaire items included: the method by which the home was heated, fuel source used for cooking, whether the family had pets in the home, whether livestock were present on the property, whether smoking was permitted in the home, and the presence of visible mold growth in the home. Individuals who lived on farms were asked additional questions about agricultural operations that occurred on site.

### 2.2. Determining size and location of swine AFOs in the county

Swine facilities in Keokuk County are comparatively smaller than operations located in northern and western Iowa and rural North Carolina. AFOs located in the county rarely have lagoons and usually store manure in pits located underneath the structure. Because the State of Iowa only requires AFOs larger than 500 animal units (1250 fully grown hogs) to file a manure management plan, many operations in the county are undocumented with the state (IDNR, 2012). Therefore, an alternative method was needed to locate all AFOs in the county and to estimate their size.

According to Section 427.1(19) of the Code of Iowa, tax exemption status may be given to structures with a qualified pollution control device that abates air or water pollution. This code includes swine confinements that use concrete storage pits or lagoons to store manure. To receive a tax credit for employing these pollution control measures, a swine confinement operator must send the IDNR a certified exemption letter with the size and location of every pit on the property. These letters are then forwarded to the corresponding counties to verify the existence of the structure and to confirm the confinement is actively raising livestock. In 2005, the Keokuk County Tax Assessor's office began tracking active AFOs with manure-storage pits. The Assessor's office also identified properties that were raising livestock with a pit or lagoon, but chose not to file a tax exemption letter with the State for various reasons. From these records, we identified 168 swine AFOs that were active within Keokuk County during the study period.

Latitudes and longitudes of all homes and AFOs were obtained from a GIS database operated by the Keokuk County Tax Assessor's office. Data on the construction year of the AFO and the area of the hog operation were also obtained from the same source. Coordinates of the homes and AFOs were imported into ArcGIS (version 9.3 Esri, Redlands, CA) and plotted. From the coordinates the distance and direction (360°) of the AFO to the home was calculated. The degree direction was then converted to 16-point compass rose. Additionally, an aerial photograph of the county was imported into ArcGIS and was used to visually verify the location of every home and AFO in the study.

### 2.3. Participant's relative environmental exposure to AFOs

In order to estimate the relative environmental exposure ( $E_{\text{relative}}$ ) to study subjects from AFOs surrounding their homes, a qualitative exposure metric was devised (Eq. (1)). This metric was developed to account for the cumulative effect of all AFOs located within a 4.8 km radius of participants' homes, while taking into account additional relevant factors. The selection of a 4.8 km buffer was based on previous studies which found adverse respiratory health outcomes within this distance (Mirabelli et al., 2006; Wing and Wolf, 2000). As this was a cross-sectional study, temporality was difficult to establish; however, AFOs that were built after the child visited the clinic were excluded from the child's relative exposure summation.

The purpose of this metric was not to predict the actual concentrations of pollutants emitted by swine AFOs, but to simply qualify study participants' potential risk of exposure. Some studies evaluating the health effects from AFOs have relied on linear distance as an estimate of exposure (Mirabelli et al., 2006; Radon et al., 2007; Wing and Wolf, 2000). However, a dispersion modeling study

by O'Shaughnessy and Altmaier (2011) found  $H_2S$ , a gas commonly emitted by AFOs, decays non-linearly as distance from an AFO increases (O'Shaughnessy and Altmaier, 2011). Therefore, the inverse square law was used in the exposure equation as opposed to a simple linear function. While this may be more representative of pollutant dispersion,  $E_{relative}$  is still a simplification of a number of factors that influence environmental contaminant generation inside a AFO, including animal density, ventilation system, and manure management (Blunden et al., 2008; Kim, 2004). Since these factors were unknown, the facility area ( $m^2$ ) determined through tax records, was used as a surrogate for the total amount of emissions produced by the facility.

A 16 point wind rose (averaged from 2001–2004) was constructed from meteorological data compiled by the IDNR from the National Weather Service's meteorological station located approximately 80 km. The wind rose data used for the exposure metric only considered speeds less than  $4 m s^{-1}$  since near source areas are affected greater during low wind conditions (Moreira et al., 2005). The percentage of time wind blew from the AFO to the home was determined by matching the 16-point wind rose to the 16-point compass rose.

$$E_{Relative} = \log \sum \frac{A}{d^2} f_w \quad (1)$$

where  $E_{relative}$  is the participant's relative AFO exposure,  $A$  is the area of the AFO ( $m^2$ ),  $d$  is the distance between AFO and residence (m) and  $f_w$  is the percentage of time wind which was blowing  $< 4 m s^{-1}$  from the AFO to the home.

#### 2.4. Statistical analysis

SAS version 9.3 (SAS Institute Inc. Cary, NC) was used for all statistical analysis performed in this study. Two outcomes were evaluated in this study: (1) physician-diagnosed childhood asthma and (2) physician-diagnosed asthma and children that have been prescribed medication for wheeze. Unadjusted logistic and covariate-adjusted correlated logistic regression analyses were performed for each outcome. Fourteen potential asthma risk factors were considered as potential covariates including age, physician-diagnosed allergies, gender, parental history of asthma, premature birth ( $< 37$  weeks), physician-diagnosed respiratory illness before the age of two years, at least one parent smoking in the home, working around livestock, cockroach problem in the home, keeping an indoor dog and/or cat, household income  $< \$40,000$ , living on a farm, parents raising livestock, and presence of mold inside the home and were analyzed first bivariate using logistic regression (PROC LOGISTIC). If data for a child was missing for any of the variables assessed, the responses were given the mode.

Backwards selection multivariable logistic regression modeling was then performed with all variables entering the initial model. Since multiple children live in the same household, demographic and parental health information could not be considered independent variables. Due to the correlated nature of the data, general estimating equations (PROC GENMOD) were used to evaluate the association between various explanatory variables and the outcomes of interest with household ID used in the repeated statement. The exchangeable working correlation structure was found to have the smallest Quasi likelihood under the Independence model Criterion (QICu) and was chosen for data analysis. The child's relative AFO exposure was evaluated two separate ways: first, as a continuous explanatory variable and second, as a categorical variable stratified by quartiles. Variables that remained in the final model were checked for two-way interactions separately. The final model included only covariates with a  $p < 0.10$  and those that were biologically plausible explanatory variables.

### 3. Results

Descriptive statistics for the study population are summarized in Table 1. The study contained 565 children with a mean age of 9.6 years. The majority of children lived in that households earned more than \$40,000 a year, had at least one parent who completed some college coursework, and resided within 3.2 km of the nearest AFO. The prevalence of physician-diagnosed allergies was 19.7%, while 28% of children in the cohort saw a health practitioner for a severe respiratory illness before the age of two years. Lifetime-asthma prevalence was significantly larger ( $p < 0.001$ ) for boys (15.9%) compared to girls (5.1%); likewise, physician-diagnosed asthma or medication for wheeze was larger in boys (15.6%) than girls (7.1%) ( $p < 0.001$ ).

A farming household was defined as having an operation of 10 acres or more in active crop production to differentiate between commercial farming and individuals farming for personal consumption. Using this definition, only 29.6% of the cohort was living on a farm during the time of the survey, with the majority

**Table 1**

Demographic characteristics of the study population.

Variable	N (%)
Number of children	565
Number of households	277
Gender	
Female	257 (45.5)
Male	308 (54.5)
Age (yrs)	
0–6	145 (25.7)
6–12	246 (43.5)
12–17	174 (30.8)
Physician-diagnosed asthma prevalence	
Female	13 (5.1)
Male	49 (15.9)
Total	62 (11.0)
Physician-diagnosed asthma or medication for wheeze	
Female	40 (7.1)
Male	88 (15.6)
Total	128 (22.7)
Child lives on a farm	167 (29.6)
Child works around livestock	40 (7.1)
Cockroach problem in the home	12 (2.1)
Child's proximity to nearest CAFO	
$\leq 1600$ m	107 (18.9)
$> 1600$ m to $\leq 3200$ m	320 (37.7)
$> 3200$ m to $\leq 4800$ m	203 (35.9)
$> 4800$ m	42 (7.4)
Highest education achieved by parents	
Did not complete high school	6 (2.2)
High school or GED	59 (21.3)
Some college	121 (43.7)
College grad or above	91 (32.9)
Indoor dog and/or cat	242 (42.8)
Parental history of asthma	45 (8.0)
Parental smoking in the home	53 (9.4)
Parents raises livestock	125 (22.1)
Parents income $< \$40,000$	132 (23.4)
Physician-diagnosed allergies	111 (19.7)
Presence of mold in the home	88 (15.6)
Premature birth ( $< 37$ weeks)	62 (11.0)
Respiratory illness $< 2$ years	158 (28.0)

of children residing in towns or rural non-farming households. Of the 165 children who were identified as living on a farm, 70.5% had parents who worked in hog or cattle production. Only seven children had parents that worked with livestock and did not reside on a farm. A small percentage of children (7.1%) indicated that they have previously worked either in a confinement or with livestock in the past.

Unadjusted associations between the two respiratory outcomes and potential risk factors are presented in Table 2. A significant positive association ( $OR = 1.29$ ,  $p = 0.043$ ) was observed between childhood asthma and  $E_{relative}$ . The magnitude of the association was slightly attenuated and no longer significant in children that were prescribed medication for wheeze or had been diagnosed with asthma ( $OR = 1.19$ ,  $p = 0.087$ ). Risk factors that were observed to be significantly associated ( $p < 0.05$ ) with both outcomes included gender, atopy, premature birth, and a respiratory illness before the age of two. Although specific information regarding the type of respiratory illness before the age of two years was not collected in this study, it was found to be the strongest factor associated with both outcomes. Parental history for asthma was defined as a child having at least one parent with a lifetime diagnosis of asthma. A significant association was observed ( $OR = 3.42$ ,  $p < 0.001$ ) for children with asthma, but not for children with medication for wheeze or asthma ( $OR = 1.80$ ,  $p = 0.078$ ). However, complete parental history of asthma was missing for 171 (30%) children and may have biased the results toward the null.

**Table 2**  
Unadjusted analysis of asthma outcomes by potential risk factors.

Variable	Physician-diagnosed asthma (n=62)		Physician-diagnosed asthma or medication for wheeze (n=128)	
	OR (95% CI)	p	OR (95% CI)	p
$E_{\text{relative}}$	1.29 (1.01–1.64)	0.043	1.19 (0.98–1.45)	0.087
Age (year)	1.08 (1.01–1.14)	0.016	0.98 (0.94–1.03)	0.260
Diagnosed allergies	6.20 (3.56–10.79)	< 0.001	4.16 (2.66–6.50)	< 0.001
Male gender	3.55 (1.88–6.70)	< 0.001	2.17 (1.43–3.30)	< 0.001
Parental history of asthma	3.42 (1.66–7.04)	< 0.001	1.80 (0.94–3.46)	0.078
Premature birth	3.84 (2.03–7.27)	< 0.001	2.24 (1.28–3.93)	0.005
Respiratory illness before 2 years	7.01 (3.96–12.41)	< 0.001	9.36 (6.02–14.57)	< 0.001
At least one parent smokes in the home	0.83 (0.32–2.17)	0.706	0.78 (0.38–1.59)	0.490
Child works around livestock	2.18 (0.96–4.97)	0.058	1.51 (0.75–3.07)	0.252
Cockroach problem in the home	1.64 (0.35–7.68)	0.523	1.14 (0.30–4.28)	0.845
Indoor dog and/or cat	1.11 (0.65–1.89)	0.694	0.85 (0.57–1.27)	0.428
Household income < \$40,000	1.40 (0.78–2.51)	0.264	1.18 (0.75–1.87)	0.463
Live on a farm	1.25 (0.72–2.19)	0.430	1.34 (0.88–2.04)	0.175
Parents raise livestock	0.83 (0.43–1.61)	0.578	0.93 (0.57–1.50)	0.750
Presence of mold in the home	1.19 (0.60–2.39)	0.618	1.54 (0.93–2.56)	0.094

Studies conducted in Keokuk County have shown that farm children regularly participate in agricultural tasks at an early age, including working with livestock (Merchant et al., 2005; Park et al., 2003). However, the KCRHS only conducted occupational surveys on children over the age of 12 years. Consequently, children's occupational exposure to livestock and AFOs was unknown for 79% of the cohort. Children who did not complete an adolescent questionnaire, either because of age restrictions or lack of participation, were treated as having no exposure. When analyzed bivariately, a near significant association was observed between children working in an AFO and/or with livestock and asthma ( $OR=2.18$ ,  $p=0.058$ ). However, this may be a spurious relationship confounded by gender and age; considering the majority of children that work with livestock were male (80%) and all were above the age of 12 years. No significant association was found between a child working with livestock and medication for wheeze or asthma ( $OR=1.51$ ,  $p=0.252$ ). Children may also be exposed to livestock via parental take-home exposure. Any child whose parents specified that they worked with livestock was considered potentially exposed. Bivariate analysis found no association between parents raising livestock and either outcomes ( $OR=0.83$ ,  $p=0.578$  asthma;  $OR=0.93$ ,  $p=0.750$  asthma or medication for wheeze).

Unadjusted analysis of environmental risk factors such as parental smoking, presence of mold in the home, and having an indoor dog and/or cat were not significant. Since the KCRHS only assessed a lifetime asthma diagnosis or medication for wheeze, households with asthmatic or atopic children may have eliminated these risk factors after their child was diagnosed.

Multivariable models which included  $E_{\text{relative}}$  are presented in Table 3. All asthma covariates were eliminated sequentially with only variables with a  $p < 0.10$  included in the final model. When analyzed as a continuous variable,  $E_{\text{relative}}$  was significantly associated with childhood asthma ( $OR=1.51$ ,  $p=0.014$ ) and medication for wheeze or asthma ( $OR=1.38$ ,  $p=0.023$ ). Furthermore, when  $E_{\text{relative}}$  was included in the model, the QICu was reduced for both outcomes, indicating addition of  $E_{\text{relative}}$  increased the goodness-of-fit.

To determine if the risk of asthma increased in a linear fashion, children were grouped into quartiles based on  $E_{\text{relative}}$ . Covariate adjusted associations between exposure quartiles and childhood asthma are shown in Table 4. No monotonic dose–response relationship was observed between increasing exposure quartiles and the prevalence of childhood asthma. All odds ratios were increased compared to the reference group, but no exposure quartile approached significance. However, when the outcome medication for wheeze or asthma was analyzed, a linear trend

was observed between exposure quartiles. Risk was increased across all exposure quartiles compared to the lowest, with the 4th quartile having the largest odds ratio ( $OR=2.40$ ,  $p=0.027$ ).

#### 4. Discussion

The aim of this study was to determine if a larger relative environmental exposure to swine AFOs was associated with two respiratory health outcomes (childhood asthma and physician-prescribed medication for wheeze or asthma). Children's relative exposure to swine AFOs was estimated using a metric that took into consideration facility area, distance, and percentage of low wind speed ( $< 4 \text{ m s}^{-1}$ ) blowing from the AFO to the home. After adjusting for recognized risk factors, a significant positive relationship was observed between increasing  $E_{\text{relative}}$  and both outcomes. To determine whether the risk increased in a linear fashion, children were grouped into quartiles according to their  $E_{\text{relative}}$  value. A monotonic dose–response relationship was observed in children that have been prescribed medication for wheeze or had been previously diagnosed with asthma, but not in children with only an asthma diagnosis. It is not clear whether the lack of a linear trend in the asthma group is due to limited power.

Childhood asthma is commonly underdiagnosed by physicians and asthma status obtained through questionnaires may not be sensitive enough to detect all cases within a cohort (Chrischilles et al., 2004; Crain et al., 1994; Joseph et al., 1996). A study investigating childhood asthma prevalence in two rural Iowa counties observed that among 13.8% of participants who reported frequent asthma symptoms, only 41.6% had been given a positive diagnosis by a physician (Chrischilles et al., 2004). Therefore, we chose to include medication for wheeze as an alternative indicator of asthma. While this most likely increased the sensitivity of non-differential asthma ascertainment, specificity was probably decreased by inclusion of more false positives. This misclassification may account for the attenuation in the odds ratio and significance level when medication for wheeze or asthma was analyzed as an outcome variable compared to asthma alone. On the other hand with increased cases we were able to detect a linear trend in the odds of medication for wheeze or asthma when children were stratified into exposure quartiles.

We were concerned that children differed significantly in terms of socioeconomic status as their proximity to an AFO increased. In stratified analysis, household income and parental education did not differ between children living within 1.6 km from the nearest AFO compared to children living greater than



**Table 3**  
Multivariable analysis for asthma outcomes.

Variable	Physician-diagnosed asthma		Physician-diagnosed asthma or medication for wheeze	
	OR (95% CI)	p	OR (95% CI)	p
<i>E</i> <sub>relative</sub>	1.51 (1.08–2.09)	0.014	1.38 (1.04–1.81)	0.023
Age (year)	1.09 (1.02–1.18)	0.009	*	*
Diagnosed allergies	4.71 (2.49–8.92)	< 0.001	3.58 (2.05–6.25)	< 0.001
Male gender	3.27 (1.53–6.97)	0.002	1.67 (1.04–2.70)	0.035
Parental history of asthma	3.27 (1.04–10.25)	0.041	*	*
Premature birth	4.04 (1.71–9.50)	0.001	1.95 (0.93–4.07)	0.078
Respiratory illness before 2 years	5.83 (3.00–11.32)	< 0.001	8.52 (5.15–14.10)	< 0.001

\* Variable not selected through backwards regression.

**Table 4**  
Relative exposure quartiles by asthma outcomes.

<i>E</i> <sub>relative</sub> exposure quartiles	Physician-diagnosed asthma <sup>a</sup>		Physician-diagnosed asthma or medication for wheeze <sup>b</sup>	
	OR (95% CI)	p	OR (95% CI)	p
1st	–	–	–	–
2nd	1.86 (0.73–4.74)	0.192	1.43 (0.67–3.08)	0.355
3rd	2.06 (0.82–5.18)	0.126	1.52 (0.71–3.26)	0.283
4th	1.71 (0.65–4.54)	0.278	2.40 (1.11–5.21)	0.027

–: Reference group.

<sup>a</sup> Adjusted for age, physician-diagnosed allergies, gender, respiratory illness before 2 years, parental history of asthma, and premature birth.

<sup>b</sup> Adjusted for physician-diagnosed allergies, gender, respiratory illness before 2 years, and premature birth.

4.8 km from the nearest AFO. Interestingly, children within 1.6 km tended to live in household that earned more income and had at least one parent that attended college compared to children living more than 4.8 km from the nearest AFO.

All significant asthma risk factors observed in this study have been found to be associated with childhood asthma in other studies. Factors such as gender (Akinbami et al., 2009), atopy (Clark, 2000; Eder et al., 2006), and premature birth (Dombkowski et al., 2008; Gessner and Chimonas, 2007) have been previously found to be strong factors contributing to the development of the disease. In addition research has shown that a viral infection before the age of two years caused by either respiratory syncytial virus (RSV) or human rhinovirus (HRV) is associated with childhood asthma (Gern, 2010; Sly et al., 2010). The causal mechanisms behind this association are still not clear and researchers are still trying to determine whether these infections contribute to the progression of the disease or demonstrate an individual's propensity toward decreased lung function which is an early indicator for asthma (Gern, 2010; Martinez, 2003; Nafstad et al., 2000; Sly et al., 2010).

Results from this study are consistent with occupational and environmental studies concerning exposure to swine confinements. Studies have routinely shown swine confinement workers have a higher rate of bronchitis, asthma-like syndrome, and asthma than the general population (Donham et al., 2007; Iversen et al., 1988; Schenker et al., 1998; Zejda et al., 1993; Merchant et al., 2005; Mirabelli et al., 2006; Sigurdarson and Kline, 2006). Although residential exposure is assumed to be orders of magnitude smaller than occupational exposures, children could be negatively impacted by swine AFOs at much smaller exposures due to their developing respiratory systems. In a large cross-sectional study ( $n=58,169$ ) Mirabelli et al. (2006) observed that children who attended school within 4.8 km of a swine confinement had a significantly larger prevalence of

physician diagnosed childhood asthma ( $PR=1.07$ , 95% CI: 1.01–1.15) (Mirabelli et al., 2006). Additionally, Sigurdarson and Kline (2006) found that children who attended an elementary school located within 800 m of a swine AFO had a significantly increased prevalence of physician-diagnosed asthma ( $OR=5.71$ ,  $p=0.004$ ) compared to children who went to a control school (nearest swine AFO > 16 km) (Sigurdarson and Kline, 2006). Our study also builds on a previous study conducted in Keokuk County which investigated farm exposures and childhood asthma. Merchant et al. (2005) observed that children who lived on a farm that raised swine and added antibiotics to their feed had a significantly higher prevalence of asthma or asthma-like symptoms compared to children who lived on a farm that did not raise swine (55.8–26.2%,  $p=0.013$ ; Merchant et al., 2005).

Several studies have indicated that children who lived on farms or had exposures to livestock early in life had a decreased prevalence of atopy and asthma (Ehrenstein et al., 2000; Ernst and Cormier, 2000; Kilpelainen et al., 2000; Riedler et al., 2001). Researchers concluded that exposure to microbes early in life may reduce the risk of developing allergic diseases including asthma. This protective effect has been termed the 'hygiene hypothesis'. When analyzed both bivariately and multivariately, no significant decrease in asthma prevalence was observed in children who lived on farms in the KCRHS cohort. This lack of a protective effect was also seen in families that raised livestock. Possible explanations for this finding are varied. Information was only available regarding the current residence of the child. Consequently, it was unknown whether the child was born on a farm or if he/she had early contact with pets and/or livestock. In addition, Keokuk County is considered entirely rural with no towns with a population greater than 2500. As a result, children living in towns or rural non-farming locales may have a similar exposure as farming children due to their proximity to agricultural activities.

This study highlights the need for greater tracking of smaller AFOs by state and local governments; since, the majority of swine facilities in the county were unregistered and not easily accessible using state databases. While previous studies have observed adverse respiratory health effects from large swine AFOs (Mirabelli et al., 2006; Sigurdarson and Kline, 2006; Wing and Wolf, 2000), this is the first study to document similar effects while including smaller, primarily unregistered facilities. This suggests that a cumulative chronic exposure to hog facilities can be as detrimental to respiratory health as an exposure from a single large swine operation. Therefore, monitoring smaller un-registered facilities by state and federal agencies may have a positive impact on rural health.

One of the many strengths of this study was the detailed information collected on participants. Due to the complex nature of asthma, it was essential to understand the medical history of the child along with the environment in which they live. The wide

range of information collected by the KCHRS allowed for the assessment of 14 potential asthma risk factors. Additionally, all risk factors identified bivariately and multivariately have been shown to be associated with childhood asthma in previous studies. Medical and questionnaire data were collected by nurses in a research clinic while homes were surveyed by a team of industrial hygienists, which ensured a high degree of reliability. The results of the study were also strengthened by the design. Selection bias was minimized due to the stratified random selection of subjects and adequate response rate for a large population-based study.

Limitations of this study include a modest sample size, incomplete “occupational” exposure information, and possible exposure misclassification. Only 62 (11%) children in the cohort had physician-diagnosed asthma. Consequently, when children were categorized according to their relative AFO exposure, there was limited power to detect difference between groups. Furthermore, “occupational” information was incomplete for 79% of the children. Since it is plausible that children living near these facilities may be more inclined to also work at them, failure to control for this potential exposure may limit the results of this study.

Possible exposure misclassification also limited the results. Round 2 of the KCHRS ended in 2004, however the Keokuk County Tax Assessor's Office only began collecting AFO information in 2005. While the date of facility construction is known, whether it was in active production during 1999–2004 is not known. Hog production is cyclical and dependent on a multitude of factors. Although an operation may have been built prior to the child's clinical assessment there is no guarantee it was in operation. AFO characteristics such as pollution control devices used by the facility, manure management, operational maintenance, and topography of the land were not available and therefore not considered. Additionally, wind rose data were collected from an off-site weather station and may not be representative of conditions in the study area. We would expect these types of exposure misclassification to be non-differential, biasing results toward the null hypothesis.

## 5. Conclusions

The goal of this study was to develop a metric to qualify children's relative environmental exposure to swine AFO and evaluate its association with prescription medication for wheeze and/or childhood asthma. We observed a significant positive association between both health outcomes and relative exposure. These results are consistent with previous environmental and occupational studies that have found an increased risk of asthma or asthma-like symptoms associated with AFO. Our study is one of the first that has investigated relative exposure to primarily smaller unregistered swine AFOs and demonstrates the need for greater tracking of smaller operations by state governments. To avoid possible exposure misclassification, future studies would benefit from collection of quantitative environmental data for residence near these facilities as opposed to estimating exposure. Additionally, more work is needed to adequately address the possible occupational exposure to children working in swine AFOs.

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## Human subjects

This study has been approved by the University of Iowa's Institutional Review Board #199308458. Please see the attached IRB approval memo.

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## References

- Akinbami, L.J., Moorman, J.E., Garbe, P.L., Sondik, E.J., 2009. Status of childhood asthma in the United States, 1980–2007. *Pediatrics* 123, S131–S145.
- Blunden, J., Aneja, V.P., Westerman, P.W., 2008. Measurement and analysis of ammonia and hydrogen sulfide emissions from a mechanically ventilated swine confinement building in North Carolina. *Atmos. Environ.* 42, 3315–3331.
- Chrischilles, E., Ahrens, R., Kuehl, A., Kelly, K., Thorne, P., Burmeister, L., Merchant, J., 2004. Asthma prevalence and morbidity among rural Iowa schoolchildren. *J. Allergy Clin. Immunol.* 113, 66–71.
- Clark, N.A., Demers, P.A., Karr, C.J., Koehoorn, M., Lencar, C., Tamburic, L., Brauer, M., 2010. Effect of early life exposure to air pollution on development of childhood asthma. *Environ. Health Perspect.* 118, 284.
- Clark, T.J.H., 2000. Asthma, 4th ed Oxford University Press, USA.
- Cole, D., Todd, L., Wing, S., 2000. Concentrated swine feeding operations and public health: a review of occupational and community health effects. *Environ. Health Perspect.* 108, 685.
- Crain, E.F., Weiss, K.B., Bijur, P.E., Hersh, M., Westbrook, L., Stein, R.E.K., 1994. An estimate of the prevalence of asthma and wheezing among inner-city children. *Pediatrics* 94, 356–362.
- Dombkowski, K.J., Leung, S.W., Gurney, J.G., 2008. Prematurity as a predictor of childhood asthma among low-income children. *Ann. Epidemiol.* 18, 290–297.
- Donham, K.J., Wing, S., Osterberg, D., Flora, J.L., Hodne, C., Thu, K.M., Thorne, P.S., 2007. Community health and socioeconomic issues surrounding concentrated animal feeding operations. *Environ. Health Perspect.* 115, 317.
- Eder, W., Ege, M.J., von Mutius, E., 2006. The asthma epidemic. *N. Engl. J. Med.* 355, 2226–2235.
- Ehrenstein, V., Mutius, V., Kries, V., 2000. Reduced risk of hay fever and asthma among children of farmers. *Clin. Exp. Allergy* 30, 187–193.
- Ernst, P., Cormier, Y., 2000. Relative scarcity of asthma and atopy among rural adolescents raised on a farm. *Am. J. Respir. Crit. Care Med.* 161, 1563–1566.
- Gern, J.E., 2010. The urban environment and childhood asthma study. *J. Allergy Clin. Immunol.* 125, 545–549.
- Gessner, B.D., Chimonas, M.A.R., 2007. Asthma is associated with preterm birth but not with small for gestational age status among a population-based cohort of Medicaid-enrolled children < 10 years of age. *Thorax* 62, 231–236.
- Iowa Department of Natural Resources (IDNR), 2012. Current Requirements for Confinements, vol. 2012.
- Iowa State University, 2009. Keokuk County Agriculture. Available from: <<http://www.extension.iastate.edu/Publications/Pm2023-54.pdf>> ) accessed 26.06.12. Last updated December, 2009.
- Iowa State University and The University of Iowa Study Group, 2002. Iowa Concentrated Animal Feeding Operation Air Quality Study. Final Report. The University of Iowa College of Public Health, Iowa City, IA.
- Islam, T., Gauderman, W.J., Berhane, K., McConnell, R., Avol, E., Peters, J.M., Gilliland, F.D., 2007. Relationship between air pollution, lung function and asthma in adolescents. *Thorax* 62, 957–963.
- Iversen, M., Dahl, R., Korsgaard, J., Hallas, T., Jensen, E., 1988. Respiratory symptoms in Danish farmers: an epidemiological study of risk factors. *Thorax* 43, 872–877.
- Joseph, C.L.M., Foxman, B., Leickly, F.E., Peterson, E., Ownby, D., 1996. Prevalence of possible undiagnosed asthma and associated morbidity among urban schoolchildren. *J. Pediatr.* 129, 735–742.
- Key, N.D., McBride, W.D., 2007. The Changing Economics of US Hog Production. US Department of Agriculture, Economic Research Service.
- Kilpelainen, M., Terho, E., Helenius, H., Koskenvuo, M., 2000. Farm environment in childhood prevents the development of allergies. *Clin. Exp. Allergy* 30, 201–208.
- Kim, J., 2004. Ambient air pollution: health hazards to children. *Pediatrics* 114, 1699.
- Maddox, L., Schwartz, D.A., 2002. The pathophysiology of asthma. *Annu. Rev. Med.* 53, 477–498.
- Martinez, F.D., 2003. Respiratory syncytial virus bronchiolitis and the pathogenesis of childhood asthma. *Pediatr. Infect. Dis. J.* 22, S76.

- McConnell, R., Berhane, K., Gilliland, F., London, S.J., Islam, T., Gauderman, W.J., Avol, E., Margolis, H.G., Peters, J.M., 2002. Asthma in exercising children exposed to ozone: a cohort study. *Lancet* 359, 386–391.
- Merchant, J.A., Naleway, A.L., Svendsen, E.R., Kelly, K.M., Burmeister, L.F., Stromquist, A.M., Taylor, C.D., Thorne, P.S., Reynolds, S.J., Sanderson, W.T., 2005. Asthma and farm exposures in a cohort of rural Iowa children. *Environ. Health Perspect.* 113, 350.
- Merchant, J.A., Stromquist, A.M., Kelly, K.M., Zwerling, C., Reynolds, S.J., Burmeister, L.E., 2002. Chronic disease and injury in an agricultural county: the Keokuk County Rural Health Cohort Study. *J. Rural Health* 18, 521–535.
- Mirabelli, M.C., Wing, S., Marshall, S.W., Wilcosky, T.C., 2006. Asthma symptoms among adolescents who attend public schools that are located near confined swine feeding operations. *Pediatrics* 118, e66–e75.
- Mochizuki, H., Shigeta, M., Tokuyama, K., Morikawa, A., 1999. Difference in airway reactivity in children with atopic vs nonatopic asthma. *Chest* 116, 619–624.
- Moorman, J.E., Rudd, R.A., Johnson, C.A., King, M., Minor, P., Bailey, C., Scalia, Akinbami, L.J., 2007. National Surveillance for Asthma—United States, 1980–2004. Department of Health and Human Services, Centers for Disease Control and Prevention.
- Moreira, D.M., Tirabassi, T., Carvalho, J.C., 2005. Plume dispersion simulation in low wind conditions in stable and convective boundary layers. *Atmos. Environ.* 39, 3643–3650.
- Nafstad, P., Magnus, P., Jaakkola, J.J.K., 2000. Early respiratory infections and childhood asthma. *Pediatrics* 106, e38.
- National Research Council's Committee on Animal Nutrition, 2003. Air Emissions from Animal Feeding Operations: Current Knowledge, Future Needs. The National Academies Press.
- O'Shaughnessy, P.T., Altmaier, R., 2011. Use of AERMOD to determine a hydrogen sulfide emission factor for swine operations by inverse modeling. *Atmos. Environ.* 45, 4617–4625.
- Park, H., Reynolds, S.J., Kelly, K.M., Stromquist, A.M., Burmeister, L.F., Zwerling, C., Merchant, J.A., 2003. Characterization of agricultural tasks performed by youth in the Keokuk County Rural Health Study. *Appl. Occup. Environ. Hyg.* 18, 418–429.
- Radon, K., Schulze, A., Ehrenstein, V., van Strien, R.T., Pram, G., Nowak, D., 2007. Environmental exposure to confined animal feeding operations and respiratory health of neighboring residents. *Epidemiology* 18, 300.
- Riedler, J., Braun-Fahrlander, C., Eder, W., Schreuer, M., Waser, M., Maisch, S., Carr, D., Schierl, R., Nowak, D., von Mutius, E., 2001. Exposure to farming in early life and development of asthma and allergy: a cross-sectional survey. *Lancet* 358, 1129–1133.
- Schenker, M., Christiani, D., Cormier, Y., Dimich-Ward, H., Doekes, G., Dosman, J., Douwes, J., Dowling, K., Enarson, D., Green, F., 1998. American Thoracic Society: respiratory health hazards in agriculture. *Am. J. Respir. Crit. Care Med.* 158, S1–S76.
- Sigurdson, S.T., Kline, J.N., 2006. School proximity to concentrated animal feeding operations and prevalence of asthma in students. *Chest* 129, 1486–1491.
- Slavin, R.G., 2002. Asthma. American College of Physicians—American Society of Internal Medicine. The University of Michigan.
- Sly, P.D., Kusel, M., Holt, P.G., 2010. Do early-life viral infections cause asthma? *J. Allergy Clin. Immunol.* 125, 1202–1205.
- Stromquist, A., Merchant, J.A., Zwerling, C.M., Burmeister, L., Sanderson, W.T., Kelly, K.M., 2009. Challenges of conducting a large rural prospective population-based Cohort study: the Keokuk County Rural Health Study. *J. Agromed.* 14, 142–149.
- USEPA, 2004. Risk Assessment Evaluation for Concentrated Animal Feeding Operations. United States Environmental Protection Agency, Cincinnati.
- Von Essen, S.G., Auvermann, B.W., 2005. Health effects from breathing air near AFOs for feeder cattle or hogs. *J. Agromed.* 10, 55.
- von Mutius, E., 2009. Gene–environment interactions in asthma. *J. Allergy Clin. Immunol.* 123, 3–11.
- Wing, S., Wolf, S., 2000. Intensive livestock operations, health, and quality of life among eastern North Carolina residents. *Environ. Health Perspect.* 108, 233.
- Zeida, J., Hurst, T., Rhodes, C., Barber, E., McDuffie, H., Dosman, J., 1993. Respiratory health of swine producers. Focus on young workers. *Chest* 103, 702–709.