

# Determinants of High Pesticide Exposure Events in the Agricultural Health Cohort Study from Enrollment (1993-1997) through Phase II (1999-2003)

K. Payne, G. Andreotti, E. Bell, A. Blair, J. Coble, M. Alavanja

**ABSTRACT.** *We conducted an analysis of the determinants of high pesticide exposure events (HPEEs), which are defined as self-reported incidents of high exposure to pesticides, fertilizers, or other chemicals in the Agricultural Health Study, a cohort of private applicators and their spouses residing in North Carolina or Iowa, and commercial applicators residing in Iowa. We examined the risk of HPEEs occurring between enrollment (Phase I: 1993-1997) and follow-up (Phase II: 1999-2003) among participants who completed the Phase II questionnaire (n = 43,149) by calculating hazard rate ratios and 95% confidence intervals using Cox proportional-hazard regression. During the follow-up period, 1,582 HPEEs were reported (3.8%). HPEE risk was significantly higher among Iowa residents, younger participants, those with a hearing deficit, a risk-taking personality, and an HPEE prior to enrollment. Among private applicators (n = 30,102), larger farm size, higher frequency and duration of pesticide use, spraying pesticides with open cab windows, using a tractor cab without a charcoal filter, repairing spray equipment, wearing work clothing more than two days without changing, not removing work boots before entering the home, and storing pesticides in the home were associated with significantly higher HPEE risk. Among commercial applicators (n = 2,326), higher frequency of pesticide use was associated with a significantly higher HPEE risk. Among spouses (n = 10,721), higher frequency of pesticide use, using an application vehicle with a cab, and storing pesticides in the home were associated with a significantly higher HPEE risk. Our findings indicate that HPEEs were associated with several modifiable pesticide handling procedures that can be targeted in safety training and education.*

**Keywords.** *Agricultural Health Study, Farmers, High pesticide exposure events, Pesticide applicators, Pesticide exposure.*

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The authors are **Kevin Payne**, PhD, Post-Doctoral Fellow, and **Gabriella Andreotti**, PhD, Epidemiologist, National Cancer Institute, Division of Cancer Epidemiology and Genetics, Rockville, Maryland; **Erin Bell**, PhD, Associate Professor, School of Public Health, University of Albany, Rensselaer, New York; **Aaron Blair**, PhD, Senior Scientist, **Joseph Coble**, PhD, former Staff Scientist, and **Michael Alavanja**, PhD, Senior Investigator, National Cancer Institute, Division of Cancer Epidemiology and Genetics, Rockville, Maryland. **Corresponding author:** Gabriella Andreotti, NCI, DCEG, 6120 Executive Blvd., Rockville, MD 20852; phone: 301-594-7902; e-mail: andreotg@mail.nih.gov.

The Agricultural Health Study (AHS) is an ongoing prospective cohort study of private applicators (mostly farmers), their spouses, and commercial applicators residing in North Carolina or Iowa. The AHS was designed to identify agricultural exposures, particularly pesticides, associated with cancer and other diseases (Alavanja et al., 1996). Use of pesticides sometimes results in high pesticide exposure events (HPEEs), which are defined as self-reported incidents of unusually high exposure to pesticides, fertilizers, or other chemicals that are sometimes associated with various acute symptoms and chronic conditions (Kamel et al., 2007; Hoppen et al., 2007). A previous article from the AHS, which used self-reported data at enrollment (Phase I questionnaire: 1993-1998), found that 16% of private applicators reported an HPEE at some time in the past (Keim and Alavanja, 2001). Work practices associated with HPEEs in a previous study using AHS Phase I questionnaire data included frequent pesticide application, delay in washing clothing after application, mixing work clothing with other household laundry, washing-up inside the home rather than outside, applying pesticides within 50 yards of the home, and storing pesticides within the home (Alavanja et al., 1999b). A nested case-control study using a specially designed questionnaire examined 36 private applicators with HPEE and found that financial difficulties and having a high risk acceptance (i.e., scoring high on a scale to assess attitudes toward high-risk behaviors) were significant risk factors for an HPEE (Alavanja et al., 2001). The most recent study used AHS Phase I and two years of Phase II follow-up questionnaire data (1999 to October 2000) and examined risk among 306 private applicators and 63 spouses (Bell et al., 2006). Main risk factors from this study include report of an HPEE prior to enrollment, increasing pesticide application days, and being an Iowa versus a North Carolina resident (Bell et al., 2006).

The purpose of the current study is to further evaluate the occurrence of HPEEs in the AHS using additional event and exposure information collected after enrollment. This report is an extension of the study conducted by Bell et al. (2006), which only examined approximately two years of data from the Phase II questionnaire from private applicators and spouses. In this study, we examine the risks of HPEEs occurring between enrollment (Phase I: 1993-1997) and follow-up (Phase II: 1999-2003) for all private applicators, their spouses, and commercial applicators who completed the Phase II questionnaire. We also account for the varying time periods between enrollment and follow-up for each individual. Among private applicators, we also examine the risks of symptoms accompanying reported HPEEs and the parts of the body commonly exposed to pesticides during the incident.

## Methods

### Study Subjects

The AHS cohort has been previously described (Alavanja et al., 1996). Briefly, the AHS cohort includes 52,395 private applicators from Iowa and North Carolina who are mostly farmers, along with 32,347 of their spouses, and 4,915 licensed commercial pesticide applicators from Iowa. Participants were enrolled between 1993 and 1997 (Phase I). Participation rates were high, with 82% of applicators seeking pesticide licenses in each state and 75% of spouses enrolling in the study. The AHS was conducted under a protocol approved by the Institutional Review Boards of the National Institutes of Health and its contractors.

## Questionnaires

At enrollment, participants completed a self-administered questionnaire collecting information on demographics, lifestyle factors, and work practices. A self-administered take-home questionnaire, given to all enrolled participants to obtain additional information, was returned by 44%. Participants who completed the take-home questionnaire were similar to those not completing the questionnaire, except for being slightly older (Tarone et al., 1997). For spouses, enrollment information was obtained from a self-administered questionnaire (81%) and a telephone interview (19%). A follow-up computer-assisted telephone interview (CATI) administered between 1999 and 2003 (Phase II) obtained updated information on enrolled participants (Alavanja et al., 2001). Participants who completed the Phase II questionnaire, which totaled 43,149 participants (30,102 private applicators, 2,326 commercial applicators, and 10,721 spouses), were eligible for this study. Questionnaires are available at the AHS website (<http://aghealth.nci.nih.gov>).

## HPEE Identification

In Phase II, participants who reported that they either used pesticides or worked on a farm since enrollment were asked the HPEE question: "Since enrollment, did you have any incidents with fertilizers, herbicides, or other pesticides that caused you an unusually high personal exposure." Participants who responded "yes" were identified as HPEE cases, and those who responded "no" were identified as non-cases. For participants reporting an HPEE, additional questions were asked in the Phase II questionnaire regarding symptoms related to the most recent incident within the last calendar year. Participants who reported a symptom related to their HPEE were classified as "symptomatic HPEEs."

## Risk Factor Information

For this study, risk factor information came from the Phase I or Phase II questionnaires (indicated in the tables). The factor "risk-taking personality" was created from four survey questions used to assess a respondent's attitude toward risk derived from Harrell (1995) and previously used in the AHS (Alavanja et al., 1999b; Alavanja et al., 2001; Bell et al., 2006). Respondents were asked to state whether they agreed or disagreed with the following statements: (Q1) "Farming [commercial pesticide work] is more dangerous than jobs in industry or manufacturing", (Q2) "Accidents are just one of the occupational hazards of farming [commercial pesticide work] that must be accepted if you are going to be in the business", (Q3) "During a normal work week [as a commercial pesticide worker] it's common for me, while doing farm work, to experience a number of 'close calls' that under different circumstances might have resulted in personal injury or property loss", and (Q4) "To make a profit [to perform a job], most farmers [commercial pesticide workers] take risks that might endanger their health." If a respondent answered three or more questions as "yes," they were considered to have a risk-taking personality. For the participants reporting an HPEE, the following additional questions were asked in the Phase II questionnaire regarding the most recent incident: (1) What part of your body was exposed? (2) Did this incident result in a healthcare visit? (3) What was the name of the chemical you were exposed to? (4) What pesticide or fertilizer-related job were you doing when the exposure occurred? and (5) What application method were you using?

## Analysis

We calculated hazard rate ratios (HR) and 95% confidence intervals (95% CI) for HPEE risk using Cox proportional-hazard regression. The time-dependent variable was the number of days between enrollment and Phase II interview for each participant be-

cause the date of the HPEE was not obtained. Each determinant for HPEE was also evaluated as a potential confounding variable for other factors. Final statistical models included factors resulting in a 10% change in the HR. We also evaluated potential effect modification by HPEE prior to enrollment and risk-taking personality using stratified analyses. HPEE risk was examined among private applicators, spouses, and commercial applicators separately. We also estimated the risk of HPEE of private applicators compared to commercial applicators from Iowa using logistic regression. AHS data release versions P1REL0712.04 and P2REL0612.03 were used for this analysis.

## Results

Of the participants included in this analysis ( $n = 43,149$ ), 1,582 (3.8%) reported an HPEE and 289 (0.7%) reported a symptomatic HPEE after enrollment. The highest frequency of HPEEs was among commercial applicators ( $n = 316$ , 13.6%), followed by private applicators ( $n = 1,088$ , 3.6%) and spouses ( $n = 178$ , 1.7%). The highest frequency of HPEEs with an accompanying symptom was among spouses ( $n = 50$ , 28.1%), followed by private applicators ( $n = 209$ , 19.2%) and commercial applicators ( $n = 30$ , 9.5%). Among participants from Iowa, commercial applicators had a 2.5-fold risk (95% CI = 2.1, 3.0) of an HPEE and a 1.6-fold risk of symptomatic HPEE (95% CI = 0.9, 2.9) compared to private applicators (data not shown). Among private applicators, only 2.2% of HPEEs were reported to a healthcare facility. Among participants reporting an HPEE, 40% reported that the event involved a pesticide (32% herbicides, 7% insecticides, and 1% fungicide) and the remaining 60% were other chemicals, which could have included fertilizers.

### Demographic, Lifestyle, and Medical Factors

Participants residing in Iowa had a higher risk of an HPEE than participants residing in North Carolina (private applicators: HR = 2.8, 95% CI = 2.4, 3.3; spouses: HR = 3.7, 95% CI = 2.3, 6.0) (table 1). Age was inversely associated with HPEE in each of the three participant groups. Private applicators between 18 and 38 years old had a 4.5-fold risk (95% CI = 3.6, 5.7) compared to private applicators age 56 and older. Private applicators with at least some college education had a 1.4-fold risk of an HPEE (95% CI = 1.3, 1.6) compared to those with a high school education or less. Education was not a significant risk factor for HPEEs among commercial applicators or spouses. Marital status was not a statistically significant determinant for an HPEE among private applicators or commercial applicators; all spouses, by definition, were married. Nearly 97% of the study population was white; thus, we could not adequately evaluate race as a risk factor.

Current smoking at enrollment was associated with a 1.5-fold risk of HPEE (95% CI = 1.1, 2.0) among commercial applicators and a 2.2-fold risk (95% CI = 1.5, 3.4) among spouses compared to those not smoking. Private applicators who smoked for over 20 years had a 1.4-fold risk (95% CI = 1.1, 1.9) of HPEE compared to private applicators who never smoked, although current or former smoking status was not a significant risk factor. Drinking alcohol was not associated with HPEE risk.

Having a hearing deficit was associated with a 1.7-fold risk (95% CI = 1.5, 2.0) for an HPEE in private applicators and a 1.4-fold risk (95% CI = 1.1, 1.8) in commercial applicators compared to those who did not report being hard of hearing. Among private applicators with a hearing deficit ( $n = 10,237$ ), risk of an HPEE was greater among those who did not wear a hearing aid (HR = 1.8, 95% CI = 1.1, 2.9) compared to those who did. No spouses had a hearing deficit and an HPEE. Wearing glasses for near- or farsightedness was not associated with HPEE risk.

Having a risk-taking personality was associated with an increased risk of HPEEs for all three participant types (private applicators: HR = 1.9, 95% CI = 1.7, 2.2; commercial applicators: HR = 1.9, 95% CI = 1.5, 2.6; spouses: HR = 1.6, 95% CI = 1.2, 2.3). Having an HPEE prior to enrollment was also associated with a higher risk of an additional HPEE (private applicators: HR = 3.5, 95% CI = 3.0, 4.3; commercial applicators: HR = 2.8, 95% CI = 1.6, 5.1). Information on HPEE prior to enrollment was not obtained for spouses. Among private applicators, the HRs for symptomatic HPEEs were similar to HPEEs overall with regard to demographic, lifestyle, and medical factors. Due to small numbers, we did not report symptomatic HPEE risks for commercial applicators and spouses. When we further adjusted for hearing deficit, risk-taking personality, HPEE prior to enrollment, and frequency of pesticide application, the associations reported in table 1 persisted, except for the link with education, which was no longer statistically significant. In addition, stratified analyses revealed no evidence of effect modification by HPEE prior to enrollment (yes, no) or risk-taking personality type (yes, no).

### **Work-Related Factors**

Table 2 shows the associations between work-related factors and HPEE risk among private applicators and commercial applicators. Private applicators with farms >1,000 acres had a 2.2-fold risk (95% CI = 1.5, 3.1) compared to those with farms <50 acres. The risk of an HPEE was also higher for private applicators who lived <200 feet from the closest field where pesticides were applied, compared to those who lived >200 feet away, although risk estimates did not increase monotonically by distance.

Frequency of pesticide application (number of application days per year) was positively associated with HPEE risk for private applicators and commercial applicators. Compared to private applicators who applied pesticides <5 days per year, the highest risk was observed for those who applied pesticides between 40 and 59 days per year (HR = 2.5, 95% CI = 1.8, 3.5) but decreased slightly for those who applied pesticides >59 days per year. For commercial applicators, those who applied pesticides >150 days per year had a 2.2-fold risk of HPEE (95% CI = 1.3, 3.8) compared to those who applied pesticides <19 days per year. Duration of pesticide application (years) was also positively associated with HPEE risk among private applicators. Compared to private applicators who applied pesticides for five years or less, those who applied pesticides for >30 years had a 2.3-fold risk of an HPEE (95% CI = 1.7, 3.2).

Several pesticide-handling procedures were associated with HPEE risk among private applicators. Spraying pesticides from a cab with open windows was associated with a 1.8-fold risk (95% CI = 1.4, 2.4), and repairing spray equipment was associated with a 2.6-fold risk (95% CI = 1.6, 4.1). Wearing the same pesticide application clothing more than two days without changing was associated with a 1.4-fold risk (95% CI = 1.0, 1.8), not removing work boots before entering the home was associated with a 1.4-fold risk (95% CI = 1.2, 1.7), and storing pesticides in the home or basement was associated with a 2.1-fold risk (95% CI = 1.8, 2.4) of HPEEs. None of these pesticide-handling procedures was associated with HPEEs among commercial applicators. Among private applicators, the associations between the farming-related factors with HPEEs were similar to the association for symptomatic HPEEs with little difference in risk estimates. Due to small numbers, we were unable to evaluate symptomatic HPEE risk among commercial applicators and spouses, as well as the type of chemical, job, and application method conducted at the time of the incident among any of the three participant groups.

**Table 1. Hazard ratios (HR) and 95% confidence intervals (CI) for high pesticide exposure events (HPEE) in relation to demographics, lifestyle, and medical factors by participant type. Boldface indicates statistical significance at two-sided  $\alpha < 0.05$ .**

Variable	Private Applicators			Symptomatic HPEE			Commercial Applicators			Spouses of Private Applicators				
	No HPEE	HPEE HR <sup>[a]</sup>	(95% CI) <sup>[a]</sup>	HPEE	HR <sup>[a]</sup>	(95% CI) <sup>[a]</sup>	No HPEE	HPEE	HR <sup>[b]</sup>	(95% CI) <sup>[b]</sup>	No HPEE	HPEE	HR <sup>[c]</sup>	(95% CI) <sup>[c]</sup>
Worked on farm or used pesticides <sup>[d]</sup>	29,014	1,088	-	209	-	-	2,010	316	-	-	10,543	178	-	-
State of residence <sup>[e]</sup>														
North Carolina	10,311	188	1.0	Ref.	44	1.0	Ref.	0	0	1.0	Ref.	2,385	19	1.0
Iowa	18,703	900	<b>2.8</b>	<b>(2.4, 3.3)</b>	165	<b>2.1</b>	<b>(1.5, 3.0)</b>	2,010	316	-	-	8,158	159	<b>3.7</b>
Age at interview <sup>[e]</sup> (years)														
≥56	11,644	208	1.0	Ref.	36	1.0	Ref.	486	50	1.0	Ref.	3,727	42	1.0
46-55	8,269	308	<b>1.8</b>	<b>(1.5, 2.1)</b>	70	<b>2.6</b>	<b>(1.7, 4.0)</b>	733	107	1.2	(0.8, 1.7)	3,250	57	1.3
39-45	5,495	313	<b>2.9</b>	<b>(2.4, 3.6)</b>	62	<b>4.1</b>	<b>(2.6, 6.5)</b>	445	78	1.4	(1.0, 2.2)	2,187	53	<b>1.6</b>
18-38	3,606	259	<b>4.5</b>	<b>(3.6, 5.7)</b>	41	<b>5.5</b>	<b>(3.1, 9.6)</b>	346	81	<b>2.0</b>	<b>(1.3, 3.2)</b>	1,378	26	1.4
Education <sup>[e]</sup>														
High school or less	15,572	432	1.0	Ref.	85	1.0	Ref.	828	125	1.0	Ref.	3,816	49	1.0
Some college	12,439	616	<b>1.4</b>	<b>(1.3, 1.6)</b>	121	<b>1.5</b>	<b>(1.1, 2.0)</b>	1,130	184	1.0	(0.8, 1.4)	6,727	129	1.3
Marital status <sup>[e]</sup>														
Married	24,963	897	1.0	Ref.	173	1.0	Ref.	1,641	247	1.0	Ref.	10,543	178	1.0
Single	3,972	189	1.0	(0.9, 1.2)	36	1.1	(0.8, 1.6)	368	68	1.0	(0.7, 1.4)	0	0	-
Smoking status <sup>[e]</sup>														
No	24,380	915	1.0	Ref.	181	1.0	Ref.	1,702	240	1.0	Ref.	9,766	152	1.0
Yes	3,970	146	1.1	(0.9, 1.3)	25	0.9	(0.6, 1.3)	308	76	<b>1.5</b>	<b>(1.1, 2.0)</b>	777	26	<b>2.2</b>
Smoked tobacco <sup>[e]</sup> (years)														
Never	15,646	642	1.0	Ref.	126	1.0	Ref.	1,007	143	1.0	Ref.	7,498	114	1.0
1-5	2,769	109	1.1	(0.9, 1.3)	20	1.0	(0.6, 1.6)	215	35	1.0	(0.7, 1.5)	801	12	1.0
6-10	2,238	84	1.1	(0.9, 1.4)	14	1.0	(0.6, 1.8)	202	32	1.1	(0.8, 1.7)	460	7	0.8
11-20	3,652	125	<b>1.3</b>	<b>(1.0, 1.6)</b>	25	1.3	(0.8, 2.2)	345	70	<b>1.4</b>	<b>(1.0, 2.0)</b>	668	20	1.6
>20	3,701	94	<b>1.4</b>	<b>(1.1, 1.9)</b>	18	1.4	(0.7, 2.7)	206	32	1.3	(0.8, 2.2)	635	16	1.8

Alcohol drinking <sup>(e)</sup>															
Never	9,360	245	1.0	Ref.	42	1.0	Ref.	250	37	1.0	Ref.	3,994	54	1.0	Ref.
<Once monthly	4,473	177	1.0	(0.9, 1.3)	44	<b>1.7</b>	<b>(1.1, 2.6)</b>	268	44	1.1	(0.7, 1.7)	3,071	54	1.0	(0.7, 1.4)
1-3 times monthly	4,824	201	0.9	(0.8, 1.2)	41	1.3	(0.8, 2.0)	378	60	1.0	(0.7, 1.6)	1,799	43	1.2	(0.8, 1.8)
Once per week	3,338	171	1.1	(0.9, 1.3)	33	1.3	(0.8, 2.2)	335	41	0.8	(0.5, 1.3)	719	8	0.6	(0.3, 1.2)
2-4 times weekly	3,915	185	1.0	(0.8, 1.2)	32	1.2	(0.7, 1.9)	509	84	1.0	(0.7, 1.6)	492	12	1.2	(0.7, 2.3)
Almost daily	1,254	55	1.1	(0.8, 1.5)	10	1.2	(0.6, 2.5)	204	36	1.0	(0.6, 1.6)	117	2	-	-
Everyday	303	10	0.9	(0.5, 1.7)	1	(+)	(+)	31	9	1.5	(0.7, 3.3)	35	2	-	-
Trouble hearing without hearing aid <sup>(d)</sup>															
No	18,014	595	1.0	Ref.	104	1.0	Ref.	1,308	192	1.0	Ref.	49	2	1.0	Ref.
Yes	10,237	473	<b>1.7</b>	<b>(1.5, 2.0)</b>	100	<b>2.1</b>	<b>(1.6, 2.8)</b>	618	113	<b>1.4</b>	<b>(1.1, 1.8)</b>	18	0	-	-
Wear hearing aid one or both ears <sup>(d)</sup>															
Yes	1,122	21	1.0	Ref.	4	1.0	Ref.	59	8	1.0	Ref.	2	0	1.0	Ref.
No	9,110	452	<b>1.8</b>	<b>(1.1, 2.9)</b>	96	2.4	(0.8, 7.6)	559	105	1.1	(0.5, 2.5)	16	0	-	-
Wear glasses for nearsightedness <sup>(d)(f)</sup>															
No	8,425	303	1.0	Ref.	57	1.0	Ref.	695	127	1.0	Ref.	1,858	36	1.0	Ref.
Yes	5,837	227	1.1	(0.9, 1.4)	43	1.1	(0.7, 1.6)	1,314	189	1.0	(0.7, 1.2)	8,685	142	1.0	(0.7, 1.4)
Wear glasses for farsightedness <sup>(d)</sup>															
No	7,323	348	1.0	Ref.	64	1.0	Ref.	-	-	-	-	-	-	-	-
Yes	6,943	179	1.1	(0.9, 1.4)	35	1.0	(0.6, 1.7)	-	-	-	-	-	-	-	-
Risk-taking personality <sup>(d)(g)</sup>															
No	23,631	762	1.0	Ref.	139	1.0	Ref.	1,717	227	1.0	Ref.	8,895	135	1.0	Ref.
Yes	5,383	326	<b>1.9</b>	<b>(1.7, 2.2)</b>	70	<b>2.3</b>	<b>(1.7, 3.1)</b>	293	89	<b>1.9</b>	<b>(1.5, 2.6)</b>	1,648	43	<b>1.6</b>	<b>(1.2, 2.3)</b>
HIPEE prior to enrollment <sup>(e)</sup>															
No	12,238	305	1.0	Ref.	61	1.0	Ref.	839	93	1.0	Ref.	-	-	-	-
Yes	2,096	224	<b>3.5</b>	<b>(3.0, 4.3)</b>	40	<b>3.3</b>	<b>(2.2, 5.1)</b>	261	73	<b>2.8</b>	<b>(1.6, 5.1)</b>	-	-	-	-

<sup>(a)</sup> Adjusted for state, age, education, current smoking status, and duration of pesticide application (years) except for factors under study.

<sup>(b)</sup> Adjusted for age, education, current smoking status, and duration of pesticide application (years) except for factors under study.

<sup>(c)</sup> Adjusted for state, age, education, current smoking status, and frequency of pesticide application (days per year) except for factors under study.

<sup>(d)</sup> Based on Phase II questionnaire at follow-up.

<sup>(e)</sup> Based on Phase I questionnaire at enrollment.

<sup>(f)</sup> Estimates for commercial applicators and spouse are for near- and farsightedness.

<sup>(g)</sup> Positive response to three out of four Phase II survey questions derived from Harrell (1995).

**Table 2. Hazard ratios (HR) and 95% confidence intervals (CI) for high pesticide exposure events (HPEE) in relation to work-related factors among private and commercial applicators. Boldface indicates statistical significance at two-sided  $\alpha < 0.05$ .**

Variable	Private Applicators							Commercial Applicators			
	No HPEE		HR <sup>[a]</sup>	(95% CI) <sup>[a]</sup>	Symptomatic HPEE			No HPEE			
HPEE	HPEE	HPEE			HR <sup>[a]</sup>	(95% CI) <sup>[a]</sup>	HPEE	HPEE	HR <sup>[b]</sup>	(95% CI) <sup>[b]</sup>	
Worked on farm or used pesticides <sup>[c]</sup>											
Either	29,014	1,088	-	-	209	-	-	2,010	316	-	-
Worked on farm	27,440	1,056	-	-	203	-	-	615	124	-	-
Used pesticides	26,012	1,060	-	-	202	-	-	2,010	316	-	-
Farm size <sup>[d]</sup> (acres planted)											
0<50	3,981	52	1.0	Ref.	12	1.0	Ref.	-	-	-	-
50-199	4,929	124	1.3	(0.9, 1.9)	28	1.8	(0.8, 3.9)	-	-	-	-
200-499	7,666	289	<b>1.5</b>	<b>(1.1, 2.1)</b>	53	1.7	(0.8, 3.7)	-	-	-	-
500-999	5,914	281	<b>1.6</b>	<b>(1.2, 2.3)</b>	50	1.8	(0.8, 3.9)	-	-	-	-
≥1000	3,618	260	<b>2.2</b>	<b>(1.5, 3.1)</b>	53	<b>2.9</b>	<b>(1.3, 6.3)</b>	-	-	-	-
Distance between field and home <sup>[c]</sup> (feet)											
≥200	17,103	529	1.0	Ref.	97	1.0	Ref.	-	-	-	-
100-199	6,638	305	<b>1.4</b>	<b>(1.2, 1.6)</b>	66	<b>1.6</b>	<b>(1.1, 2.2)</b>	-	-	-	-
50-99	3,205	173	<b>1.6</b>	<b>(1.3, 1.9)</b>	33	<b>1.5</b>	<b>(1.0, 2.3)</b>	-	-	-	-
0<50	1,518	72	<b>1.4</b>	<b>(1.1, 1.9)</b>	12	1.1	(0.6, 2.2)	-	-	-	-
Frequency of pesticide application <sup>[c]</sup> (days per year)											
0<5	5,045	92	1.0	Ref.	15	1.0	Ref.	-	-	-	-
5-9	6,626	181	1.2	(0.9, 1.5)	38	1.5	(0.8, 3.0)	-	-	-	-
10-19 <sup>[e]</sup>	8,396	351	<b>1.5</b>	<b>(1.1, 1.9)</b>	62	1.7	(0.9, 3.3)	630	55	1.0	Ref.
20-39	5,179	280	<b>1.8</b>	<b>(1.4, 2.3)</b>	64	<b>2.6</b>	<b>(1.4, 5.1)</b>	461	56	1.4	(0.9, 2.1)
40-59	1,249	79	<b>2.5</b>	<b>(1.8, 3.5)</b>	18	<b>3.6</b>	<b>(1.7, 8.0)</b>	188	36	<b>2.0</b>	<b>(1.3, 3.2)</b>
60-150	772	39	<b>1.9</b>	<b>(1.2, 2.9)</b>	6	1.4	(0.4, 4.4)	618	146	<b>2.5</b>	<b>(1.8, 3.6)</b>
≥150	156	11	1.9	(0.8, 4.4)	2	(+)	(+)	111	23	<b>2.2</b>	<b>(1.3, 3.8)</b>
Duration of pesticide application <sup>[d]</sup> (years)											
0<6	3,466	149	1.0	Ref.	28	1.0	Ref.	630	103	1.0	Ref.
6-10	4,007	137	0.9	(0.7, 1.1)	23	0.9	(0.5, 1.5)	394	61	1.1	(0.8, 1.5)
11-20	9,207	388	<b>1.3</b>	<b>(1.1, 1.7)</b>	73	1.4	(0.9, 2.3)	551	82	1.2	(0.9, 1.7)
21-30	6,991	259	<b>1.9</b>	<b>(1.5, 2.5)</b>	58	<b>2.3</b>	<b>(1.3, 4.1)</b>	211	25	1.2	(0.7, 2.0)
≥30	3,904	103	<b>2.3</b>	<b>(1.7, 3.2)</b>	22	<b>2.7</b>	<b>(1.3, 5.6)</b>	63	6	1.2	(0.5, 3.0)
Personal protective equipment used <sup>[c]</sup>											
No	13,431	629	1.0	Ref.	110	1.0	Ref.	684	155	1.0	Ref.
Yes	10,995	405	0.9	(0.8, 1.1)	88	1.2	(0.9, 1.6)	989	126	0.7	(0.4, 1.1)
Pesticide application vehicle with open or closed cab <sup>[c]</sup>											
Open	6,970	224	1.0	Ref.	48	1.0	Ref.	365	32	1.0	Ref.
Closed	11,960	664	0.8	(0.7, 1.0)	126	0.8	(0.5, 1.2)	789	189	2.6	(1.7, 3.9)
Spray pesticides from cab with windows open or closed <sup>[c]</sup>											
Closed	11,197	606	1.0	Ref.	109	1.0	Ref.	721	174	1.0	Ref.
Open	738	58	<b>1.8</b>	<b>(1.4, 2.4)</b>	17	<b>3.1</b>	<b>(1.8, 5.4)</b>	66	15	1.2	(0.5, 1.5)
Tractor cab has charcoal filter <sup>[c]</sup>											
Yes	2,991	177	1.0	Ref.	25	1.0	Ref.	537	135	1.0	Ref.
No	8,318	458	1.1	(0.9, 1.4)	96	<b>1.7</b>	<b>(1.1, 2.8)</b>	220	49	1.0	(0.7, 1.5)
Repair spray equipment <sup>[c]</sup>											
No	1,828	28	1.0	Ref.	6	1.0	Ref.	274	27	1.0	Ref.
Yes	24,056	1,031	<b>2.6</b>	<b>(1.6, 4.1)</b>	196	<b>3.3</b>	<b>(1.0, 10.3)</b>	1,715	289	1.5	(0.9, 2.3)
Bathe after pesticide handling <sup>[c]</sup>											
Yes	9,626	279	1.0	Ref.	56	1.0	Ref.	1,228	211	1.0	Ref.
No	16,265	779	1.1	(1.0, 1.3)	145	1.1	(0.8, 1.5)	765	105	0.8	(0.9, 1.6)



**Table 2 (cont'd). Hazard ratios (HR) and 95% confidence intervals (CI) for high pesticide exposure events (HPEE) in relation to work-related factors among private and commercial applicators. Boldface indicates statistical significance at two-sided  $\alpha < 0.05$ .**

Variable	Private Applicators							Commercial Applicators			
	No HPEE	HPEE	HR <sup>[a]</sup>	(95% CI) <sup>[a]</sup>	Symptomatic HPEE HPEE	HR <sup>[a]</sup>	(95% CI) <sup>[a]</sup>	No HPEE	HPEE	HR <sup>[b]</sup>	(95% CI) <sup>[b]</sup>
Wear work clothing more than two days <sup>[c]</sup>											
No	24,682	998	1.0	Ref.	187	1.0	Ref.	1,925	309	1.0	Ref.
Yes	1,226	60	<b>1.4</b>	<b>(1.0, 1.8)</b>	14	<b>1.8</b>	<b>(1.0, 3.1)</b>	71	6	0.6	(0.2, 1.4)
Wash work clothing separately <sup>[c]</sup>											
Yes	18,742	761	1.0	Ref.	137	1.0	Ref.	1,574	251	1.0	Ref.
No	6,727	287	<b>1.1</b>	<b>(1.0, 1.3)</b>	63	1.3	(0.9, 1.8)	399	63	1.1	(0.8, 1.5)
Remove work boots before entering home <sup>[c]</sup>											
Yes	22,696	824	1.0	Ref.	147	1.0	Ref.	1,721	261	1.0	Ref.
No	6,015	262	<b>1.4</b>	<b>(1.2, 1.7)</b>	62	<b>1.9</b>	<b>(1.4, 2.6)</b>	271	54	1.0	(0.7, 1.5)
Store pesticides in home <sup>[c]</sup>											
No	25,140	821	1.0	Ref.	162	1.0	Ref.	1,865	283	1.0	Ref.
Yes	3,777	267	<b>2.1</b>	<b>(1.8, 2.4)</b>	47	<b>1.9</b>	<b>(1.3, 2.7)</b>	130	33	0.7	(0.4, 1.3)
Use well for drinking water <sup>[c]</sup>											
Yes	19,507	711	1.0	Ref.	136	1.0	Ref.	522	93	1.0	Ref.
No	9,501	376	0.9	(0.8, 1.1)	72	0.9	(0.7, 1.3)	1,488	223	0.8	(0.6, 1.5)

<sup>[a]</sup> Private applicator portion adjusted for state, age, education, current smoking status, duration of pesticide application (years), and farm size except for factors under study.

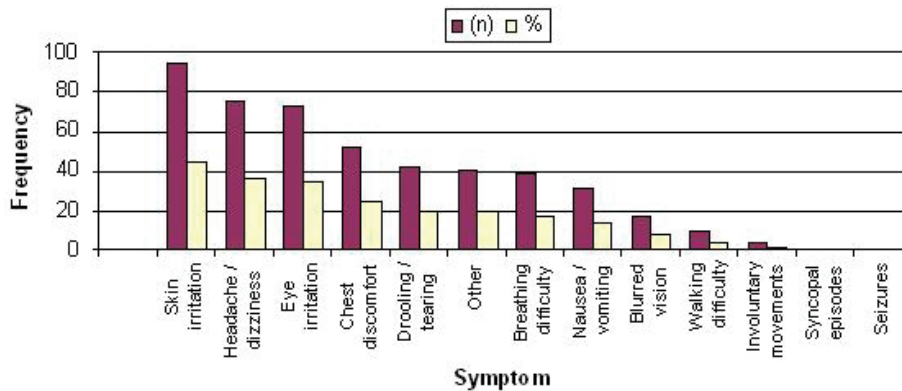
<sup>[b]</sup> Commercial applicator portion adjusted for age, education, current smoking status, and duration of pesticide application (years) except for factors under study.

<sup>[c]</sup> Based on Phase II questionnaire at follow-up.

<sup>[d]</sup> Based on Phase I questionnaire at enrollment.

<sup>[e]</sup>  $\leq 19$  commercial applicators.

Table 3 shows the associations between work-related factors and HPEE risk among spouses. Spouses who applied pesticides for >20 days per year had a 2.2-fold risk (95% CI = 1.3, 3.7) compared to spouses applying pesticides for <5 days per year. In addition, spouses who sprayed pesticides from a vehicle with an enclosed cab had a 2.5-fold risk (95% CI = 1.0, 6.2). Storing pesticides in the home or basement was associated with a 1.9-fold risk (95% CI = 1.4, 2.5) among spouses.



**Figure 1. Distribution of symptoms associated with HPEE among private applicators reporting symptoms ( $n = 209$ ). Most common symptoms: skin irritation ( $n = 92$ , 44%), headache/dizziness ( $n = 77$ , 37%), and eye irritation ( $n = 75$ , 36%).**

**Table 3. Hazard ratios (HR) and 95% confidence interval (CI) for high pesticide exposure events (HPEE) in relation to work-related factors among spouses of private applicators. Boldface indicates statistical significance at two-sided  $\alpha < 0.05$ .**

Variable		No HPEE	HPEE	HR <sup>[a]</sup>	(95% CI) <sup>[a]</sup>
Worked on farm or used pesticides <sup>[b]</sup>	Either	10,543	178	-	-
	Worked on farm	6,913	144	-	-
	Used pesticides	10,543	178	-	-
Distance between field and home <sup>[c]</sup> (feet)	≥200	4,905	76	1.0	Ref.
	100-199	2,439	50	1.3	(0.9, 1.9)
	50-99	1,782	31	1.1	(0.7, 1.7)
	0<50	1,131	20	1.2	(0.7, 2.0)
Frequency of pesticide application <sup>[b]</sup> (days per year)	0<5	6,253	84	1.0	Ref.
	5-9	2,530	44	1.3	(0.9, 1.9)
	10-19	1,207	33	<b>2.0</b>	<b>(1.4, 3.1)</b>
	≥20	505	17	<b>2.2</b>	<b>(1.3, 3.7)</b>
Personal protective equipment used <sup>[b]</sup>	No	5,354	92	1.0	Ref.
	Yes	4,748	77	1.0	(0.7, 1.3)
Pesticide application vehicle with open or closed cab <sup>[b]</sup>	Open cab	546	8	1.0	Ref.
	Closed cab	244	14	<b>2.5</b>	<b>(1.0, 6.2)</b>
Spray pesticides from cab with windows open or closed <sup>[b]</sup>	Windows closed	201	13	1.0	Ref.
	Windows open	36	1	-	-
Tractor cab has charcoal filter <sup>[b]</sup>	Yes	67	3	1.0	Ref.
	No	85	8	1.9	(0.5, 7.4)
Repair spray equipment <sup>[b]</sup>	No	490	8	1.0	Ref.
	Yes	333	14	1.9	(0.8, 4.6)
Bathe after pesticide handling <sup>[b]</sup>	Yes	4,781	76	1.0	Ref.
	No	5,680	101	1.0	(0.8, 1.4)
Wear work clothing more than two days <sup>[b]</sup>	No	10,046	170	1.0	Ref.
	Yes	425	7	0.9	(0.4, 2.0)
Wash work clothing separately <sup>[b]</sup>	Yes	5,516	103	1.0	Ref.
	No	4,942	74	0.8	(0.6, 1.1)
Remove work boots before entering home <sup>[b]</sup>	Yes	8,203	141	1.0	Ref.
	No	1,364	26	1.2	(0.8, 1.9)
Store pesticides in home <sup>[b]</sup>	No	7,963	106	1.0	Ref.
	Yes	2,520	72	<b>1.9</b>	<b>(1.4, 2.5)</b>
Use well for drinking water <sup>[b]</sup>	Yes	7,027	108	1.0	Ref.
	No	3,511	70	1.2	(0.9, 1.6)

<sup>[a]</sup> Adjusted for state, age, education, current smoking status, and frequency of pesticide application (days per year) except for factors under study.

<sup>[b]</sup> Based on Phase II questionnaire at follow-up.

<sup>[c]</sup> Based on Phase I questionnaire at enrollment.

### HPEE-Related Symptoms and Exposure Sites

Among private applicators reporting symptoms associated with an HPEE ( $n = 209$ ), the most common symptoms were skin irritation ( $n = 92$ , 44%), headache/dizziness ( $n = 77$ , 37%), and eye irritation ( $n = 75$ , 36%) (fig. 1). Comparing subjects with symptomatic ( $n = 209$ ) and non-symptomatic HPEEs ( $n = 194$ ) in relation to the part of the body that was exposed, we found significant increased risk of symptomatic HPEE when the body part exposed was the head (HR = 1.4, 95% CI = 1.0, 1.8), the face (HR = 1.8, 95% CI = 1.3, 2.4), the lung (HR = 1.6, 95% CI = 1.3, 2.2), and the digestive tract (HR = 1.8, 95% CI = 1.2, 2.7), but a significant inverse association against symptomatic HPEE when the body part exposed was the torso (HR = 0.7, 95% CI = 0.5, 0.9).

## Discussion

In this study among AHS participants, we examined the determinants of HPEEs occurring between enrollment (Phase I: 1993-1997) and follow-up (Phase II: 1999-2003). During the follow-up period, 3.8% of the study population reported an HPEE. We identified several demographic, lifestyle, medical, and work-related factors that were significantly associated with an excess risk of HPEEs. As in previous analyses (Alavanja et al., 1999b; Bell et al., 2006), participants from Iowa had a higher risk of HPEEs compared to those from North Carolina, which could not be explained by the lifestyle and work-related risk factors we examined. It has been suggested that the association may be linked to longer application times per day in Iowa (Alavanja et al., 1999a). Similarly, the higher risk among commercial applicators compared to private applicators and their spouses may reflect their higher frequency of pesticide application, or specific commercial pesticide handling procedures that we did not evaluate in the AHS.

Our findings for the effects of young age, high risk-taking personality, and previous HPEEs are consistent with previous analyses (Alavanja et al., 1999b; Alavanja et al., 2001; Bell et al., 2006) and appear to be independent risk factors for HPEE. Frequency of pesticide application did not explain the age effect, despite the significant inverse correlation between age and frequency of pesticide application ( $r^2 = -0.3$ ,  $p < 0.0001$ ). We compared the frequency of several demographic, lifestyle, medical, and work-related factors between participants with and without high-risk personality or prior HPEE but found no significant differences, suggesting that inexperience due to young age and personality type are independent risk factors. Our finding for a higher HPEE risk among those with more education is consistent with previous results (Bell et al., 2006). This finding is also consistent with results from a study of occupational injuries among Belgian farmers, where higher education level was statistically associated with occupational injury (Van den Broucke and Colémont, 2011). It was suggested that this finding could have been linked to an interaction with age, which we did not find. Higher education may be linked to a riskier or more demanding workload, or a higher likelihood of reporting the event. Reasons for the higher risk among smokers, which was not previously reported, are unclear. Additional data on whether subjects were smoking while the event occurred could help explain this association.

Our findings of a higher HPEE risk among hearing-impaired private applicators resemble previous findings reporting that private applicators with a hearing deficit had higher odds of farm-related injury than those without a hearing deficit (Hwang et al., 2001; Sprince et al., 2003). Reasons for a higher risk among the hearing impaired and not the vision impaired are unclear. Since risks were higher among those who did not wear a hearing aid compared to those who did, a possibility is that these persons are less able to detect and prevent potential dangers that could be detected by sound.

As in earlier reports (Alavanja et al., 1999b; Alavanja et al., 2001; Bell et al., 2006), we found several work-related factors, such as larger farm size, shorter distance between the fields and home, and higher frequency and duration of pesticide application, that were independent determinants of HPEEs among private applicators after adjustments were made. Similar to the findings of Bell et al. (2006), we also found associations for several pesticide-handling activities among private applicators, including spraying pesticides from a cab with open windows, repairing spray equipment, wearing work clothes for more than two days without changing, not removing work boots before entering the home, and storing pesticides in the home. The first two activities listed above may be di-

rectly linked to an HPEE, but the latter three behaviors may be an indication of the level of care used when working with pesticides. Thus, several pesticide-handling behaviors may be modifiable through intervention and training (e.g., change work clothing daily, remove work boots before entering the home, and do not store pesticides in the home) (Quandt et al., 2001).

Among the private applicators reporting an HPEE, 19.2% reported a symptomatic HPEE. Of the symptomatic HPEEs, 11.5% were reported to a healthcare facility, and only 2.2% of all HPEEs were reported to a healthcare facility. This under-enumeration of pesticide exposure events was also found in a previous study of poison control centers, which obtain data from healthcare facilities (Mehler et al., 2006). When comparing the determinants for HPEEs and symptomatic HPEEs among private applicators (tables 1 and 2), no measurable differences in the associations were noted.

The AHS is a unique cohort with detailed information on pesticide and other agricultural, lifestyle, and medical factors. HPEEs were newly occurring events since establishment of the cohort through follow-up. We were also able to examine determinants of HPEEs among three applicator types who may have different pesticide exposures and, thus, different risk factors for HPEEs. Although AHS participants are able to provide reliable information on pesticide use (Hoppin et al., 2002; Blair et al., 2002), all data were self-reported. Since there is no standard definition of an HPEE or symptomatic HPEE, characterization of an HPEE is subjective and potentially prone to misclassification that could result in a reduced estimation of risk. Although results for symptomatic and all HPEEs were similar, which provides some confirmation of HPEE occurrence, symptoms due to other causes could have coincidentally occurred at the time of HPEE. Due to small numbers, we were unable to evaluate symptomatic HPEE risk among commercial applicators and spouses, as well as the type of chemical, job, and application method conducted at the time of the incident among any of the three participant groups. In addition, other than “pesticide (herbicide, insecticide, fungicide)” or “other chemical,” the agent related to the HPEE could not be evaluated.

In conclusion, we identified several risk factors for HPEEs among AHS participants, including Iowa residence, young age, hearing impairment, risk-taking personality, and a previous HPEE. Among private applicators, several work-related factors (e.g., larger farm size, shorter distance between field and home, and higher frequency and duration of pesticide application) and pesticide handling practices (e.g., repairing spray equipment, wearing work clothes for more than two days, not removing work boots before entering the home, and storing pesticides in the home), some of which may be modifiable, were also associated with a higher risk of HPEEs. Findings from this study can be used to identify high-risk subgroups, as well as high-risk activities or behaviors that can be targeted in safety training and education.

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