Suicide and Pesticide Use among Pesticide Applicators and Their Spouses in the Agricultural Health Study

John D. Beard,1 David M. Umbach,2 Jane A. Hoppin,3 Marie Richards,4 Michael C. R. Alavanja,5 Aaron Blair,5 Dale P. Sandler,2 and Freya Kamel3

1Department of Health Science, College of Life Sciences, Brigham Young University, Provo, Utah, USA; 2Biostatistics Branch, and Epidemiology Branch, National Institute of Environmental Health Sciences, National Institutes of Health, Department of Health and Human Services, Research Triangle Park, North Carolina, USA; 4Westat, Durham, North Carolina, USA; 5Occupational and Environmental Epidemiology Branch, Division of Cancer Epidemiology and Genetics, National Cancer Institute, National Institutes of Health, Department of Health and Human Services, Rockville, Maryland, USA

BACKGROUND: An association may exist between pesticide exposure and suicide. OBJECTIVE: We sought to evaluate the existence of an association between pesticide use and suicide using data from the Agricultural Health Study (AHS), a prospective cohort study of licensed pesticide applicators and their spouses in Iowa and North Carolina.

METHODS: Via linkage to state mortality files and the National Death Index, we identified 110 suicides occurring between enrollment in the AHS (from 1993 to 1997) and 31 May 2009, among 81,998 cohort members contributing 1,092,943 person-years of follow-up. The average length of follow-up was 13.3 years. AHS participants provided data on pesticide use and potential confounders via self-administered questionnaires at enrollment. We evaluated several measures of pesticide use: use of any pesticide, use of any of 5 specific pesticides, cumulative lifetime days of use and intensity-adjusted cumulative lifetime days of use of 22 specific pesticides, and ever use of 10 functional and chemical classes of pesticides. We used Cox proportional hazards regression models to estimate adjusted hazard ratios and 95% confidence intervals.

RESULTS: After adjusting for age at enrollment, sex, number of children in family, frequency of alcohol consumption during the past 12 months, and smoking status, we found no association between prior pesticide use and suicide in applicators and their spouses. Results were the same for applicators and spouses together or for applicators alone and were consistent across several measures of pesticide use.

CONCLUSIONS: Our findings do not support an association between moderate pesticide use and suicide.

KEY WORDS: farmers, pesticide applicators, pesticides, spouses, suicide. Environ Health Perspect 119:1610–1615 (2011). http://dx.doi.org/10.1289/ehp.1103413 [Online 13 July 2011]

Several studies have reported higher suicide rates among farmers than the general population (Blair et al. 1993; Browning et al. 2008; Gunderson et al. 1993; Lee et al. 2002; Melzer et al. 2008; Miller and Burns 2008; Page and Fragar 2002; Stallones 1990), although two studies found lower rates among Canadian farmers (Pickett et al. 1993, 1999). A review noted higher suicide rates among farmers than any other occupational group in the United Kingdom (Gregoire 2002).

Other studies suggested associations between chronic exposure to pesticides and suicide among farmers and other agricultural populations. In Australia, pesticide applicators had higher suicide rates than the general population (MacFarlane et al. 2009, 2010), whereas applicators in Italy had a lower rate of accidents and suicide (Torchio et al. 1994). Parrón et al. (1996) found higher suicide rates in an intensive agricultural area of southeastern Spain than in other areas with similar demographic and socioeconomic compositions; they tentatively attributed the increased rates to pesticide exposure. Colorado farmers potentially exposed to pesticides had higher suicide rates than the general population (Stallones 2006), and ecological and case studies suggested an association between organophosphate pesticide (OP) use and suicide (London et al. 2005).

The Agricultural Health Study (AHS) is a large, prospective cohort study of private pesticide applicators (mostly farmers), commercial applicators, and spouses of private applicators in Iowa and North Carolina. It was designed to study associations between cancer and other chronic diseases and farm-related exposures (Alavanja et al. 1996). Previously, AHS participants in the highest category of use of chlorpyrifos, an OP, were reported to be twice as likely to commit suicide as those who never used chlorpyrifos (Lee et al. 2007). Because that study was based on few cases and evaluated only one pesticide, we wanted to evaluate more fully the possible associations between the use of pesticides, particularly OPs, and suicide among applicators and their spouses in the AHS.

METHODS

Population and case definition. The AHS cohort, enrolled from 1993 to 1997, provided data on demographic and lifestyle factors, pesticide use, and other agricultural exposures at enrollment (Alavanja et al. 1996). Most private and commercial applicators were men (97% and 96%, respectively), whereas most spouses were women (99%). Mortality data including date and cause of death were obtained by linking the cohort to state mortality files and the National Death Index. We used the International Classification of Diseases, 9th Revision (ICD-9) [World Health Organization (WHO) 1977] codes to identify suicides from 1993 to 1998 and 10th Revision (ICD-10) (WHO 1992) codes for those from 1999 to 2009. ICD-9 codes beginning with E95 or 95 or ICD-10 codes X60–X84 identified suicides listed as underlying or contributing causes of death. We excluded 129 individuals < 18 years of age at enrollment, 1 individual from a couple in which the private applicator and spouse had both committed suicide (the excluded individual was randomly chosen from the couple to avoid correlated death times), and an additional 7,528 cohort members missing covariate information. The analysis included a total of 81,988 cohort members: 48,098 private applicators [contributing 647,006 person-years (PY)], 4,781 commercial applicators (68,240 PY), and 29,119 spouses of private applicators (377,697 PY). The average length of follow-up was 13.3 years. We identified 110 suicides that occurred between enrollment and 31 May 2009.

The institutional review boards (IRBs) of the National Institutes of Health, Battelle Centers for Public Health Research and Evaluation (North Carolina field station), the University of Iowa (Iowa field station), and Westat (study coordinating center) approved this study, and the IRB of Brigham Young University exempted it. The study was explained to all potential participants, who indicated consent by returning the enrollment questionnaire.

Address correspondence to F. Kamel, Epidemiology Branch, National Institute of Environmental Health Sciences, 111 T.W. Alexander Dr., A3-05, Research Triangle Park, NC 27709 USA. Telephone: (919) 541-1581. Fax: (919) 541-2511. E-mail: kamel@niehs.nih.gov

We thank the field stations in Iowa (University of Iowa: C. Lynch, P. Gillette, and E. Heywood) and North Carolina (Battelle: C. Knott and M. Hayslip) for conducting the Agricultural Health Study (AHS) and Westat (K. Torres, S. Legum, and M. Dunn) for central study coordination. We thank the participants of the AHS for their contribution to this research.

This work was supported by the Intramural Research Program of the National Institutes of Health, National Institute of Environmental Health Sciences (NIEHS) (Z01 ES04930), the National Cancer Institute (Z01 CP044008), and NIEHS Award T32ES007018. M.R. is employed by Westat (Durham, North Carolina), an employee-owned company. The authors declare they have no actual or potential competing financial interests. Received 6 January 2011; accepted 12 July 2011.
Exposure assessment. Applicators and spouses provided information on pesticide use and other factors via questionnaires completed at enrollment (AHS 2011). This information included years of use (duration) and average days per year of use (frequency) for any pesticide in addition to ever use for 50 specific pesticides. For applicators, information was also collected on duration and frequency of use for 22 of the 50 pesticides. We evaluated suicide risk in relation to 10 pesticide categories (four functional: fumigants, fungicides, herbicides, and insecticides; and six chemical: phenoxy herbicides, triazine herbicides, carbamates, organochlorine insecticides, organophosphate insecticides, and pyrethroid insecticides) as well as individual pesticides and overall pesticide use.

For both applicators and spouses, we evaluated cumulative lifetime days of use of any pesticide. For applicators only, we also evaluated cumulative lifetime days of use and intensity-adjusted cumulative lifetime days of use for 22 individual pesticides, although we present results for only the 17 pesticides for which there were at least five exposed cases. Duration and frequency of use data were collected in seven and eight categories, respectively. Using values set to the midpoint of each category, or 50\% greater than the lower bound in the highest category, we determined an applicator’s cumulative lifetime days of use for any pesticide and for each specific pesticide as the product of the duration and frequency values. We categorized cumulative lifetime days of use of any pesticide into quartiles based on the distribution of use for all applicators and spouses. We categorized specific pesticides into three levels based on the distribution of use for all applicators: a) none, b) used for less than or equal to the median lifetime days of use, and c) used for more than the median lifetime days. We also evaluated intensity-adjusted cumulative lifetime days of use, calculated as previously described (Dosemeci et al. 2002) and again categorized in three levels: none, ≤ median, > median.

Statistical analysis. We employed Cox proportional hazards regression models to estimate hazard ratios (HR) and 95\% confidence intervals (CIs) for the association of suicide with each measure of pesticide use. survival. Time periods were defined as the time (in days) between enrollment in the AHS and death for those who died from suicide (n = 110) or some other cause (n = 5,980) or the time between enrollment and 31 May 2009, for study participants still alive (n = 75,908). We ran models for applicators only and for applicators and spouses combined. There were too few suicides among spouses (n = 9) to analyze data on spouses alone. Possible confounding variables identified from prior reports (categorized as in Table 1) included age, sex, state of residence, race/ethnicity, education level, marital status, number of children in family (as a measure of social connection), size of farm worked last year, frequency of alcohol consumption during the past 12 months, smoking status, and ever diagnosed with heart disease or diabetes (as measures of chronic disease). We did not consider depression as a potential confounder, as it may be an intervening variable. Although spouses were not asked about number of children in family, farm size, or ever being diagnosed with heart disease, we inferred spouses’ answers for the first two items from applicators’ responses and based the last item on spouses’ responses to questions on myocardial infarction, angina, and arrhythmia.

We evaluated all covariates significantly associated with suicide in both unadjusted and age- and sex-adjusted models as potential confounders (α = 0.05). We then performed manual backward selection using α = 0.05 to select a base model from the covariates identified in the first step. As an alternative model selection method, we performed manual forward selection using α = 0.05 and selected the same model as with the backward selection method. We evaluated whether additional covariates should be included in the base model with likelihood ratio tests (α = 0.05) and evaluated model fit using the Akaike information criterion and the Schwarz Bayesian criterion.

### Table 1. Characteristics of suicide cases and all pesticide applicators and spouses.

| Characteristic                        | Casesa | Totala | Crude HR (95\% CI) | Adjusted HRb (95\% CI) |
|--------------------------------------|--------|--------|-------------------|------------------------|
| Age at enrollment (years)            |        |        |                   |                        |
| 18–35                                | 27     | 164    | 1.14 (0.68, 1.91) | 1.09 (0.65, 1.82)     |
| 36–45                                | 32     | 243    | 331.257           | Reference              |
| 46–65                                | 36     | 217    | 442.276           | 0.84 (0.52, 1.35)     |
| > 65                                 | 15     | 79     | 74.056            | 2.07 (1.12, 3.82)     |
| Sex                                  |        |        |                   |                        |
| Male                                 | 100    | 648    | 698.643           | Reference              |
| Female                               | 10     | 54     | 394.300           | 0.17 (0.09, 0.33)     |
| State of residence                   |        |        |                   |                        |
| Iowa                                 | 61     | 406    | 743.676           | Reference              |
| North Carolina                       | 49     | 296    | 349.267           | 1.72 (1.18, 2.50)     |
| Applicator type or spouse            |        |        |                   |                        |
| Private applicator                   | 89     | 569    | 647.086           | Reference              |
| Commercial applicator                | 12     | 81     | 68.240            | 1.30 (0.71, 2.37)     |
| Spouse of (private applicator)       | 9      | 51     | 377.697           | 0.17 (0.09, 0.34)     |
| Race/ethnicity                       |        |        |                   |                        |
| White, non-Hispanic                  | 102    | 669    | 1,060.879         | Reference              |
| Other                                | 7      | 24     | 3,238             | 2.37 (1.10, 5.10)     |
| Education level                      |        |        |                   |                        |
| ≤ Some high school                   | 10     | 53     | 73.003            | 1.39 (0.71, 2.76)     |
| High school graduate                 | 48     | 324    | 489.551           | Reference              |
| GED, 1–3 years of vocational education beyond high school, or some college | 37 | 224 | 298.743 | 1.26 (0.82, 1.94) |
| ≥ College graduate                   | 13     | 87     | 212.110           | 0.63 (0.34, 1.16)     |
| Marital status                       |        |        |                   |                        |
| Married or living as married         | 87     | 572    | 970.990           | Reference              |
| Divorced or separated                | 11     | 61     | 33.299            | 3.72 (1.99, 6.97)     |
| Widowed, never married, or other     | 12     | 69     | 67.845            | 1.54 (0.94, 2.42)     |
| Number of children in family         |        |        |                   |                        |
| ≤ 1                                  | 44     | 265    | 266.403           | Reference              |
| > 1                                  | 66     | 437    | 826.540           | 0.48 (0.33, 0.70)     |
| Size of farm worked last year        |        |        |                   |                        |
| Did not work on a farm or < 5 acres  | 8      | 41     | 80.244            | Reference              |
| ≥ 5 acres                            | 81     | 503    | 922.473           | 0.88 (0.43, 1.82)     |
| Frequency of alcohol consumption during past 12 months |        |        |                   |                        |
| Never                                | 38     | 232    | 372.767           | Reference              |
| ≤ Every day                          | 67     | 435    | 688.157           | Reference              |
| Every day                            | 5      | 35     | 10.129            | 5.04 (2.03, 12.51)    |
| Smoking status                       |        |        |                   |                        |
| Never                                | 39     | 275    | 658.739           | Reference              |
| Past                                 | 32     | 194    | 277.039           | 1.95 (1.22, 3.12)     |
| Current                              | 39     | 234    | 157.164           | 4.20 (2.09, 6.55)     |
| Ever diagnosed with heart disease    |        |        |                   |                        |
| No                                   | 100    | 657    | 1,016.855         | Reference              |
| Yes                                  | 5      | 14     | 5.077             | 0.85 (0.43, 1.68)     |
| Ever diagnosed with diabetes (other than white pregnant) |        |        |                   |                        |
| No                                   | 101    | 653    | 1,048.599         | Reference              |
| Yes                                  | 7      | 43     | 31.850            | 2.26 (1.05, 4.87)     |
| Ever diagnosed with depression       |        |        |                   |                        |
| No                                   | 85     | 586    | 1,022.481         | Reference              |
| Yes                                  | 18     | 85     | 53.221            | 4.06 (2.44, 6.75)     |

*aInformation for specific covariates was missing for 0–8\% of participants. bAdjusted for age at enrollment and sex.*
The applicator-only base model included age at enrollment (18–35, 36–45, 46–65, > 65 years), number of children in family (≤ 1, > 1), frequency of alcohol consumption during the past 12 months (never, < every day, every day), and smoking status (never, past, current). The base model for applicators and spouses together also included sex.

### Table 2. Suicide and pesticide use among applicators and spouses.

| Variable | Cases¹ | Total² | Adjusted HR³ (95% CI) |
|----------|--------|--------|-----------------------|
| Years personally mixed or applied pesticides | n | PY | n | PY |
| None | 7 54 | 13,904 | 180,992 | Reference |
| ≤ 5 | 29 152 | 13,009 | 175,839 | 1.53 (0.60, 3.87) |
| > 5 | 73 493 | 50,952 | 681,370 | 0.83 (0.33, 2.08) |
| Days per year personally mixed or applied pesticides | n | | | |
| None | 8 59 | 14,124 | 183,728 | Reference |
| < 20 | 71 466 | 46,745 | 622,313 | 0.90 (0.42, 2.29) |
| ≥ 20 | 30 175 | 16,987 | 232,178 | 0.89 (0.36, 2.20) |
| Cumulative lifetime days personally mixed or applied pesticides | ≤ 9 | 22 129 | 20,736 | 271,553 | Reference |
| > 9–109 | 33 220 | 21,524 | 287,320 | 0.65 (0.37, 1.16) |
| > 109–370 | 26 162 | 19,747 | 265,712 | 0.51 (0.27, 0.94) |
| > 370 | 26 169 | 15,777 | 212,577 | 0.61 (0.33, 1.13) |
| Medical visits related to pesticide use⁴ | No | 91 592 | 49,022 | 663,393 | Reference |
| Yes | 9 57 | 3,492 | 47,305 | 1.32 (0.66, 2.62) |
| Functional pesticide classes ever personally mixed or applied | Fumigants | No | 85 542 | 68,238 | 920,494 | Reference |
| | Yes | 25 160 | 12,178 | 164,901 | 0.98 (0.62, 1.54) |
| Fungicides | No | 74 470 | 61,607 | 818,170 | Reference |
| | Yes | 36 232 | 19,761 | 266,561 | 0.89 (0.59, 1.34) |
| Herbicides | No | 14 83 | 20,326 | 265,005 | Reference |
| | Yes | 96 619 | 61,406 | 824,414 | 0.69 (0.35, 1.36) |
| Insecticides | No | 18 112 | 22,312 | 291,593 | Reference |
| | Yes | 92 580 | 59,560 | 799,710 | 0.86 (0.49, 1.49) |
| Chemical pesticide classes ever personally mixed or applied | Phenoxy herbicides | No | 37 219 | 25,338 | 336,166 | Reference |
| | Yes | 67 455 | 40,178 | 542,779 | 0.70 (0.45, 1.16) |
| Triazine herbicides | No | 38 225 | 25,769 | 342,148 | Reference |
| | Yes | 66 449 | 39,747 | 536,796 | 0.71 (0.47, 1.09) |
| Carbamates | No | 48 309 | 39,193 | 518,868 | Reference |
| | Yes | 62 393 | 42,656 | 572,294 | 0.80 (0.54, 1.17) |
| Organochlorine insecticides | No | 66 445 | 54,499 | 726,683 | Reference |
| | Yes | 44 257 | 26,745 | 356,697 | 0.80 (0.58, 1.15) |
| Organophosphate insecticides | No | 26 170 | 28,870 | 377,315 | Reference |
| | Yes | 84 532 | 52,979 | 713,702 | 0.82 (0.50, 1.33) |
| Pyrethroid insecticides | No | 87 538 | 68,400 | 907,912 | Reference |
| | Yes | 23 164 | 13,326 | 181,574 | 1.08 (0.68, 1.74) |

Abbreviations: 2,4-D, [2,4-dichlorophenoxy]acetic acid; 2,4,5-T, [2,4,5-trichlorophenoxy]acetic acid; 2,4,5-TP, (RS)-2-(2,4,5-trichlorophenoxy)propionic acid; DDT, 1,1,1-trichloro-2,2-bis(chlorophenylethylene); DDE, 2,2-dichlorovinyl dimethyl phosphate; EPTC, 3-ethyl dipropyl(thiocarbamate). Information for specific pesticide covariates was missing for 0–20% of participants. Adjusted for age at enrollment, sex, number of children in family, frequency of alcohol consumption during the past 12 months, and smoking status. Category boundaries set at the quartiles of the distribution of cumulative lifetime days of pesticide use for all applicators and spouses. Not asked on the spouse questionnaire. Only results for applicators are shown. Fumigants included aluminum phosphide, methyl bromide, ethylene dibromide, carbon tetrachloride, and ethylene dibromide. Fungicides included benomyl, clorone, thiophanate, and maneb. Herbicides included 2,4-D, 2,4,5-T, 2,4,5-TP, alachlor, atrazine, butachlor, chlormuron, cyanazine, dicamba, EPTC, glyphosate, imazaquin, imazethapyr, metolachlor, metribuzin, parquat, pendimethalin, petrolleum oil, and trifluralin. Insecticides included aldicarb, aldrin, azinphos, butoxphos, diazinon, dieldrin, endosulfan, fenitrofarb, fenitrothion, fenitrothion, parathion, parathion methyl, and permethrin. Organophosphate insecticides included chlorpyrifos, coumaphos, DEF, diazinon, fenosulfuron, malathion, parathion, parathion methyl, and propoxur. Pyrethroid insecticides included permethrin (for animals) and permethrin (for crops).

Additional analyses included stratifying models by state of residence, number of children in family, and use of chemical-resistant gloves (applicants only). We formally compared HRs from the two strata using a 95% CI constructed from the standard error of the difference between HRs. To additional models, we added state, marital status, race/ethnicity, ever being diagnosed with diabetes, or cumulative lifetime days of use of any pesticide. We evaluated all four functional classes of pesticides together in a single model. Additionally, we evaluated carbamates, herbicides, organochlorine insecticides, OPs, and pyrethroid insecticides together in another model. Some analyses were repeated, restricting the sample to male applicators, applicators who personally used pesticides, individuals who did not report a physician diagnosis of depression, or cohort members ≤ 50 years of age at enrollment (because pesticide use among younger applicators is probably less likely to change during follow-up than use among older applicators). We separately evaluated suicides committed within 5 years of enrollment or more than 5 years past enrollment. We evaluated pesticide use during the year prior to enrollment. Finally, we used within-category medians to assess dose–response trends in cumulative lifetime days of use and intensity-adjusted cumulative lifetime days of use.

We used the P1REL090600 release of the Phase I data set, the REL090500.00 release of the demographic data set, and the REL201004.00 release of the mortality data set for this study and performed all analyses with SAS version 9.2 (SAS Institute Inc., Cary, NC).

### Results

In models adjusted for age at enrollment and sex, risk for suicide was significantly greater if participants a) were > 65 years of age compared with 36–45 years of age, b) were living in North Carolina, c) were of a race/ethnicity other than white/non-Hispanic, d) were divorced or separated compared with married or living as married, e) drank alcohol every day during the 12 months prior to enrollment compared with drank alcohol < every day, f) were current smokers compared with never smokers, or g) had ever been diagnosed with diabetes or depression (Table 1). Suicide risk was significantly lower for women than men and for participants with > 1 child compared with ≤ 1 child (Table 1).

We found little evidence that suicide was associated with overall pesticide use among applicators and spouses combined (Table 2). We saw no significant dose–response relationships between pesticide use (measured by duration, frequency, or cumulative lifetime days of use of any pesticide) and suicide. Only 37% of suicide cases (n = 41), all applicants, provided information on experiencing a high pesticide
exposure event, and only seven cases experienced one (HR = 1.13; 95% CI: 0.50, 2.57). No cases reported being diagnosed with pesticide poisoning, but medical visits related to pesticide use were not significantly associated with suicide among applicators (Table 2).

For no specific functional or chemical class of pesticides, including OPs, was ever use significantly associated with suicide (Table 2). Only use of pyrethroid insecticides had an HR of > 1.0 (HR = 1.09; 95% CI: 0.68, 1.74), but that was not significant.

Among applicators and spouses together, ever use of individual pesticides was typically inversely associated with suicide, although estimates were often based on small numbers of exposed cases (Table 3). Five herbicides (atrazine, dicamba, imazethapyr, metolachlor, and pendimethalin) showed significant inverse associations; no positive association was statistically significant. The HR for (2,4,5-trichlorophenoxy)acetic acid (2,4,5-T), however, was elevated (HR = 1.55; 95% CI: 0.95, 2.53).

Among applicators alone, none of the 22 individual pesticides showed a significant dose–response relationship between cumulative lifetime days of use and suicide (Table 4). Repeating those analyses with intensity-adjusted cumulative lifetime days of use, we found HRs that were generally < 1.0 but not significant (data not shown). We found significant inverse dose–response relationships between three intensity-adjusted pesticides and suicide: (2,4-dichlorophenoxy)acetic acid (2,4-D) (≤ 381 days vs. none: HR = 0.85; 95% CI: 0.53, 1.37; > 381 days vs. none: HR = 0.65; 95% CI: 0.33, 0.96; \( p_{\text{trend}} = 0.04 \)), metolachlor (≤ 221 days vs. none: HR = 0.49; 95% CI: 0.26, 0.91; > 221 days vs. none: HR = 0.47; 95% CI: 0.25, 0.87; \( p_{\text{trend}} = 0.03 \)), and terbufos (≤ 189 days vs. none: HR = 0.71; 95% CI: 0.38, 1.31; > 189 days vs. none: HR = 0.45; 95% CI: 0.22, 0.95; \( p_{\text{trend}} = 0.04 \)).

When we stratified by state of residence or number of children in family separately and used the ever-use herbicide variables for applicators and spouses, we observed the same results in each stratum; generally inverse associations between herbicides and suicide with a few being significant (data not shown). Formal comparison of the stratum-specific HRs showed no significant differences. Data on use of chemical-resistant gloves were available only for applicators. Stratification by this variable yielded similar results in both strata for general use and herbicide variables (data not shown).

Results remained unchanged when state, marital status, race/ethnicity, ever being diagnosed with diabetes, or cumulative lifetime days of use of any pesticide were added to the models one at a time (data not shown). Evaluating all four functional pesticide classes together in a single model or evaluating carbamates, herbicides, organochlorine insecticides, OPs, and pyrethroid insecticides together in another model did not change results (data not shown). Excluding cohort members who had been diagnosed with depression changed results slightly: a few more pesticides were inversely associated with suicide and a few more inverse associations were significant (data not shown). Restricting analyses to male applicators, to applicators who personally used pesticides, or to cohort members ≤ 50 years of age at enrollment did not change results (data not shown). Likewise, evaluating pesticide use during the year prior to the enrollment of cohort members in the AHS did not change results (data not shown).

Evaluating suicides committed more than 5 years after enrollment in the AHS showed no significant associations between suicide and general pesticide use or the functional and chemical class pesticide variables, although most HRs were slightly more negative (data not shown). Similarly we found no significant associations between pesticide use and suicide committed within 5 years of enrollment (data not shown).

### Table 3. Suicide and ever use of specific pesticides among applicators and spouses.

| Herbicide | Ever personally mixed or applieda | Casesa | Totala | Adjusted HRb,c (95% CI) |
|-----------|---------------------------------|--------|--------|------------------------|
| DDVP      | 15                              | 89     | 109,723| 0.80 (0.46, 1.41)      |
| Chlorothalonil | 13                           | 83     | 33,921 | 1.55 (0.97, 2.47)      |
| Heptachlor | 9                              | 57     | 7,613  | 0.80 (0.39, 1.64)      |
| Phenamethoxycarbonylurea | 7            | 48     | 5,330  | 0.64 (0.30, 1.40)      |
| Malathion | 62                             | 388    | 548,502| 0.93 (0.61, 1.42)      |
| Carbofuran | 23                           | 181    | 184,258| 0.99 (0.61, 1.59)      |
| Lindane   | 14                             | 99     | 125,975| 0.92 (0.52, 1.63)      |
| Flockyphos | 77                           | 509    | 167,712| 0.94 (0.61, 1.45)      |
| Malathion | 62                             | 388    | 548,502| 0.93 (0.61, 1.42)      |
| Carbofuran | 23                           | 181    | 184,258| 0.99 (0.61, 1.59)      |
| Lindane   | 14                             | 99     | 125,975| 0.92 (0.52, 1.63)      |
| Flockyphos | 77                           | 509    | 167,712| 0.94 (0.61, 1.45)      |
| Metribuzin | 33                           | 233    | 310,544| 0.77 (0.50, 1.19)      |
| Metolachlor | 38                          | 252    | 374,305| 0.68 (0.44, 1.03)      |
| Atrazine  | 56                             | 402    | 506,172| 0.64 (0.43, 0.96)      |
| Butylate  | 26                             | 213    | 221,059| 0.91 (0.58, 1.45)      |
| Chloromuron ethyl | 26            | 194    | 264,933| 0.66 (0.42, 1.05)      |
| Cyazine   | 28                             | 188    | 292,910| 0.70 (0.45, 1.10)      |
| Dichamba  | 33                             | 271    | 356,274| 0.63 (0.41, 0.98)      |
| EPTC      | 17                             | 148    | 145,053| 0.97 (0.57, 1.68)      |
| Glyophosphate | 77                         | 509    | 167,712| 0.94 (0.61, 1.45)      |
| Imazethapyr | 22                       | 161    | 301,466| 0.49 (0.30, 0.80)      |
| Metolachlor | 28                          | 169    | 330,200| 0.54 (0.35, 0.84)      |
| Methribuzin | 33                         | 233    | 310,443| 0.77 (0.50, 1.30)      |
| Paraquat  | 19                             | 152    | 172,340| 0.70 (0.42, 1.16)      |
| Pendimethalin | 30                       | 196    | 320,020| 0.56 (0.36, 0.87)      |
| Petroleum oil | 32                       | 211    | 324,356| 0.65 (0.41, 1.00)      |
| Trifluralin | 41                           | 290    | 315,427| 0.79 (0.52, 1.22)      |

Abbreviations: 2,4-D, (2,4-dichlorophenoxy)acetic acid; 2,4,5-T, (2,4,5-trichlorophenoxy)acetic acid; 2,4,5-TP, (2,4,5-trichlorophenoxy)propionic acid; DDT, 1,1,1-trichloro-2,2-bis(chloromethyl)ethane; DDVP, 2,2-dichlorovinyl dimethyl phosphate; EPTC, S-ethyl dipropyl(thiocarbamate).

*a*Information for specific pesticides was missing for 1–6% of participants.

*b*Adjusted for age at enrollment, sex, number of children in family, frequency of alcohol consumption during the past 12 months, and smoking status. *For each pesticide, the applicators and spouses who did not use the pesticide served as the reference group. *Fewer than five cases used aluminum phosphide, coumaphos, dieldrin, trichlorfon, or zinc.
Discussion

We found no association between pesticide use up to enrollment in the AHS and subsequent incidence of suicide in pesticide applicators and their spouses. This finding was consistent for use of any pesticide or individual pesticides, for functional or chemical classes, and for cumulative lifetime days of pesticide use. Results were the same for applicators and spouses together or for applicators only.

Although many studies have reported higher suicide rates among farmers and pesticide applicators than the general population (Blair et al. 1993; Browning et al. 2008; Gunderson et al. 1993; Lee et al. 2002; MacFarlane et al. 2009, 2010; Meltzer et al. 2008; Miller and Burns 2008; Page and Fragar 2002; Stallones 1999), others have found lower rates (Pickett et al. 1993, 1999; Torchio et al. 1994). A recent mortality analysis showed lower suicide rates among AHS participants than among the general populations of Iowa and North Carolina at least 15 years of age, although deaths due to unintentional injuries were elevated (Waggoner et al. 2011). The lower suicide rate in the AHS could reflect misclassification of suicides as unintentional injuries (e.g., collision with objects).

Another possible explanation for the lower suicide rate in the AHS is that individuals at risk of suicide may be less likely to enroll initially. This self-selection, if nondifferential by exposure, should not bias estimated HRs, although it might reduce precision. To reduce the influence of the healthy worker effect on their standardized mortality ratios (SMRs), Waggoner et al. (2011) calculated relative SMRs (rSMRs), a ratio of a cause-specific SMR and the SMR for all other causes except the cause of interest. The rSMR for suicide among applicators was 1.06 (95% CI: 0.87, 1.28) (Waggoner JK, personal communication), suggesting that the deficit in suicides observed in the AHS may be due to the healthy worker effect.

Previous studies that reported higher suicide rates among farmers and pesticide applicators had less-detailed pesticide exposure information than that available in the AHS (London et al. 2002; Stallones 1999, 2002).

Table 4. Suicide and dose response for specific pesticides among applicators.

| Cumulative lifetime days of use | Cases | Total | Adjusted HR (95% CI) |
|---------------------------------|-------|-------|---------------------|
|                                | n     | PY    |                     |
| **Fungicides**                  |       |       |                     |
| None                            | 84    | 546   | 44,681 604,613      | Reference |
| ≤ 26                            | 9     | 59    | 3,919 53,240        | 0.96 (0.49, 1.98) |
| > 26                            | 5     | 24    | 3,467 47,046        | 0.62 (0.25, 1.53) |
| **Fungicides**                  |       |       |                     |
| None                            | 89    | 577   | 47,968 648,713      | Reference |
| ≤ 28                            | 6     | 29    | 2,041 27,768        | 1.32 (0.58, 3.03) |
| > 28                            | 6     | 45    | 2,035 27,983        | 1.31 (0.57, 3.01) |
| **Herbicides**                  |       |       |                     |
| None                            | 34    | 211   | 13,153 178,829      | Reference |
| ≤ 64                            | 36    | 245   | 20,023 270,683      | 0.79 (0.49, 1.27) |
| > 64                            | 25    | 165   | 18,453 249,665      | 0.61 (0.36, 1.04) |
| **Chlorothalonil**              |       |       |                     |
| None                            | 54    | 353   | 24,026 325,520      | Reference |
| ≤ 51                            | 17    | 106   | 13,169 177,726      | 0.62 (0.36, 1.08) |
| > 51                            | 18    | 118   | 12,351 168,066      | 0.69 (0.40, 1.18) |
| **Atrazine**                    |       |       |                     |
| None                            | 45    | 259   | 16,342 222,136      | Reference |
| ≤ 56                            | 25    | 152   | 18,518 250,121      | 0.56 (0.34, 0.93) |
| > 56                            | 27    | 219   | 17,104 231,261      | 0.68 (0.41, 1.10) |
| **Cyanazine**                   |       |       |                     |
| None                            | 64    | 402   | 29,498 395,275      | Reference |
| ≤ 39                            | 15    | 84    | 10,993 147,671      | 0.74 (0.42, 1.30) |
| > 39                            | 12    | 94    | 9,376 128,369       | 0.67 (0.36, 1.25) |
| **Dicamba**                     |       |       |                     |
| None                            | 61    | 343   | 24,905 337,385      | Reference |
| ≤ 39                            | 14    | 133   | 13,824 186,574      | 0.49 (0.27, 0.88) |
| > 39                            | 15    | 108   | 10,737 146,204      | 0.67 (0.37, 1.19) |
| **EPTC**                        |       |       |                     |
| None                            | 73    | 446   | 39,292 531,770      | Reference |
| ≤ 25                            | 7     | 66    | 6,184 83,741        | 0.69 (0.32, 1.51) |
| > 25                            | 9     | 75    | 3,797 52,139        | 1.36 (0.68, 2.74) |
| **Glyphosate**                  |       |       |                     |
| None                            | 24    | 136   | 12,692 171,041      | Reference |
| ≤ 39                            | 42    | 276   | 21,334 286,296      | 1.04 (0.63, 1.72) |
| > 39                            | 30    | 209   | 17,954 244,520      | 0.88 (0.51, 1.50) |

Abbreviations: 2,4-D, 2,4-dichlorophenoxyacetic acid; EPTC, S-ethyl dipropyl(thiocarbamate).

In 2002, Stallones reported higher suicide rates among farmers and pesticide applicators than the general population. Although many studies have reported higher suicide rates among farmers and pesticide applicators than the general population (Blair et al. 1993; Browning et al. 2008; Gunderson et al. 1993; Lee et al. 2002; MacFarlane et al. 2009, 2010; Meltzer et al. 2008; Miller and Burns 2008; Page and Fragar 2002; Stallones 1999, 2002) other studies have found lower rates (Pickett et al. 1993, 1999; Torchio et al. 1994). A recent mortality analysis showed lower suicide rates among AHS participants than among the general populations of Iowa and North Carolina at least 15 years of age, although deaths due to unintentional injuries were elevated (Waggoner et al. 2011). The lower suicide rate in the AHS could reflect misclassification of suicides as unintentional injuries (e.g., collision with objects).

Another possible explanation for the lower suicide rate in the AHS is that individuals at risk of suicide may be less likely to enroll initially. This self-selection, if nondifferential by exposure, should not bias estimated HRs, although it might reduce precision. To reduce the influence of the healthy worker effect on their standardized mortality ratios (SMRs), Waggoner et al. (2011) calculated relative SMRs (rSMRs), a ratio of a cause-specific SMR and the SMR for all other causes except the cause of interest. The rSMR for suicide among applicators was 1.06 (95% CI: 0.87, 1.28) (Waggoner JK, personal communication), suggesting that the deficit in suicides observed in the AHS may be due to the healthy worker effect.

Previous studies that reported higher suicide rates among farmers and pesticide applicators had less-detailed pesticide exposure information than that available in the AHS (London et al. 2002; Stallones 1999, 2002).
with insecticides, and previous finding from the AHS that suggested agricultural chemicals. We did not replicate a disordered personality traits/disorders (e.g., factors such as alcohol/substance use, mood disorders, and social isolation, frequent alcohol consumption, stress, stress in general, or other problems that have experienced mental problems, financial strain, and intensity of use. We were able to control for potential confounding factors. Finally, suicide from death certificates is a relatively valid outcome (Moyer et al. 1989).

Limitations include the small number of suicides (n = 110), which meant low power for estimating HRs for some individual pesticides. Further, participants were farmer owners/operators and their spouses or they were commercial applicators, that is, not farm workers. Therefore, results may not be generalizable to farm workers who may be more highly exposed than AHS farmers. Some information potentially useful for a suicide analysis was unavailable from AHS questionnaires. For example, information on financial situation or pertinent life events such as divorce or death of a family member was unavailable, as was information on personality or access to mental health care. Measures of acute high-intensity pesticide exposure were available for most of the cohort, particularly suicide cases, and dose–response information was available for only 22 of 50 pesticides. Using data on past pesticide use instead of ongoing use could also misclassify pesticide use if ongoing use, and not past use, is what increases suicide risk.

In conclusion, we found little evidence that pesticide use increases suicide risk in pesticide applicators and their spouses. This finding, although based on relatively few suicides, was consistent across multiple measures of pesticide use and was robust to varying analytic strategies. Although this null finding needs confirmation in different populations, it could be reassuring to farming populations.

**REFERENCES**

AHS (Agricultural Health Study). 2011. Full Text of Questionnaires. Available: http://aghealth.nci.nih.gov/overviews/questionnaires.html (accessed 13 December 2010).

Alavanja MCR, Sandler D, McMasters S, Zahn S, McDonnell C, Lynch C, et al. 1996. The Agricultural Health Study. Environ Health Perspect 104:362–369.

Belsey C, Stallones L, Hoppin JA, Alavanja MC, Blair A, Keeffe T, et al. 2006. Depression and pesticide exposures in female spouses of licensed pesticide applicators in the Agricultural Health Study cohort. J Occup Environ Med 48:1005–1013.

Belsey C, Stallones L, Hoppin JA, Alavanja MC, Blair A, Keeffe T, et al. 2008. Depression and pesticide exposures among private pesticide applicators in the Agricultural Health Study. Environ Health Perspect 116:1713–1719.

Blair A, Dosemeci M, Heiman EM. 1993. Cancer and other causes of death among male and female farmers from twenty-three states. Am J Ind Med 24:742.

Booth N, Briscoe M, Powell R. 2000. Suicide in the farming community: methods used and contact with health services. Occup Environ Med 57:642–644.

Brasington SR, Westneat SC, Knight RH. 2008. Suicides among farmers in three southeastern states, 1990–1998. J Agr Saf Health 14:461–472.

Dosemeci M, Alavanja MC, Rowland AS, Mage D, Zahn SH, Rothman N, et al. 2002. A quantitative approach for estimating exposure to pesticides in the Agricultural Health Study. Ann Occup Hyg 46:245–260.

Goldney RD. 2002. A global view of suicidal behaviour. Emerg Health Perspect 104:362–369.