High Pesticide Exposure Events Among Farmers and Spouses Enrolled in the Agricultural Health Study

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ABSTRACT. *We completed a nested case-control analysis of factors associated with reporting a high pesticide exposure event (HPEE) by pesticide applicators and spouses during the five years since enrollment in the Agricultural Health Study (AHS). Cases and controls were identified from the 16,415 private pesticide applicators and 14,045 spouses with completed five-year follow-up interviews as of October 2000. Among the applicators, 306 cases with at least one HPEE in the five years since enrollment and 612 controls, randomly selected from those without a reported HPEE, were identified for analysis. Among the spouses, 63 cases were identified and 126 controls were selected. Risk for a new HPEE was increased among applicators reporting at enrollment ever having an HPEE with an odds ratio (OR) of 3.8 (95% CI: 2.7, 5.3). Compared to applicators who applied pesticides fewer than 5 days per year, the ORs ranged from 1.4 (95% CI: 0.9, 2.2) for 6 to 10 days per year to 2.2 (95% CI: 1.4, 3.6) for more than 20 application days per year. The incidence of HPEE among Iowa applicators was much greater (8.8/1000 applicators) than among North Carolina applicators (2.0/1000). Spouses reported fewer HPEEs compared to applicators (2/1000 spouses). Overall, the observed risk factors for new HPEEs among applicators are similar to risk factors observed in previous cross-sectional analyses of HPEE history. Further, only 13% of applicators and 22% of spouses with symptoms resulting from HPEE sought medical care, suggesting that pesticide poisoning surveillance data may seriously underreport the frequency of such events.*

Keywords. *Accidents, Agricultural pesticides, Pesticide exposure events.*

Although current research suggests that agricultural workers in the U.S. are healthier than the general population, they have higher rates of certain cancers, asthma, and neurologic diseases (Alavanja et al., 1996; Blair et al., 2005; Kamel et al., 2003). While the causes of these patterns of disease among farmers are unknown, exposures common to farmers (i.e., pesticides) have been suggested as possible risk factors (Alavanja et al., 2004; Alavanja et al., 1996; Kamel and Hoppin, 2004). The Agricultural Health Study (AHS) has enrolled licensed pesticide applicators in Iowa and North Carolina (N.C.) and their spouses to assess the relationship between pesticide and other agricultural exposures and health outcomes.

Pesticide exposure to farmers is a result of both their day-to-day farming operations ("chronic exposure") and unusual events such as spills and accidents that cause exposures at levels higher than what they normally experience ("acute exposure"). The reporting

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of pesticide poisonings is incomplete nationally, especially for those working in agriculture (USGAO, 2000). Given that case ascertainment based solely on pesticide poisoning reports may not sufficiently identify individuals at risk for high pesticide exposure events (HPEE), it is important to characterize this unique population both for identifying individuals at risk and evaluating health effects associated with these high-exposure episodes.

Since there is no standardized definition for HPEE, we relied on self-reports from the participants in the AHS for past analyses. At enrollment into the study cohort, applicators were asked: "Have you ever had an incident or experience while using any type of pesticide which caused you unusually high personal exposure?" Fourteen percent of the 22,884 applicators completing both baseline questionnaires at enrollment into the study cohort reported a history of at least one HPEE. Analyses of this group of applicators showed that HPEE risk per applicator increased with pesticide application days. In addition, HPEE risk was greater for the following three groups: males, applicators with at least some college compared to those with less than a high school education, and applicators living in Iowa (Alavanja et al., 1999). In a second study, farmers in Iowa who recalled having at least one HPEE during the twelve-month period prior to the interview (Alavanja et al., 2001), and a group of farmers who did not report such an event, were asked a series of questions pertaining to their pesticide use practices. Scoring high on a risk-acceptance scale and poor financial condition of the farm contributed to HPEE risk with odds ratios (OR) and confidence intervals (CI) of 3.8 (1.4-11.2) and 4.6 (1.5-16.6), respectively.

Since previous analyses were limited to lifetime history of HPEE and Iowa applicators, we used the data from the five-year follow-up interview of the AHS cohort to examine risk factors associated with new HPEEs in both Iowa and North Carolina study participants. Given that information on HPEEs was not gathered from spouses at the time of enrollment, we were able to assess the risk of HPEE in this group for the first time.

Methods

Cases and controls were selected from applicators and spouses enrolled in the AHS cohort. The methods used to assemble this cohort have been previously described (Alavanja et al., 1996). Briefly, 52,395 privately licensed pesticide applicators living in Iowa and North Carolina and 32,347 spouses of the licensed applicators were enrolled between December 1993 and December 1997. In 1999, a five-year follow-up of the cohort began, which includes the administration of a computer-assisted telephone interview (CATI). As of October 2000, 16,415 applicators and 14,045 spouses had completed the CATI questionnaire. This interview collected information from licensed applicators and spouses regarding the number of HPEEs that occurred in the five years since enrollment into the AHS, as well as specific information pertaining to the HPEE if it occurred in the 12 months prior to the interview.

Cases and controls were identified from the private pesticide applicators and spouses with completed CATI questionnaires as of October 2000. Cases were defined as all those who answered "yes" to the question: "Since (the year of enrollment), did you have any incidents with fertilizers, herbicides, or other pesticides that caused you an unusually high personal exposure?" Controls (2 per case) were randomly selected from those who answered "no" to the same question. Among the applicators, 306 cases with at least one HPEE in the five years since enrollment and 612 controls were identified for analysis. Among the spouses, 63 cases and 126 controls were identified. A second, more restrictive, case group of individuals who had experienced a HPEE in the year

prior to the interview (referred to as HPEE-12) was examined separately given that they were more likely to remember the event in greater detail compared to those recalling events occurring up to five years previously. Applicators with these more recent events were asked whether or not symptoms occurred as a result of the HPEE. Therefore, individuals reporting an HPEE in the year prior to the interview with (referred to as HPEE-12S) and without (referred to as HPEE-12NS) reported symptoms were also evaluated separately.

CATI Interview

Demographic factors (race and marital status), farm characteristics (farm size, proximity of home to fields where pesticides were applied, source of drinking water), and pesticide work practices (number of pesticide application days per year, use of protective clothing, bathing after working with pesticides, washing work clothes separately, storing pesticides in the home) were obtained from the CATI questionnaire for both applicators and spouses. Previous history of HPEE, age, and education status were obtained from the enrollment questionnaire. In addition, for respondents who indicated that the HPEE occurred in the year prior to the interview (108 applicators; 33 spouses), information specific to that most recent event was obtained, including the pesticide used when the HPEE occurred, resulting symptoms, and work activity at the time of the event.

Statistical Analyses

Both HPEE and HPEE-12 case definitions were evaluated separately. To assess associations with HPEE, unadjusted odds ratios (OR) and 95% confidence intervals (CI) were calculated for each of the demographic, farm, and pesticide work characteristics comparing HPEE and HPEE-12 cases to controls. The continuous variables (age, farm size, and days of pesticide application) were categorized by quartile cutpoints. Characteristics with unadjusted OR of less than or equal to 0.8 or greater than or equal to 1.3 were examined in a multivariable logistic regression model. Variables that met the criteria were entered or removed singly into the model using both a forward and backward selection process. The model was evaluated for confounding and model stability after each step. The final model included the dependent variable (HPEE) and the variables selected in this modeling process.

To evaluate whether the estimates derived from the final model would vary by state or for number of pesticide application days per year, the final model was evaluated separately for each state of residence and categories of pesticide application days. Both CI precision (width) and whether or not the CI included one were used to identify associations that were noteworthy. Given that the goal of this analysis was to assess patterns of associations, precise measures that included 0.8 or greater as the lower limit of the confidence interval or findings that were consistent with prior reports were considered for model inclusion even if not statistically significant in the strictest sense. Finally, the distribution of characteristics specific to the most recent HPEE was described by symptom status.

Results

Applicators

Of the 16,415 applicators with completed questionnaires, 306 reported having at least one HPEE since enrollment, with 135 of the 306 (46%) reporting multiple HPEEs over the five-year period. Of the 135, 99 (73%) had five or fewer events. Of the 306 applicators reporting an HPEE, 108 (35%) indicated that at least one event had occurred

in the 12-month period prior to the interview. Thus, the one-year incidence rate of at least one HPEE per year was 108/16,416 = 6.5/1000 applicators per year. Stratified by state of residence, the one-year incidence rates of HPEE among Iowa and North Carolinian applicators were 8.8/1000 and 2.0/1000, respectively. For those reporting an HPEE with symptoms in the year prior to the interview (n = 54), 35 (65%) reported multiple HPEEs over the five-year period. Of the 35, 22 (63%) had five or fewer events.

The distributions of demographic, farm, and pesticide work practice characteristics are presented in table 1 for the HPEE, HPEE-12S, and control groups. When compared to the same control group, the distribution of risk factors and magnitude of the unadjusted ORs for HPEE and HPEE-12 were the same. Similarly, the distribution of risk factors for applicators with one reported HPEE was similar to the distribution observed for those with two or more HPEEs in the same five-year period. Thus, only the results for HPEE and HPEE-12S are presented.

Demographic Characteristics

All of the applicators were men, and 97% were white. Applicators who reported "ever" having an HPEE at the time of enrollment into the AHS had the greatest risk of a new event in the five years since enrollment (OR: 3.7; 95% CI: 2.7, 4.9). Risk was inversely associated with quartiles of age. Compared to applicators greater than or equal to 53 years old at the time of enrollment, ORs ranged from 2.6 (95% CI: 1.7, 3.9) for those less than 38 years of age to 1.1 (95% CI: 0.7, 1.8) for those 46 and older. Residents of Iowa had twice the risk of North Carolinians, and applicators with a high school education were less likely to experience an event compared to those with a college education.

For the HPEE-12S applicators, reporting "ever" having an HPEE at enrollment was also related to risk of an HPEE in the past year (OR: 2.7; 95% CI: 1.5, 4.8). HPEE plus symptom risk was inversely related with high school education compared to those with a college education (OR: 0.6; 95% CI: 0.3, 1.1).

Farm Characteristics

Of the farm characteristics examined, farm size (i.e., $\geq$800 acres vs. <200 acres) and distance of the home from fields where pesticides were applied (i.e., 50-199 ft vs. >200 ft) were related to HPEE with ORs of 1.8 (95% CI: 1.2, 2.6) and 1.5 (95% CI: 1.1, 1.9), respectively. Similar results were observed for the HPEE-12S applicators with ORs of 2.1 (95% CI: 1.0, 4.4) and 2.0 (95% CI: 1.1, 3.5), respectively.

Pesticide Work Characteristics

HPEE risk increased with categories of pesticide application days per year. When compared to fewer than 5 pesticide application days per year, ORs ranged from 1.5 (95% CI: 1.0, 2.2) for 6 to 10 days per year to a high of 3.1 (95% CI: 2.0, 4.7) for more than 20 application days per year. Trends were similar for the HPEE-12S applicators. Not removing work boots when entering the home was associated with increased risk (1.6 OR, 95% CI: 1.2, 2.3) overall and in the subset of recent HPEE with symptoms. Applicators and spouses were asked if they "normally wear" personal protective equipment (PPE) while applying pesticides. Wearing any type of personal protective equipment (i.e., gloves, masks, or coveralls) when applying pesticides reduced HPEE risk only slightly compared to those who did not wear PPE. However, while the numbers were small, HPEE risk with symptoms increased for applicators who did not wear gloves when applying insecticides, fungicides, and fumigants.

Table 1. Distribution of pesticide applicator characteristics by high pesticide exposure status (HPEE), high pesticide exposure status with symptoms (HPEE-12S), no HPEE (controls), and unadjusted ORs for applicators at the five-year follow-up of the AHS cohort in 1999-2000.

Variable	No HPEE (controls)	HPEE	Unadjusted OR (95% CI)[a]	HPEE 12S	Unadjusted OR (95% CI)[b]

Total	612	306		54	
Demographic characteristics					
HPEE reported at enrollment into cohort					
HPEE reported	126	149	3.7 (2.7, 4.9)	22	2.7 (1.5, 4.8)
No HPEE reported	474	152	Referent	31	Referent
Missing	12	5		1	
State of residence					
Iowa	504	276	1.9 (1.3, 3.0)	47	1.4 (0.6, 3.3)
North Carolina	108	30	Referent	7	Referent
Missing	0	0			
Race					
White	592	294	NA[c]	54	NA
Non-white	5	1		0	
Missing	15	11			
Age in years 18-38	145	110	2.6 (1.7, 3.9)	16	2.0 (0.9, 4.7)
39-45	145	97	2.3 (1.5, 3.5)	24	3.0 (1.4, 6.7)
46-55	157	51	1.1 (0.7, 1.8)	5	0.6 (0.2, 1.8)
≥56	165	48	Referent	9	Referent
Education					
≤High school education	305	118	0.6 (0.5, 0.8)	21	0.6 (0.3, 1.1)
≥Some college	289	177	Referent	33	Referent
Missing	18	11			
Marital status					
Married	529	265	1.0 (0.7, 1.5)	49	1.5 (0.6, 3.9)
Not married	82	41	Referent	5	Referent
Missing	1	0			
Farm characteristics					
Size of farm					
≥801 acres	130	88	1.8 (1.2, 2.6)	19	2.1 (1.0, 4.4)
415- 800.5 acres	159	82	1.3 (0.9, 2.0)	11	1.0 (0.4, 2.3)
201-414.5 acres	153	71	1.2 (0.8, 1.8)	12	1.1 (0.5, 2.5)
≤200.5 acres	170	65	Referent	12	Referent
Distance of home from field where pesticides are applied					
<50-199 ft	247	153	1.5 (1.1, 1.9)	31	2.0 (1.1, 3.5)
200 ft to 1/4 mile	362	153	Referent	23	Referent
Missing	3	0			
Uses well for drinking water					
Yes	434	209	0.9 (0.7, 1.2)	40	1.2 (0.6, 2.4)
No	178	97	Referent	14	Referent
Tractor has enclosed cab					
No	150	73	0.8 (0.5, 1.1)	15	1.0 (0.5, 1.9)

Yes	281	180	Referent	28	Referent
Missing	181	53		11	
Repairs own spraying or mixing equipment					
No	30	4	NA	1	NA
Yes	527	294		51	
Missing	55	8		2	

Table 1 (cont'd).

Variable	No HPEE (controls)	HPEE	Unadjusted (95% CI)[a]	OR HPEE 12S	Unadjusted OR (95% CI)[b]
Pesticide work characteristics					
Number of pesticide applications (days per year)					
1-5	197	60	Referent	9	Referent
6-11	170	77	1.5 (1.0, 2.2)	14	1.8 (0.8, 4.3)
12-20	109	86	2.6 (1.7,3.9)	10	2.0 (0.8, 5.1)
>20	80	75	3.1 (2.0, 4.7)	19	5.2 (2.3, 12.0)
Missing	56	8			
Wears protective clothing when applying pesticides[d]					
Gloves	219	108	0.8 (0.6, 1.1)	21	1.1 (0.6, 2.0)
Boots or overalls	56	23	0.7 (0.4, 1.2)	4	NA
Mask or face shield	42	18	0.7 (0.4, 1.3)	2	NA
None	295	173	Referent	26	Referent
Wears gloves when applying fumigants					
No	309	183	1.0 (0.6, 1.7)	31	2.2 (0.6, 8.0)
Yes	43	25	Referent	7	Referent
Does not use fumigants	162	72		9	
Wears gloves when applying fungicides					
No	312	183	1.1 (0.6, 1.8)	31	2.7 (0.7, 10.3)
Yes	45	25	Referent	5	Referent
Does not use fungicides	157	72		11	
Wears gloves when applying herbicides					
No	332	183	1.0 (0.7, 1.4)	28	0.5 (0.1, 2.2)
Yes	171	95	Referent	19	Referent
Does not use herbicides	11	2		0	
Wears gloves when applying insecticides					
No	326	193	1.3 (0.9, 1.8)	32	2.3 (0.8, 6.5)
Yes	140	65	Referent	12	Referent
Does not use insecticides	48	22		3	
Bathes after applying or mixing pesticides					
No	377	220	1.3 (1.0, 1.8)	37	1.2 (0.6, 2.2)
Yes	177	78	Referent	15	Referent
Missing	58	8		2	

Removes work boots when entering home					
No	110	81	1.6 (1.2, 2.3)	18	2.3 (1.2, 4.2)
Yes	500	225	Referent	36	Referent
Missing	2	0			
Washes clothes worn to mix/apply pesticide separately					
No	126	79	1.2 (0.9, 1.7)	19	2.1 (1.1, 3.8)
Yes	423	215	Referent	31	Referent
Missing	63	12			
Wears the same clothes worn to mix/apply pesticides more than one day in a row					
No	529	278	0.7 (0.4, 1.3)	47	0.5 (0.2, 1.3)
Yes	27	20	Referent	5	Referent
Missing	56	8			
Stores pesticides in the home					
No	498	219	0.6 (0.4, 0.8)	45	1.1 (0.5, 2.4)
Yes	113	87	Referent	9	Referent
Missing	1	0			

[a] Unadjusted OR for individuals with HPEE compared to those without HPEE.

[b] Unadjusted OR for HPEE-12s applicators compared to those without HPEE.

[c] NA = less than five exposed cases, OR not determined. [d] Categories not mutually exclusive.

Logistic Regression Model

Using the previously described criteria, the following variables were evaluated in a logistic regression model: history of HPEE reported at enrollment into the cohort, state of residence, age, education status, distance of fields from home, having a tractor with an enclosed cab, pesticide application days, wearing gloves when working with pesticides, bathing after a pesticide accident, not removing work boots when entering the home, storing pesticides in the home, and washing work clothes with other laundry. Of these, previous HPEE reported at enrollment, state of residence, categories of days of pesticide application per year, storing pesticides in the home, wearing work boots in the home, and categories of age were the variables most strongly associated with HPEE risk and remained in the final logistic regression model. The ORs for these six variables are provided in table 2.

Overall, the patterns observed for HPEE in the full analysis were maintained when the logistic model was stratified on categories of pesticide application days per year (i.e., 1-5, 6-10, 11-20, ≥20) and state of residence. One exception was wearing work boots when entering the home. An increased risk of HPEE was observed for applicators reporting wearing work boots in the home among Iowa applicators (OR: 1.8; 95% CI: 1.2, 2.7) but not among North Carolina applicators (OR: 0.7; 95% CI: 0.3, 2.2).

Spouses

Of the 14,045 spouses with completed five-year follow-up questionnaires, 63 reported having at least one HPEE in the five years since enrollment, and 33 reported having an HPEE in the 12-month period prior to the interview. Given that all of the HPEEs reported in the year prior to the interview were from residents of Iowa, the yearly incidence in Iowa was 33/9989 = 3/1000 spouses. Twenty-eight of the 63 (44%) spouses reported multiple HPEEs during the five-year period between enrollment and interview. Fifteen reported five or fewer HPEEs, 12 experienced 6 to 20 events, while only 1 reported more than 20 events over the five-year period. For HPEE-12S spouses (n = 18), 12 (67%) reported multiple HPEEs over the five-year period. Of the 12, 6

(50%) had five or fewer events, 4 (33%) reported 6 to 20 separate events, and 1 (8%) reported more than 20 HPEEs in the five-year period.

Demographic, farm, and pesticide work practice characteristics by HPEE and HPEE plus symptoms for spouses are reported in table 3. The numbers were insufficient to examine quartiles of farm size and days of pesticide application per year; thus, these covariates were dichotomized.

Demographic Characteristics

All but two of the spouses of licensed applicators in this analysis were female, 93% were Iowa residents, and 98% were white. As with the applicators, both categories of age and education were associated with HPEE when unadjusted for other characteristics. The youngest age group (less than 37 years of age) had the highest HPEE risk with an OR of 2.5 (95% CI: 1.0, 5.9). When compared to those with a college education, spouses with a high school education (OR: 0.4; 95% CI: 0.2, 0.9) were less likely to experience an HPEE. For the HPEE-12S spouses, all were white and from Iowa.

Farm Characteristics

No association was observed for those living in close proximity to fields where pesticides were applied, the use of a well for the primary source of drinking water, or using a tractor with an enclosed cab for both the HPEE and HPEE-12S case definitions.

Table 2. Adjusted ORs (95% CI) for HPEE since enrollment, for HPEE in 12 months prior to interview (with and without symptoms), and for HPEE since enrollment stratified on state of residence and categories of pesticide application days.

		HPEE in Previous 12 Months			State of Residence		No. of Pesticide Applications (days per year)			
Variable	HPEE	HPEE 12[a]	HPEE 12NS[b]	HPEE 12S[c]	Iowa	N.C.	1-5	6-11	12-20	>20
HPEE reported at enrollment										
Yes	3.8 (2.7, 5.3)	3.1 (1.9, 4.9)	3.6 (1.9, 6.6)	2.5 (1.3, 4.6)	4.1 (2.8, 6.1)	2.4 (0.9, 6.7)	6.6 (3.3, 13.3)	3.5 (1.9, 7.3)	3.7 (1.9, 6.0)	3.0 (1.5, Ref.
No	Ref.[d]						Ref.	Ref.	Ref.	Ref.
State of residence										
Iowa	2.0 (1.2, 3.2)	1.9 (0.9, 4.0)	2.4 (0.8, 7.1)	1.8 (0.7, 4.5)	NA[e]	NA	1.7 (0.7, 4.2)	2.2 (0.8, 6.6)	2.3 (0.8, 7.0)	2.0 (0.8, 5.1)
N.C.	Ref.	Ref.	Ref.	Ref.			Ref.	Ref.	Ref.	Ref.
Age in years										
18-38	2.1 (1.3, 3.4)	1.8 (0.9, 3.9)	3.0 (1.0, 10.1)	1.2 (0.5, 3.0)	1.9 (1.1, 3.2)	3.5 (1.0, 13.0)	3.8 (1.4, 10.3)	1.6 (0.7, 3.6)	1.8 (0.6, 5.9)	1.8 (0.5, 7.0)
39-45	1.8 (1.1, 3.0)	2.5 (1.2, 5.2)	3.5 (1.1, 11.0)	2.1 (0.8, 5.1)	1.7 (1.0, 2.8)	3.2 (0.8, 13.6)	4.1 (1.6, 10.8)	0.7 (0.3, 1.7)	1.1 (0.4, 3.7)	3.5 (0.9, 3.6)
46-55								0.7 (0.3, 1.6)	0.6 (0.2, 1.9)	0.7 (0.2, 3.2)
≥56	0.9 (0.6, 1.5)	0.8 (0.4, 2.0)	1.6 (0.5, 5.7)	0.5 (0.1, 1.5)	0.9 (0.5, 1.5)	1.4 (0.3, 6.7)	2.2 (0.8, 5.6)			
	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Number of pesticide applications (days per year)										
	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	NA	NA	NA	NA

1-5	1.4 (0.9, 2.2)	1.7 (0.8, 3.4)	1.5 (0.5, 3.9)	1.8 (0.7, 4.5)	1.5 (1.0, 2.4)	1.0 (0.3, 3.7)				
6-11	2.1 (1.3, 3.3)	2.6 (1.3, 5.3)	3.4 (1.3, 8.6)	1.7 (0.6, 4.7)	2.2 (1.4, 3.6)	1.2 (0.3, 4.7)				
12-20	2.2 (1.4, 3.6)	3.7 (1.8, 7.5)	3.0 (1.1, 8.3)	4.2 (1.7, 10.7)	2.4 (1.4, 4.0)	2.0 (0.6, 6.7)				
>20										
Removes work boots when entering the home										
No	1.6 (1.1, 2.4)	1.6 (1.0, 2.8)	1.2 (0.6, 2.6)	2.1 (1.1, 4.2)	1.8 (1.2, 2.7)	0.7 (0.3, 2.2)	2.3 (1.1, 5.1)	1.2 (0.6, 2.4)	2.1 (0.1, 4.6)	1.2 (0.6, 2.7)
Yes	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Stores pesticides in the home										
No	0.7 (0.5, 0.9)	0.8 (0.4, 1.3)	0.5 (0.2, 1.0)	1.2 (0.5, 2.6)	0.7 (0.5, 1.0)	0.3 (0.1, 1.6)	0.7 (0.3, 1.7)	0.6 (0.3, 1.1)	0.6 (0.3, 1.2)	1.0 (0.4, 2.2)
Yes	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.

[a] HPEE-12 = HPEE reported in 12 months prior to interview (n = 108).

[b] HPEE-12NS = HPEE from previous 12 months that did not result in symptoms (n = 54).

[c] HPEE-12S = HPEE from previous 12 months that resulted in symptoms (n = 54).

[d] Ref. = referent.

[e] Factor not included in the logistic regression model since the model is stratified on the same factor.

Table 3. Distribution of spouse characteristics by high pesticide exposure status (HPEE), high pesticide exposure status with symptoms (HPEE-12S), no HPEE (controls), and unadjusted ORs for spouses at the five-year follow-up of the AHS cohort in 1999-2000.

Variable	No HPEE (controls)	HPEE	Unadjusted OR (95% CI)[a]	HPEE 12S	Unadjusted OR (95% CI)[b]
Total	126	63		18	
Demographic characteristics					
State of residence					
Iowa	116	59	NA[c]	18	NA
North Carolina	10	4		0	
Missing	0	0			
Race					
White	125	61	NA	18	NA
Non-white	0	0		0	
Missing	1	2			
Age in years 18-37	27	20	2.5 (1.0, 5.9)	8	NA
38-43	28	16	1.9 (0.8, 4.6)	1	
44-52	31	15	1.6 (0.7, 3.9)	6	

≥53	40	12	Referent	3	
Education ≤High school	48	11	0.4 (0.2, 0.9)	3	NA
≥College	75	39	Referent	11	
Missing	3	13		4	
Farm characteristics					
Size of farm in acres					
≥201 acres	5	11	1.3 (0.3, 5.7)	4	NA
≤200.5 acres	6	10	Referent	14	
Missing	115	42		0	
Distance of home from the fields					
<50-199 ft	66	31	0.9 (0.5, 1.6)	8	0.7 (0.3, 2.0)
200 ft-1/4 mile	60	32	Referent	10	Referent
Use well for source of drinking water					
Yes	82	43	1.2 (0.6, 2.2)	13	1.4 (0.5, 4.2)
No	44	20	Referent	5	Referent
Tractor has enclosed cab					
No	7	3	NA	0	NA
Yes	5	8		3	
Missing	114	52		15	
Repairs own spraying or mixing equipment					
No	3	3	NA	0	NA
Yes	9	8		3	
Missing	114	52		15	

Table 3 (cont'd).

Variable	No HPEE (controls)	HPEE	Unadjusted (95% CI)[a]	ORHPEE 12S	Unadjusted OR (95% CI)[b]
Total	126	63		18	
Pesticide work characteristics					
Number of pesticide application days per year					
≥6	38	27	1.7 (0.9, 3.2)	11	3.6 (1.3, 10)
1-5	87	36	Referent	7	Referent
Missing	1	0			
Wears protective clothing when applying pesticides[d]					
Gloves	61	20	0.5 (0.3, 1.0)	5	0.4 (0.1, 1.3)
Boots or overalls	6	1	NA[e]		
Mask or face shield	1	0	NA	0	NA
None	56	36	Referent	11	Referent
Bathes after applying or mixing pesticides					
No	82	35	0.7 (0.4, 1.3)	10	0.7 (0.3, 2.1)

Yes	43	27	Referent	7	Referent
Missing	1	1		1	
Removes work boots when entering the home					
No	37	15	0.8 (0.4, 1.5)	3	NA
Yes	89	47	Referent	14	
Missing	0	1		1	
Washes clothes worn to mix/apply pesticides separately					
No	58	23	0.7 (0.4, 1.3)	7	0.8 (0.3, 2.3)
Yes	68	39	Referent	10	Referent
Missing	0	1		1	
Wears the same clothes worn to mix/apply pesti cides more than one day in a row					
No	120	60	NA	16	NA
Yes	5	2		1	
Missing	1	1		1	
Stores pesticide in the home					
No	87	36	0.6 (0.3, 1.1)	12	0.9 (0.3, 2.6)
Yes	39	27	Referent	6	Referent
Missing	0	0		0	

[a] Unadjusted OR for individuals with HPEE compared to those without HPEE.

[b] Unadjusted OR for individuals with HPEE and symptoms compared to those without HPEE.

[c] NA = less than five exposed cases, OR not determined.

[d] Categories not mutually exclusive.

[e] NA = less than five exposed cases, OR not determined.

Pesticide Work Practices

Spouses who applied pesticides more than 6 days per year were more likely to experience an HPEE compared to those who applied for fewer than 5 days per year (OR: 1.7; 95% CI: 0.9, 3.2). HPEE risk decreased for those spouses who wore gloves when applying pesticides and who did not store pesticides in the home, with ORs of 0.5 (95% CI: 0.3, 1.0) and 0.6 (95% CI: 0.3, 1.1), respectively. No other characteristics were associated with HPEE.

Logistic Regression Model

Only two variables remained in the final logistic regression model for HPEE; spouses with a high school education were far less likely to experience an HPEE compared to spouses with a college education, with an adjusted OR of 0.4 (95% CI: 0.2, 0.9). A similar

OR was observed for those who wore gloves while applying pesticides (compared to spouses who did not) (OR: 0.5; 95% CI: 0.3, 1.0). Numbers were too small to calculate adjusted ORs for HPEE-12S.

Symptoms Status for HPEE in the 12 Months Prior to Interview:

Applicators and Spouses

The distribution of characteristics for those with a HPEE in the year prior to the interview is described for both spouses and applicators in tables 4 and 5. Given the small numbers, only the distributions are provided.

Applicators and spouses who reported that their HPEE occurred in the twelve months prior to the interview were asked if they experienced symptoms related to the HPEE. Fifty-four (50%) of the 108 applicators with an HPEE in the twelve months prior to the interview reported one or more symptoms, with the vast majority (n = 52) reporting multiple symptoms. Their distribution is presented in table 4. The most common symptoms were skin irritation (21%), eye irritation (17%), headache (16%), tearing (9%), and chest discomfort (9%). Only 7 (13%) individuals sought care after the event, with one of the seven hospitalized. Applicators with symptoms were more likely to report exposure to the head or neck area than those without symptoms (32% versus 10%).

Eighteen (55%) of the 33 spouses with an HPEE in the twelve months prior to the interview reported one or more symptoms, with most (n = 12) reporting multiple symptoms. Headache (17%), skin irritation (14%), difficulty breathing (10%), and difficulty walking (10%) were the most common complaints. Four (22%) sought care and none were hospitalized.

Pesticides Used at Time of Event

Among the HPEE-12 applicators, 30% of those with symptoms reported using insecticides at the time of the event. In contrast, 6% of applicators without symptoms reported using insecticides. A similar pattern was not observed among spouses.

Table 4. Symptoms resulting from an HPEE in the year prior to interview reported by applicators and spouses (applicators n = 108; spouses n = 33).

	Applicators (%)	Spouses (%)
Number reporting no symptoms	54	15
Number reporting at least one symptom[a]	54	18
Blurred vision	4 (4)	0 (0)
Convulsions	0 (0)	0 (0)
Difficulty breathing	7 (6)	4 (10)
Difficulty walking	2 (2)	4 (10)
Tearing or drooling	10 (9)	2 (5)
Eye irritation	19 (17)	2 (5)
Headache or dizziness	18 (16)	7 (17)
Pass out	0 (0)	0 (0)
Nausea	11 (10)	6 (14)
Skin irritant	24 (21)	10 (24)
Chest discomfort	10 (9)	2 (5)
Involuntary movements	0 (0)	1 (2)

[a] Symptoms are not mutually exclusive (individuals could report multiple symptoms); the 54 applicators with symptoms reported a total of 105 symptoms; the 18 spouses with symptoms reported a total of 38 symptoms.

Table 5. Distribution (%) of covariates by symptom status for applicators and spouses with an HPEE in the year prior to interview (AHS, 1999-2000).

	Applicators (n = 108)	Spouses (n = 33)

All Symptoms	Symptoms[a]	No symptoms	Symptoms	No symptoms
HPEE in last year	54 (50%)	54 (50%)	18 (55%)	15 (45%)
Activity at time of HPEE				
Mixing	5 (9)	13 (24)	2 (11)	1 (7)
Loading	9 (17)	7 (13)	1 (6)	1 (7)
Applying	29 (54)	26 (48)	7 (39)	10 (67)
Cleaning	6 (11)	4 (7)	1 (6)	0 (0)
Clean spill	0 (0)	2 (4)	0 (0)	0 (0)
Other	5 (9)	2 (4)	7 (39)	3 (20)
If applying: method used[b]				
Vehicle	17 (59)	13 (50)	2 (29)	1 (10)
Hand spray	6 (21)	11 (42)	4 (57)	3 (30)
Backpack	1 (3)	0 (0)	0 (0)	1 (10)
Sprayer	1 (3)	1 (4)	1 (14)	0 (0)
Pre-applied to seed	0	1 (4)	0 (0)	0 (0)
Other	4 (14)	0 (0)	0 (0)	5 (50)
Body part in contact with chemical				
Head	38 (32)	18 (10)	8 (22)	10 (29)
Hand	24 (20)	32 (33)	11(30)	7 (20)
Chest	25 (21)	37 (39)	8 (22)	10 (29)
Other	31 (26)	9 (9)	10 (27)	8 (23)
Sought care				
Yes	7 (13)	0 (0)	4 (22)	0 (0)
No	47 (87)	54 (100)	14 (78)	15 (100)
If you sought care, were you hospitalized?				
Yes	1		0	
No	6		4	
Pesticide used at time of HPEE				
Insecticide	16 (30)	3 (6)	2 (11)	4 (27)
Herbicide	17 (31)	45 (83)	7 (39)	6 (40)
Fungicide	2 (4)	1 (1)	0 (0)	2 (13)
Unknown	19 (35)	5 (9)	9 (50)	3 (20)
Washed within one hour after HPEE				
No	22 (41)	14 (26)	7 (41)	6 (40)
Yes	32 (59)	40 (74)	10 (59)	9 (60)
Reported history of HPEE at enrollment				
Yes	35 (65)	40 (74)	12 (67)	11 (73)
No	19 (35)	14 (26)	6 (33)	4 (27)

[a] Symptoms = applicators and spouses who experienced at least one symptom (n = 54 for applicators and n = 18 for spouses).

[b] Applies only to those who indicated that they were applying pesticides at time of HPEE (n = 55 for applicators and n = 17 for spouses.

Activity at Time of HPEE

Applying pesticides was the most common activity at the time of the reported HPEE (54% of applicators with symptoms and 48% of applicators without symptoms). For spouses with symptoms, the two most common activities at the time of the HPEE were application (39%) and "other" (39%), while 67% of those without symptoms reported that they were applying pesticides at the time of the event.

Discussion

We observed an increased risk of HPEE among private pesticide applicators with increasing pesticide application days, history of HPEE at enrollment, decreasing age, storing pesticides in the home, living in Iowa, and not removing work boots when entering the home. Of those with an HPEE in the 12 months prior to the interview, 50% of applicators and 55% of spouses reported symptoms related to the HPEE. Only 13% of the applicators with symptoms and 22% of the spouses with symptoms sought care (and would come to the attention of medical personnel responsible for reporting pesticide exposure events).

As previously observed, applicators and spouses living in Iowa had an increased HPEE risk compared to North Carolinians. In an earlier analysis of lifetime HPEE history (Alavanja et al., 1999), risk was lower for North Carolina compared to Iowa applicators with an OR of 0.7 (95% CI: 0.6, 0.8). The yearly incidence of 6.0 HPEE per 1000 applicators observed in the previous nested case-control study of Iowa farmers (Alavanja et al., 2001) was lower than the rate of 8.8/1000 for Iowa farmers we observed in this new analysis. It is not clear why the incidence increased slightly, but the increase may be the result of different reporting patterns over the time period of study. While the incidence of 2.0 events per 1000 North Carolina farmers was substantially lower than either observation from Iowa, analyses stratified by state of residence showed that individual HPEE risk factors were similar in both states, with one exception. Removing work boots in the home reduced risk for applicators in Iowa but was not associated with HPEE for applicators living in North Carolina. Crop type, farm size, and pesticide application days differ for the two states (Alavanja et al., 1999). In our previous analyses, controlling for these factors attenuated but did not explain the total difference by state. Therefore, given the consistency of this finding across our analyses, it is possible that HPEE incidence is reported differentially by applicators in Iowa and North Carolina. Given the lack of a standard definition for HPEE, it is probable that North Carolinian applicators interpret and reported HPEE differentially than Iowa applicators; however, we had no data to assess this possibility for the analyses described here. Interpretation and/or reporting differences by state of residence will be examined in future assessments of this cohort.

In previous analyses of HPEE in the AHS cohort, characteristics related to modifiable work practices such as storing pesticides in the home, washing work clothes with family clothes, and scoring high on a risk-acceptance scale were all related with increased HPEE risk (Alavanja et al., 1999; Alavanja et al., 2001). We observed similar results here, with HPEE risk increasing for applicators who stored pesticides in the home and who did not remove work boots when entering the home. While we do not believe that these characteristics are causative risk factors for HPEE, they may be an indication of the care used when working with pesticides.

The probability of experiencing an HPEE increases with cumulative lifetime pesticide application days (Alavanja et al., 1999; Mage et al., 2000). As expected, similar results were observed in our analysis; applicators with the greatest number of pesticide application days per year were more likely to have a new HPEE compared to those with the fewest application days. Given the strong association with number of

application days, we performed analyses stratified by application days to assess whether the pattern of additional risk factors remained the same. While stratification reduced the sample size (generating less precise estimates), age, not removing work boots when entering the home, storing pesticides in the home, state of residence, and history of HPEE continued to be associated with HPEE.

The consistency of the observable risk factors across studies suggests that work and pesticide handling practices may play an important role in HPEE risk. Thus, if these characteristics are not modified, multiple HPEEs may be more likely to occur over the working history of the farmer. In this analysis, when compared to controls, applicators with a new HPEE were more likely to have reported a history of HPEE at enrollment into the study cohort. This finding may be the result of the self-reported nature of the outcome (applicators may be more likely to recall events if they have reported them previously). However, the 149 applicators in this analysis with a history of HPEE represent only 5% of the applicators who reported ever experiencing an HPEE at enrollment, suggesting that differential recall may not explain this finding. In addition, 46% of the applicators in this analysis reported multiple events over the five-year follow-up period. If HPEEs are related to adverse health effects, then the most vulnerable population may be those individuals who are at risk for multiple events over a working lifetime.

In a previous analysis of applicators who reported a history of HPEE at enrollment, pesticides used at the time of the HPEE differed from those used on a general basis; they were more likely to be insecticides (Keim and Alavanja, 2001). The majority of the applicators in this analysis used herbicides at the time of the HPEE, the most commonly used pesticide in this study population (Keim and Alavanja, 2001). However, applicators using insecticides were more likely to report symptoms associated with the HPEE. While all pesticides are toxic, the level of toxicity varies widely by pesticide function, class, and specific type (Klaassen and Watkins, 2003). Many of the most commonly used insecticides (i.e., organophosphates) function by altering the nervous system and are not selective (i.e., they may affect non-target species) (Klaassen and Watkins, 2003). For example, organophosphates were recently listed as the pesticide class most often reported as the type used at the time of poisoning or symptomatic illness (USEPA, 1999). A similar pattern was observed in our analysis, with 16 of the applicators using insecticides at the time of the HPEE reporting symptoms. In theory, the correct use of PPE when working with acutely toxic pesticides should prevent the onset of symptoms even when HPEEs occur. As with the previous analyses, (Alavanja et al., 1999; Alavanja et al., 2001), general use of PPE did not differ by HPEE or symptom status for applicators. However, a reduction in risk of HPEE with symptoms was observed among applicators who reported wearing gloves when applying insecticides in general (not specifically at the time of the HPEE). Interestingly, risk increased for applicators who reported wearing gloves when applying herbicides. Given that we did not have information on the use of PPE at the time of the HPEE itself, we were unable to adequately evaluate the association between use of protective equipment and HPEE.

Several studies have shown that younger individuals are at an increased risk of farm injuries and pesticide poisonings (Hwang et al., 2001; Lewis et al., 1998; Zhou and Roseman, 1994). Younger farmers may have a greater work responsibility on the farm, which would increase their probability of having an event (Mage et al., 2000), or they may be less experienced than older farmers and at greater risk for accidents. Both younger age and college education were risk factors for HPEE in the unadjusted analysis. However, when controlling for age, the association with education for applicators was attenuated. In our study cohort, younger farmers are more likely to have

a college education than older farmers. Thus, the unadjusted findings with education status may be the result of the correlation of age with education level.

For the first time, we were able to examine HPEE among spouses enrolled in the AHS cohort. The incidence rate was much lower for spouses than for the male licensed pesticide applicators. In previous analyses (Alavanja et al., 1999), female licensed applicators were less likely to have an HPEE compared to male applicators; however, this gender differential was attenuated when the analyses were adjusted for job and work characteristics. Although the small numbers of spouses in this analysis made it difficult to fully assess differences, some observations are pertinent. For example, when asked to report the work activity at the time of the HPEE, the majority of farmers reported "applying pesticides," while many of the spouses reported "other" activities such as walking by a freshly treated field.

Given the uncertainty in the definition of HPEE, we also evaluated HPEE that occurred in the year prior to the interview and a more specific definition, HPEE plus symptoms. While this reduced the power of our study (creating wider confidence intervals), the overall pattern of risk factors was unchanged with this more specific definition.

A strength of this study is the fact that it is nested within the agricultural cohort, a study group of applicators and their spouses. This provided us with the opportunity to examine newly acquired events in the years since enrollment in a cohort where exposures can be well characterized. However, there are limitations that should be considered. The most significant limitation is the lack of a standard definition of HPEE. An average dose resulting from these unusually high events is not known. The continued follow-up of the AHS cohort will provide us with the opportunity to develop a more specific definition of HPEE and to understand the potential dose associated with such events.

While there may be potential for recall bias, given that the information on characteristics pertaining to HPEE were gathered as part of a large cohort-wide questionnaire that was not specific to HPEE, the potential for such bias is reduced. However, for the HPEE-specific covariates, differential recall by applicators with and without symptoms cannot be ruled out. For example, 35% of HPEE applicators with symptoms could not recall the pesticide used at the time of the event, compared to 9% of those without symptoms. Given the small numbers for the symptom analysis and the uncertainty of the HPEE definition, we were unable to fully evaluate whether or not these observed differences were a statistical artifact or a true difference in self-reporting. Given the ongoing assessment of this cohort, we will be able to evaluate these issues more fully in future analyses.

Finally, many of the risk factors examined here were factors that relate to the "general" work practices and characteristics of the applicator or spouse. For example, we did not have data on PPE use at the time of HPEE, only in relation to what the applicator or spouse normally wore when working with pesticides. While some data specifically pertained to the HPEE (i.e., pesticide used at the time of the event), this information was only gathered for those events occurring in the year prior to the interview (and not the full five years); thus, small numbers made the complete evaluation of these factors difficult.

In addition, while we examined incident events within a cohort, we could not take full advantage of the prospective nature of the study. Some of the key exposure variables were reported at the same time as the new HPEEs, while others (e.g., age at enrollment, and history of HPEE) were obtained at enrollment. Detailed baseline data on pesticide use practices were obtained only for the 40% who had returned a supplemental questionnaire (Alavanja et al., 1999; Tarone et al., 1997). At the time of this analysis, the number of incident events (n = 306) was too small to restrict the

analysis to those with a returned supplemental questionnaire and assess pesticide use practices prospectively as a risk factor for HPEE. This analytical approach will be used in future follow-up studies of the cohort.

In summary, HPEE risk factors observed in this analysis of new events were similar to those previously reported for HPEE lifetime history among applicators. While incidence was lower for North Carolina applicators, risk factors were consistent for each state. Overall, spouses experienced a much lower incidence of HPEE compared to applicators. Developing an improved definition of HPEE and examining predictive risk factors for applicators and spouses will be the focus of future analyses of HPEE in this cohort of farmers and their spouses.

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