Chronic Bronchitis Among Nonsmoking Farm Women in the Agricultural Health Study

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Objective: The purpose of this study was to examine agricultural risk factors for chronic bronchitis among nonsmoking farm women. **Methods:** *We used self-reported enrollment data from the 21,541 nonsmoking women in the Agricultural Health Study to evaluate occupational risk factors for prevalent chronic bronchitis among farm women. Odds ratios (ORs) for chronic bronchitis for occupational exposures were adjusted for age, state, and related agricultural exposures.* **Results:** *Applying manure and driving combines were independently associated with chronic bronchitis. Off-farm job exposures associated with chronic bronchitis were organic dusts, asbestos, gasoline, and solvents. Five pesticides were associated with chronic bronchitis after multivariate adjustment and sensitivity analyses: dichlorvos (OR = 1.63, 95% CI = 1.01, 2.61), DDT (OR = 1.67, 95% CI = 1.13, 2.47), cyanazine (OR = 1.88, 95% CI = 1.00, 3.54), paraquat (OR = 1.91, 95% CI = 1.02, 3.55), and methyl bromide (OR = 1.82, 95% CI = 1.02, 3.24).* **Conclusion:** *Pesticides as well as grain and dust exposures were associated with chronic bronchitis among nonsmoking farm women.* (J Occup Environ Med. 2007;49:574–583)

Farmers and agricultural workers have increased prevalence of chronic bronchitis despite lower rates of smoking.[1–4] Farm work, livestock production, and occupational dust and grain exposure contribute to chronic bronchitis.[5] Longitudinal studies of chronic bronchitis in farming populations suggest that the disease is work-related,[6] and that inhalation exposures to such potential hazards as organic dusts, bacteria, endotoxins, and gases contribute to chronic bronchitis risk.[7,8]

Recent US data show that the prevalence of chronic bronchitis increased in both men and women from 1982 to 1996 and is now higher in women than in men.[9] Little is known about the role of occupational exposures, including farm exposures, in chronic bronchitis among women. Women have been underrepresented in many occupational studies of chronic bronchitis. Studies of farming populations have included women to some extent.[5,10,11] However, many of these studies have limited their exposure assessment to crop and animal production information[5] or to specific agricultural activities[11] or farm types.[10] Only one study to date[1] assessed the risk among nonsmoking farm women, but this study lacked detailed information on agricultural exposures. Few studies have had sufficient power to study nonsmokers alone and none to date have investigated potential associations with pesticides. To investigate occupational risk factors, including pesticides, for chronic bronchitis among nonsmoking farm women, we used data from

the Agricultural Health Study (AHS), a large cohort study conducted to characterize health risks associated with farming.

Materials and Methods

The AHS is a large, prospective study of Iowa and North Carolina pesticide applicators and their spouses.[12] The study enrolled more than 52,000 licensed private pesticide applicators, mostly farmers, from 1993 to 1997. The AHS enrolled 82% of the licensed private pesticide applicators in Iowa and North Carolina when they received their pesticide certification training between 1993 and 1997. A total of 32,347 spouses (75% of those eligible) enrolled in the study using a self-administered questionnaire that applicators brought home to their spouses.

We conducted a cross-sectional analysis of chronic bronchitis and agricultural exposures using the spouse enrollment data. Our analytical sample was limited to the 21,541 nonsmoking female spouses who provided complete information on age, smoking, and chronic bronchitis and were at least 20 years old at enrollment. We defined a nonsmoker as someone who reported that they had not smoked 100 cigarettes in their lifetime. As a result, we excluded all male spouses ($N = 220$), smokers ($N = 8503$), those without smoking history data ($n = 1845$), and those younger than 20 or missing age ($N = 14$), or missing age at diagnosis ($N = 35$). We did not study female pesticide applicators ($n = 454$) because exposure information differed for applicators and spouses. Chronic bronchitis was defined as a self-report of doctor-diagnosed chronic bronchitis at age 20 or older based on the response on the spouse questionnaire (Has a DOCTOR ever told you that you had (been diagnosed with) chronic bronchitis? If yes, how old were you when a doctor first told you? <20, 20 to 39, 40 to 59, 60+). We limited the analysis to nonsmoking women to minimize the potential for confounding by this im-

portant chronic bronchitis risk factor. To help limit possible misreporting of disease, we also excluded 189 women who reported being diagnosed before age 20.

We assessed exposure and outcome using data primarily provided by the spouses with additional information on farm characteristics from the questionnaire completed by the applicator at enrollment. The spouse questionnaire provided information on demographics, medical history, current farm activities, job history, and lifetime pesticide use. The applicator questionnaire provided information on farm type, farm size, and applicator smoking history, as a measure of spouse passive smoking at home. The exposures of interest for this analysis were 1) current farm activities, 2) lifetime nonfarm job history, and 3) lifetime pesticide history.

Current farm activities reported on the spouse questionnaire included crop activities, animal exposures, solvent use, maintenance work, and use of farm equipment. For the nonfarm job held the longest, women were asked about ever-exposure to 19 potential occupational hazards including organic dusts, inorganic dusts, chemicals, and fumes. For these nonfarm job exposures, we limited the analysis to those participants who reported having a job off the farm.

Spouses reported total years and days of use of any pesticide and ever-use of 50 specific pesticides. The questionnaire also provided information on recent residential pesticide use. We assessed exposure as follows: 1) ever-use of any pesticide, 2) ever-use of each pesticide functional group (herbicides, insecticides, fungicides, and fumigants), 3) ever-use of each insecticide class (carbamates, organochlorines, organophosphates, and pyrethroids), and 4) ever-use of each of 50 individual chemicals. In addition, we assessed cumulative lifetime exposure to any pesticide: 1) total years mixed or applied pesticides, 2) total

days per year mixed or applied pesticides, and 3) total lifetime days (the product of 1 and 2). Because farm women have distinct patterns of pesticide use, we used variables that describe broad patterns of pesticide use with regard to the five most commonly used chemicals (2,4-D, glyphosate, diazinon, carbaryl, malathion) and agricultural pesticides as described by Kirrane et al.[13] We used a five-level variable characterizing these patterns: 1) no pesticide use, 2) only residential (general use) pesticides, 3) one or more of the five most commonly used pesticides, 4) one or two agricultural pesticides used in addition to any of the five most commonly used pesticides, and 5) three or more agricultural pesticides used in addition to any of the five most commonly used pesticides.[13]

To assess potential associations between occupational exposures and chronic bronchitis, we used a logistic regression model that controlled for state and age (10-year categories) to estimate odds ratios (ORs) and 95% confidence intervals (CIs). The model with age and state was our base model in which we evaluated all other covariates and exposures of interest. We used goodness-of-fit tests to assess whether other covariates (eg, spousal smoking, body mass index [BMI]) were important model predictors. In addition, we used a 10% change in the estimate criterion to identify whether a covariate was a potential confounder. We created a home environmental tobacco smoke variable based on whether the spouse's husband had a history of smoking. Among other potential confounders, race and education were not associated with the outcome, and current BMI did not confound our results; thus, we did not include these variables in the base model. We limited our analysis to exposures reported by at least five cases. We assessed each potential risk factor individually in the base model, and then in groups of related factors, evaluating current ac-

tivities separately from lifetime activities. For current farm activities, we considered four groups of related factors: 1) crop activities—apply chemical fertilizer, apply manure fertilizer, hand-pick crops, plant, and till the soil; 2) solvent use—paint, gasoline for cleaning, and other solvents (paint stripper, benzene, turpentine); 3) maintenance activities—weld, repair engines, and grind metal; and 4) farm equipment—combines, diesel tractors, gasoline tractors, and trucks. Fitting all variables in a group in a single model allowed us to control for closely related activities, which may serve as mutual confounders. For nonfarm occupational activities, associations with chronic bronchitis were assessed within the following groups: 1) organic dusts—cotton, wood, and grain; 2) inorganic dusts—mineral, sand, and asbestos; 3) chemicals—solvents, gasoline, and pesticides; and 4) fumes—welding, engine exhaust, and lead solder. For lifetime pesticide exposure history, we assessed dose-response for increasing categories (lifetime days, years, days per year, and patterns of pesticide use) and performed χ^2 tests for trend using these categories. Once all models were fitted, we assessed the Spearman correlations among statistically significant exposures from the different groups to evaluate potential confounding more broadly. We considered odds ratios statistically significant when the 95% confidence interval excluded 1.0.

We used the data set release P1REL0310 from the AHS. The AHS questionnaires are available at http://www.aghealth.org/qnaires.pdf. All statistical analyses were performed using SAS version 9.0 (SAS Institute, Cary, NC).

Results

A total of 583 (2.7%) nonsmoking farm women reported doctor-diagnosed chronic bronchitis after age 20 (Table 1). Participants were predominantly from Iowa, white, and ranged in age at enrollment from 20 to 88 years. Prevalence of chronic bronchitis increased with increasing age and increasing BMI. Women who reported chronic bronchitis were more likely than controls to report a history of other respiratory conditions, including asthma and emphysema. The majority of women reported growing up on a farm; these women were less likely to report chronic bronchitis (odds ratio [OR] = 0.81, 95% confidence interval [CI] = 0.68, 0.97). Comparison of the crude data presented in Table 1 suggested that spousal smoking was associated with chronic bronchitis. However, after controlling for age and state, chronic bronchitis was not associated with the husband smoking at home (OR = 1.12, 95% CI = 0.94, 1.33).

Among related crop activities, chronic bronchitis was associated with applying manure as fertilizer (OR = 1.58, 95% CI = 1.18, 2.12), but not with applying chemical fertilizer (Table 2). We saw no association of chronic bronchitis with current animal exposures with frequency of personal contact or with living on a farm where animals were produced. Modeled individually, painting, using gasoline for cleaning, and using other solvents (eg, paint stripper, benzene, and turpentine)

TABLE 1

General Characteristics of 21,541 Nonsmoking Farm Women in the Agricultural Health Study (1993–1997) by Chronic Bronchitis Status

Characteristic	Chronic Bronchitis* (N = 583‡)		Controls (N = 20,958‡)	
	N	%	N	%
Age (yrs)				
20–39	90	15	6610	32
40–49	155	27	5834	28
50–59	163	28	4855	23
60–69	137	24	2939	14
70+	38	7	720	3
State of residence				
Iowa	336	58	15,188	72
North Carolina	247	42	5770	28
Race				
White	553	97	20,127	98
Other	18	3	469	2
Education				
High School grad and below	276	54	8408	45
Beyond high school	233	46	10,460	55
BMI (kg/m^2)				
Underweight (14–18.49)	6	1	269	2
Normal (18.5–24.9)	150	34	7072	48
Overweight (25–29.9)	147	34	4690	32
Obese (30–58)	134	31	2634	18
Respiratory conditions				
Asthma	145	25	796	4
Emphysema	8	1	30	0
Farm life and other				
Raised on farm†	364	63	13,321	64
Lived/worked on farm >40 yrs	289	50	7921	38
Farm size >1000 acres	43	7	2738	13
Job off farm (ever)	515	89	18,305	88
Lifestyle				
Current alcohol use	213	37	10,702	51
Husband ever smoke	268	48	8010	39

*Self-report of a doctor's diagnosis of chronic bronchitis in patients older than 20 years.
†Lived at least half of life on a farm before the age of 18 years.
‡Numbers may not add up to totals due to missing data.

TABLE 2
Current Occupational Farm Exposures and the Association With Prevalent Chronic Bronchitis Among Nonsmoking Farm Women in the Agricultural Health Study (1993–1997)

Current Farm Activities	Chronic Bronchitis (n = 583) %	Controls (n = 20,958) %	Odds Ratio†	95% Confidence Interval†	Odds Ratio*	95% Confidence Interval*
Crop activities						
Apply chemical fertilizer	13	11	0.99	(0.76, 1.27)	0.84	(0.61, 1.15)
Apply manure	16	11	1.39	(1.10, 1.75)	1.58	(1.18, 2.12)
Hand-pick crops	31	25	1.11	(0.92, 1.34)	1.17	(0.92, 1.48)
Plant	27	23	1.00	(0.82, 1.21)	0.82	(0.62, 1.08)
Till the soil	23	25	1.06	(0.86, 1.29)	0.99	(0.79, 1.25)
Animals raised						
Beef cattle	36	34	1.10	(0.92, 1.32)	1.07	(0.87, 1.30)
Dairy cattle	9	10	1.00	(0.74, 1.36)	0.95	(0.69, 1.31)
Poultry	14	13	1.15	(0.90, 1.47)	1.15	(0.88, 1.51)
Sheep	7	8	1.21	(0.80, 1.57)	1.03	(0.71, 1.49)
Swine/hogs	28	34	1.10	(0.91, 1.36)	1.07	(0.86, 1.32)
Solvent use						
Gas as solvent	18	15	1.50	(1.19, 1.89)	1.28	(0.96, 1.70)
Other solvent‡	22	19	1.42	(1.15, 1.75)	1.27	(0.94, 1.70)
Paint	33	32	1.27	(1.06, 1.54)	1.04	(0.80, 1.35)
Maintenance activities						
Grind metal	1	1	1.27	(0.56, 2.87)	1.20	(0.51, 2.86)
Repair engines	2	1	1.44	(0.71, 2.94)	1.29	(0.58, 2.87)
Farm equipment operated						
Combines	13	11	1.49	(1.15, 1.92)	1.57	(1.18, 2.10)
Diesel tractors	31	34	1.06	(0.88, 1.29)	0.80	(0.62, 1.03)
Gasoline tractors	28	26	1.24	(1.02, 1.51)	1.21	(0.94, 1.55)
Trucks	40	38	1.16	(0.97, 1.39)	1.13	(0.93, 1.37)

*Multivariate adjusted: adjusted for age, state, and variables within each group (crop activities, animals, solvent use, maintenance, and farm equipment).
†Adjusted for age, state.
‡Paint stripper, benzene, turpentine for cleaning.

were each statistically significantly associated with chronic bronchitis. However, when modeled together, the odds ratios for both gasoline and other solvents were attenuated and painting was no longer associated with chronic bronchitis. In the model with all four types of equipment, the association with combines (OR = 1.57, 95% CI = 1.18, 2.10) was much greater than with any other farm equipment.

Most farm women (88%) reported ever having a job off the farm, though only 44% reported exposure to at least 1 of the 19 agents listed on the questionnaire (Table 3). In models containing the organic dust variables, each of the organic dusts—cotton, grain, and wood—was significantly associated with chronic bronchitis. Among inorganic dusts, only the association with asbestos was statistically signif-

icant, (OR = 1.56, 95% CI = 1.11, 2.20). Of the chemicals, gasoline (OR = 1.88, 95% CI = 1.23, 2.88) and solvents (OR = 1.58, 95% CI = 1.18, 2.10) were associated with chronic bronchitis.

Although short-term use of pesticides appeared to be associated with chronic bronchitis, we saw no trend with increasing duration of use categories (Table 4). Chronic bronchitis was associated with increasing days of use, although the dose-response trend was not strictly monotonic (P trend = 0.001). The risk of chronic bronchitis was increased among women who applied pesticides 120 days or more in their lifetimes (OR = 1.50, 95% CI = 1.17, 1.91). Women who used three or more agricultural pesticides in addition to the most commonly used pesticides (glyphosate, 2,4-D, malathion, diazinon, carbaryl) had an in-

creased risk of chronic bronchitis (OR = 1.58, 95% CI = 1.19, 2.09). However, those who used fewer agricultural pesticides showed no elevated risk.

Fifty-two percent of the women reported ever-use of at least one pesticide in their lifetime (Table 5). We saw little evidence of an overall pesticide association. There was no association between overall use of pesticides and chronic bronchitis (OR = 1.14, 95% CI = 0.97, 1.35), and when we constructed models that contained the four functional groups, we did not observe a significant association. In this mutually adjusted model, the odds ratio for insecticides was 1.20 (95% CI = 0.98, 1.47). Among the four insecticide groups, there was no increased risk of chronic bronchitis.

In evaluating the 50 individual pesticides, 42 had five or more ex-

TABLE 3
Off-Farm Occupational Exposures and the Association With Prevalent Chronic Bronchitis Among Nonsmoking Farm Women in the Agricultural Health Study (1993–1997)

Longest Held Off-Farm Job Exposure‡	Chronic Bronchitis (n = 515) %	Controls (n = 18,305) %	Odds Ratio*	95% Confidence Interval*	Odds Ratio†	95% Confidence Interval†
Organic dusts						
Cotton dust	7	3	1.92	(1.35, 2.74)	1.81	(1.27, 2.59)
Grain dust	4	3	1.84	(1.16, 2.92)	1.59	(0.99, 2.55)
Wood dust	6	3	2.21	(1.55, 3.23)	1.98	(1.34, 2.93)
Inorganic dusts						
Asbestos	8	5	1.59	(1.13, 2.22)	1.56	(1.11, 2.20)
Mineral/mining	2	2	1.16	(0.57, 2.37)	0.97	(0.47, 2.01)
Silica/sand dust	2	2	1.50	(0.81, 2.77)	1.38	(0.74, 2.57)
Chemicals						
Gasoline	5	3	2.11	(1.41, 3.18)	1.88	(1.23, 2.88)
Pesticides	4	4	1.19	(0.76, 1.88)	0.95	(0.59, 1.53)
Solvents	12	9	1.69	(1.28, 2.23)	1.58	(1.18, 2.10)
Fumes						
Engine exhaust	6	5	1.44	(0.98, 2.11)	1.39	(0.92, 2.08)
Lead solder	2	1	2.38	(1.27,4.43)	2.30	(1.18, 4.48)
Welding fumes	2	2	1.34	(0.73, 2.46)	0.91	(0.46, 1.81)

*Adjusted for age, state.
†Multivariate adjusted: adjusted for age, state, and variables within each group (organic dusts, inorganic dusts, chemicals, fumes).
‡Analysis limited to those (88%) reporting having had a job off the farm; 66% reported none of the listed exposures.

posed cases. Of these, 18 were associated with chronic bronchitis in the age- and state-adjusted base models (Table 6). Among the insecticides, three organochlorines (dieldrin, DDT, and lindane), four organophosphates (diazinon, dichlorvos, malathion, and parathion), and two carbamates (carbaryl and carbofuran) were significantly associated with chronic bronchitis. Herbicides that were statistically significant in the single pesticide base models were 2,4-D, alachlor, atrazine, cyanazine, metribuzin, paraquat, and petroleum oil. The fungicide chlorothalonil and the fumigant methyl bromide were also statistically significant after base-model adjustment. After adjusting for the all pesticides in their respective groups, some associations were attenuated. Among the organochlorine insecticides, the OR for DDT remained elevated and statistically significant after group adjustment (OR = 1.67, 95% CI = 1.13, 2.47); the OR for dieldrin remained high (OR = 2.53, 95% CI = 0.84, 7.56). Among organophosphate insecticides, only the association between dichlorvos and

chronic bronchitis remained statistically significant (OR = 1.63, 95% CI = 1.01, 2.61) after adjusting for other organophosphates. In models that included all herbicides, cyanazine (OR = 1.88, 95% CI = 1.00, 3.54) and paraquat (OR = 1.91, 95% CI = 1.02, 3.55) remained elevated. Only one fumigant (methyl bromide) had at least five cases, and it was associated with chronic bronchitis (OR = 1.82, 95% CI = 1.02, 3.24).

People with chronic bronchitis may also have other respiratory conditions, such as asthma. In our sample, 25% of the women who reported chronic bronchitis also reported a history of asthma. As a sensitivity analysis to evaluate whether the observed associations with chronic bronchitis were potentially due to associations with asthma, we reran all the models after excluding the 941 individuals who reported asthma from both the case (n = 145) and control group (n = 796). For most exposures, the observed associations with chronic bronchitis remained elevated, though with some attenuation. For current farm activities (Table 2), the odds ratio for

manure went from 1.58 to 1.36 (95% CI = 0.96, 1.92). For off-the-farm jobs (Table 3), the association with grain dust increased from 1.59 to 1.98 (95% CI = 1.19, 3.31) when asthmatics were excluded from the sample. The associations for cotton and wood dust were reduced to 1.6 and 1.5, respectively. We saw no change in the associations with frequency of pesticide usage (Table 4), but did see an attenuation of the odds ratio for use of three or more agricultural chemicals from 1.58 to 1.36 (95% CI = 0.97, 1.90). For the pesticide groups (Table 5), the odds ratio for fungicides increased from 1.45 to 1.87 (95% CI = 1.01, 3.44); there was no change in the other odds ratios. For the individual pesticides (Table 6), when asthmatics were removed from the sample, the associations for carbofuran, parathion, and petroleum oil went away. For carbofuran, the odds ratio decreased from 1.68 to 0.95; for parathion, the odds ratio decreased from 1.48 to 1.01; for petroleum oil, the odds ratio went from 1.54 to 1.13. These were the only observed associations that were eliminated when

TABLE 4
Cumulative Lifetime Pesticide Exposure and the Association With Prevalent Chronic Bronchitis Among Nonsmoking Farm Women in the AHS (1993–1997)

	Chronic Bronchitis (n = 583) %	Controls (n = 20,958) %	Odds Ratio*	95% Confidence Interval	P Trend†
Duration of pesticide use					
Years					0.12
None	51	49	1.00		
1	5	5	1.51	(1.00, 2.26)	
2–5	10	13	0.99	(0.72, 1.35)	
6–10	9	9	1.18	(0.85, 1.64)	
11–20	12	12	1.14	(0.85, 1.53)	
21–30	7	6	1.18	(0.82, 1.70)	
30+	8	5	1.30	(0.91, 1.85)	
Days per year					0.001
None	51	49	1.00		
1–5	22	25	1.02	(0.75, 1.38)	
5–9	11	11	1.35	(1.00, 1.84)	
10–19	10	8	1.80	(1.22, 2.66)	
20–39	6	3	1.57	(0.84, 2.91)	
40+	2	1	1.79	(1.20, 2.67)	
Lifetime days‡					0.02
None	51	49	1.00		
1–9	12	13	1.20	(0.89, 1.61)	
10–39	9	12	0.90	(0.65, 1.25)	
40–119	11	12	1.02	(0.76, 1.37)	
120–7000	19	12	1.50	(1.17, 1.91)	
Pesticide use patterns§					0.01
None	35	37	1.00		
Residential pesticides‖	9	9	1.17	(0.86, 1.59)	
Most used pesticides#	30	31	1.11	(0.90, 1.38)	
1–2 Agricultural pesticides**	13	13	1.09	(0.83, 1.43)	
3+ Agricultural pesticides††	13	9	1.58	(1.19, 2.09)	

*Odds ratios adjusted for age and state.
†χ^2 test for trend based on categories shown.
‡Total lifetime days is the product of the midpoints of year and days-per-year categories.
§As defined by Kirrane et al, 2004.[13]
‖Reported using pesticides for home or garden only.
#Exposure to at least one commonly used pesticide: glyphosate, 2,4-D, malathion, diazinon, carbaryl.
**1 to 2 predominantly agricultural pesticides in addition to the commonly used products.
††3 or more predominantly agricultural pesticides in addition to the commonly used products.

we excluded asthmatic subjects. The odds ratios for DDT and dichlorvos were attenuated but the odds ratio remained elevated and consistent with an association with chronic bronchitis (OR_{DDT} = 1.58, 95% CI = 1.00, 2.52; $OR_{dichlorvos}$ = 1.56, 95% CI = 0.88, 2.78). The odds ratio for dieldrin was attenuated as well, but based only on two exposed cases. The odds ratio for cyanazine increased from 1.88 to 2.30 (95% CI = 1.07, 4.91). Taken overall, this sensitivity analysis suggests that the ob-served associations with chronic bronchitis are not due to potential underlying associations with asthma with the exception of the results for carbofuran, parathion, and petroleum oil.

To evaluate whether correlated exposures could be responsible for our findings, we assessed the Spearman correlations between pairs of the significant exposures. We saw no evidence of strong correlations among variables, with most correlations being less than 0.25. The strongest correlation was between using gasoline as a solvent and other solvents (R = 0.52), but was controlled for in our mutually-adjusted models. The correlation between manure application and driving combines was 0.22; thus, we did not consider one a potential confounder of the other.

Discussion

Farm women have been overlooked in the evaluation of respiratory hazards of agriculture although they commonly perform tasks that are similar to those performed by men.[2,13] Chronic bronchitis among farmers has been associated with occupational exposures[1,2,4–6,14,15]; women who have similar exposures may have similar risks as their male counterparts. Other studies that have evaluated farm women have been limited to broad farm characteristics,[5] use of occupational codes for farming,[1,11] or to a small focused farming activity such as dairy operations,[10] thus limiting the comparison among farming activities. The large number of nonsmoking women in the AHS provides a unique opportunity to assess potential occupational exposures and activities for chronic bronchitis without confounding by smoking. We evaluated associations with dusts, grains, and animals, the exposures most studied for chronic bronchitis among farmers, as well as with personal pesticide use.

Handling manure and driving combines were significantly associated with chronic bronchitis among farm women. These activities were not highly correlated. Use of manure as fertilizer, but not chemical fertilizer, was associated with chronic bronchitis, consistent with research on animal confinement farming.[16] Dried fecal material produces organic dusts which may cause chronic bronchitis, and manure produces gases such as sulfuric acid and ammonia that have also been associated with chronic bronchitis.[16,17] We did not find associations between current animal exposures and chronic bron-

TABLE 5

Lifetime Pesticide Exposure and the Association With Prevalent Chronic Bronchitis Among Nonsmoking Farm Women in the Agricultural Health Study (1993–1997)

	Chronic Bronchitis (n = 583) %	Controls (n = 20,958) %	Odds Ratio†	95% Confidence Interval†	Odds Ratio*	95% Confidence Interval*
Any pesticide	58	56	1.14	(0.97, 1.35)		—
Functional group						
Insecticides	45	39	1.29	(1.09, 1.53)	1.20	(0.98, 1.47)
Herbicides	36	37	1.07	(0.90, 1.28)	0.91	(0.74, 1.12)
Fungicides	7	4	1.35	(0.96, 1.89)	1.22	(0.84, 1.78)
Fumigants	3	2	1.51	(0.91, 2.53)	1.45	(0.84, 2.52)
Insecticide class						
Carbamates	37	31	1.23	(1.03, 1.46)	1.01	(0.81, 1.26)
Organophosphates	31	25	1.35	(1.12, 1.62)	1.22	(0.95, 1.56)
Organochlorines	11	7	1.37	(1.05, 1.80)	1.21	(0.88, 1.66)
Pyrethroids	6	5	1.33	(0.91, 1.93)	1.13	(0.76, 1.68)

*Multivariate adjusted: adjusted for age, state, and variables within each group (functional group or insecticide class).
†Adjusted for age, state.

chitis, unlike several studies that show that the prevalence of chronic bronchitis was highest among farmers with animals,[5,6,18,19] but this difference is most likely due to our having only current data on animal exposures.

Occupational exposures are known to contribute to chronic bronchitis among workers both in agricultural and industrial settings.[4] Off-farm work-related exposures to dusts were independently associated with chronic bronchitis in our study. Results for organic dusts were consistent with previous research.[14,20] Grain, wood, and cotton dusts have been associated with chronic bronchitis, chronic wheezing symptoms, a reduction in lung function, and airflow limitation.[14,20]

To our knowledge, we are the first to investigate specific pesticides and chronic bronchitis, although pesticides have been associated with other respiratory conditions, such as wheezing,[21,22] asthma,[23] restrictive lung function,[24] and chronic cough.[25] Whereas ever-use of any pesticide was not associated with chronic bronchitis, the use of some specific pesticides was. Of the 42 pesticides, three insecticides (dichlorvos, DDT, and carbofuran), two herbicides (cyanazine and paraquat), and one fumigant (methyl bromide) were

positively associated with chronic bronchitis after adjusting for other related pesticides. The association with carbofuran went away when asthmatics were removed from the sample, suggesting that asthmatics were driving this association; carbofuran has been associated with asthma among Saskatchewan farmers.[23] We could see no obvious commonalities among the pesticides associated with chronic bronchitis; information on the long-term respiratory effects of these chemicals is very limited. Dichlorvos is an organophosphate insecticide used to control many insects and parasitic infections on animals[26]; it was associated with current wheeze among commercial pesticide applicators in the AHS.[22] DDT is an organochlorine insecticide that was banned for use in the United States in 1972[26]; most studies on DDT have been focused on its reproductive and carcinogenic effects and not long-term pulmonary effects. Paraquat is a broadleaf herbicide associated with pulmonary fibrosis[16] as well as current wheeze among farmers in the AHS.[21] Cyanazine is a triazine herbicide with no previously identified adverse long-term respiratory effect. Methyl bromide is a fumigant that has been associated with chest pain and shortness of breath after acute

exposures in two case reports of grain storage workers.[27] We had no data on frequency of use of specific pesticides. However, we saw some evidence of increased chronic bronchitis with increased days of pesticide application and use of three or more agricultural pesticides. Although some of the insecticides may be associated with use on animals or in animal operations (eg, dichlorvos), it is unlikely that the herbicides are associated with animal operations in the past. Methyl bromide use might be associated with historic grain storage activities. Whether the observed relationships with chronic bronchitis are due to the pesticide application itself or other correlated farm activities cannot be resolved in our data.

Our reliance on self-reported information on doctor diagnosis to assess disease status may have resulted in misclassification of disease. Chronic bronchitis is defined as the presence of productive cough and phlegm for at least 3 months in each of 2 successive years. We did not have symptom data. Reported physician diagnoses may overestimate disease compared with direct use of symptom criteria.[28] We attempted to improve our case definition by restricting our population to those reporting diagnosis after age 20.

TABLE 6
Lifetime Pesticide Exposure and the Association With Prevalent Chronic Bronchitis Among Nonsmoking Farm Women in the Agricultural Health Study (1993–1997)

Pesticide	Chronic Bronchitis (n = 583) %	Controls (n = 20,958) %	Odds Ratio†	95% Confidence Interval†	Odds Ratio*	95% Confidence Interval*
Insecticides						
Carbamates						
Carbaryl	37	31	1.22	(1.03, 1.45)	1.19	(0.99, 1.42)
Carbofuran	3	2	1.77	(1.09, 2.87)	1.68	(1.03, 2.74)
Organochlorines						
Aldrin	1	1	1.05	(0.43, 2.57)	0.70	(0.23, 2.13)
Chlordane	6	4	1.25	(0.86, 1.81)	1.00	(0.65, 1.55)
Dieldrin	1	0.3	2.52	(1.01, 6.34)	2.53	(0.84, 7.56)
DDT	7	3	1.64	(1.16, 2.30)	1.67	(1.13, 2.47)
Heptachlor	1	1	1.09	(0.44, 2.68)	0.68	(0.22, 2.04)
Lindane	3	1	1.80	(1.04, 3.11)	1.49	(0.80, 2.78)
Organophosphates						
Chlorpyrifos	5	4	1.43	(0.97, 2.10)	1.21	(0.74, 1.98)
Coumaphos	1	1	0.75	(0.31, 1.82)	0.43	(0.15, 1.19)
Diazinon	14	10	1.47	(1.15, 1.88)	1.19	(0.89, 1.61)
Dichlorvos	4	3	1.83	(1.20, 2.80)	1.63	(1.01, 2.61)
Fonofos	3	2	1.56	(0.90, 2.69)	1.26	(0.61, 2.60)
Malathion	24	19	1.34	(1.10, 1.63)	1.21	(0.95, 1.53)
Parathion	2	1	1.96	(1.03, 3.74)	1.48	(0.72, 3.03)
Phorate	3	2	1.57	(0.93, 2.66)	1.38	(0.72, 2.64)
Terbufos	3	3	1.14	(0.69, 1.90)	0.66	(0.33, 1.32)
Pyrethroids						
Permethrin (crop)	2	2	1.13	(0.61, 2.07)	1.05	(0.56, 1.96)
Permethrin (animals)	4	4	1.47	(0.96, 2.26)	1.53	(0.99, 2.38)
Herbicides						
2,4-D	16	15	1.29	(1.02, 1.63)	1.20	(0.89, 1.63)
2,4,5-T	1	1	1.23	(0.50, 3.02)	0.97	(0.37, 2.51)
Alachlor	6	4	1.65	(1.15, 2.38)	1.28	(0.72, 2.26)
Atrazine	6	4	1.45	(1.00, 2.09)	0.91	(0.51, 1.61)
Butylate	1	1	1.12	(0.55, 2.28)	0.75	(0.32, 1.77)
Cyanazine	4	3	1.84	(1.20, 2.81)	1.88	(1.00, 3.54)
Chlorimuron-ethyl	1	2	0.86	(0.42, 1.74)	0.60	(0.26, 1.37)
Dicamba	5	4	1.39	(0.92, 2.10)	1.12	(0.64, 1.95)
EPTC	1	1	0.95	(0.42, 2.16)	0.59	(0.22, 1.54)
Glyphosate	33	33	1.07	(0.89, 1.29)	0.94	(0.76, 1.17)
Imazethapyr	3	3	1.25	(0.76, 2.05)	0.91	(0.45, 1.83)
Metolachlor	4	3	1.36	(0.87, 2.13)	1.07	(0.56, 2.03)
Metribuzin	3	2	1.77	(1.04, 3.00)	1.48	(0.69, 3.17)
Paraquat	2	1	1.94	(1.09, 3.44)	1.91	(1.02, 3.55)
Pendimethalin	2	1	1.01	(0.57, 1.81)	0.63	(0.30, 1.32)
Petroleum oil	5	3	1.68	(1.14, 2.49)	1.54	(0.95, 2.49)
Trifluralin	5	5	1.19	(0.81, 1.74)	0.89	(0.53, 1.51)
Fungicides						
Benomyl	1	1	1.46	(0.71, 3.01)	1.21	(0.52, 2.78)
Captan	3	2	1.26	(0.76, 2.10)	1.10	(0.61, 1.97)
Chlorothalonil	2	1	2.07	(1.11, 3.85)	1.69	(0.80, 3.57)
Maneb/nancozeb	2	1	1.30	(0.74, 2.29)	1.12	(0.58, 2.16)
Metalaxyl	2	1	1.47	(0.81, 2.66)	1.22	(0.62, 2.38)
Fumigants						
Methylbromide	2	1	1.82	(1.02, 3.24)	—	

*Multivariate adjusted: adjusted for age, state, and variables within each group (organophosphates, organochlorines, carbamates, pyrethroids, fungicides, and fumigants).
†Adjusted for age, state.

Reassuringly, the prevalence of self-reported chronic bronchitis (2.7%) among nonsmoking women in the AHS was similar to the prevalence (3%) among nonsmoking California farmers[29] and among nonsmoking Finnish women (3%).[30] Other population-based surveys of occupational exposures and chronic bronchitis have relied on self-reported doctor diagnosis of chronic bronchitis[31,32] and have seen the expected patterns

of exposure disease relationships (eg, smoking) as those that have used the more conventional symptom criterion. People with chronic bronchitis frequently have a history of asthma as well, and the risk factors for these outcomes may be similar. When we excluded people who reported a history of asthma, we saw an attenuation of some of the associations, but only the elevated risks for carbofuran, parathion, and petroleum oil went away entirely. This observation suggests that the majority of our findings are not driven by people with asthma in the sample.

Agricultural work is accompanied by concurrent hazards. A recent study of women in the AHS[13] showed that women who applied agricultural pesticides were more likely to engage in farm activities such as driving combines, planting crops, or applying fertilizer than were women who did not apply pesticides. Thus, an increase in chronic bronchitis among farm women who used pesticides could be confounded by other exposures. Although our ability to model current activities and lifetime pesticide use together was limited, we attempted to control for confounding by adjusting for sets of factors with the strongest correlations. In our final analyses of the correlation structure, we did not see evidence of strong correlations among the factors associated with chronic bronchitis in our data. We did not observe any correlations between the farm activities and pesticides.

The cross-sectional nature of this analysis of prevalent chronic bronchitis limits full evaluation of farming hazards, because much of the data was based on current farm activities. Current farming activities are often used as surrogates for past activities, but evidence suggests that chronic bronchitis may result in a change in farming habits. Tupi and colleagues[33] showed that farmers with chronic bronchitis planned to reduce, finish, or change the line of farm production more than twice as often as healthy farmers, and that 37% considered health reasons to be the main determinant of a change in future activities. In a population-based study of Norwegian farmers, chronic bronchitis symptoms were associated with a change in farm operation, retirement, or both. Thus, our results may underestimate the impact of farming exposures if before enrollment women changed their farm exposures as a result of diagnosis. This potential underestimation may be evident in the lack of association we found between disease and current animal exposures. However, the study benefited by having information on lifetime pesticide use and exposures related to the longest held occupation. Furthermore, farmers in the AHS provide plausible[34] and reliable[35] information regarding their pesticide use.

Few studies to date have evaluated the role of specific agricultural activities and chronic bronchitis among farm women. Most population-based studies have relied on simple exposure surrogates. Our cross-sectional study on farm women and occupational hazards among lifelong nonsmokers is the largest to date. This study benefited from the high participation rate (75%), which may minimize selection bias, and from sufficient sample size to explore the association of disease with a variety of agricultural and occupational exposures. By restricting the analysis to lifelong nonsmokers, we were able to evaluate these exposures without confounding by smoking, the major risk factor for chronic bronchitis. With information on lifetime pesticide use and occupational history, we were able to evaluate exposures not previously considered among farm women. Our results suggest that farm women have similar risk factors as men and that some specific pesticides may also be associated with chronic bronchitis.

Acknowledgments

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Erratum

Reference Omitted

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