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Animal production, insecticide use and self-reported symptoms and diagnoses of COPD, including chronic bronchitis, in the Agricultural Health Study

Jessica L. Rinsky[a], **David B. Richardson**[a], **Kathleen Kreiss**[b], **Leena Nylander-French**[c], **Laura E. Beane Freeman**[d], **Stephanie J. London**[e], **Paul K. Henneberger**[b], **Jane A. Hoppin**[f,*]

[a]Department of Epidemiology, Gillings School of Global Public Health, University of North Carolina, Chapel Hill, NC, United States of America

[b]National Institute for Occupational Safety and Health, Centers for Disease Control and Prevention, Morgantown, WV, United States of America

[c]Department of Environmental Sciences and Engineering, Gillings School of Global Public Health, University of North Carolina, Chapel Hill, NC, United States of America

[d]Occupational and Environmental Epidemiology Branch, National Cancer Institute, National Institutes of Health, Department of Health and Human Services, Rockville, MD, United States of America

[e]Epidemiology Branch, National Institute of Environmental Health Sciences, National Institutes of Health, Department of Health and Human Services, Research Triangle Park, NC, United States of America

[f]Department of Biological Sciences, Center for Human Health and the Environment, North Carolina State University, Raleigh, NC, United States of America

Abstract

Background: Occupational exposure to animal production is associated with chronic bronchitis symptoms; however, few studies consider associations with chronic obstructive pulmonary disease (COPD). We estimated associations between animal production activities and prevalence of self-reported COPD among farmers in the Agricultural Health Study.

Methods: During a 2005–2010 interview, farmers self-reported information about: their operations (i.e., size, type, number of animals, insecticide use), respiratory symptoms, and COPD diagnoses (i.e., COPD, chronic bronchitis, emphysema). Operations were classified as small or medium/large based on regulatory definitions. Farmers were classified as having a COPD diagnosis, chronic bronchitis symptoms (cough and phlegm for ≥3 months during 2 consecutive

[*]Corresponding author at: Department of Biological Sciences, Campus Box 7633, North Carolina State University, Raleigh, NC 27695-7633, United States of America. jahoppin@ncsu.edu (J.A. Hoppin).

Appendix A. Supplementary data
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years), or both. Polytomous logistic regression was used to estimate odds ratios (OR) and 95% confidence intervals (CI).

Results: Of 22,491 participating farmers (median age: 59years), 922 (4%) reported a COPD diagnosis only, 254 (1%) reported a diagnosis and symptoms, and 962 (4%) reported symptoms only. Compared to raising no commercial animals, raising animals on a medium/large operation was positively associated with chronic bronchitis symptoms with (OR: 1.59; 95% CI: 1.16, 2.18) and withouta diagnosis (OR: 1.69; 95% CI: 1.42, 2.01). Ever use of multiple organophosphates, carbaryl, lindane, and permethrin were positively associated with chronic bronchitis symptoms.

Conclusion: Animal production work, including insecticide use, was positively associated with chronic bronchitis symptoms; but not consistently with COPD diagnosis alone. Our results support the need for further investigation into the role of animal production-related exposures in the etiology of COPD and better respiratory protection for agricultural workers.

Keywords

Epidemiology; Occupational health; Environmental health; Pesticide

1. Introduction

Chronic obstructive pulmonary disease (COPD), a general term now used to refer to chronic bronchitis, emphysema, and other causes of airway obstruction, is an important cause of morbidity and mortality in the United States. COPD arises from an enhanced chronic inflammatory response in the airways to particles or gases (Maitra and Kumar, 2007). Although smoking is the most important risk factor for COPD, 15–20% of COPD in the United States may be related to occupational exposures, with this proportion being 30–48% for never smokers (Balmes et al., 2003; Trupin et al., 2003; Wurtz et al., 2015).

Elevated rates of COPD have been observed for farmers, especially those in the animal production industry (NIOSH, 2007). Workers involved in food animal production are exposed to respiratory irritants including organic dusts, gases and chemicals (ATS, 1998; Radon et al., 2002a; O'Shaughnessy et al., 2012; Senthilselvan et al., 2011). The concentration of irritants varies by characteristics of the production environment, with the highest concentrations often found in industrial animal production facilities where large numbers of animals are raised in confinement (ATS, 1998; Radon et al., 2002a; O'Shaughnessy et al., 2012; Senthilselvan et al., 2011). Organic dust and endotoxin levels in animal production facilities are associated with increased prevalence of COPD manifestations including chronic cough and phlegm, chronic bronchitis, and airway obstruction (ATS, 1998; Senthilselvan et al., 2011). Evidence also suggests a link between pesticide exposure and COPD, (de Jong et al., 2014; Hoppin, 2014; Hoppin et al., 2007; Sprince et al., 2000) including insecticides commonly used to control pests in the animal production environment (Hoppin et al., 2007).

Despite recognition of a link between exposures in the animal production environment and chronic bronchitis symptoms, assessment of the association between occupational exposure to animal production and manifestations of the category of disease referred to as COPD has been limited and is necessary to understand the potential burden of COPD in agricultural populations and relevant occupational exposures (Monso et al., 2004). To examine this, we estimated associations between occupational exposure to animals and types of insecticides potentially used in animal production, and self-reported chronic bronchitis symptoms and COPD diagnoses among farmers participating in the Agricultural Health Study (AHS).

2. Methods

2.1. Study population

The AHS enrolled 52,394 private pesticide applicators (mostly farmers), hereafter referred to as “farmers,” when they presented for a restricted use pesticide license in Iowa and North Carolina during 1993–1997 (Alavanja et al., 1996) (Fig. 1). This analysis is restricted to the 24,171 farmers who responded to the 2005–2010 follow-up interview, during which information about respiratory symptoms was solicited from all participants. Previous publications have described AHS participation over time (Hoppin et al., 2012; Rinsky et al., 2017; Montgomery et al., 2010), and the implications of restriction to the 2005–2010 follow-up interview participants (46% of farmers who enrolled) (Rinsky et al., 2017).

From the 2005–2010 population, we excluded 683 farmers because of missing COPD information and 997 farmers because of missing covariate data resulting in an analysis population of 22,491.

All farmers included in this analysis provided information on demographics, lifestyle, medical history and farming activities through an enrollment questionnaire (1993–1997). This analysis was approved by all relevant Institutional Review Boards. Participants indicated initial informed consent by completing the enrollment questionnaire. Questionnaires are available on the study web site (http://www.aghealth.nih.gov/collaboration/questionnaires.html).

2.2. Exposure assessment

We used self-reported information about raising animals and personal use of insecticides registered for use on or around animals as proxies for occupational exposure to the animal production environment. Fig. 1 illustrates information collected at each interview.

2.2.1. Animal production—At enrollment, farmers responded to the question “What are the major income producing crops and animals you are currently raising on your farm?” and “Last year, how many poultry/livestock were there on the farm?” Responses to the latter question were recorded in categories of the number of poultry and livestock. During the two follow-up interviews farmers were asked “What type of animals did you have” and “How many of each animal did you have” in the year prior to interview (1999–2003) and since the time of last interview (2005–2010). Differences in detail and reference points at each interview prohibited us from combining information across interviews; instead, we created variables indicating the presence and number of each animal type reported at each interview.

To characterize the scale of the operation, we applied US Environmental Protection Agency regulatory definitions for small, medium, and large concentrated animal feeding operations

(CAFOs), which incorporate information about animal type and weight (U.S. EPA, 2012). Assuming animals were of mature weight, we categorized farmers into those working on: 1) an operation with no animals; 2) a small animal operation; or, 3) a medium/large animal operation. Small operations included those raising animals on pasture and possibly small industrial operations. Medium/large operations are likely to be industrial, raising animals in confinement, and, therefore, were considered as one category. We categorized operations based on each animal type separately and based on all animals on the property; results for the latter are presented here to account for production of multiple animal types on one property.

2.2.2. Insecticide use—We used responses to the question, "Have you applied insecticides to farm animals in the past 12 months?" asked at enrollment to assess general exposure to insecticides used on animals.

To assess specific insecticide use, we examined personal use of insecticides belonging to major insecticide classes formerly or currently registered for use on animals or in and around animal production facilities. We limited our analysis to insecticides used by at least 1% of the cohort. With these criteria, we evaluated ever use of 18 insecticides including nine organophosphates, one carbamate, one organochlorine, and seven pyrethroids. Twelve of the evaluated insecticides have been used in or around animal confinement areas, while the remaining six are members of the same insecticide classes but were not approved for animal use.

For insecticides asked about on the enrollment questionnaire, and based on personal use information provided at each interview (Supplementary Table 1), AHS researchers created lifetime personal ever and days of use variables for each pesticide at each interview as described previously (Hoppin et al., 2012). The lifetime exposure variables created following the 2005–2010 interview represent the most complete lifetime exposure variables available for this analysis. We categorized lifetime days of use into three categories (never users, users reporting ≤median days of use, users reporting > median days of use) based on the distribution among the study population.

2.3. Outcome assessment

During the 2005–2010 interview, farmers were asked, "Have you ever been diagnosed with" chronic bronchitis, emphysema, and COPD, in three separate questions (Supplementary Table S2). Farmers also reported whether they typically cough, bring up phlegm, and the duration of each of these symptoms. COPD encompasses multiple conditions with chronic cough and phlegm being the defining symptoms (ATS, 2004). Physician diagnosis of COPD can vary based on criteria used and requires the patient to present for care. To capture the potential variety of manifestations and severity in COPD among farmers, we used self-reported symptoms and diagnosis to define multiple disease categories, as has been done previously (ATS, 2004).

1. **COPD diagnosis only:** Physician's diagnosis of COPD, chronic bronchitis, or emphysema; but, no report of symptoms meeting the classical definition of

chronic bronchitis (cough and phlegm for ≥three months during two consecutive years (ATS, 2004)).

2. **COPD-related diagnosis and chronic bronchitis symptoms:** Physician's diagnosis of COPD, chronic bronchitis, or emphysema; and, symptoms consistent with the classical definition of chronic bronchitis.

3. **Chronic bronchitis symptoms only:** Symptoms consistent with the classical definition of chronic bronchitis; but, no report of a physician's diagnosis of COPD, chronic bronchitis or emphysema.

4. **No COPD:** Farmers who did not report a diagnosis or symptoms consistent with chronic bronchitis.

2.4. Statistical analysis

We evaluated prevalent COPD diagnosis and chronic bronchitis symptoms reported during the 2005–2010 interview. We were unable to evaluate disease incidence because diagnoses and symptoms were not collected from all farmers at enrollment, prohibiting our ability to confidently exclude prevalent cases and because the questions used to collect exposure information at each interview did not provide a clear temporal ordering of exposure and disease.

We examined the distribution of demographic and lifestyle characteristics reported at enrollment for all participants, and by disease status. We also examined the distribution of animal production and insecticide use at each interview overall and by disease status to identify temporal variation in animal production or insecticide use during the study period. Based on literature and directed acyclic graphs (DAG), (Greenland et al., 1999) we identified age, state, gender, education, and smoking as potential confounders of associations between animal production, insecticide use, and COPD outcomes. We saw no evidence of correlation among the insecticides to suggest potential confounding by correlated exposures.

To control for confounding we used stabilized inverse probability of exposure weights (IPEW), which create a "pseudo-population" where the distributions of confounding variables are similar across exposure groups. This is a form of direct standardization that results in no association between the exposure and confounders in the analysis population (Cole and Hernan, 2008). To derive exposure weights, we used linear, logistic, or polytomous logistic regression models for continuous, binary, and multi-level exposures, respectively, to estimate the predicted probability of exposure, conditional on the identified con- founders (categorized as shown in Table 1). We assigned each individual a weight equal to the inverse of the predicted probability that the person had his/her observed exposure. To stabilize the weights, we multiplied each weight by the marginal probability of the individual's observed exposure status.

We applied IPEW to polytomous logistic regression models to estimate standardized prevalence odds ratios (ORs). Each model included the exposure as the only explanatory variable. To account for within-subject correlation induced by weighting, we used a robust variance estimator to estimate standard errors and 95% confidence intervals (CIs) (Cole and

Hernan, 2008). We used previously described methods to evaluate the appropriateness of IPEW (Cole and Hernan, 2008). We present results estimated using untruncated IPEW because these weights demonstrated means close to one with few extreme values (Supplementary Table S3).

Although the number of farmers raising animals and actively using insecticides declined during the study period, these patterns did not differ by COPD status and closely aligned with aging of the cohort and temporal trends in animal production and insecticide use in the United States (US EPA, 2011; US EPA, 2000; Pew Commission on Industrial Farm Animal Production, 2008). Further, estimates of associations with COPD status were similar for exposure variables defined at each interview with the most complete and detailed information available from the 2005–2010 interview. Consequently, we present only associations between COPD status and animal production reported during the 2005–2010 interview and the lifetime insecticide use variables.

We evaluated smoking (never, former, current), early-life exposure to farm animals (yes, no), and state of residence (Iowa, North Carolina) as potential effect-measure modifiers. Associations did not differ across these variables; consequently, we present only overall results.

2.5. Sensitivity analyses

We conducted several sensitivity analyses. We excluded farmers < 40 years old at enrollment (N = 6310) because these individuals may require longer follow-up to observe COPD. We also excluded farmers reporting a physician's diagnosis of asthma (N = 1533), as asthma symptoms may overlap with symptoms of chronic bronchitis (Gibson and Simpson, 2009) and have been found to be related to use of pesticides (Hoppin et al., 2006; Henneberger et al., 2014) and work with animals (Hoppin et al., 2006; Henneberger et al., 2014; Omland, 2002). Additionally, we excluded farmers suspected to have COPD at enrollment (N = 849) based on reported age at diagnosis or symptom onset. Results of these analyses did not alter conclusions and are not presented here. Finally, to determine if an independent effect of insecticides existed, we adjusted insecticide ever-use models for animal production variables. All statistical analyses were conducted in SAS v9.3 (Cary, NC).

3. Results

Of the 22,491 farmers, a majority were male (97%) and ranged in age at the 2005–2010 interview from 27 to 97 years old (median age: 59 years). Forty-four percent of farmers were ever smokers and 13% were current smokers. Among participating farmers, 922 (4%) reported a COPD diagnosis only, 254 (1%) reported both a COPD diagnosis and chronic bronchitis symptoms, and 962 (4%) reported chronic bronchitis symptoms only (Table 1). The median age of disease onset was 52 years old (range: 18–90); the median age of onset was 55 years for diagnosis and 49 years for symptoms. Current or former smoking were more common among those reporting a COPD diagnosis or chronic bronchitis symptoms.

3.1. Animal exposures

Overall, raising animals was not positively associated with having a COPD diagnosis without chronic bronchitis symptoms with the exception of raising sheep/goats; raising hogs was inversely associated with a COPD diagnosis (Table 2). However, farmers raising hogs had greater odds of chronic bronchitis symptoms with and without a COPD diagnosis while those raising poultry and beef cattle had greater odds of chronic bronchitis symptoms only compared to farmers raising no animals. Farmers raising dairy cattle had greater odds of diagnosis and symptoms; however, this estimate is based on a small number of cases raising dairy cattle.

Reporting a COPD diagnosis without chronic bronchitis symptoms, was inversely associated with raising animals on a small and medium/ large operation. However, farmers working on small operations had 1.31 (95% CI: 1.13, 1.51) times the odds of COPD diagnosis and chronic bronchitis symptoms compared with farmers raising no animals. Working on a medium/large operation was positively associated with chronic bronchitis symptoms with (OR: 1.59; 95% CI: 1.16, 2.18) and without a diagnosis (OR: 1.69; 95% CI: 1.42, 2.01) (Fig. 2).

3.2. Insecticide use

3.2.1. Insecticides ever approved for use on or around animals—Applying insecticides to animals or animal shelters in the year prior to enrollment was associated with a greater burden of chronic bronchitis symptoms with (OR: 1.39; 95% CI: 1.08, 1.78) and without (OR: 1.21; 95% CI: 1.05, 1.38) a COPD diagnosis (Table 3).

Of the 12 insecticides ever approved for use on animals, eight were associated with at least one COPD-related outcome. The only insecticide associated with all three COPD-related categories was diazinon. Otherwise, use of the following insecticides was associated with increased chronic bronchitis symptoms with and without a COPD diagnosis: coumaphos, diazinon, malathion, carbaryl, permethrin (animals), and lindane. Ever use of dichlorvos was associated with greater odds of chronic bronchitis symptoms alone. Personal use of pyrethrins was associated with greater odds of chronic bronchitis symptoms and a COPD diagnosis; however, this was based on a small number of cases reporting use. Results remained similar, though less precise, when controlling for types of animals raised (Supplementary Table S4).

When lifetime days of use were modeled, personal use of couma- phos, dichlorvos, and permethrin (animals) was associated with elevated odds of chronic bronchitis symptoms with or without a COPD diagnosis; for all, the largest OR was observed at the highest levels of use (Supplementary Table S5). Similar patterns remained when estimates were adjusted for types of animals raised (Supplementary Table S6).

3.2.2. Insecticides never approved for use on or around animals—Of the six insecticides never approved for use on animals, three were associated with at least one COPD-related outcome. Parathion was positively associated with chronic bronchitis symptoms with or without COPD diagnosis. Phorate was inversely associated with COPD diagnosis alone, while permethrin (for crops) was positively associated with COPD diagnosis in the absence of chronic bronchitis symptoms.

When lifetime days of use were considered, permethrin (crops) was associated with COPD diagnosis irrespective of chronic bronchitis symptoms (Supplementary Table S5). Similar patterns remained when estimates were adjusted for types of animals raised (Supplementary Table S6).

4. Discussion

Occupational exposure to animal production has been previously linked to COPD-related manifestations including short-term decline in pulmonary function (ATS, 1998; Monso et al., 2004; Omland, 2002), symptoms of respiratory irritation (ATS, 1998; Senthilselvan et al., 2007), and increased risk of cough and phlegm (ATS, 1998; Omland, 2002). Among AHS participants, we observed evidence to support a link between animal production work, including exposure to animals and insecticide use, and a greater burden of chronic bronchitis symptoms whether a COPD diagnosis was reported or not; however, we observed only limited evidence of associations between animal production work and COPD diagnoses independent of chronic bronchitis symptoms.

Raising hogs, poultry, and beef cattle were associated with a greater burden of chronic bronchitis symptoms. Farmers producing animals on medium/large operations likely using industrial production methods had approximately 60% greater odds of chronic bronchitis symptoms irrespective of a COPD diagnosis. Researchers have previously found greater prevalence of chronic bronchitis (ATS, 1998; Melbostad et al., 1997; Mauny et al., 1997; Chaudemanche et al., 2003; Gainet et al., 2007) and cough and phlegm (ATS, 1998; Senthilselvan et al., 2007; Chaudemanche et al., 2003) among farmers and farm workers involved in production of hogs, poultry, and cattle (mostly dairy), mainly in industrial settings. The respiratory effects of occupational exposure to beef cattle production have not been well studied but researchers have documented similar levels of organic dust and endotoxin in cattle feedlots as levels found in hog confinement facilities (Von Essen et al., 2010; McEachran et al., 2015).

The observed associations between personal use of insecticides and chronic bronchitis symptoms support mounting evidence that use of insecticides may either play a role in the etiology or exacerbation of COPD-related manifestations or serve as a marker of other relevant exposures. General use of pesticides has been linked with chronic bronchitis in a case-control study in Lebanon (Salameh et al., 2006) and reduced pulmonary function and higher prevalence of airway obstruction among two population-based cohorts in The Netherlands (de Jong et al., 2014). Among rural residents of Beijing, China, use of insecticides was associated with twice the odds of cough and phlegm production (Zhang et al., 2002). Similar to our results for farmers who reported directly applying insecticides to farm animals, farmers in the Iowa Farm Family Health and Hazard Surveillance Project who applied insecticides to livestock had twice the odds of phlegm than farmers who did not apply insecticides, but who raised livestock (Sprince et al., 2000).

Most previous work investigating COPD-related outcomes and animal production lacks information on type, frequency and duration of pesticides used (Hoppin, 2014). Using the AHS, we were able to quantify associations between COPD-related outcomes and specific insecticides. Use of insecticides ever approved for use on or around animals demonstrated multiple positive associations with chronic bronchitis symptoms. However, many of these insecticides are also used for purposes other than treating animals or their enclosures (North Carolina Cooperative Extension Service, 2014). We also found that ever use of several of the insecticides never approved for use on or around animals were associated with greater odds of chronic bronchitis symptoms, COPD diagnosis, or both. Therefore, the associations reported here cannot be attributed solely to animal production. Additional work with detailed personal exposure information is necessary to better elucidate the interrelationships between animal exposures and insecticide use on COPD.

With the exception of permethrin, pyrethroids were not consistently associated with increased odds of chronic bronchitis symptoms or COPD diagnosis. Use of pyrethroids has increased since the 1970s while the use of the more acutely toxic organophosphates has declined (US EPA, 2013). Because pyrethroid use is more common, the potential respiratory health effects of exposure should be examined.

Associations were not consistently observed between raising animals, insecticide use and COPD diagnosis independent of chronic bronchitis symptoms. It is possible that the biological response to animal production exposures may manifest in chronic bronchitis symptoms but not lead to a COPD diagnosis. This hypothesis aligns with what has been observed for other dusty trades (Becklake, 1985). Limitations in our exposure assessment may also explain some of the discrepancy. Presence of animals on a property is a crude proxy for personal exposure to respiratory irritants in animal production. Additional information is necessary to understand each farmers' potential exposures including lifetime duration and intensity of animal production work and details about the production environment including age of animals, confinement practices, waste management systems, and insecticide use. Future work would be strengthened by including this information and objective measures of irritants, and considering the interaction between such exposures. It is also possible that exposure misclassification operated differently in analyses of COPD-related diagnosis and symptoms. For example, if farmers with a COPD diagnosis limited personal exposure to animal production, a healthy-worker survivor effect would be stronger in analysis of diagnosis than symptoms (Chenard et al., 2007; Radon et al., 2002b; Thelin and Hoglund, 1994).

To capture the full burden of COPD-related outcomes, we considered both diagnoses and symptoms consistent with the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria for COPD, which includes symptoms as a key aspect of defining disease severity (GOLD, 2011). The prevalence of COPD-related diagnosis among AHS farmers was similar to the age-adjusted prevalence in the general population (6%) (Iowa: 5%; North Carolina: 7%), (Kosacz et al., 2012) despite a lower prevalence of smoking compared to the general population (CDC, 2010). The prevalence of chronic bronchitis symptoms was lower than estimates of chronic bronchitis symptoms from other US studies of animal confinement workers (7–25%) (ATS, 1998; Omland, 2002). Varying approaches to measure COPD burden may explain some of these differences. For example, when spirometry is used, COPD prevalence among individuals involved in animal production (17%) (Monso et al., 2004) and the general public (10–20%) (Tilert et al., 2013) is consistently greater than what we found here. This is not surprising, as reliance on self-report is known to result in an underestimate of COPD compared with spirometry (Trupin et al., 2003; Mannino et al., 2002; Halbert et al., 2006; Barr et al., 2002). Although spirometry or clinical confirmation of case status is useful in confirming COPD cases, spirometry also identifies those with subclinical obstruction. Reliance on self-reported diagnosis and symptoms does not exclude those who have not accessed care to receive spirometry or a diagnosis and may be more representative of clinically relevant disease; especially in populations with limited access to care (Barr et al., 2002).

Our analysis was restricted to farmers responding to the 2005–2010 interview. Restriction was necessary because COPD-related outcomes were not available for all participants prior to this interview. We previously examined the impact of non-participation in the 2005–2010 interview on estimation of exposure-disease associations (Rinsky et al., 2017). The previous analysis suggested that animal production, use of insecticides, and COPD-related outcomes are not strongly associated with response to the 2005–2010 interview and that effect estimates generated from 2005–2010 respondents should be similar to those that would have been generated from the full cohort had complete information been available (Rinsky et al., 2017; Daniel et al., 2012; Westreich, 2012).

In this analysis, we were unable to establish the temporal ordering of exposure and COPD outcomes, and therefore could not directly assess incident disease. Our differential findings for those with COPD diagnoses without chronic bronchitis symptoms, suggest that diagnosed workers may be more likely to have changed their agricultural practices. Future work, with detailed information about timing of exposure and disease onset is needed to directly assess COPD risk in populations working in animal production. The AHS allows researchers to evaluate the potential health risks of agricultural exposures by comparing exposed farmers to unexposed farmers rather than the general population. However, AHS participants were recruited on the basis of being private pesticide applicators and therefore, few participants are truly unexposed to all pesticides. When multiple pesticides are independently associated with disease risk, having no clear unexposed group limits the ability to observe associations (Rose, 1985). Because the AHS includes only pesticide applicator farm owners and operators, these results may not be generalizable to all animal operation operators, or to farm workers who may experience a different intensity and duration of exposure to the animal production environment.

Several design elements of the AHS strengthened this analysis. The large sample size and extensive information about demographics and lifestyle factors allowed for confounding control and exploration of effect modification by important covariates. The ability to consider modification by smoking revealed that the observed associations were present among never, former, and current smokers alike. Because the AHS continues to follow farmers who change farming activities or even cease farm work, concerns common to cross-sectional studies regarding exclusion of farmers who have left work are reduced. In addition, although there are limitations to our exposure assessment, the AHS provides one of the most detailed assessments of personal insecticide use available.

These results provide more evidence that animal production work and personal use of specific insecticides are associated with a greater burden of chronic bronchitis symptoms. The results support the call for further research into the role of occupational exposures, specifically animal production work, in the etiology of COPD manifestations and the need to provide better protections for farmers and agricultural workers. This analysis also demonstrates the need for prospective studies of farmers and farm workers in the United States to be conducted with improved information on personal exposure to animal production and other farming activities. Addressing these limitations will allow the scientific and farming communities to better understand effects of exposure to animal production and insecticide use on respiratory health.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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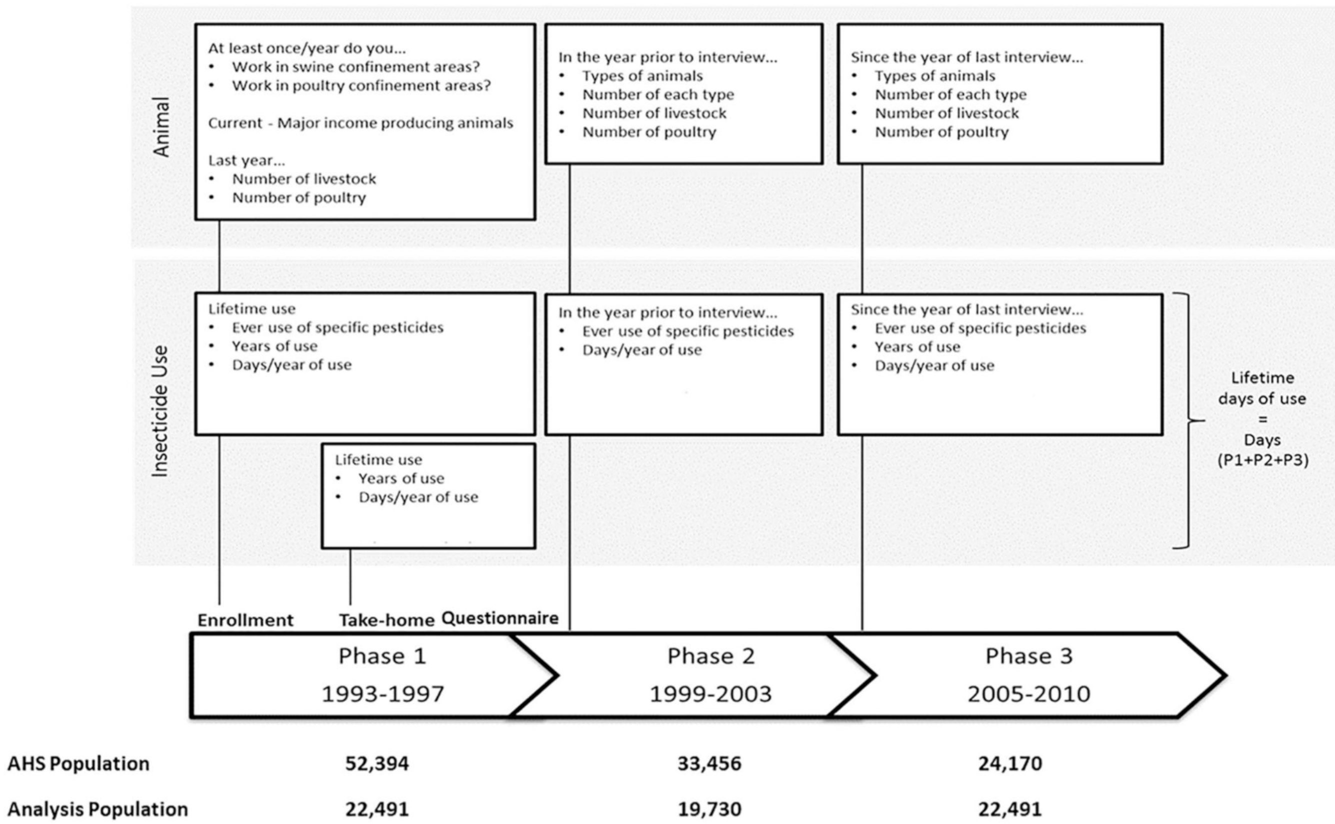

Fig. 1.

Participation in interviews and report of animal production and pesticide use information by phase in the Agricultural Health Study and the current analysis.

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Outcome	Operation Size	Cases	No COPD	OR	95% CI
COPD diagnosis only	No animals	603	10631	1	
	Small	256	6760	0.88	0.76, 1.02
	Medium/large	63	2962	0.72	0.58, 0.89
COPD diagnosis & symptoms	No animals	158	10631	1	
	Small	72	6760	1.03	0.78, 1.36
	Medium/large	24	2962	1.59	1.16, 2.18
COPD-related symptoms only	No animals	455	10631	1	
	Small	339	6760	1.31	1.13, 1.51
	Medium/large	168	2962	1.69	1.42, 2.01

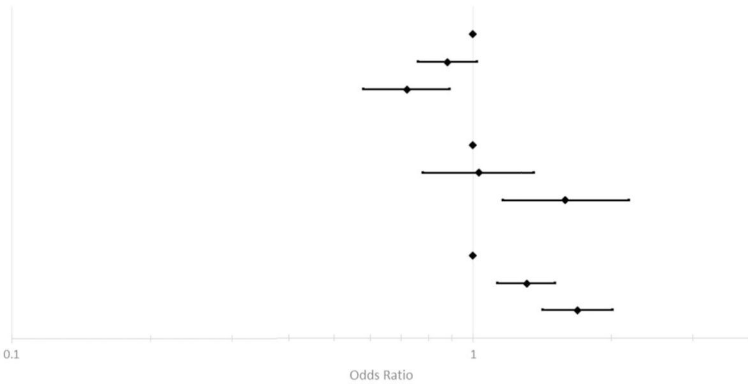

Fig. 2.

Associations between size of animal operation[a] and COPD status among 22,491 farmers participating in the 2005–2010 interview, Agricultural Health Study. [a]Size of animal production was determined using the number of animals produced on a farmer’s property and categorized using the regulatory definitions of CAFOs (U.S. EPA, 2012). Large and medium operations are likely to be raising animals in confinement.

Table 1

Distribution of demographic and lifestyle characteristics by COPD diagnosis and symptoms among 22,491 farmers participating in the 2005–2010 interview, Agricultural Health Study.

	No COPD		COPD diagnosis only[a]		COPD diagnosis & chronic bronchitis symptoms[b]		Chronic bronchitis symptoms only[c]	
Participant characteristics[d]	***N* = 20,353**	**%**	***N* = 922**	**%**	***N* = 254**	**%**	***N* = 962**	**%**
Age (2005–2010 interview)								
<50 years	4540	22	69	7	13	5	195	20
50–59 years	6295	31	177	19	49	19	295	31
60–69 years	5090	25	286	31	72	28	224	23
70–79years	3574	18	297	32	97	38	188	20
80+ years	854	4	93	10	23	9	60	6
State								
Iowa	13,771	68	437	47	140	55	711	74
North Carolina	6582	32	485	53	114	45	251	26
Gender								
Female	565	3	33	4	7	3	16	2
Male	19,788	97	889	96	247	97	946	98
Race/ethnicity								
White, non-Hispanic	19,519	96	841	91	217	85	920	96
Other	477	2	26	3	11	4	11	1
Missing	357		55		26		31	
Education								
< High school degree	1441	7	138	15	49	19	77	8
High school graduate/GED	9330	46	448	49	129	51	458	48
Some college	5283	26	203	22	53	21	261	27
≥College graduate	4299	21	133	14	23	9	166	17
Marital status								
Married/living as married	17,769	87	842	92	224	89	855	89
Other	2566	13	78	8	28	11	103	11

Participant characteristics[d]	No COPD N = 20,353	%	COPD diagnosis only[a] N= 922	%	COPD diagnosis & chronic bronchitis symptoms[b] N= 254	%	Chronic bronchitis symptoms only[c] N= 962	%
Missing	18		2		2		4	
Smoking status								
Never	11,721	58	278	30	51	20	438	46
Former	6381	31	396	43	113	44	288	30
Current	2251	11	248	27	90	35	236	25
Alcohol consumption[e]								
None	6733	34	370	42	90	38	251	27
Light drinker	12,562	64	492	58	139	59	650	70
Heavy drinker	308	2	11	1	8	3	26	3
Missing	750		49		17		35	
Size of farm (acres)								
Didn’t work on farm/none	633	3	43	5	13	6	34	4
<5	711	4	49	6	15	7	35	4
5–49	1804	10	143	17	32	14	74	8
50–199	3460	18	185	23	42	19	157	17
200–499	5499	29	204	25	55	24	287	32
500–999	4310	23	120	15	41	18	204	22
> 1000	2550	13	75	9	27	12	119	13
Missing	1386		103		29		52	
Early life exposure to farm environment (2005–2010 interview)								
Yes	18,203	90	838	91	231	91	884	92
No	2110	10	82	9	23	9	75	8
Missing	40		2		0		3	
Ever received doctor diagnosis of asthma (2005–2010 interview)								
Yes	1086	5	253	28	85	34	109	11
No	19,256	95	666	72	167	66	850	89
Missing	11		3		2		3	

[a] Reported diagnosis of chronic bronchitis, emphysema or COPD without symptoms.

[b]Chronic cough and phlegm for more than three months in at least two consecutive years and a diagnosis of chronic bronchitis, emphysema, or COPD.

[c]Chronic cough and phlegm for ≥ three months during two consecutive years without a reported diagnosis of chronic bronchitis, emphysema or COPD.

[d]All characteristics were reported at enrollment unless otherwise specified.

[e]Heavy drinkers reported consuming five or more drinks on the same occasion on each of five or more days in the past 30 days, light drinkers reported consuming at least one drink on at least one day during the past 12months but did not qualify as a heavy drinker (NIAA, 2015).

Table 2

Associations between raising animals and COPD diagnosis and chronic bronchitis symptoms among 22,491 farmers participating in the 2005–2010 interview, Agricultural Health Study.

	No COPD		COPD diagnosis only[a]				COPD diagnosis & chronic bronchitis symptoms[b]				Chronic bronchitis symptoms only[c]			
			Cases		OR[d]	95% CI	Cases		OR[d]	95% CI	Cases		OR[d]	95% CI
	N = 20353	%	N = 922	%			N = 254	%			N = 962	%		
Type of Animal Raised														
Hogs	3208	16	62	7	0.72	0.58, 0.88	24	9	1.41	1.05, 1.89	184	19	1.25	1.06, 1.47
Poultry/Eggs	982	5	38	4	0.96	0.70, 1.32	9	4	1.02	0.57, 1.81	54	6	1.29	0.98, 1.70
Beef cattle	6906	34	246	27	0.95	0.82, 1.09	75	30	1.07	0.83, 1.39	376	39	1.29	1.13, 1.47
Dairy cattle	816	4	21	2	0.92	0.65, 1.31	9	4	1.63	0.98, 2.70	32	3	0.88	0.62, 1.25
Sheep/Goats	703	3	31	3	1.26	0.91, 1.75	3	1	-[e]		35	4	1.04	0.87, 1.24

OR = odds ratio.

CI = confidence interval.

[a]Reported diagnosis of chronic bronchitis, emphysema or COPD without symptoms.

[b]Chronic cough and phlegm for more than three months in at least two consecutive years and a diagnosis of chronic bronchitis, emphysema, or COPD.

[c]Chronic cough and phlegm for ≥ three months during two consecutive years without a reported diagnosis of chronic bronchitis, emphysema or COPD.

[d]ORs were estimated using IPEW to address confounding. Weights were estimated using age at the 2005–2010 interview, state, gender, smoking status, and education categorized as shown in Table 1.

[e]OR not calculated because there were < 5 exposed cases.

Table 3

Associations between ever use of selected insecticides and COPD diagnosis and chronic bronchitis symptoms among 22,491 farmers participating in the 2005–2010 interview, Agricultural Health Study.

	No COPD		COPD diagnosis only[a]				COPD diagnosis & chronic bronchitis symptoms[b]				Chronic bronchitis symptoms only[c]			
			Cases		OR[d]	95% CI	Cases		OR[d]	95% CI	Cases		OR[d]	95% CI
Exposure	**N = 20353**	**%**	**N = 922**	**%**			**N = 254**	**%**			**N = 962**	**%**		
Insecticide application to farm animals in past 12 months[e]	6524	32	221	24	1.03	0.90, 1.19	79	31	1.39	1.08, 1.78	348	36	1.21	1.05, 1.38
Ever approved for use on or around animals														
Organophosphates														
Chlorpyrifos	9488	47	375	41	0.96	0.84, 1.10	114	45	1.13	0.88, 1.44	475	49	1.12	0.98, 1.27
Coumaphos	1841	9	90	10	1.12	0.90, 1.40	28	11	1.30	0.88, 1.92	112	12	1.27	1.04, 1.57
Diazinon	7155	35	396	43	1.18	1.03, 1.35	110	43	1.42	1.10, 1.83	372	39	1.34	1.05, 1.72
Dichlorvos	2380	12	86	9	0.97	0.79, 1.20	34	13	1.26	0.88, 1.81	144	15	1.39	1.16, 1.66
Malathion	15135	74	673	73	1.03	0.88, 1.20	207	81	1.85	1.32, 2.60	749	78	1.22	1.05, 1.43
Carbamates														
Carbaryl	12142	60	634	69	1.05	0.92, 1.20	180	71	1.28	0.99, 1.66	602	63	1.28	1.11, 1.47
Pyrethroids														
Permethrin (animals)	3580	18	102	11	0.95	0.80, 1.14	41	16	1.35	1.00, 1.83	208	22	1.41	1.21, 1.65
Pyrethrins[f]	318	2	11	1	0.81	0.44, 1.48	5	2	2.61	1.36, 5.02	15	2	1.05	0.62, 1.78
Cyfluthrin[f]	1648	8	33	4	0.79	0.60, 1.04	11	4	0.65	0.37, 1.15	84	9	1.11	0.88, 1.41
Lambda Cyhalothrin[f]	791	4	19	2	1.00	0.71, 1.41	1	0	-[d]		33	3	1.01	0.72, 1.42
Esfenvalerate[f]	354	2	12	1	1.02	0.60, 1.71	3	1	-[g]		11	1	0.93	0.54, 1.58
Organochlorines														
Lindane	4762	23	218	24	1.07	0.91, 1.24	80	31	1.50	1.14, 1.96	304	31	1.48	1.29, 1.71
Never approved for use on or around animals														
Organophosphates														
Parathion	3258	16	203	22	1.06	0.89, 1.27	59	23	1.41	1.04, 1.90	176	18	1.29	1.10, 1.52

	No COPD		COPD diagnosis only[a]				COPD diagnosis & chronic bronchitis symptoms[b]				Chronic bronchitis symptoms only[c]			
			Cases		OR[d]	95% CI	Cases		OR[d]	95% CI	Cases		OR[d]	95% CI
Exposure	**N = 20353**	**%**	**N = 922**	**%**			**N = 254**	**%**			**N = 962**	**%**		
Phorate	7163	35	262	28	0.84	0.73, 0.97	100	39	1.24	0.96, 1.60	387	40	1.01	0.88, 1.16
Fonofos	4421	22	148	16	0.90	0.77, 1.06	62	24	1.20	0.90, 1.61	249	26	1.05	0.89, 1.22
Terbufos	7984	39	292	32	1.07	0.94, 1.22	99	39	1.22	0.95, 1.57	400	42	1.00	0.87, 1.14
Pyrethroids														
Permethrin (crops)	3117	15	140	15	1.29	1.09, 1.52	33	13	1.18	0.85, 1.63	136	14	0.99	0.83, 1.19
Tefluthrin[f]	692	3	18	2	0.77	0.51, 1.16	6	2	1.08	0.56, 2.10	42	4	0.95	0.66, 1.37

OR = odds ratio.

CI = confidence interval.

[a] Reported diagnosis of chronic bronchitis, emphysema or COPD without symptoms.

[b] Chronic cough and phlegm for more than three months in at least two consecutive years and a diagnosis of chronic bronchitis, emphysema, or COPD.

[c] Chronic cough and phlegm for ≥three months during two consecutive years without a reported diagnosis of chronic bronchitis, emphysema or COPD.

[d] ORs were estimated using IPEW to address confounding. Weights were estimated using age at the 2005–2010 interview, state, gender, smoking status and education categorized as shown in Table 1.

[e] Reported at enrollment.

[f] Use information from the 2005–2010 interview only.

[g] OR not calculated because there were < 5 exposed cases.