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Prevalence of exposure to solvents, metals, grain dust, and other hazards among farmers in the Agricultural Health Study

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Exposures to multiple chemical, physical, and biological agents in agricultural work environments can result in confounding that may obscure or distort risks observed in epidemiologic studies. The Agricultural Health Study (AHS) is a large epidemiology study being conducted to investigate health risks among pesticide applicators and their families. During enrollment in the AHS, questionnaires were administered to over 52,000 licensed pesticide applicators from North Carolina and Iowa, who were mostly farmers. Questions about the frequency of various farming tasks were used to estimate the prevalence of exposure to solvents (25%), metals (68%), grain dusts (65%), diesel exhaust fumes (93%), and other hazards, including exposure to pesticides. Most of the farmers in the AHS reported performing routine maintenance tasks at least once a month, such as painting (63%), welding (64%), and repair of pesticide equipment (58%). The majority of farmers (74% in North Carolina; 59% in Iowa) reported holding nonfarm jobs, of which the most frequent were construction and transportation. The majority of the farmers enrolled in the AHS (55%) also reported that they mixed or applied pesticides on 10 or more days per year. The associations between the use of pesticides and the frequency with which the farmers in the AHS reported performing various types of specific farming activities were assessed to evaluate potential confounding. Confounding risk ratios calculated for these activities suggest that the magnitude of bias due to confounding is likely to be minimal.
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Introduction

Farmers perform a wide variety of different tasks required for the planting, cultivation, and harvesting of crops; the care and feeding of livestock; and the repair and maintenance of buildings and mechanical equipment. These tasks can involve potential exposure to agricultural chemicals, such as pesticides and fertilizers. Exposure to engine exhaust fumes can occur when driving tractors and exposure to airborne particulates can occur when tilling the soil. Exposure to solvent vapors and metal fumes can occur during the maintenance and repair of machinery and equipment. General summaries of the health hazards associated with agricultural work environments can be readily obtained from the published literature (Shaver and Tong, 1991). However, the assessment of exposure to specific environmental agents for individual farmers in epidemiologic studies can be quite challenging due to seasonal and day-to-day variability in their activities (Poppendorf and Donham, 1991). Thus, epidemiologic studies of farmers have typically resorted to relatively crude classifications of exposure status based on surrogates such as occupation, type of crop, or geographic region (Blair et al., 1992).

The Agricultural Health Study (AHS) is a large prospective cohort study being conducted to characterize the health risks associated with exposure to pesticides and other hazards in the agricultural work environment. A complete description of the study has been published previously (Alavanja et al., 1996). In short, the study enrolled over 52,000 private pesticide applicators, primarily farmers, from North Carolina and Iowa between December 1993 and December 1997 using a self-administered and a take-home questionnaire. The responses to questions about farming tasks and activities in these questionnaires were used to estimate the prevalence of exposure to a variety of agents among farmers in the AHS cohort.

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Table 1. Percentage of farmers by type of crop and type of livestock in the agricultural health study.

	North Carolina farmers	Iowa farmers
Number of subjects enrolled	20,529	31,598
Median age at enrollment	51	47
Number of subjects who completed take-home questionnaire	8108 (39%)	14,801 (47%)
Major crops (percentage of farmers)	Tobacco (37) Soybeans (37) Field corn (35)	Field corn (82) Soybeans (75) Hay (34)
Acres planted (percentage of farmers)		
None	4	<1
<5	11	<1
5–49	24	2
50–199	21	16
200–499	15	35
500–999	10	29
1000 or more	9	18
Major livestock (percentage of farmers)	Cattle (23) Hogs (8) Poultry (5)	Hogs (41) Cattle (40) Dairy (5)
Number of livestock (other than poultry, %)		
None	54	23
<50	24	8
50–99	8	8
100–499	8	25
500–999	1	17
1000 or more	4	19

Exposure to multiple chemical, biological, or physical hazards in the agricultural work environment can potentially confound health risks associated with exposure to pesticides. A factor that is associated with both the disease and the exposure of interest can cause bias in risk estimates that either exaggerates or obscures causal associations. The magnitude of bias due to confounding depends, in part, on the strength of the association between the confounding factor and the exposure of interest. The confounding risk ratio (CRR) is defined as the ratio of the unadjusted relative risk to the relative risk adjusted for the confounding factor. The CRR provides a general measure to evaluate the potential magnitude of bias due to confounding (Breslow and Day, 1980; Wacholder et al., 2000). The questionnaires completed by the pesticide applicators enrolled in the AHS were analyzed to assess the strength of associations between the use of pesticides and the frequency of other farming activities. These associations were used to calculate CRRs for these activities.

Methods

Enrollment questionnaires completed by 52,127 private pesticide applicators from Iowa and North Carolina were analyzed, and descriptive statistics were generated to summarize the prevalence of exposure to various agents. To apply restricted pesticides in North Carolina, applicators must have a pesticide applicator's license, while in Iowa, individuals must obtain a certification issued by the Department of Agriculture. Both states offer training classes, during which enrollment in the AHS was offered. These applicators are referred to as farmers, since 88% reported that they currently worked on a farm. In addition to farmers, approximately 5200 commercial pesticide applicators were enrolled in the AHS, but they were not primarily farmers and, therefore, were excluded from this analysis.

The enrollment questionnaire collected basic demographic information, as well as information on farm tasks and activities. Farmers were asked to identify their major income-producing crops and the number of acres planted in the past year, as well as the type and number of major income-producing livestock. A take-home questionnaire was distributed to be completed later and returned in the mail. The take-home questionnaire was designed to supplement the information from the enrollment questionnaire and to obtain greater detail on the frequency with which various farming tasks were performed.

Farming practices in North Carolina and Iowa were compared based on the percentage of farmers in each state that reported various types of crops and livestock, as well as the frequency with which farmers performed various farming tasks and maintenance activities. Seasonal variation in tasks was assessed by asking for separate responses for the summer and winter seasons. The responses to questions

Table 2. The percentage of farmers who reported various activities by state from the AHS enrollment questionnaire.

Which of the following activities do you perform at least once each year?	North Carolina (n=20,529) [%]	Iowa (n=31,598) [%]
Maintenance activities		
Paint	47	74
Weld	43	78
Repair pesticide application equipment	49	64
Repair engines	38	43
Replace asbestos brake linings	18	13
Crop handling		
Handle stored grain	32	86
Handle stored hay	36	64
Grind animal feed	17	59
Load or unload silage	6	29
Animal-related activities		
Perform veterinary services	25	65
Work in swine confinement areas	7	38
Butcher animals	14	13
Work in poultry confinement areas	6	2
Do not do any of above	7	1

about the frequency and duration of pesticide use were evaluated to determine the distribution in the total number of years and the number of days per year that these farmers personally mixed or applied pesticides. The average number of years and the average number of days per year that farmers mixed or applied pesticides by state were calculated by multiplying the percentage of farmers in each range by the midpoint of the range, and summing the products.

Solvents are sometimes mixed with pesticides, so farmers were asked whether they mixed solvents with various types of pesticides. They were also asked about the frequency with which they used solvents to clean their hands or equipment.

The take-home questionnaire also asked about nonfarm jobs held the longest, and the number of years on that job. A checklist of 20 specific agents found in various industrial settings was included in the questionnaire for self-report of nonfarm exposures. The nonfarm jobs were coded using the occupation and industry codes from the Standard Occupational Classification (SOC) Manual (US Department of Commerce, 1980) and the Standard Industrial Classification (SIC) Manual (Office of Management and Budget, 1987). The occupation and industry codes were then tabulated to identify the most frequently held nonfarm occupations and industries. The percentage of farmers who held nonfarm jobs and reported exposure to one or more of these 20 agents was calculated.

The potential for bias in risks estimates from exposure to pesticides due to confounding from exposures to agents other than pesticides was investigated by calculating CRRs. The farmers were dichotomized based on whether they mixed or applied pesticides on 10 or more days per year. They were then grouped based on whether they performed each of the 12 activities listed in the take-home questionnaire one or more times a month. The proportion of farmers who performed the activity one or more times a month among those farmers who mixed or applied pesticides on 10 or more days per year was compared with the proportion of farmers who performed the activity one or more times a month among those who mixed or applied pesticides less than 10 days per year. A CRR for each of the 12 farming activities listed in the take-home questionnaire was calculated using the equation in the Appendix.

Table 3. The percentage of farmers who reported performing various activities by frequency and state from the AHS take-home questionnaire.

During the last growing season, how many days did you do the following activities?	Days per season	North Carolina (n=8,108)		Iowa (n=14,801)	
		%	Average days per season	%	Average days per season
Till the soil	Never	11	34	4	28
	1–10	29		23	
	11–30	27		50	
	31–100	26		22	
	>100	7		2	
Drive combines	Never	46	16	8	24
	1–10	21		20	
	11–30	18		52	
	31–100	13		19	
	>100	2		0	
Apply natural fertilizer	Never	55	8	26	28
	1–10	29		23	
	11–30	12		32	
	31–100	3		12	
	>100	2		8	
Plant crops	Never	11	22	9	17
	1–10	34		22	
	11–30	42		64	
	31–100	11		5	
	>100	3		0	
Apply chemical fertilizer	Never	18	16	20	10
	1–10	42		45	
	11–30	32		33	
	31–100	6		2	
	>100	2		0	
Handpick crops	Never	40	18	83	2
	1–10	27		15	
	11–30	20		2	
	31–100	9		0	
	>100	5		0	

Results

Enrollment questionnaires were completed by 20,529 farmers from North Carolina and 31,598 farmers from Iowa (Table 1). The decade of birth ranged from the 1930s through the 1970s, with a median age at enrollment of 51 and 47 for North Carolina and Iowa farmers, respectively. The farmers who completed the enrollment questionnaire were mostly white males (95%). A higher percentage of females (4.5% vs. 1.4%) and nonwhites (7.9% vs. 0.2%) was enrolled in North Carolina compared with Iowa. In addition to the enrollment questionnaire, 8108 (39%)

Table 4. Percentage of farmers who reported performing various farming tasks by frequency, season, and state from the AHS take-home questionnaire.

How often do you personally do the following activities?		North Carolina (n=8,101)		Iowa (n=14,801)	
		Summer	Winter	Summer	Winter
Drive diesel tractor	Daily	13	9	4	23
	Weekly	45	35	4	42
	Monthly	24	31		25
	<1 Month	18	24		10
Drive gasoline tractor	Daily	24	2	1	10
	Weekly	25	12	4	27
	Monthly	5	28	2	29
	<1 Month	47	58	2	34
Drive trucks	Daily	22	34	1	13
	Weekly	16	27	2	21
	Monthly	8	18	2	24
	<1 Month	54	21	3	42
Grind metal	Daily	1	1		2
	Weekly	11	10	2	17
	Monthly	37	34	5	54
	<1 Month	51	55	2	28
Welding	Daily	1	1		1
	Weekly	10	9	2	15
	Monthly	30	29	4	49
	<1 Month	59	61	2	34
Repair engines	Daily	1	1		1
	Weekly	4	4		4
	Monthly	30	28	3	30
	<1 Month	64	67	5	65
Use gasoline to clean hands or equipment	Daily	1	0		0
	Weekly	4	3		3
	Monthly	24	20	3	23
	<1 Month	71	76	5	74
Use solvents to clean equipment	Daily	1	1		1
	Weekly	2	2		3
	Monthly	19	16	2	16
	<1 Month	79	81	7	81
Paint	Daily	0	0		0
	Weekly	1	1		1
	Monthly	24	21	4	18
	<1 Month	75	77	5	80
Grind animal feed	Daily	1	1		8
	Weekly	3	4	3	33
	Monthly	8	9	1	12
	<1 Month	88	86	4	46
Perform veterinary procedures	Daily	1	1		1
	Weekly	2	3	1	11
	Monthly	11	14	3	32
	<1 Month	86	83	5	56
Milk cows	Daily	2	2		6
	Weekly	1	1		0
	Monthly	1	1		1
	<1 Month	96	96	9	93

farmers from North Carolina and 14,801 (47%) farmers from Iowa also completed the take-home questionnaire.

Major differences between the two states were seen in the various types of crops and livestock reported (Table 1). In North Carolina, 37% of farmers reported growing tobacco and soybeans and 35% reported field corn as their major crops. In Iowa, 82% of farmers reported growing field corn, 75% reported soybeans, and 34% reported hay as their major crops. Cattle were the major livestock reported by North Carolina farmers (23%), while hogs were the major livestock reported by Iowa farmers (41%). The majority of farmers in Iowa grew field corn, while farmers in the North Carolina tended to have more diversity in the types of crops grown. The average acres planted in Iowa were larger than in North Carolina, with an average of 587 vs. 274 acres planted, respectively. Iowa farmers raised more livestock, and were more likely to report having over 100 livestock compared with North Carolina (51% vs. 13%). In North Carolina, 48% of farmers reported no livestock, while in Iowa, 22% reported no livestock.

Iowa farmers reported performing maintenance activities such as painting, welding, and repair of pesticide application equipment more often than farmers in North Carolina. Iowa farmers were also more likely to perform activities involving exposure to grain dust, such as handling stored grain and grinding animal feed (Table 2). Along with having more livestock, Iowa farmers performed animal-related tasks such as veterinary services and working in swine confinement areas more often than farmers in North Carolina. There was a broad distribution in the frequency of most tasks reported. For example, 11% and 4% of farmers from North Carolina and Iowa, respectively, reported that they never tilled the soil, while 7% and 2% reported that they tilled the soil more than 100 days per season. Despite the smaller acreage, North Carolina farmers reported that they tilled the soil an average of 34 days per growing season, while Iowa farmers tilled the soil an average of 28 days per season (Table 3). A higher percentage of North Carolina farmers planted crops, applied chemical fertilizer, and handpicked crops on 30 or more days per season, while a higher percentage of Iowa farmers drove combines and applied natural fertilizer on 30 or more days per season.

In North Carolina, 82% of farmers reported that they drove a diesel tractor at least monthly, and 13% drove diesel tractors on a daily basis during the summer (Table 4). In Iowa, 97% of farmers reported that they drove a diesel tractor at least once a month, and 49% drove diesel tractors on a daily basis. The majority of farmers from both states drove trucks and gasoline tractors at least monthly. Over 50% of farmers in Iowa, but not in North Carolina, reported that they grinded or welded metal at least once a month. More than 25% of farmers from both states reported that they repaired engines, used gasoline, or solvent to clean equipment, and painted at least once a month. Approximately 46% of Iowa farmers performed veterinary procedures where they came in contact with animal blood one or more times per month compared with 18% of North Carolina farmers (Table 4).

Over 89% of the North Carolina farmers and 98% of the Iowa farmers who completed the enrollment questionnaire reported that they personally mixed or applied pesticides one or more times per season (Table 5). The most frequently reported duration for the total years that they mixed or applied pesticides was 11–20 years, with an average of 17 years in both states. In North Carolina, 57% of the farmers reported that they mixed or applied pesticides on 10 or more days per year, while in Iowa, 54% of farmers mixed or applied 10 or more days per year. The most frequent range for the days per year with which these farmers reported applying or mixing pesticides was 10–19 days per year. Solvents were used as an additive when mixing pesticides by 8% of farmers (Table 6).

The majority of farmers in both states had, at some point in their careers, worked at a nonfarm job, 74% in North Carolina and 59% in Iowa (Table 7). The most frequently reported nonfarm occupations included construction, transportation (e.g., truck driver), and mechanic. The most

Table 5. The percentage of farmers who mix or apply pesticides by duration and frequency from the AHS enrollment questionnaire.

	North Carolina (n=20,529) [%]	Iowa (n=31,598) [%]
During your lifetime, have you ever personally mixed or applied any pesticides?		
Yes	89	98
No	2	1
No response	9	1
How many years did you personally mix or apply pesticides?		
1 or less	3	2
2–5	13	9
6–10	16	14
11–20	28	33
21–30	19	25
More than 30	13	12
No response	8	5
Average number of years	17	17
How many days per year did you personally mix or apply pesticides?		
Less than 5	17	15
5–9	16	26
10–19	22	32
20–39	20	17
40–59	8	3
60–150	6	1
More than 150	1	<1
No response	10	6
Average number of days per year	27	18

Table 6. Percentage of farmers who used solvents as an additive when mixing pesticides.

Type of pesticide	North Carolina (n=8,108) [%]	Iowa (n=14,801) [%]
Animal insecticides	4.5	4.9
Herbicides	2.8	4.1
Crop insecticides	1.2	0.7
Fungicides	0.6	0.2
Any of the above	7.1	8.7

frequently reported industries were construction, trucking, and food products. Engine exhaust, gasoline, solvents, and welding fumes were the most frequently reported exposures for nonfarm jobs (Table 8). The proportion of farmers who reported exposure to the various agents listed on the questionnaire was similar between the two states; however, exposure to wood dust was more common in North Carolina, while exposure to grain dust was more common in Iowa.

Among the farmers from both states who completed the take-home questionnaire, 57% reported that they mixed or applied pesticides on 10 or more days per year. The farmers who mixed or applied pesticides on 10 or more days per year were also more likely to perform 10 of 12 activities listed in the take-home questionnaire (Table 9), including maintenance activities such as repairing engines, grinding metal, and welding at least once a month, as compared with farmers who mixed or applied pesticides less often.

Table 7. Percentage of farmers who held nonfarm jobs by type of occupation and industry.

		North Carolina (n=8,108) [%]	Iowa (n=14,801) [%]
Did you ever have a job off a farm?			
Yes		74	59
How many years did you have this job?			
<1		6	14
2–5		18	36
6–10		16	20
11–20		21	16
>20		39	14
For the nonfarm job you held the longest, what was your job? (top five)			
SOC	*Occupation*		
64	Construction trades	10	11
82	Transportation occupations	6	10
61	Mechanics and repairers	8	9
77	Fabricators, assemblers, handworking	4	7
68	Precision production occupations	7	5
What industry was the job in? (top five)			
SIC	*Industry*		
15	Construction	13	13
42	Trucking and warehousing	5	7
20	Food products	2	9
39	Manufacturing	3	7
35	Industrial machinery and equipment	2	8

Table 8. Percentage of farmers reporting exposures in nonfarm jobs by agent.

Exposure agent	North Carolina (n=5,972) [%]	Iowa (n=8,739) [%]
Pesticides	7	7
Engine exhaust	20	21
Gasoline	16	15
Solvents	16	16
Welding fumes	16	16
Wood dust	14	8
Grain dust	4	10
Cotton dust	5	<1
Silica dust	5	4
Mineral dust	2	1
Asbestos	8	4
Lead solder	5	4
Lead	3	2
Cadmium	1	<1
Mercury	1	<1
Electroplating fumes	1	1
Other metals	4	3
Pneumatic drills	6	7
X-ray radiation	2	1
None of the above	21	15

Table 9. Hypothetical CRRs based on proportion of farmers reporting various activities among those who mix or apply pesticides 10 or more days per year compared with those who mix or apply pesticides less than 10 days per year.

Activity performed one or more times per month	Mix or apply pesticides 10 or more days per year		CRR
	Yes (p_1) [%]	No (p_2) [%]	
Repair engines	74	62	1.07
Grind metal	73	62	1.07
Weld	69	58	1.07
Drive trucks	45	35	1.07
Use gasoline to clean	42	35	1.05
Use solvent to clean	28	22	1.05
Paint	39	35	1.03
Drive diesel tractor	95	90	1.02
Contact animal blood	38	35	1.02
Grind animal feed	41	40	1.01
Drive gasoline tractor	71	71	1.00
Milk cows	2	3	0.97

p_1=proportion of farmers who perform this activity one or more times per month and who mix or apply pesticides 10 or more days per year.
p_2=proportion of farmers who perform this activity one of more times per month and who mix or apply pesticides less than 10 days per year.
CRR calculated for hypothetical relative risk of 2.0 for this activity.

The strength of the association between the farming activities and the use of pesticides was assessed based on the proportion of farmers who reported performing each activity at least once a month among the farmers who mixed or applied pesticides on 10 or more days per year compared with the proportion of farmers who performed the activity at least once a month among farmers who mixed or applied pesticides on less than 10 days per year. For example, 25% of all respondents reported the use of solvents to clean equipment at least once a month. Among the farmers who mixed or applied pesticides on 10 or more days per year, 28% reported the use of solvents to clean equipment at least once a month. Among farmers who mixed or applied less than 10 days per year, only 22% reported the use of solvents to clean equipment at least once a month. Thus, farmers who reported more frequent use of pesticides were 27% more likely to report use of solvents compared with farmers who reported less frequent use of pesticides.

Similar comparisons between farmers who mixed or applied pesticides on 10 or more days per year and less than 10 days per year were made for each of the 12 farming tasks in Table 9. The relative proportions were then used to calculate CRRs for each task. When assuming a crude relative risk of 2.0 for the task, the hypothetical CRR values ranged from 0.97 to 1.07. A maximum CRR of 1.07 indicates a maximum bias of 7% in risk estimates for exposure to pesticides due to confounding from these other activities (Table 9).

Discussion

The extensive information on pesticide use collected in the AHS enrollment and take-home questionnaires provides an excellent opportunity to investigate the disease risks associated with the use of specific pesticides. However, the diverse nature and the seasonal variability of the farming tasks and activities create substantial challenges for exposure assessment in the agricultural work environments. Questionnaires like those used in the AHS and other studies are important tools for collection of exposure information of individual subjects and assessment of the prevalence of exposure to various hazards among farmers. A telephone survey of California farm operators was conducted in 1993 to collect information on the percentage and frequency with which farmers performed farming tasks, with an emphasis on evaluating exposure to dust and respiratory hazards (Nieuwenhuijsen et al., 1997). A comparison between this survey and the results presented here is limited due to differences in the specific questions and regional agricultural practices; however, a difference in the frequency of reported activities is apparent. In California, 31% of farmer operators reported planting or seeding during the previous 12 months, while in the AHS survey, 89% of farmers in North Carolina and 91% in Iowa reported planting crops. In California, 19% of farm operators reported hand-harvesting, while in the AHS survey, 60% and 17% reported handpicking crops in North Carolina and Iowa, respectively.

The use of questionnaires to assess exposures among farmers in the AHS has several limitations. While over 52,000 farmers completed the enrollment questionnaires, only 44% of these farmers completed the take-home questionnaire. However, a previous analysis revealed that the farmers who completed the take-home questionnaire were, for most characteristics, similar to those who completed only the enrollment questionnaire (Tarone et al., 1997). Another limitation is that the AHS cohort was established to investigate potential effects among pesticide applicators and, therefore, the statistics on use of pesticides and other activities presented here may not necessarily represent the total population of farmers in these two states.

Chronic diseases such as cancer often have multiple etiologies that are not well understood. A major objective of epidemiologic studies of farmers is to identify etiologic agents among the multiple exposures found in agricultural work environments and to quantify their relative importance to disease risks. When evaluating causal associations between exposure and disease, the possibility of confounding must be considered. To result in substantial confounding, a factor must be strongly associated with both the suspected etiologic agent and the disease of interest. Conversely, if a factor is not associated with the exposure of interest, then there is no potential for confounding regardless of the association between the confounding factor and the outcome of interest (Blair et al., 1995). Thus, the potential for confounding can be assessed by evaluating the strength of the association between the confounding factor and the exposure of interest.

The potential for confounding was demonstrated in a study of leukemia risk and occupation conducted in Iowa and Minnesota. In this study, an elevated risk of leukemia was detected among workers employed in agricultural industries, as well as in occupations with possible exposure to solvents (Blair et al., 2000). In a separate study, an analysis of the ingredients of 8000 pesticides identified 71 different solvents, several of which have been identified by IARC as human carcinogens (Petrelli et al., 1993). The authors recommended that exposure to solvents be considered as a potential risk factor during investigations of cancer risk among farmers.

Among the AHS cohort, the farmers who apply pesticides more often were also more likely to use solvents. Thus, an increased risk of a particular disease among farmers who use pesticides could be confounded by exposures to solvents, resulting in a possible bias in the estimate of disease risk from exposure to pesticides alone. In the AHS cohort, 28% of the farmers who mixed or applied pesticides on 10 or more days per year also reported the use of solvents to clean equipment at least once a month, compared with 22% of farmers who mixed or applied pesticides less than 10 days per year. If the use of solvents doubles the risk of disease, then the calculated CRR for solvents would be 1.05. This value can be interpreted to mean that confounding due to the use of solvents would cause no more than a 5% positive bias in the risk for pesticide use. If the relative risk from use of solvents is less than 2.0, then the maximum bias would be less than 5%. If the relative risk from use of solvents was, for example, as high as 5.0 — a relative strong relative risk, then the corresponding value of the CRR would be 1.13, and the potential bias would be 13%. These CRR values are only hypothetical since no actual diseases are considered in this analysis. A relative risk of 2.0 for the strength of the association between the confounder and disease was selected as a plausible value that was large enough for concern, yet small enough to possibly avoid recognition as a significant source of confounding. Bias in observed association from recognized confounding factors, such as smoking, can be addressed using standard statistical methods, such as stratification or multiple logistic regression models (Breslow and Day, 1980).

The calculation of the CRR requires several assumptions and provides only a crude estimate of the potential for confounding. It requires a dichotomous classification for exposure to both the agent of interest and the confounding agent. The annual frequency of pesticide use was reported in the seven categories shown in Table 5. For this analysis, these seven categories were collapsed into two categories (i.e., less than 10 days per year and 10 or more days per year) to provide two approximately equally sized groups for comparison. More than one confounding variable may exist, and some farmers may have residential and nonoccupational exposures to these substances that are not reflected in the questionnaire responses. Thus, the calculation of a CRR may oversimplify complex exposure scenarios, and more sophisticated approaches, such as multivariate regressions and factor analysis, are required to more rigorously examine confounding when epidemiological analyses for specific diseases are conducted. These general conclusions about the potential magnitude of confounding must be interpreted with caution, and do not preclude the need to investigate confounding for specific diseases and types of pesticides.

While farmers experience an overall lower mortality rate compared with the general population, elevated rates for certain types of cancer that suggest environmental causes have been detected (Blair et al., 1995; Davis et al., 1992). Limitations in the information on exposure to specific pesticides, as well as other hazardous agents in the agricultural work environment, have precluded a more detailed analysis of specific exposures. In the AHS, the detailed information collected on frequency of farming tasks and activities has been analyzed to assess exposure to pesticides as well as other potential hazards. The similar proportions of farmers who performed various farming activities among farmers who reported more frequent use of pesticides compared with farmers who reported less frequent use of pesticides indicate that substantial bias due to unrecognized confounding from these activities in estimates of disease risks from exposure to pesticides is unlikely.

Appendix: CRR

The CRR (Table 10) is defined as the ratio of the risk estimate obtained when ignoring confounding divided by the risk estimate obtained after adjustment for confounding. The CRR provides a general measure to estimate the magnitude of bias from a confounding factor (Breslow and Day, 1980). The CRR is calculated from the prevalence of exposure to the confounding factor among subjects who are exposed to the agent of interest (p_1), the prevalence of exposure to the confounding factor among subjects who are not exposed to the agent of interest (p_2), and the strength of the association between the confounding factor and the disease (OR_c). Interestingly, the CRR is not affected by the strength of the association between the exposure and outcome of interest. Given an exposure of interest (E), and a confounding factor (C), the CRR is calculated from Eq. (1):

$$\mathrm{CRR} = \mathrm{OR_p}/\mathrm{OR_a} = [\mathrm{OR_c}p_1 + (1-p_1)]/[\mathrm{OR_c}p_2 + (1-p_2)] \quad (1)$$

where:

OR_a=odds ratio after stratification by C (adjusted);
OR_p=odds ratio ignoring C (crude or pooled);
OR_c=odds ratio for confounder C after stratification by exposure E;
p_1=prevalence of exposure to C among those exposed to E;
p_2=prevalence of exposure to C among those not exposed to E.

Table 10. CRRs for different risks from confounding exposure (OR_c) and prevalences of exposure to confounding variable among subjects exposed to E (p_1) and not exposed to E (p_2).

Prevalence of exposure		CRRs		
p_1	p_2	OR_c=2	OR_c=5	OR_c=10
0.1	0.05	1.05	1.17	1.31
0.3	0.15	1.08	1.22	1.32
0.5	0.30	1.15	1.36	1.49
0.9	0.50	1.31	1.84	1.80

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