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Pesticide exposure and self-reported incident depression among wives in the Agricultural Health Study

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ABSTRACT

Background: Depression in women is a public health problem. Studies have reported positive associations between pesticides and depression, but few studies were prospective or presented results for women separately.
Objectives: We evaluated associations between pesticide exposure and incident depression among farmers' wives in the Agricultural Health Study, a prospective cohort study in Iowa and North Carolina.
Methods: We used data on 16,893 wives who did not report physician-diagnosed depression at enrollment (1993–1997) and who completed a follow-up telephone interview (2005–2010). Among these wives, 1054 reported physician diagnoses of depression at follow-up. We collected information on potential confounders and on ever use of any pesticide, 11 functional and chemical classes of pesticides, and 50 specific pesticides by wives and their husbands via self-administered questionnaires at enrollment. We used inverse probability weighting to adjust for potential confounders and to account for possible selection bias induced by the death or loss of 10,639 wives during follow-up. We used log-binomial regression models to estimate risk ratios and 95% confidence intervals.
Results: After weighting for age at enrollment, state of residence, education level, diabetes diagnosis, and drop out, wives' incident depression was positively associated with diagnosed pesticide poisoning, but was not associated with ever using any pesticide. Use of individual pesticides or functional or chemical classes of pesticides was generally not associated with wives' depression. Among wives who never used pesticides, husbands' ever use of individual pesticides or functional or chemical classes of pesticides was generally not associated with wives' incident depression.
Conclusions: Our study adds further evidence that high level pesticide exposure, such as pesticide poisoning, is associated with increased risk of depression and sets a lower bound on the level of exposure related to depression, thereby providing reassurance that the moderate levels of pesticide exposure experienced by farmers' wives likely do not increase risk.

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1. Introduction

The lifetime prevalence of doctor diagnosed depression among American women was recently reported as 20.2%, which was almost double the prevalence (11.1%) in American men (Strine et al., 2008). Although the cause of the higher prevalence of depression among women, and the cause of depression in general, remains unknown, it has been hypothesized to involve both biological susceptibilities and environmental risk factors (Kessler, 2003).

Higher rates of depression and other psychiatric conditions have been linked to exposure to pesticides, particularly organophosphate insecticides, and living on or near farms (Bazylewicz-Walczak et al., 1999; Beseler and Stallones, 2008; Beseler et al., 2006, 2008; Carruth and Logan, 2002; London et al., 2005; Mackenzie Ross et al., 2010; Meyer et al., 2010; Rehner et al., 2000; Salvi et al., 2003; Stallones and Beseler, 2002a, 2002b; Villeneuve et al., 2009; Wesseling et al., 2010). Only a few of the previous studies of pesticide exposure and depression, however, were prospective (Bazylewicz-Walczak et al., 1999; Beseler and

Abbreviations: 2,4-D, 2-(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)propanonic acid; CI, Confidence interval; DDT, 1,1,1-trichloro-2,2-bis(4-chlorophenyl)ethane; EPTC, *S*-ethyl dipropyl(thiocarbamate); IQR, Interquartile range; NIEHS, National Institute of Environmental Health Sciences; RR, Risk ratio.

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Stallones, 2008; Salvi et al., 2003). The largest of these was a longitudinal study of about 600 farmers and their spouses in Colorado (Beseler and Stallones, 2008). In that study, depression was assessed annually for three years using the Center for Epidemiological Studies-Depression Scale (Beseler and Stallones, 2008), which assesses depression during the past week (Radloff, 1977). Farmers and their spouses who reported past pesticide poisoning at baseline were twice as likely to be classified as depressed during follow-up compared to those who did not report pesticide poisoning (Beseler and Stallones, 2008). However, associations for women were not reported separately from men in that study and associations between depression and specific pesticides, pesticide classes, or chronic, low-dose pesticide exposure were not assessed.

Four studies have evaluated pesticide exposure and depression in women (Bazylewicz-Walczak et al., 1999; Beseler et al., 2006; Carruth and Logan, 2002; Meyer et al., 2010). Bazylewicz-Walczak et al. (1999) administered the Profile of Mood States to 51 women working in the gardening industry in Poland (26 exposed to organophosphate insecticides for one season, March–June, and 25 not exposed) and found exposed women experienced greater tension, depression, and fatigue compared to unexposed women. A cross-sectional survey of 657 randomly sampled farm women in Louisiana found that women who reported pesticide use were more likely to report depressive symptoms than those who did not use pesticides (Carruth and Logan, 2002). Residents of an agricultural area of Brazil with an intensive use of pesticides had higher rates of hospitalization for mood disorders (*International Classification of Diseases, 10th Revision* codes F30-F39) than two reference areas (Meyer et al., 2010). In the Agricultural Health Study, wives who had ever received a physician-diagnosis of pesticide poisoning were more likely to report ever receiving a physician-diagnosis of depression than those without pesticide poisoning (Beseler et al., 2006). Relationships between specific pesticides and depression were not evaluated in any of these studies.

The Agricultural Health Study is a prospective cohort study of 57,310 licensed pesticide applicators (private and commercial) in Iowa and North Carolina and 32,345 spouses of private applicators. It was designed to assess associations between pesticides and other agricultural hazards and cancer and non-cancer endpoints (Alavanja et al., 1996). In addition to the study of wives (Beseler et al., 2006), a higher prevalence of depression was previously reported among male private pesticide applicators in the Agricultural Health Study who experienced a past pesticide poisoning or who reported ever using pesticides from several different pesticide classes (Beseler et al., 2008). Neither study, however, evaluated relationships between specific pesticides and depression and both used cross-sectional designs (Beseler et al., 2006, 2008). The current analysis evaluates associations between both general and specific pesticide use and self-reported, incident depression among wives in the Agricultural Health Study.

2. Materials and methods

2.1. Study population and case definition (Fig. 1)

The Agricultural Health Study cohort was assembled in 1993–1997 by enrolling pesticide applicators who were at state facilities to receive or renew their pesticide-use licenses (Alavanja et al., 1996); 84% of eligible applicators enrolled by completing a questionnaire. Additional questionnaires were sent home with married private applicators to enroll their spouses (Alavanja et al., 1996); 32,345 spouses (75% of those eligible) enrolled. We excluded 4380 spouses from this analysis because they were male (219; < 1%), reported having been diagnosed with depression by a physician at enrollment (2252; 7%; prevalent depression), were missing data on depression at enrollment (1345; 4%), or were missing covariate data (564; 2%).

Incident depression was ascertained through a follow-up telephone interview completed in 2005–2010. On average, the time between enrollment in the Agricultural Health Study and the follow-up interview was 11.9 years. Of 27,965 eligible wives, 10,639 (38%) did not complete the follow-up interview (1342 because of death). We further excluded 433 wives because they reported an age at depression diagnosis prior to their age at enrollment in the Agricultural Health Study (402; 1%; prevalent depression) or were missing data on age at depression diagnosis (31; < 1%). In total, we included 16,893 wives in this analysis: 1054 (6%) who reported ever having been diagnosed with depression (incident depression cases) and 15,839 (94%) who did not (non-cases) (Fig. 1).

Information on depression was ascertained using four different questions (Agricultural Health Study, 2012). Prevalent depression was ascertained via the enrollment questionnaire using the question "Has a DOCTOR ever told you that you had (been diagnosed with)…[d]epression requiring medication? (No, Yes)". Incident depression was ascertained through a follow-up telephone interview via the question "Have you ever been diagnosed with depression? (No, Yes)". Age at depression diagnosis was ascertained at follow-up via the question "How old were you when you were first diagnosed with depression? (years)". We assigned any wife who reported an age at depression diagnosis that was less than her age at enrollment to have prevalent depression. Treatment of depression with medications was ascertained among incident cases at follow-up via the question "Are you currently taking any prescribed medicines for depression? (No, Yes)". We used all incident depression cases for our main analyses, but conducted a sensitivity analysis in which we refit models restricting incident depression cases to wives who had taken medication for their depression.

The Agricultural Health Study was approved by the Institutional Review Boards of the National Institutes of Health and its contractors; the current analysis involving coded data was exempted from review by the Institutional Review Board of the University of North Carolina at Chapel Hill. All participants provided implied informed consent by completing and returning the enrollment questionnaires after the study was explained to them.

2.2. Exposure assessment

Information on demographics, medical conditions, lifestyle, pesticide use, and other agricultural hazards and practices was collected from wives and their applicator husbands via self-administered questionnaires at enrollment in the Agricultural Health Study (Agricultural Health Study, 2012; Alavanja et al., 1996). Exposure variables used in this analysis included wives' and husbands' ever use of (1) any pesticide, (2) 11 pesticide classes (four functional: fumigants, fungicides, herbicides, and insecticides; and seven chemical: carbamates, chloroacetanilide herbicides, organochlorine insecticides, organophosphate insecticides, phenoxy herbicides, pyrethroid insecticides, and triazine herbicides), and (3) 50 individual pesticides. We present results for only those pesticides for which there were at

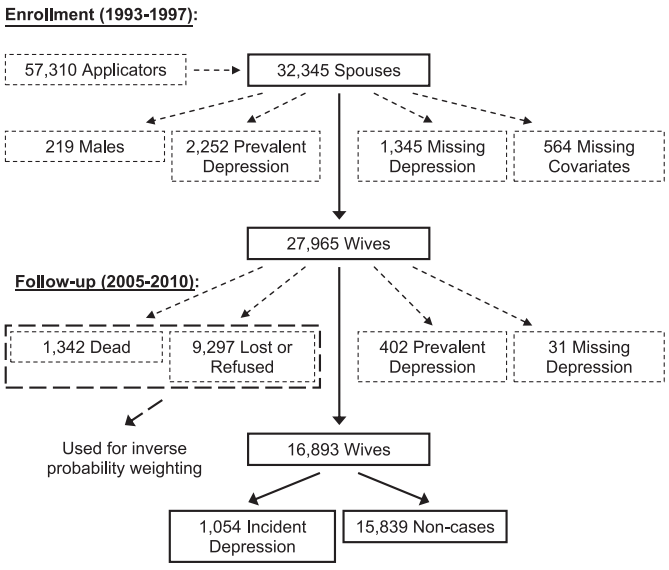

Fig. 1. Flow diagram depicting the study population for an analysis of pesticide use and self-reported, incident depression in wives from Iowa and North Carolina enrolled in the Agricultural Health Study. Boxes or lines marked with solid lines represent individuals who remained in the study after each step shown, whereas boxes or lines marked with small dashes represent individuals who were excluded after each step shown (see Section 2.1 for more details). Boxes or lines marked with large dashes represent individuals who, although not directly included in the analysis, were incorporated into the analysis via inverse probability weighting (see Section 2.3 for more details).