Environmental Exposure to Confined Animal Feeding Operations and Respiratory Health of Neighboring Residents

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Background: Despite public concern about potential adverse health effects of concentrated animal feeding operations, objectively assessed data on environmental exposure to concentrated animal feeding operations and respiratory health are sparse. We aimed to assess respiratory health in neighbors of confined animal feeding operations.

Methods: A survey was done in 2002–2004 among all adults (18–45 years old) living in 4 rural German towns with a high density of confined animal feeding operations. Questionnaire data were available for 6937 (68%) eligible subjects. In a random sample we measured the following outcomes: specific IgE to common and farm-specific allergens, lung function, and bronchial hyperresponsiveness to methacholine. Exposure was measured by collecting data on odor annoyance and geo-coded data on the number of animal houses within 500 m of the home. Locally optimal estimating and smoothing scatter plots were used to model the association between exposure and outcome. Analyses were restricted to subjects without private or professional contact with farming environments.

Results: The prevalence of self-reported asthma symptoms and nasal allergies increased with self-reported odor annoyance. The number of animal houses was a predictor of self-reported wheeze and decreased forced expiratory volume in 1 second, but not allergic rhinitis or specific sensitization. Self-reported exposure and results of clinical measurements were poorly correlated.

Conclusions: Confined animal feeding operations may contribute to the burden of respiratory disease among their neighbors. Our findings underline the importance of objective assessment of exposure and outcome in environmental epidemiology.

(*Epidemiology* 2007;18: 300–308)

Submitted 25 August 2006; accepted 12 December 2006.

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***Editors' note:** A commentary on this article appears on page 309.*

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ISSN: 1044-3983/07/1803-0300
DOI: 10.1097/01.ede.0000259966.62137.84

Exposures inside animal houses include gases (eg, ammonia and hydrogen sulfide) and organic dusts containing fungi, bacteria, and their constituents (eg, beta-(1,3-) glucans, endotoxins).[1,2] The adverse effects of these exposures on respiratory health of farmers and farm workers have long been established (as reviewed by Radon[2] and by Kirkhorn and Garry[3]). Occupationally exposed persons have increased risks of chronic bronchitis and asthma-like syndrome,[3–5] bronchial hyperresponsiveness,[6] and sensitization against farm-specific allergens,[7,8] as well as inflammation of the upper and lower respiratory tract.[2,3]

In recent years, animal production in North America and many European countries has shifted from small family-owned farms to confined animal feeding operations that house large numbers of animals. In Lower Saxony in north-west Germany, the number of confined animal feeding operations has increased substantially over the last 20–30 years. The major animal production in this area consists of poultry (74 million animals in 2001) and swine (6.5 million animals in 2001) housed in about 30,000 production facilities.

Emissions from confined animal feeding operations and the spraying of the animal wastes on the surrounding fields can result in environmental exposure to gases, organic dusts, bacteria, fungi, endotoxins, and residues of veterinary antibiotics.[9,10] Neighbors of large-scale animal production facilities are frequently annoyed by the associated odor.[11–13] According to several studies, this annoyance may decrease the quality of life,[9,11,12,14,15] impair mental health[9,15,16] and reduce immune function.[17]

Neighbors are frequently concerned about negative effects of confined animal feeding operations on their respiratory health. A number of surveys have been conducted on the association between environmental exposures to emission of confined animal feeding operations and respiratory health in children[18–20] and adults[15,16] living in close proximity to these facilities. These surveys suggest a higher prevalence of asthma symptoms in subjects potentially exposed to emissions of confined animal feeding operations.

At the same time, many studies have indicated a lower prevalence of respiratory allergies among subjects with farm-animal contact in early infancy.[21–23] These studies, however, were mainly conducted in areas with traditional farming.

One major challenge of studying health effects of environmental exposure to confined animal feeding operations is objective assessment of exposure and outcome. Subjects concerned about potential health effects may be both more aware of symptoms and more likely to report exposure, compared with less concerned neighbors or persons with an economic interest in confined animal feeding operations (eg, farm workers).[24–26] In addition the validity of self-reported respiratory symptoms varies largely by socioeconomic status.[27] These methodologic limitations may bias studies that rely solely on self-report of symptoms or exposures.

The aim of the Lower Saxony Lung Study was to study potential adverse effects of environmental exposures to emissions from confined animal feeding operations on respiratory health. Exposure and outcome were ascertained using self-reports as well as objective measurement.

METHODS

Study Subjects

The study was conducted in 4 rural towns in Lower Saxony, northwestern Germany, with a high density of animal feeding operations (Table 1). The animal production focused primarily on pigs and poultry. All adults age 18 to 44 years with German citizenship, registered in the population registries of these towns, formed the target population (n = 10,252). The registry provided information on home addresses, age, and sex of the target population. The study was performed consecutively in the 4 communities between 2002 and 2004, using the same instruments and measurements throughout the study period. To reduce reporting bias the study was introduced as a study on respiratory health in rural areas.

TABLE 1. Description of the Study Towns and Characteristics of the Study Population by Town, Lower Saxony, Germany

	Town 1	Town 2	Town 3	Town 4
Area; km^2	42	79	100	113
No. of inhabitants	2652	5805	7562	12,577
No. of animals				
Cattle	960	11,836	11,554	17,610
Pigs	24,300	98,926	45,958	87,448
Chicken	1,382,000	1,884,647	176,527	506,790
Turkey	161,600	n/a	397,244	642,369
Study population				
Participants*; no. (%)	630 (23.8)	1114 (19.2)	1432 (18.9)	2380 (18.9)
Descriptive data				
Age (yrs); mean ± SD	33.6 ± 7.4	32.9 ± 7.7	33.0 ± 7.3	33.7 ± 7.3
Sex (female); no. (%)	303 (48.1)	540 (48.5)	720 (50.3)	1190 (50.0)
Farm subjects†; no. (%)	363 (57.6)	623 (55.9)	755 (52.7)	1390 (58.4)
Education >12 yrs; no. (%)	127 (20.5)	377 (34.2)	315 (22.2)	484 (20.6)
Measures of exposure				
Ambient endotoxin concentration (EU/m^3) measured at 32 study sites[28]; geometric mean ± SD	3.0 ± 2.2	n/a	n/a	n/a
Number of animal houses within 500 m; median (range)	7 (0 to 18)	3 (0 to 15)	3 (0 to 12)	4 (0 to 20)
Self-reported odor annoyance; no. (%)				
Not at all	118 (19.1)	531 (48.1)	611 (43.3)	851 (36.4)
Somewhat	236 (38.1)	482 (43.7)	631 (44.7)	1124 (48.1)
Moderately	126 (20.4)	62 (5.6)	121 (8.6)	244 (10.4)
Strongly	139 (22.5)	29 (2.6)	49 (3.5)	119 (5.1)
Outcomes: questionnaire-based				
Wheezing without having a cold; no. (%)	108 (17.2)	123 (11.1)	182 (12.8)	266 (11.2)
Physician diagnosed asthma; no. (%)	52 (8.3)	62 (5.6)	86 (6.1)	134 (5.7)
Allergic rhinitis; no. (%)	82 (13.2)	151 (13.6)	196 (13.8)	307 (13.1)
Outcomes: clinical measurements				
Specific IgE to common allergens >0.35 IU/mL; no. (%)	64 (27.1)	139 (24.0)	124 (26.4)	267 (21.8)
Specific IgE to agricultural allergens >0.35 IU/mL; no. (%)	10 (4.2)	8 (1.4)	15 (3.2)	26 (2.1)
Bronchial hyperresponsiveness to methacholine; no. (%)	57 (42.9)	176 (42.6)	128 (40.3)	400 (41.7)
FEV_1 (% predicted); mean ± SD	99.3 ± 14.4	102.7 ± 14.0	98.8 ± 13.0	104.3 ± 13.2

n/a indicates not available.
*Participants in the questionnaire part of the study born in the former western part of Germany; % of inhabitants.
†Lived on a farm in first 3 years of life or had regular farm animal contact during childhood, lived or worked on a farm at the time of the study.

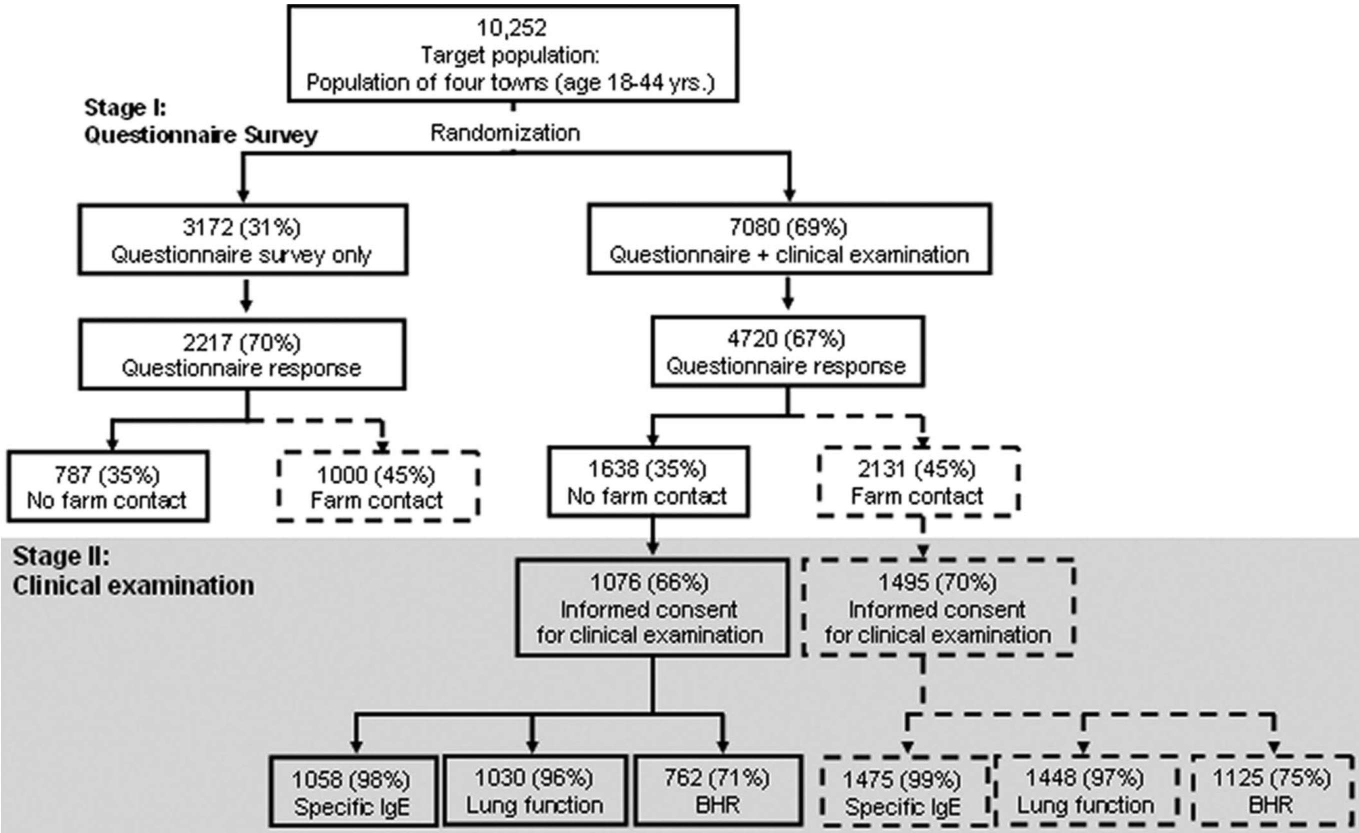

FIGURE 1. Flow chart of the study. Farm contact during childhood (living on a farm or regular contact to farm animals during the first 3 years of life) or at the time of the study (living or working on a farm). (Does not add up to 100% due to missing data on farm contact.)

Before the study, the target population of each town was divided at random into 2 groups. All residents were sent a mail-in questionnaire (Fig. 1). In addition, parts of the population were randomly selected and invited to take part in the clinical examinations (n = 7080). Nonresponders of both groups received up to 2 postal reminders and a phone call. To assess potential selection bias, subjects declining to participate at phone contact were asked 10 items of the main questionnaire. In the first town, 59 home visits were also done in attempt to reduce attrition. However, this measure (which was extremely time-consuming) resulted in only 3 additional returned questionnaires, and so was dropped. Overall, 68% of the eligible population completed the questionnaire. The study was approved by the Medical Ethical Committee of the Ludwig-Maximilians-University Munich, and the Lower Saxony Medical Board.

Questionnaire

The 74 items of the questionnaire were taken mainly from existing, validated questionnaire instruments (questionnaire available from the authors by request). The questionnaire covered 6 main areas:

Sociodemographic Data

These included occupational exposures, smoking patterns, and childhood environment. Questions were taken from the European Community Respiratory Health Survey questionnaire.[29]

Respiratory Symptoms

The items of the European Community Respiratory Health Survey questionnaire were used to assess symptoms of asthma, allergic rhinitis, atopic eczema, and chronic bronchitis.[29]

Farm-Animal Contact During Childhood and at the Time of the Survey

These items were taken from the Allergy and Endotoxin study.[21]

Odor and Noise Annoyance

These items were taken from the German National Health Survey.[30] Irrelevant items on noise annoyance were included to reduce reporting bias.

Confined Animal Feeding Operations Within 500 m of the Home and Work Environment, as Well as During Childhood

These questions were developed for the present study and included items on type, number, and proximity of confined animal feeding operations.

Prior to the study, the reliability of the questionnaire was assessed among 53 inhabitants of another rural town in the study area.[31] This pilot study indicated a moderate to good reliability of most questionnaire items. Only a few questions had poor reliability and were thus not used in the analysis: details of exposure to confined animal feeding operations in childhood, and in the current home and work environment.

Medical Examination

Medical examination consisted of blood sampling and pulmonary function testing—followed by bronchial challenge with methacholine. Procedures were done according to the European Community Respiratory Health Survey protocol.[29] Only subjects born in former West Germany were eligible for medical examination, to ensure similar childhood environments. Informed consent for medical examination was obtained for 66% of eligible subjects (Fig. 1).

We measured specific IgE against a mix of inhalant allergens (Timothy grass, rye, mugwort, birch, *Dermatophagoides pteronyssinus*, *Cladosporium herbarum*, cat, and dog) in serum samples (Pharmacia, Freiburg, Germany). This group of allergens are summarized here as SX1. In addition, samples were tested for specific IgE against a mix of common agricultural antigens (chicken, turkey, pig, cattle, *Aspergillus fumigatus*) summarized here as AX1.

Lung function was measured with a spirometer (Jaeger, Würzburg, Germany) according to American Thoracic Society criteria,[32] and is shown as percent of predicted function, derived from sex, height, and age standards.[33] The European Community Respiratory Health Survey protocol for stepwise methacholine challenge was adapted for the APS dosimeter (Jaeger, Würzburg, Germany).[34] Briefly, doubling or quadrupling doses were used until a drop in forced expiratory volume in 1 second (FEV_1) of 20% occurred (maximum cumulative dose: 1.2 mg). One study nurse did all pulmonary function testing and bronchial challenges throughout the study period.

Exposure Definition

Exposure to confined animal feeding operations was defined by the self-reported level of odor annoyance in the home environment ("How annoyed are you by odor in and around your home?"). The question on odor annoyance was assessed on a 4-point Likert scale from "not at all" to "strongly." Ninety percent of subjects reporting to be at least somewhat annoyed by odors in the home environment reported that agricultural sources (spraying of the fields, confined animal feeding operations) were the major source of odor.

Separate exposure estimates were developed on the basis of number of animal houses within 500 m (0.3 miles) around participants' home. This distance was chosen because microbial emissions can be measured up to 500 m from confined animal feeding operations.[35] For this approach each home address was geo-coded. The number of animal houses within 500 m of each home was provided by local authorities. The information was based on the most recent (year 2000) mandatory information about farming facilities. Owing to confidentiality issues, the actual number, type of animals, and geographic coordinates of the animal houses could not be used.

Outcome Definition

Based on the questionnaire data, we used the following conditions as self-reported outcomes: wheeze without a cold during the last 12 months, physician diagnosis of asthma (ever), and symptoms of allergic rhinitis ("Do you have nasal allergies, eg, hay fever"). Allergic sensitization was defined as a specific IgE concentration of 0.35 kU/L or higher in serum samples.[29] Age-, sex- and height-standardized FEV_1 was used to evaluate bronchial obstruction. Finally, bronchial hyperresponsiveness to methacholine challenge was defined as more than a 20% drop in FEV_1.

Statistical Methods

Analyses were restricted to subjects born in the former West Germany. Group differences were assessed using χ^2 test for categorical variables. Continuous variables were compared using Mann-Whitney-*U* test (2 group comparisons) or Kruskal-Wallis-ANOVA (multiple group comparison).

TABLE 2. General Characteristics of the Rural Study Population* Stratified by Farm Contact†

	Farm (n = 3131)	Nonfarm (n = 2425)
Sex (female); no. (%)	1539 (49.2)	1214 (50.1)
Age (yrs); mean ± SD	34.0 ± 7.3	32.5 ± 7.5
Active and passive smoke exposure; no. (%)		
Not at all	938 (30.4)	661 (27.7)
Only ETS	379 (12.3)	329 (13.8)
Ex smoker	659 (21.4)	478 (20.0)
Current smoker	1108 (35.9)	919 (38.5)
Education >12 yrs; no. (%)	695 (22.5)	608 (25.3)
Family history of allergic disease; no. (%)	898 (31.6)	698 (32.2)
Three or more siblings; no. (%)	1819 (58.9)	1026 (43.3)
Exposures		
Self-reported odor annoyance; no. (%)		
Not at all	1180 (38.3)	931 (38.9)
Somewhat	1411 (45.8)	1062 (44.4)
Moderately	302 (9.8)	251 (10.5)
Strongly	186 (6.0)	150 (6.3)
Number of animal houses within 500 m of the home; median (range)	4 (0 to 19)	3 (0 to 20)
Outcomes: questionnaire-based		
Wheezing without having a cold; no. (%)	357 (11.5)	322 (13.4)
Doctors' diagnosed asthma; no. (%)	157 (5.1)	177 (7.3)
Allergic rhinitis; no. (%)	327 (10.6)	409 (17.0)
Outcomes: clinical measurements		
Specific IgE to common allergens >0.35 IU/mL; no. (%)	285 (19.5)	309 (29.6)
Specific IgE to agricultural allergens >0.35 IU/mL; no. (%)	34 (2.3)	25 (2.4)
Bronchial hyperresponsiveness to methacholine; no. (%)	439 (40.4)	322 (43.7)
FEV_1 (% predicted); no. (%)	103.1 ± 13.6	101.4 ± 13.7

ETS indicates environmental tobacco smoke exposure.
*Born in the former western part of Germany.
†Lived on a farm in first 3 years of life or had regular farm animal contact during childhood, lived or worked on a farm at the time of the study.

All multiple regression models were adjusted a priori for sex, age, passive and active smoking, level of education, family history of allergic disease, and the number of siblings.

To assess the linearity of the association between number of animal houses within 500 m of the home and the health outcomes under study, we used locally optimal estimating and smoothing scatter (LOESS) plots using bandwidth of 0.6. These models were adjusted for the above-mentioned potential confounders. Based on the results of the analyses for the outcome of wheezing, the number of animal houses in the home environment was categorized at the resulting cut-off values (≤5, ≤10, ≤12, and >12 animal houses).

Logistic regression analysis was used to calculate outcome odds ratios (ORs) with 95% confidence intervals (CIs) for the animal house categories, as well as the self-assessed odor annoyance in the home environment. Linear regression analysis was used to calculate differences in lung function parameters between different groups. Analyses were performed using SAS v 9.02 (SAS, Cary NC) and S-Plus (Insightful Corporation, Seattle, WA).

RESULTS

Participation and Nonresponder Characteristics

Based on information from the population registry, participants were more likely than nonparticipants to be female (51% vs. 43%) while the 2 groups did not differ on age (mean 33 years). Comparing the 433 subjects who answered only the short questionnaire with other participants, the former were less likely to have been born in former West Germany (81% vs. 86%), more likely to have lived on a farm during the first 3 years of life (46% vs. 37%), and more likely to ever have smoked (61% vs. 56%). No meaningful differences were seen with respect to prevalence of asthma or allergic rhinitis.

Descriptive Data

Characteristics of the Study Population and Exposure by Town

The median number of animal houses within 500 m of the home environment was highest in Town 1 (7; range 0–18) and lowest in Town 3 (3; range 0–12; Table 1). In line with this finding, subjects living in Town 1 were on average more annoyed by odor in the home environment. Endotoxin measurements at 32 study sites in Town 1 indicated endotoxin levels of up to 23 EU/m^3 (geometric mean 3.0 EU/m^3; geometric standard deviation 2.2 EU/m^3).[28]

The 4 towns differed with respect to level of education (Table 1). The percentage of subjects with regular farm contact was highest in Town 4.

Questionnaire-based outcomes indicated a higher prevalence of wheezing in Town 1 (Table 1). The mean FEV_1 was lowest in Towns 1 and 3.

Comparison of Farm and Nonfarm Subjects

The general characteristics of subjects with and without regular farm contact are compared in Table 2. Regular farm

TABLE 3. Prevalence and Adjusted Odds Ratios of Respiratory Symptoms and Disease by Level of Odor Annoyance for Subjects Without Regular Farm Contact

Level of Odor Annoyance	No.*	Prevalence %	OR†	(95% CI)	Prevalence %	OR†	(95% CI)	Prevalence %	OR†	(95% CI)
Symptoms										
		Wheezing Without Cold			**Physician-Diagnosed Asthma**			**Allergic Rhinitis**		
Not at all‡	788	10.8	1.00		5.8	1.00		15.2	1.00	
Somewhat	919	12.2	1.23	(0.90 to 1.68)	8.0	1.40	(0.95 to 2.06)	17.0	1.09	(0.83 to 1.42)
Moderately	215	19.8	2.19	(1.42 to 3.37)	8.4	1.51	(0.84 to 2.73)	22.2	1.49	(1.00 to 2.22)
Strongly	116	26.7	2.96	(1.80 to 4.86)	12.9	2.51	(1.32 to 4.75)	25.0	1.81	(1.11 to 2.97)
Clinical Measurements										
		Specific IgE to Common Allergens >0.35 IU/mL			**Bronchial Hyperresponsiveness to Methacholine**			**FEV_1% Predicted§**		
Not at all‡	289	28.1	1.00		41.2	1.00		101.9 ± 12.8¶	0.0‖	
Somewhat	452	29.5	1.11	(0.79 to 1.57)	46.6	1.21	(0.83 to 1.76)	100.8 ± 13.9¶	−1.5	(−4.0 to 1.0)‖
Moderately	102	37.4	1.71	(1.02 to 2.87)	41.8	0.92	(0.50 to 1.69)	102.3 ± 14.8¶	0.2	(−3.7 to 4.2)‖
Strongly	53	27.5	1.02	(0.51 to 2.03)	42.4	1.12	(0.50 to 2.49)	102.6 ± 12.8¶	−0.1	(−5.2 to 5.0)‖

*No. missing for wheezing, 9; asthma, 3; allergic rhinitis, 17; IgE, 25; bronchial hyperresponsiveness, 274; and FEV_1, 43.
†Adjusted for age (5 categories), sex, active and passive smoke exposure, level of education, number of siblings, and parental allergies.
‡Reference category.
§Additionally adjusted for passive smoke exposure during childhood
¶Mean ± SD.
‖Adjusted mean difference in % predicted (95% CI).

contact was defined as living on a farm during the first 3 years of life (n = 2560), regular farm animal contact during childhood (n = 2810), living (n = 1060), or working on a farm at the time of the study (n = 490) (overall n = 3131; 56%; Fig. 1).

Compared with the nonfarm population, the farm population was, on average, older, and had lower prevalence of smokers, lower average level of education, and more siblings (Table 2). The prevalence of wheezing without a cold, physician-diagnosed asthma, allergic rhinitis, and sensitization against common allergens were lower among farm subjects than among the nonfarm population. Likewise, mean FEV_1 values were higher among farm subjects. There was no difference between subjects with and without farm contact with respect to bronchial hyperresponsivness.

Overall, only 59 subjects were sensitized to agricultural allergens. None of them was sensitized exclusively to agricultural allergens. Therefore, only specific IgE to common allergen was considered relevant for the multivariate analyses.

The level of odor annoyance did not differ between farm and nonfarm subjects. The mean number of animal houses within 500 m of the home environment was slightly higher among farm subjects (median 4; range 0–19) than among nonfarm subjects (3; 0–20). The remaining analyses were restricted to subjects without regular farm contact (n = 2425), since for them environmental exposures to farm emissions were considered relevant.

Respiratory Health

The odds for all respiratory symptoms and for physician-diagnosed asthma increased with increasing self-reported level of odor annoyance (Table 3). In contrast, no associations were seen between self-reported odor annoyance and any of the clinical outcomes.

While constant at lower exposure levels, the LOESS smoothers suggested an increase in wheezing without a cold when there were large numbers of animal houses in the home vicinity (Fig. 2A). In addition, FEV_1 dropped with increasing number of animal houses (Fig. 2B). In contrast, for sensitization to common allergens the prevalence was slightly decreased at high exposure levels; however, confidence intervals were wide (Fig. 2C).

The odds for wheezing without a cold was increased for subjects having more than 12 animal houses within 500 m of their home (Table 4). These subjects also had lower mean FEV_1 values as compared with subjects with 5 or fewer animal houses within 500 m of their home (mean difference

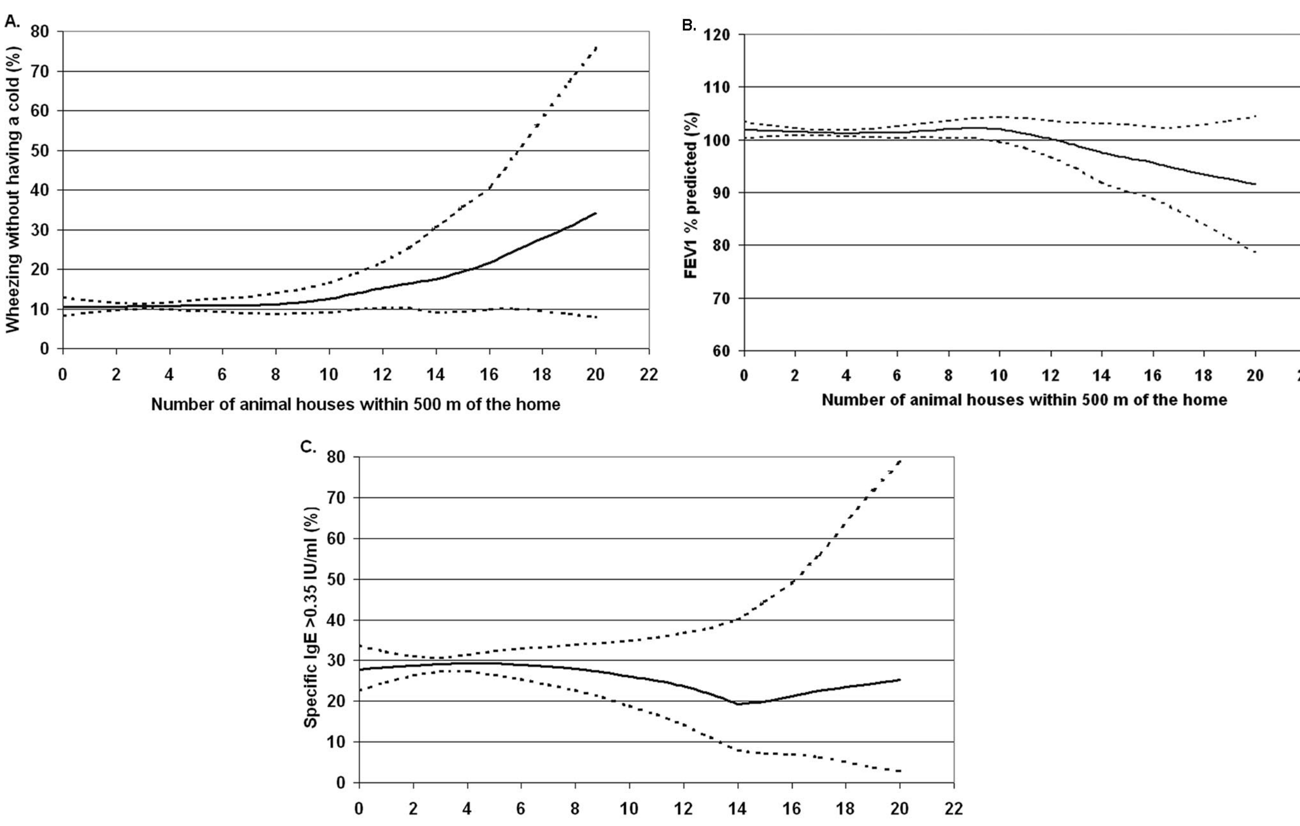

FIGURE 2. Smoothed plots (solid lines) with 95% confidence intervals (dashed lines) of number of animal houses within 500 m of the home and (A) wheezing without cold, % (B) FEV_1% predicted, and (C) sensitization to common allergens. Adjusted for age, sex, active and passive smoke exposure, level of education, number of siblings, and parental allergies. FEV_1% predicted additionally adjusted for passive smoke exposure during childhood.

TABLE 4. Prevalence and Adjusted Odds Ratios of Respiratory Symptoms and Disease by Number of Animal Houses Within 500 m for Subjects Without Regular Farm Contact

No. of animal houses within 500 m	No.*	Prevalence %	OR†	(95% CI)	Prevalence %	OR†	(95% CI)	Prevalence %	OR†	(95% CI)
		Symptoms								
		Wheezing Without Cold			Physician-Diagnosed Asthma			Allergic Rhinitis		
≤5‡	1343	12.3	1.00		7.9	1.00		17.4	1.00	
≤10	416	11.9	1.00	(0.70 to 1.42)	5.3	0.69	(0.42 to 1.11)	15.4	0.91	(0.66 to 1.24)
≤12	48	18.8	1.62	(0.74 to 3.53)	8.3	1.23	(0.43 to 3.54)	18.8	1.20	(0.56 to 2.57)
>12	48	27.1	2.45	(1.22 to 4.90)	10.4	1.18	(0.45 to 3.10)	22.9	1.29	(0.64 to 2.60)
		Clinical Measurements								
		Specific IgE to Common Allergens >0.35 IU/mL			Bronchial Hyperresponsiveness to Methacholine			FEV_1% Predicted§		
≤5‡	580	29.4	1.00		46.1	1.00		101.5 ± 13.2‖	0.0¶	
≤10	186	28.0	0.95	(0.65 to 1.39)	40.5	0.72	(0.47 to 1.10)	101.5 ± 13.6‖	−0.1	(−2.8 to 2.6)¶
≤12	22	36.4	1.38	(0.55 to 3.47)	29.4	0.50	(0.17 to 1.49)	103.7 ± 12.8‖	0.2	(−6.9 to 7.3)¶
>12	22	19.1	0.54	(0.17 to 1.69)	33.3	0.38	(0.11 to 1.31)	93.8 ± 12.6‖	−7.4	(−14.4 to −0.4)¶

*No. missing for wheezing, 9; asthma, 3; allergic rhinitis, 17; IgE, 25; bronchial hyperresponsiveness, 274; and FEV_1, 43.
†Adjusted for age (5 categories), sex, active and passive smoke exposure, level of education, number of siblings, and parental allergies.
‡Reference category.
§Additionally adjusted for passive smoke exposure during childhood.
‖Mean ± SD.
¶Adjusted mean difference in % predicted (95% CI).

= 7.1%; 95% CI = 2.9%–11.9%). In contrast, no important associations were seen with the number of animal houses for allergic rhinitis, sensitization, doctor's diagnosed asthma or bronchial hyperresponsiveness.

DISCUSSION

Our study suggests that a high density of confined animal feeding operations close to a residential area adversely affects respiratory health. The observed health effects point to asthma-like syndrome similar to those seen in farmers. In addition, our study underlines the importance of using objective measurements for exposure and disease in environmental epidemiology.

The strengths of our study were objective assessment of exposure and outcome, in addition to self-reported data of the participants. Furthermore, there was a reasonable response rate among a large population-based sample of rural subjects. Nonparticipants were mainly persons born outside former West Germany and thus would have been excluded from the analyses. To further reduce selection bias, a random sample of the population was asked to undergo a medical examination. The clinical measurements were done according to standardized procedures with thorough quality control.

At the same time, failure to test a considerable proportion of subjects for bronchial hyperresponsiveness could have introduced selection bias. As the proportion of asthmatics was the same (6%) among those who participated in the clinical measurements and those who did not, no major bias is anticipated. The subjects' lack of awareness of the number of animal houses in the home vicinity is also expected to help avoid selection bias.

Comparing self-reported data on number of confined animal feeding operations within 500 m of the home with data provided by the local authorities yielded a low level of agreement (17%; data not shown). Furthermore, in our pilot study the intraindividual test–retest reliability for the number of animal houses in the home environment was low.[31] Therefore, self-reported number of confined animal feeding operations in the home environment seems to be a poor indicator of actual exposure, which might bias results.[24–26] This is supported by our finding that self-reported odor annoyance was associated only with self-reported symptoms and disease, but not with clinical measurements.

One problem with the government data on number of animal houses in the home vicinity is that they cover all animal houses regardless of size, type and number of animals kept, and type of ventilation. For confidentiality reasons we were unable to obtain more detailed data. Therefore, some misclassification of exposure has to be anticipated, which might lead to an underestimation of effects. Nevertheless, our endotoxin measurements in 1 town indicated a moderate agreement between number of animal houses within 500 m of the home environment and level of endotoxin exposure measured in the home environment (Spearman's rho = 0.31).[28] Unfortunately, the number of measurements done (n = 32) does not allow use of these measurements as markers of exposure. Exposure to confined animal feeding operations is determined by emission both from the confined animal feeding operations and from spraying of manure on the surrounding fields. Emissions are thus predicted not by the animal houses alone, and may vary from day to day. This variability is also indicated by the moderate test–retest reliability of the question on the level of odor annoyance in the home environment (kappa = 0.51).[31] To overcome this problem, long-term measurements of such chemicals as ammonia at several points in the study area would be required. Using such exposure data, the individual exposure at the participants' home could be modeled by GIS models.

Another source of error might stem from the fact that the registry of animal houses was last updated in 2000, while the study was done between 2002 and 2004. Furthermore, only data on animal houses in the vicinity of participants' homes were available. Personal exposure assessment would be necessary to overcome this problem. Our study population reported spending, on average, 102 (±33) hours per week at home. Adjusting our analyses for number of hours at home did not change our results.

In addition, our results might be biased by having drawn samples from different towns. Stratifying the data by town did not indicate effect modification by town. Nevertheless, due to small sample sizes, especially in the higher exposure categories, confidence intervals by town were wide (data not shown). Likewise, neither adjusting the analyses for study town nor the use of GLM mixed-effect models changed the results considerably (data not shown).

The association between number of animal houses near the home and wheezing, as well as FEV_1, are similar to those observed in farmers and farm workers and might be an indication of asthma-like syndrome.[2,4,36–38] We restricted our study population to those without private or occupational contact to farming environments. This was done because the environmental exposures to emissions from confined animal feeding operations are considered to be small compared with exposures inside animal houses or exposures levels experienced of those who live on a farm,[1,8,23] and thus of minor importance for respiratory health. Repeating our analyses for subjects with farm contact, no association between number of animal houses in home vicinity and respiratory symptoms and disease could be shown. However, the association between self-reported odor annoyance and self-reported respiratory symptoms and disease were similar to those in subjects without farm contact (data not shown).

Adverse effects were seen only among subjects with a high number of animal houses in the immediate home vicinity. As this was the first study using number of animal houses as an exposure proxy, and clinical measurements to assess the outcome, we did not have the benefit of predefined cut-off values. In addition, due to the higher population density in Europe and different farming practices, the exposure is thought to differ considerably from that in the USA.[10,17,39] Therefore, LOESS smoothers have been used to elicit cut-off levels. Furthermore, due to exposure misclassification, the exact cut-off point cannot be identified from our data. To confirm our results, further epidemiologic studies are needed in areas with intensive animal production.

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