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National Health Interview Survey Mortality Among US Farmers and Pesticide Applicators

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Background *The mortality experience of pesticide-exposed workers across the US has not been thoroughly studied.*
Methods *Cox regression mortality analyses adjusted for the complex sample survey design were performed on mortality-linked 1986–1994 National Health Interview Survey (NHIS) data.*
Results *Nine thousand four hundred seventy-one farmers and pesticide applicators with 571 deaths were compared to 438,228 other US workers with 11,992 deaths. Age-adjusted risk of accidental death, as well as cancers of the nervous and lymphatic/hematopoietic systems, was significantly elevated in male and female pesticide-exposed workers; breast, prostate, and testicular cancer mortality risks were not elevated.*
Conclusions *Compared to all other workers, farmers and pesticide applicators were at greater risk of accidental mortality. These pesticide-exposed workers were not at an increased risk of cancers possibly associated with exposure to estrogen analogue compounds, but were at an increased risk of hematopoietic and nervous system cancers. NHIS mortality follow-up represents an important occupational health surveillance instrument.* Am. J. Ind. Med. 43:227–233, 2003. *© 2003 Wiley-Liss, Inc.*

KEY WORDS: cancer mortality; mortality; farmers; pesticide applicators; National Health Interview Survey

INTRODUCTION

Exposure to pesticides has become ubiquitous to workers and to the general public due to increasing and extensive applications and environmental contamination. The acute health effects of pesticides in humans are well documented, if under-reported under current surveillance systems; chronic health effects are currently being investigated [WHO, 1990; Levine and Doull, 1992; Maroni and Fait, 1993; Dich et al., 1997; Fleming and Herzstein, 1997]. The most obvious groups in which to best study the chronic effects of pesticides in humans are those occupational groups who apply pesticides in high doses as part of their daily activities over many years, including pesticide manufacturers, pesticide applicators, farmers, golf-course superintendents, and veterinarians [Dich et al., 1997]. Genotoxicity studies and some recent epidemiologic studies in these occupationally exposed populations, particularly among farmers and pesticide applicators, point to the real possibility of carcinogenic and other chronic health effects of pesticide exposure [Maroni and Fait, 1993; Blair and Zahm, 1995; Dich et al., 1997; Fleming et al., 1997, 1999a,b; Council on Scientific Affairs, 1988; Dich and Wiklund, 1998].

Despite a variety of methodologic issues including multiple pesticide exposures with inadequate exposure data, small sample sizes, and variable populations [Blair and Hoar Zahm, 1990; Blondell, 1990; Cordes and Foster, 1991;

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Munro et al., 1992; Doe and Paddle, 1994; Dich et al., 1997; Fleming et al., 1997; Cantor and Silberman, 1999], some conclusions can be drawn from the aggregate of available chronic disease studies in pesticide-exposed worker populations. Farmers and pesticide applicators (the main worker groups that have been studied since they are the largest groups with the highest occupational exposures) have tended to be healthier compared to the general population, especially with respect to cardiovascular disease and the diseases associated with heavy tobacco and ethanol use. However, in general, farmers and pesticide applicators have been shown to be at an increased risk of morbidity and mortality from accidents, some of this possibly directly related to occupational pesticide exposure (e.g., aerial sprayers) [Barthel, 1986; Cantor and Silberman, 1999]. Farmers, in particular, have been more likely to die from infectious and nonmalignant respiratory diseases [WHO, 1990; Maroni and Fait, 1993; McDuffie, 1994; Alavanja et al., 1994; Dich et al., 1997; Fleming et al., 1997; Acquavella and Olsen, 1998; Dich and Wiklund, 1998; Fleming et al., 1999b].

With respect to cancer, in most studies pesticide applicator groups (as opposed to farmers) have been shown to be at somewhat increased risk of cancer compared to the general population and other worker groups [Dich et al., 1997]. Worker populations exposed to the phenoxy acids and other herbicides may be at an increased risk for soft tissue sarcoma and non-Hodgkin's lymphoma [Zahm and Blair, 1992; Zahm et al., 1993]; in addition, brain cancer appears to be increased not only in these populations, but also possibly in their offspring [Zahm and Ward, 1998]. Farmers have consistently shown an increased risks of leukemia, multiple myeloma, and prostate cancer [Acquavella and Olsen, 1998; Dich and Wiklund, 1998; Acquavella, 1999; Fleming et al., 1999a]. Pesticide applicators have shown an increased risk of lung and testicular cancer [Figa-Talamanca et al., 1993; Pesatori et al., 1994; Fleming et al., 1999a]. Both farmers and pesticide applicators have been reported to have an elevated risks of stomach cancers [Dich et al., 1997]. Increased skin cancer risk has been seen in pesticide applicators, although this elevation in risk may be due to ultraviolet exposure rather than the pesticide use [WHO, 1990; Maroni and Fait, 1993; Alavanja et al., 1994; McDuffie, 1994; Dich et al., 1997; Fleming et al., 1997, 1999a; Dich and Wiklund, 1998].

The National Health Interview Survey (NHIS) is a multipurpose household survey of the US civilian non-institutionalized population conducted annually since 1957. From 1986 to 1994, 447,699 US workers, aged 18 years and older, participated in a probability sampling of the entire noninstitutionalized US population including all US workers. Recently, NHIS conducted a mortality follow-up with the cause of death through December 31, 1997. The NHIS database allows for longitudinal analysis of mortality data as a retrospective cohort study, as well as cross-sectional and trend analysis of the aggregate morbidity data. Thus, the NHIS database represents a unique opportunity to explore new research hypotheses, and to use the data as a surveillance tool to evaluate time trends and occupational disease in the US for the last 2 decades in both genders and in a variety of race-ethnic subpopulations. The primary objective of this preliminary study using this important database was to assess overall and cause-specific mortality patterns for pesticide-exposed workers, specifically farmers and pesticide applicators, compared to all other US workers in the NHIS cohort.

MATERIALS AND METHODS

NHIS is a continuous multipurpose and multistage probability area survey of the US civilian non-institutionalized population living at addressed dwellings, and it has been conducted since 1957 [Botman and Jack, 1995; NCHS, 1998, 2001]. Every week a probability sample of households is interviewed by trained personnel to obtain information about the characteristics of each member of the household [Liao et al., 1998]. NHIS survey response rate has reportedly ranged from 95 to 98% [Wagener and Winn, 1991].

Information on employment during the 2 weeks prior to the interview was collected for all persons aged 18 years or older in order to determine the person's employment status. ''Farmer'' and ''Pesticide Applicator'' were defined using Standardized Occupational Codes (SOC codes) provided in the NHIS database [NCHS, 1989]. For the purposes of this study, farmers and pesticide applicators were identified as ''pesticide-exposed workers'' as opposed to ''other occupations'' (i.e., all other employed persons aged 18 years and older). Data are not available for all participants with regards to confounding variables such as tobacco use, although this information is available for some participants in specific annual supplements.

Beginning with the 1986 survey year, information was collected by the NCHS to perform a mortality follow-up through linkage with the National Death Index (NDI). The linkage is complete through December 31, 1997, and includes all participants from the 1986-94 NHIS survey years. The linkage was performed completely by computer. The linkage used an algorithm with a match class and score; on an average, the linkage was reportedly 97% complete [NCHS, 2001].

Statistical Methods

Because of the multi-stage sampling design, all analyses were performed with adjustments for sample weights and design effects using the SUDAAN statistical package [Research Triangle Institute, 2002]. The study sample was defined as persons aged 18 years and older who reported working within the 2 weeks prior to their participation in the NHIS 1986–1994 surveys. Only those under 18 years of age and those with insufficient information to permit linkage to NDI were considered ineligible and excluded from the present analysis. Sample weights were further adjusted for analysis of data from combined survey years, as specified by Botman and Jack [1995]. Mortality analyses were performed using Cox Regression models (Proc Survival in SUDAAN) [Cox, 1972].

RESULTS

There were a total of 447,669 persons aged 18 years and older who reported working within the 2 weeks prior to their participation in the NHIS 1986–1994 surveys (Table I). Among these US workers, 208,855 (46.6%) were women. The mean age $\pm$ standard deviation was 38.9 ± 12.9 years.

Within the pesticide exposed worker cohort, there were 178 pesticide applicators and 9,293 farmers. There were 7 (3.9%) female pesticide applicators, and 1,718 (18.5%) female farmers. After adjusting for multiple comparisons, at the time of NHIS interview, farmers were significantly older than pesticide applicators (44.0 ± 16.2 years vs. 38.7 ± 12.7 years; $P < 0.001$) and than the "other occupations" cohort not typically exposed to pesticides (44.0 ± 16.2 vs. 38.8 ± 12.8 years; $P < 0.001$). As a pesticide-exposed group, farmers and pesticide applicators together were significantly older compared to the "other occupations" cohort (43.9 ± 16.2 vs. 38.8 ± 12.8 years; P-value < 0.001).

In the entire NHIS worker cohort, there were a total of 12,563 deaths. There were 562 deaths among farmers and 9 deaths among the pesticide applicators. Table II illustrates both the large number of cause specific deaths among the comparison cohort of non-pesticide-exposed workers, as well as the comparatively small number of deaths by specific cause among the pesticide exposed workers. Nevertheless, these relatively small numbers are sufficiently large for hypothesis-testing purposes. For example, to test the specific hypothesis that prostate cancer risk would be increased among farmers and pesticide applicators combined, the sample size was large enough to detect as statistically significant a risk ratio of 1.54 at an alpha level of 0.05 with a power of 90% (a risk ratio smaller than the risk ratios reported in the literature) [Botman and Jack, 1995; Fleming et al., 1999b].

Shown in Table III are the unadjusted and age adjusted risk ratios of mortality, by gender, comparing the pesticide-exposed workers (i.e., pesticide applicators and farmers together) to the rest of the NHIS worker cohort. Using the unadjusted risk ratios, there were statistically significant differences between both male and female pesticide-exposed workers compared to the rest of the worker cohort for almost all the cause specific deaths presented, including overall mortality, heart disease, overall cancer and many different types of cancers. However, after adjustment for age, only overall (risk ratio = 1.3; 95% CI = 1.2–1.5), cardiovascular disease (1.4 [1.2–1.7]), and motor vehicles and accidental deaths (2.1 [1.6–2.8]) were significantly increased for the combined pesticide-exposed population compared to all other US workers. Overall cancer mortality was significantly increased (1.2 [1.1–1.4]), in particular nervous system cancer (2.4 [1.3–4.6]) and lymphatic/hematopoietic cancer (2.2 [1.5–3.2]). Both accidental (3.2 [1.5–6.9]) and lymphatic/hematopoietic cancer (3.6 [1.6–8.2]) deaths were particularly elevated among the female pesticide-exposed workers. Mortality due to infectious agents as well as breast, prostate, and genital cancers were not significantly elevated in pesticide-exposed workers; however these results are based on the small number of deaths. Due to the low number of "pesticide applicators," further comparisons between farmers and pesticide applicators were not performed.

DISCUSSION

In the NHIS population based sample of US workers, pesticide applicators and farmers, in general, were healthier than other US workers, and farmers were healthier than pesticide applicators. Compared to all other US workers,

TABLE I. Demographic Characteristics and the Number of Deaths Among NHIS Participants Working at the Time of the Surveys (1986–1994)

Occupation	Male N (%)	Female N (%)	Total N (%)	Mean age (SD) Male	Mean age (SD) Female	Mean age (SD) Overall	Number of deaths Male	Number of deaths Female	Number of deaths Overall
Pesticide applicators	171 (96.1)	7 (3.9)	178	38.5 (12.9)	42.1 (8.1)	38.7 (12.7)[a]	9	0	9
Farmers	7,575 (81.5)	1,718 (18.5)	9,293	43.9 (16.6)	44.4 (14.6)	44.0 (16.2)[a]	503	59	562
Pesticide applicators and farmers	7,746 (81.8%)	1,725 (18.2)	9,471	43.7 (16.5)	44.4 (14.6)	43.9 (16.2)[a]	512	59	571
Non-pesticide exposed other occupations	231,098 (52.7)	207,130 (47.3)	438,228	39.0 (12.9)	38.6 (12.8)	38.8 (12.8)[a]	8,078	3,914	11,992
Total	238,844 (53.4)	208,855 (46.6)	447,699	39.2 (13.0)	38.6 (12.8)	38.9 (12.9)	8,590	3,973	12,563

[a]All overall mean ages were significantly different ($P < 0.001$) after adjustment for multiple comparisons: farmers versus pesticide applicators; farmers versus all other workers; pesticide-exposed workers versus all other workers.

TABLE II. Frequency of Major Cause-Specific Number of Deaths by Occupation and Gender Among NHIS Participants Working at the Time of the Surveys (1986–1994)

	Pesticide exposed workers		Other occupations		Total	
Cause of death	Male	Female	Male	Female	Male	Female
All causes	512	59	8,078	3,914	8,590	3,973
Infectious disease	9	0	454	116	463	116
Respiratory disease	16	2	394	198	410	200
Cardiovascular disease	211	20	2,729	1,084	2,940	1,104
Nervous system disease	5	1	83	46	88	47
Overall cancer	161	23	2,515	1,699	2,676	1,722
Nervous system cancer	9	2	86	55	95	57
Digestive cancer	37	4	682	333	719	337
Respiratory cancer	45	1	884	391	929	392
Breast cancer	0	2	7	382	7	384
Prostate cancer	22	—	177	—	199	—
Genital cancer	22	1	182	183	204	184
Urinary cancer	5	1	112	35	117	36
Lymphatic/hematopoietic cancer	20	7	266	150	286	157
Motor vehicle and other accidents	37	7	630	223	667	230

these pesticide-exposed workers were generally less likely to die from a variety of site-specific chronic diseases. In particular, these workers were significantly less likely to die from tobacco-associated chronic diseases (i.e., respiratory disease and respiratory cancers). Infectious disease mortality risk was also lower in pesticide applicators and farmers.

There was a significantly increased risk of age adjusted mortality due to motor vehicles and accidents. This elevation

TABLE III. Mortality Experience of Pesticide Exposed Workers Versus all Other Occupations: Crude and Age-Adjusted Risk Ratios (RR) and 95% Confidence Intervals for Overall and Major Cause-Specific Mortality Among NHIS Participants Working at the Time of the Survey (1986–1994)

	Unadjusted			Age adjusted		
Cause of death	Male RR (95% CI)	Female RR (95% CI)	Total RR (95% CI)	Male RR (95% CI)	Female RR (95% CI)	Total RR (95% CI)
All causes	1.9 (1.7–2.2)	1.9 (1.4–2.5)	2.2 (1.9–2.5)	1.2 (1.1–1.3)	1.1 (0.8–1.4)	1.3 (1.2–1.5)
Infectious disease	0.5 (0.3–1.0)	[a]	0.6 (0.3–1.2)	0.5 (0.3–1.0)	[a]	0.6 (0.3–1.2)
Respiratory disease	1.3 (0.8–2.2)	1.1 (0.3–4.4)	1.5 (0.9–2.4)	0.6 (0.4–1.0)	0.5 (0.1–2.1)	0.7 (0.4–1.1)
Heart disease	2.3 (2.0–2.8)	2.3 (1.5–3.6)	2.8 (2.4–3.3)	1.2 (1.0–1.4)	1.1 (0.7–1.8)	1.4 (1.2–1.7)
Nervous system disease	2.0 (0.8–5.3)	2.4 (0.3–18.7)	2.3 (1.0–5.6)	1.4 (0.6–3.3)	1.1 (0.4–2.9)	1.7 (0.2–13.3)
Overall cancer	2.0 (1.7–2.3)	1.7 (1.1–2.6)	2.1 (1.8–2.4)	1.2 (1.0–1.4)	1.0 (0.7–1.5)	1.2 (1.1–1.4)
Nervous system cancer	2.9 (1.4–5.9)	3.2 (0.9–11.9)	3.3 (1.8–6.1)	2.1 (1.0–4.5)	2.4 (0.6–8.8)	2.4 (1.3–4.6)
Digestive cancers	1.5 (1.1–2.0)	1.3 (0.5–3.4)	1.8 (1.3–2.4)	0.9 (0.7–1.2)	0.7 (0.3–1.7)	1.0 (0.7–1.4)
Respiratory cancers	1.6 (1.2–2.2)	0.3 (0.0–2.3)	1.7 (1.3–2.4)	1.0 (0.7–1.3)	0.2 (0.02–1.3)	1.0 (0.8–1.4)
Breast cancers	[a]	0.5 (0.1–2.1)	[a]	[a]	0.4 (0.1–1.5)	[a]
Prostate cancers	3.4 (2.1–5.8)	[a]	[a]	1.3 (0.8–2.2)	[a]	[a]
Genital cancers	3.4 (2.0–5.6)	0.6 (0.1–4.3)	2.7 (1.7–4.5)	1.3 (0.8–2.2)	0.4 (0.1–2.7)	1.3 (0.8–2.1)
Urinary cancers	2.1 (0.7–5.9)	2.9 (0.4–20.9)	2.7 (1.0–7.1)	1.2 (0.4–3.6)	1.6 (0.2–10.5)	1.6 (0.6–4.1)
Lymphatic/hematopoietic cancer	2.6 (1.7–4.2)	6.1 (2.7–13.8)	3.4 (2.3–5.1)	1.7 (1.1–2.7)	3.6 (1.6–8.2)	2.2 (1.5–3.2)
Motor vehicle and other accidents	1.7 (1.2–2.3)	3.4 (1.6–7.2)	2.3 (1.7–3.0)	1.6 (1.2–2.2)	3.2 (1.5–6.9)	2.1 (1.6–2.8)

[a]The empty cells are due to no or small number of deaths.

has been reported in previous studies, particularly in subpopulations of pesticide-exposed workers such as aerial sprayers. In addition to exposure to farm and other machinery, neurologic effects of exposure to many pesticides may be a factor in this consistently reported increased risk of accidents [WHO, 1990; Levine and Doull, 1992; Maroni and Fait, 1993; Dich et al., 1997; Fleming et al., 1997; USDHHS, 1998; Cantor and Silberman, 1999].

Increased risk of mortality from the nervous system and lymphatic/hematopoietic cancers has been reported in other studies in pesticide workers, particularly from non-Hodgkin's lymphoma. There is previously published literature associating the use of the phenoxy herbicides with an increased risk of both non-Hodgkin's lymphoma and soft tissue sarcoma [Zahm and Blair, 1992; Zahm et al., 1993; Dich et al., 1997], although not the organochlorine pesticides [Baris et al., 1998]. Nervous system cancer has been reported among farmers. Brain cancer, in particular, appears to be increased in these worker populations, as well as possibly in their offspring [Zahm and Ward, 1998].

Of note, farmers were found to be significantly older, on average, than the rest of the US workforce. This nationwide trend of an aging agricultural workforce has been confirmed by other sources [US Bureau of Census, 1998].

Data Limitations

These analyses suffer from many of the data limitations seen in previous epidemiologic studies of pesticide-exposed workers. Limitations include issues related to the healthy worker effect, lack of individual exposure measures, possible misclassification of other pesticide-exposed workers, and relatively small number of deaths. However, the use of the US worker population as the major comparison population is appropriate for issues of the healthy worker effect and other biases [Breslow and Day, 1980; Checkoway et al., 1989; Monson, 1990]. As with many previous studies, individual and cohort-specific confounding factors (such as smoking), and detailed pesticide exposure information were not obtained for this cohort. The lack of these data is an important limitation on any conclusions that could be drawn from these analyses.

Males

With regards to mortality among male pesticide-exposed workers, the only significantly elevated age adjusted mortality was due to motor vehicles and accidents, and mortality from risk of lymphatic/hematopoietic cancers.

Although not seen in this study, a significantly elevated prostate cancer risk, particularly cancer incidence more than cancer mortality, has been a consistent finding in most previous farmer studies [Dich and Wiklund, 1998; Fleming et al., 1999a,b, 2000]. As a plausible explanation, exposures to the organochlorine pesticides as possible estrogen analogues and their possible relation to worldwide increases in testicular cancer and prostate cancer have been indicated [Strohmer et al., 1993; Toppari et al., 1996; Fleming et al., 2000]. In support of the present study's results, current theories report the possible protective effects of vitamin D exposure against prostate cancer risk, given the presumed high occupational ultraviolet exposure of agricultural workers and their reportedly high rates of skin cancer [Hanchette and Schwartz, 1992].

Females

The number of female farmers and pesticide applicators was relatively small, as was the number of deaths in this subpopulation; nevertheless, this study is one of the largest to report mortality rates among female workers with occupational pesticide exposure. With the exception of mortality from accidents, and nervous system and lymphatic/hematopoietic cancer, pesticide-exposed women were in general healthier than other US female workers. Similar to other studies, the risk of lymphatic/hematopoietic cancers was somewhat elevated among both genders of pesticide-exposed workers, particularly among the women workers [Blair et al., 1985; Brown et al., 1991; Zahm and Blair, 1992; Figa-Talamanca et al., 1993; Dich et al., 1997; Fleming and Herzstein, 1997].

Breast cancer mortality was not significantly elevated, despite possible occupational exposure to organochlorine pesticides. Very few studies exist on occupational exposure to organochlorines in women with data that can be used to test current hypotheses concerning the possible etiologic relationship between exposure to organochlorines (as estrogen analogues) and the increased risk of breast cancer. Nevertheless, the present study supports the lack of breast cancer risk seen in other occupational pesticide-exposed groups [Wolff et al., 1993; Krieger et al., 1994; Dich et al., 1997; Fleming and Herzstein, 1997; Fleming et al., 1999a,b].

CONCLUSION

The present study is the first to evaluate the mortality experience of farmers and pesticide applicators over the past 2 decades using a sample representative of the entire adult US population with a comparison of all other US adult workers. Additional analyses using this same NHIS linked data set to take advantage of person years, as well as morbidity endpoints, will be performed to evaluate trends and other health outcomes among these at risk occupational groups.

Researchers in occupational health are urged to seek out this important and publicly available resource. The NHIS database and mortality follow-up represent a probability sample of the entire US population, with the ability to compare both morbidity and mortality among US workers.

Furthermore, as noted by NIOSH [1997] and the English Registrar's Decennial Reports [1995], databases such as the NHIS surveys and mortality follow-up can be used not only to target studies of work-related conditions and to add to the body of evidence generated from epidemiologic studies, but also to provide surveillance data for establishing priorities, and for tracking progress towards the elimination of preventable diseases [Drever, 1995; NIOSH, 1997].

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