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Animal production and wheeze in the Agricultural Health Study: interactions with atopy, asthma, and smoking

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Background: Exposure to animals, their feeds, and by-products contribute to respiratory symptoms among farmers.
Aims: To investigate the role of animal exposures and wheeze, and to assess whether their impact differs among susceptible subgroups, including atopics, asthmatics, and smokers.
Methods: Using the Agricultural Health Study, a cohort of pesticide applicators in Iowa and North Carolina enrolled in 1994–97, wheeze associated with animal production was evaluated and interactions among susceptible subgroups assessed. Logistic regression models were used to examine risk factors for wheeze in the past year among 20 468 farmers.
Results: Individuals raising animals requiring direct contact had the highest odds ratios (OR) for wheeze (OR_{dairy} = 1.26; OR_{eggs} = 1.70). A significant dose response was observed for both the number of poultry and the number of livestock on the farm. Farmers who performed veterinary procedures on a daily basis had an OR of 1.51. The odds of wheeze associated with poultry production was greater among atopic than non-atopic individuals. Milking cows daily increased the odds of wheeze in all individuals, with the largest association observed among atopic asthmatic individuals. The impact of dairy, poultry, and egg production varied among smoking groups. Past smokers had the highest odds ratios, followed by never smokers, and then current smokers. The OR_{eggs} was 2.88 among past smokers but only 1.46 for never smokers. The OR_{eggs} for current smokers of 0.80 might reflect self selection of exposure among smokers.
Conclusions: Results are consistent with animal production and respiratory symptoms, and suggest that subgroups may respond differently to exposure.

Farmers are exposed to many respiratory hazards at work and have higher rates of asthma and respiratory symptoms than other workers.[1–6] Individuals involved in animal production have greater prevalence of respiratory symptoms than other farmers and other rural residents. Increased respiratory symptoms and decreased lung function have been observed among dairy, swine, and poultry workers in North America, Europe, and New Zealand,[7–16] and among veterinary surgeons.[3]

Animal production involves exposure to a variety of agents besides the animals themselves. Potential respiratory hazards associated with animal production include inorganic dust from soil; organic dust containing microorganisms, mycotoxins, endotoxins, animal feed particles, and allergens; disinfectants, including quaternary ammonium compounds; and ammonia and hydrogen sulphide produced from anaerobic processes.[1 17–20] Grains and hay have also been associated with increased respiratory symptoms among animal producers.[21]

Main messages

- Animals and animal related exposures remain important triggers for wheeze among adult farmers.
- Poultry related exposures were more important predictors of wheeze than hog related exposures.
- Atopic individuals working with poultry had higher odds of wheeze than non-atopic individuals with the same exposure.
- A healthy smoker effect or a self selection of exposure was observed. Current smokers, while having the highest odds of wheeze overall, had lower odds of wheeze for working with dairy cattle, eggs, and poultry than expected, while past smokers had higher odds of wheeze than anticipated for these exposures.

Allergens and farm related antigens may trigger different responses among individuals with atopy and asthma.[20 22–24] The reported contribution of atopy to respiratory symptoms among adult farmers is not consistent. Among animal confinement workers, an asthma-like syndrome is not related to atopy.[25] However, disinfectant use among pig farmers in France contributed to atopic sensitisation and subsequent respiratory symptoms.[20] Smoking status has also been suggested to modify or enhance the effect of animal related farm exposures.[2 8 26–28]

Animal production practices differ around the world as a result of climate, culture, and regulations. Few regions represent the heterogeneity and breadth of agricultural practices to assess the contribution of a wide variety of animal handling activities in one sample. To explore the impact of animal production on respiratory symptoms of farmers and to assess whether atopics, asthmatics, and smokers respond differently to exposure, we assessed the odds of wheeze associated with

Policy implications

- While farmers are exposed to a wide array of respiratory irritants, we can identify particular animals and exposures which contribute to wheezing among adult farmers.
- Since wheeze is a symptom of respiratory morbidity among farmers, further research using more quantitative measures of respiratory impairment will allow recommendations to prevent respiratory morbidity among farmers.

Abbreviations: AHS, Agricultural Health Study; CI, confidence interval; NS, non-significant; OR, odds ratio

Table 1 Demographic and medical characteristics of farmers in the Agricultural Health Study by wheeze status, 1994–97

	All participants (n=20468)				
	Wheeze n=3838		No wheeze n=16630		
	n	%	n	%	p value†
Age category					
<20 years	28	1	108	1	0.009
21–30 years	294	8	1156	7	
31–40 years	917	24	3628	23	
41–50 years	986	26	4296	26	
51–60 years	814	21	3922	24	
61–70 years	617	16	2762	17	
>70 years	182	5	758	5	
Race					NS
White	3722	98	16090	98	
Other	78	2	361	2	
Sex					NS
Female	89	2	402	2	
Male	3749	98	16228	98	
State					<0.01
Iowa	2423	63	11496	69	
North Carolina	1415	37	5134	31	
Smoking status					
Never	1680	44	9497	57	
Past	1255	33	5399	33	<0.01‡
Current	903	24	1734	10	<0.01‡
Atopy*: asthma status					
No atopy: no asthma	2667	69	14860	89	
Atopy: no asthma	498	13	1407	8	<0.01§
No atopy: asthma	309	8	127	1	<0.01§
Atopy: asthma	364	9	236	1	<0.01§

*Atopy defined as self report of hay fever or eczema.
†p value for χ^2 test.
‡Compared to never smokers.
§Compared to no atopy, no asthma.

animal production among farmers in the Agricultural Health Study in the USA. The association between pesticide application to livestock and crops and wheeze was evaluated previously.[29]

MATERIALS AND METHODS

This cross sectional analysis of animal exposures and wheeze was conducted among farmers in the Agricultural Health Study (AHS). The AHS is a cohort of certified pesticide applicators and their spouses in Iowa and North Carolina enrolled between 1994 and 1997. Details of enrolment are described elsewhere.[30] Approximately 52 000 private pesticide applicators, primarily farmers, enrolled in the study by completing a questionnaire at pesticide certification; 82.4% of eligible applicators enrolled. A total of 22 756 of these (44%) returned a second more detailed questionnaire, which included questions regarding wheeze and asthma history. Applicators who did or did not return the second questionnaire were similar with regard to demographic characteristics, farming practices, and medical history including asthma.[31] The study population for this analysis was limited to applicators who returned both questionnaires. The AHS has been reviewed and approved by institutional review boards at the National Institutes of Health, the University of Iowa, and Battelle Life Sciences.

We obtained information regarding animal related farm activities and potential confounders from both questionnaires. These questionnaires described current farm activities, animals raised, farm tasks, pesticide application, smoking history, demographics, and medical information regarding wheeze and doctor diagnosis of ever having asthma, eczema, or hay fever. Detailed information was provided regarding specific animal raising activities including veterinary procedures, milking, and butchering, as well as grain and feed handling.

The outcome, wheeze in the past year, was based on the question: "How many episodes of wheezing or whistling in your chest have you had in the past 12 months?" Any positive response was included in the wheeze group. Information on other respiratory symptoms in the past year was not collected.

We evaluated animals and related exposures as risk factors for wheeze using a common logistic regression model controlling for age in 10-year categories, state, smoking history (current, past, never), history of asthma and atopy (four levels), and an interaction term between current smoking and history of asthma. The role of smoking on wheeze was investigated using a variety of parameters, including smoking status at enrolment (current, former, never), pack years, and cigarettes per day. Smoking status at enrolment and an interaction term between current smoking and history of asthma provided the best fit for the data and were included in all models. Atopy history was defined as a self report of a doctor diagnosis of either eczema or hay fever. We evaluated animal related farm activities in the past year, both dichotomously using ever/never responses and continuously using frequency of the activity. We compared farmers with the animal exposure of interest to those without this exposure; we did not exclude other animal exposures from the referent group. χ^2 tests for trend were performed using the questionnaire frequency categories. We evaluated whether history of atopy and/or asthma influenced response to exposure by adding terms for both two way (for example, atopy*exposure) and three way interactions (for example, atopy*asthma*exposure) with exposure to the base model. We used likelihood ratio tests to evaluate the interaction terms. When the p value for the three way interaction term was greater than 0.25, we refit the model without the three way interaction for that particular exposure and then reported the results for the two way interactions. We evaluated whether smoking history influenced response to exposure by including two interaction terms in the base

Table 2 Odds ratios for wheeze in the past year and animal production activities among farmers in the Agricultural Health Study, 1994–97

Animal production exposures	Wheeze n=3838		No wheeze n=16630		Odds ratio†	95% CI
	n	%	n	%		
Animals raised						
Beef cattle	1474	38.4	6430	38.7	1.06	0.98 to 1.14
Dairy cattle	231	6	899	5.4	1.26	1.08 to 1.48
Hogs	1256	32.7	5642	33.9	1.13	1.03 to 1.23
Sheep	149	3.9	642	3.9	1.10	0.91 to 1.34
Poultry	188	4.9	576	3.5	1.36	1.13 to 1.62
Eggs	75	2	201	1.2	1.70	1.28 to 2.26
Any animal	2297	59.9	10041	60.4	1.13	1.04 to 1.23
Grain handling activities‡						
Grind animal feed	1721	44.8	7668	46.1	1.14	1.05 to 1.24
Handle stored grain	2656	69.2	11778	70.8	1.13	1.02 to 1.24
Handle stored hay	2217	57.8	9502	57.1	1.10	1.02 to 1.19
Load/unload silage	784	20.4	3423	20.6	1.09	0.99 to 1.20
Animal contact activities‡						
Butcher animals	606	15.8	2030	12.2	1.31	1.18 to 1.45
Milk cows	236	6.3	893	5.5	1.31	1.12 to 1.52
Veterinary procedures	2042	53	8806	53	1.16	1.07 to 1.26
Work in swine areas	1098	29	4655	28.4	1.21	1.11 to 1.32

†Odds ratios adjusted for age, state, smoking (past and current), atopy-asthma status, and asthma*current smoking.
Referent group is those who did not participate in that activity.
‡At least once in the past year; at least once per month for milking cows.

Table 3 Dose response models for animal activities among farmers in the Agricultural Health Study, 1994–97

Animal production	Wheeze n=3838		No wheeze n=16630		Odds ratio†	95% CI	p trend
	n	%	n	%			
Livestock on farm							0.0042
None	1219	34	5139	33	1.00		
<50	540	15	2153	14	1.09	0.96 to 1.23	
50–99	287	8	1259	8	1.09	0.93 to 1.26	
100–499	692	19	3168	20	1.12	1.00 to 1.26	
500–999	415	12	1925	12	1.16	1.01 to 1.34	
⩾1000	470	13	2046	13	1.19	1.04 to 1.36	
Poultry on farm							0.006
None	3185	89	14029	91	1.00		
<50	177	5	742	5	1.06	0.88 to 1.27	
50–99	48	1	198	1	1.06	0.75 to 1.48	
100–499	48	1	195	1	1.14	0.81 to 1.60	
⩾500	112	3	328	2	1.39	1.10 to 1.75	
Milk cows							0.0008
Never or < once/month	3490	93	15373	94	1.00		
Monthly	45	1	147	1	1.25	0.87 to 1.80	
Weekly	26	1	96	1	1.25	0.79 to 1.99	
Daily	183	5	705	4	1.33	1.11 to 1.58	
Veterinary procedures							<0.0001
Never or < once/month	2239	60	9866	61	1.00		
Monthly	1068	29	4634	28	1.18	1.08 to 1.29	
Weekly	361	10	1563	10	1.16	1.01 to 1.33	
Daily	75	2	230	1	1.51	1.14 to 2.01	
Grind feed							0.148
Never or < once/month	2265	60	9424	58	1.00		
Monthly	422	11	1850	11	1.05	0.93 to 1.18	
Weekly	859	23	4115	25	1.04	0.94 to 1.16	
Daily	216	6	967	6	1.14	0.96 to 1.35	

†Odds ratios adjusted for age, state, smoking (past and current), atopy-asthma status, and asthma*current smoking.

model, current smoking*exposure and past smoking*exposure, and using a likelihood ratio test with two degrees of freedom. All statistical analysis was done using SAS (Cary, NC).

RESULTS

A total of 20 468 farmers had complete information on all base model covariates. Respondents were predominantly white males; they ranged in age from 16 to 88 years at the time of enrolment (table 1). Nineteen per cent reported at least one episode of wheeze in the year before enrolment. Five per cent reported a doctor diagnosis of asthma, with 54% of these individuals diagnosed before age 20; 11% had a history of eczema or hay fever, our atopy definition. Both current and former smokers were more likely to report wheeze in the past year than never smokers.

Individuals reported the number and types of animals raised on the farm in the year prior to enrolment, as well as information regarding animal related tasks occurring at least once in the past year (for example, milking cows, veterinary procedures, and handling animal feed and grain). Table 2 presents the exposure prevalences and the adjusted odds

Table 4 Odds ratios for animal exposures and wheeze by atopy and asthma status among farmers in the Agricultural Health Study

Exposure Atopy/asthma status	Exposure prevalence						p interaction‡	
	Wheeze		No wheeze					
	n	%	n	%	Odds ratio†	95% CI	Atopy	Asthma
Animals								
Beef cattle							0.02	0.34
No atopy: no asthma	1006	68	5760	90	1.03	0.94 to 1.12		
Atopy: no asthma	205	14	524	8	1.29	1.04 to 1.60		
No atopy: asthma	136	9	99	2	0.85	0.61 to 1.19		
Atopy: asthma	127	9	47	1	1.25	0.82 to 1.92		
Dairy cattle							–	–§
No atopy: no asthma	162	70	822	91	1.28	1.04 to 1.48		
Atopy: no asthma	26	11	63	7	1.19	0.74 to 1.92		
No atopy: asthma	18	8	11	1	1.10	0.51 to 2.37		
Atopy: asthma	25	11	3	0.3	3.84	1.14 to 12.98		
Hogs							0.17	0.93
No atopy: no asthma	900	72	5172	92	1.09	0.99 to 1.20		
Atopy: no asthma	149	12	366	6	1.34	1.06 to 1.69		
No atopy: asthma	108	9	64	1	1.22	0.85 to 1.77		
Atopy: asthma	99	8	40	1	1.14	0.73 to 1.78		
Sheep							0.99	0.58
No atopy: no asthma	104	70	572	89	1.13	0.91 to 1.40		
Atopy: no asthma	18	12	53	8	1.08	0.62 to 1.88		
No atopy: asthma	15	10	12	2	0.87	0.40 to 1.40		
Atopy: asthma	12	8	5	1	1.05	0.36 to 3.04		
Poultry							0.05	0.5
No atopy: no asthma	124	66	517	90	1.29	1.05 to 1.58		
Atopy: no asthma	30	16	43	7	2.02	1.24 to 3.28		
No atopy: asthma	19	10	13	2	0.95	0.46 to 1.92		
Atopy: asthma	15	8	3	1	2.03	0.58 to 7.18		
Eggs							0.04	0.48
No atopy: no asthma	50	67	186	93	1.55	1.12 to 2.14		
Atopy: no asthma	12	16	9	4	4.36	1.80 to 10.53		
No atopy: asthma	9	12	5	2	1.20	0.39 to 3.65		
Atopy: asthma	4	5	1	1	1.55	0.17 to 14.18		
Animal production activities								
Milk cows							–	–¶
No atopy: no asthma	163	69	810	91	1.26	1.05 to 1.50		
Atopy: no asthma	31	13	73	8	1.24	0.79 to 1.93		
No atopy: asthma	18	8	8	1	1.53	0.65 to 3.58		
Atopy: asthma	24	10	2	0.2	5.51	1.28 to 23.72		
Veterinary procedures							0.23	0.41
No atopy: no asthma	1422	70	7927	90	1.22	1.11 to 1.33		
Atopy: no asthma	259	13	694	8	1.32	1.06 to 1.65		
No atopy: asthma	171	8	120	1	0.95	0.67 to 1.36		
Atopy: asthma	190	9	65	1	1.44	0.93 to 2.23		
Butcher animals							0.36	0.37
No atopy: no asthma	418	69	1816	89	1.27	1.13 to 1.43		
Atopy: no asthma	86	14	179	9	1.41	1.06 to 1.87		
No atopy: asthma	51	8	24	1	1.40	0.83 to 2.35		
Atopy: asthma	51	8	11	1	2.06	1.03 to 4.10		
Swine work							0.88	0.41
No atopy: no asthma	794	72	4277	91	1.19	1.08 to 1.32		
Atopy: no asthma	120	11	316	7	1.24	0.96 to 1.58		
No atopy: asthma	98	9	49	1	1.55	1.04 to 2.29		
Atopy: asthma	93	8	37	1	1.15	0.73 to 1.81		
Grind feed							0.25	0.91
No atopy: no asthma	1217	71	6979	91	1.11	1.02 to 1.22		
Atopy: no asthma	203	12	537	7	1.30	1.04 to 1.61		
No atopy: asthma	153	9	93	1	1.21	0.86 to 1.69		
Atopy: asthma	148	9	59	1	1.17	0.77 to 1.77		
Handle grain							0.48	0.14
No atopy: no asthma	1840	69	10606	90	1.09	0.98 to 1.21		
Atopy: no asthma	333	13	927	8	1.21	0.96 to 1.52		
No atopy: asthma	258	10	156	1	1.45	1.01 to 2.08		
Atopy: asthma	225	8	89	1	1.34	0.85 to 2.13		

†Odds ratios adjusted for age, state, smoking (past and current), atopy-asthma status, and asthma*current smoking.
Referent group is those with same asthma-atopy status who did not participate in that activity.
‡p value for two way cross product interaction terms. If atopy*asthma*exposure interactions were present at p<0.25, two way interactions were not reported.
§p value for atopy*asthma*dairy interaction term = 0.097.
¶p value for atopy*asthma*milk cows interaction term = 0.15.

ratios for each type of animal activity. Poultry and eggs are presented separately as they represent different patterns of production and exposure. Individuals who raised eggs had the highest odds of wheeze of all types of animal production (OR

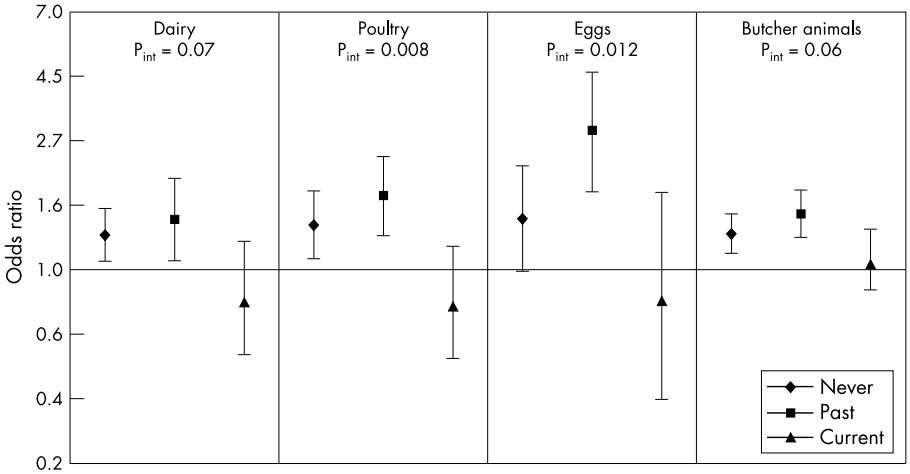

Figure 1 Odds ratios by smoking status for selected animal activities adjusted for main effects of smoking among farmers in the Agricultural Health Study. Odds ratios adjusted for age, state, smoking (past and current), asthma-atopy status, and asthma*current smoking. Odds ratios are compared to the non-exposed in each smoking category. The p value for interaction is based on a two degree of freedom test compared to a model without smoking interaction terms.

1.70, 95% CI 1.28 to 2.26). In general, activities that involved direct contact with animals had higher odds ratios than those that did not. When all types of animals were included in the same logistic model, there was some attenuation of the individual ORs; however, the ORs for dairy cattle, hogs, and eggs remained significantly different from 1.0. Odds ratios were increased for butchering animals (OR 1.31, 95% CI 1.18 to 1.45) and performing veterinary procedures (OR 1.16, 95% CI 1.11 to 1.32). When these two activities were included in the same model, there was little attenuation in the observed odds ratios, suggesting independent risk factors.

Dose-response models were consistent with an increased odds of wheeze with both the number of animals on the farm and the frequency of animal contact activities (table 3). For poultry, the odds ratio for having 500 or more birds at a time was 1.39 (95% CI 1.10 to 1.75) with a significant dose response (p trend = 0.006). For livestock (type of livestock was not specified), raising 1000 or more animals at any one time had an odds ratio of 1.19 (95% CI 1.04 to 1.36, p trend = 0.0042). A significant dose response trend was observed with increasing frequency of veterinary procedures, with individuals who reported performing veterinary procedures daily having an odds ratio of 1.51 (95% CI 1.14 to 2.01, p trend <0.0001). Information on the frequency of butchering animals was not collected.

Atopy, asthma, and smoking status may modify responses to respiratory triggers, and thus, these groups may differ in odds of wheeze for a given exposure. Since individuals with both atopy and asthma may have a different response to exposure than individuals with only one of these conditions, we present the odds ratios separately based on atopy and asthma status (table 4). Three way interactions among atopy, asthma, and exposure were observed only for atopic asthmatic individuals working with dairy cattle ($p_{interaction}$ = 0.097) and milking cows ($p_{interaction}$ = 0.15). The odds ratio for milking cows for atopic asthmatics was 5.51 (95% CI 1.28 to 23.72). We had low power to detect three way interactions given the small number of non-wheezing individuals in the atopy-asthma subgroups. For poultry, eggs, and beef cattle, exposed atopic individuals exhibited a higher odds of wheeze than predicted by the combination of atopy alone and exposure alone. Atopic farmers without asthma who produced eggs had an odds ratio for wheeze of 4.36 (95% CI 1.80 to 10.53) compared to atopic farmers not involved in egg production.

We observed statistical interactions between smoking status (never, past, and current) and four exposures: dairy cattle, poultry, eggs, and butchering animals. Current smokers were more likely to wheeze overall (table 1). However, the odds ratios for these exposures were smaller among current smokers than among past smokers and never smokers (fig 1). In particular, past smokers exhibited the largest increase in wheeze associated with egg production (OR 2.88, 95% CI 1.81 to 4.59).

DISCUSSION

Poultry, pig, and dairy production have been associated with respiratory symptoms among farmers.[1 8 9 11–14 16 25 28 32–35] Working in animal confinement areas and having direct contact with animals result in exposure to a wide array of agents.[1 36] Our data suggest important roles for activities involving frequent animal contact, such as poultry and egg production, milking cows, and performing veterinary procedures. These associations are likely to be due to different agents. Poultry production involves work in confined spaces and exposure to bird antigens, while milking cows and veterinary procedures generally involve mammals, which have different handling practices and antigens. Individual responsiveness to these agents as well as the probability of exposure is influenced by atopy, asthma, and smoking.[1 2 8 20 23 25–28 37] Smoking status and atopy had significant interactions with poultry and eggs, while atopic asthmatic status influenced wheeze risk among dairy farmers.

Poultry production in our study area, Iowa and North Carolina, is a mass production industry and characterised by three primary types: turkeys, broilers (chickens), and eggs. All involve raising birds in confined spaces. While most of the focus on workers in animal confinement areas has centred on hog production, poultry workers have a higher incidence of acute and chronic respiratory symptoms, lower baseline lung function, and greater declines in respiratory function over a workshift as measured by FEV_1 than other workers.[9 10 16 38–41] Respiratory effects are greater among those with more animal contact, both frequency and duration.[16 40] High concentrations of respiratory toxicants including ammonia, viable bacteria, organic dust, and endotoxin have been observed in poultry facilities; respiratory effects of these agents have been observed in a dose dependent fashion.[36 38 42 43] While we have no measured values of respiratory toxicants, our findings for poultry workers are consistent with increased respiratory symptoms with increasing exposure, as indicated by the observed dose-response for the number of birds present on the farm and the higher odds ratio for egg production than for poultry production.

Raising and handling mammals, such as dairy cattle and hogs, are associated with different types of respiratory toxicants than poultry production. Among European farmers, pig farmers had more work related symptoms and were 50% more likely to wheeze than cattle farmers.[15] Our data suggest that individuals who work in swine confinement areas are more likely to wheeze than beef cattle farmers. Among Ohio

farmers, inverse dose-response trends for non-cold wheeze were observed for number of cattle and number of hogs raised,[44] whereas our results support a positive dose-response trend for the number of livestock on the farm. Besides farmers, veterinarians have extensive animal contact and have higher rates of respiratory symptoms and occupational asthma.[3 45] In the Netherlands, large animal veterinarians were three times more likely to wheeze than other veterinarians, and twice as likely as swine workers to suffer an asthma attack.[45] For individuals reporting performing daily veterinary procedures, we observed a 50% higher odds of wheeze compared to subjects not performing veterinary procedures.

The role of atopy in asthma and respiratory symptoms, especially among adults, has been questioned.[24] Several studies suggest that while farmers who have higher exposure to antigens have higher levels of sensitisation, as measured by skin prick tests or serum IgG and IgE levels, this sensitisation does not influence respiratory symptoms.[32 46–48] However, other studies suggest that atopic sensitisation does influence respiratory symptoms among adult farmers.[17 49] While we have no serum measures of allergic sensitisation, we observed higher odds of wheeze among self reported atopic individuals raising eggs, poultry, and beef cattle over and above what would be expected by the independent effects of these exposures and atopy on wheeze risk. Our results are consistent with studies indicating that poultry workers have an allergic respiratory response, while hog farmers do not.[36 50–52]

Health based selection is characteristic of farming. Danish pig farmers[53] and grain processing workers[54] with respiratory symptoms were more likely to leave the industry than those without symptoms. Finnish farmers with farmer's lung and chronic bronchitis reported decreasing or eliminating their farm activities more often than other farmers.[55] In light of this potential self selection, interpreting the differential impact of exposure among atopics, asthmatics, and smokers on wheeze risk in this cross sectional analysis is challenging. It is unclear whether severe atopics and asthmatics may refrain from engaging in animal production activities. A healthy worker effect may have resulted in underestimation of the true odds of wheeze associated with animal exposure.

Current smokers, while having a higher prevalence of wheeze than other individuals overall, had a lower odds of wheeze associated with animal production after controlling for the independent effect of current smoking. In contrast, past smokers had the highest odds of wheeze when exposed to animals; this response was above that associated with past smoking alone. Former smokers may be individuals who developed reactive airway disease and quit smoking in order to continue in animal production (that is, they could not work with animals if they continued to smoke). Our data suggest a "healthy smoker effect" based on the ability to tolerate both cigarette smoke and animal exposures[56]; however, we have no way to evaluate this in our cross sectional data. Previous studies of farmers suggest increased respiratory symptoms among exposed smokers, but few have sufficient power to explore this interaction.[11 27]

Selection of an appropriate comparison population is a common concern for studies of respiratory symptoms among farmers. Farmers, in general, are healthier than the rest of the population and tend to smoke less, but have daily exposure to a vast array of respiratory hazards. Other studies of animal farmers have used non-farming rural or working class populations as their referents to address exposure to airborne contaminants on farms.[7] We observed increased odds of wheeze among farmers raising animals compared to other farmers in the AHS. The prevalence of wheeze among these US farmers is higher than in the general US population.[57] Given that our comparison group had a slightly higher likelihood of respiratory symptoms, our odds ratios could underestimate the impact of these exposures in the general population. Additionally, we chose to compare the odds of wheeze due to each animal exposure to those without that specific animal exposure, and thus have included individuals with other animal exposures in our comparisons. When we compared individuals raising specific animals to those who did not report raising any animals in the past year, we observed a slight increase in the odds ratios compared to those reported here. We did not have information on past involvement with animal handling, so we cannot determine whether historic exposures to animals affects the propensity to wheeze currently. While differences in referent groups make comparisons across studies challenging, Kimbell-Dunn and colleagues[12] observed odds ratios of a similar magnitude to ours among New Zealand farmers; for example, the odds ratio for pig exposure and current asthma was 1.3 (95% CI 0.9 to 2.0).

Wheeze is just one of a constellation of common respiratory symptoms, including cough, phlegm, and shortness of breath. Wheeze is a common and characteristic symptom of asthma, associated with reversible bronchoconstriction. Chronic wheeze can also be a symptom of chronic obstructive pulmonary disease. Most individuals who reported wheeze had two or fewer episodes of wheeze in a year, suggesting mild disease. When we ran models excluding individuals with a history of respiratory disease, we saw essentially the same results as the whole sample. We relied on self reported questionnaire information for this analysis. Self administered questionnaires have been shown to be reliable and reproducible regarding respiratory symptoms, particularly wheeze, and doctor diagnosis of asthma.[58 59] Most other large studies of farming populations have been conducted in a similar manner,[11 12 15 21 44 60] however, these studies, unlike ours, were primarily focused on respiratory symptoms and have more detailed information regarding symptom severity and medication use. However, compared to other respiratory studies of farmers, our study was much larger and has much more detailed information regarding farming exposures and has the ability to compare across heterogeneous exposures and to assess differences among potential susceptible individuals.

Few studies of respiratory symptoms in farmers have been able to compare across a broad range of agricultural practices to explore the impact of animal exposures. Among our large sample of farmers in Iowa and North Carolina, we observed an increased odds of wheeze among farmers involved in animal handling, with the highest odds ratios associated with poultry and egg production. Increasing frequency of animal contact was associated with an increased odds of wheeze as shown by milking cows, veterinary procedures, and the number of animals raised. Our results are consistent with an allergic responsiveness to poultry, but not to hogs. While wheeze represents only one of a constellation of respiratory symptoms, these results are consistent with increased respiratory symptoms among animal handlers, and suggest that the extent of these symptoms may be modified by other predisposing factors such as atopy or smoking history. Given that farmers in general have higher rates of respiratory symptoms than the general population and that the severity of respiratory symptoms will influence the extent of animal contact, our results may underestimate the impact of these exposures.

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