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Organic solvent exposure and depressive symptoms among licensed pesticide applicators in the Agricultural Health Study

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Abstract

Purpose—Although organic solvents are often used in agricultural operations, neurotoxic effects of solvent exposure have not been extensively studied among famers. The current analysis examined associations between questionnaire-based metrics of organic solvent exposure and depressive symptoms among farmers.

Methods—Results from 692 male Agricultural Health Study participants were analyzed. Solvent type and exposure duration were assessed by questionnaire. An "ever-use" variable and years of use categories were constructed for exposure to gasoline, paint/lacquer thinner, petroleum distillates, and any solvent. Depressive symptoms were ascertained with the Center for Epidemiologic Studies Depression Scale (CES-D); scores were analyzed separately as continuous (0-60) and dichotomous (<16 versus ≥ 16) variables. Multivariate linear and logistic regression models were used to estimate crude and adjusted associations between measures of solvent exposure and CES-D score.

Results—Forty-one percent of the sample reported some solvent exposure. The mean CES-D score was 6.5 (SD=6.4; median=5; range=0 – 44); 92% of the sample had a score below 16. After adjusting for covariates, statistically significant associations were observed between ever-use of any solvent, long duration of any solvent exposure, ever-use of gasoline, ever-use of petroleum distillates, and short duration of petroleum distillate exposure and continuous CES-D score ($p<0.05$). Although nearly all associations were positive, fewer statistically significant associations were observed between metrics of solvent exposure and the dichotomized CES-D variable.

Conclusions—Solvent exposures were associated with depressive symptoms among farmers. Efforts to limit exposure to organic solvents may reduce the risk of depressive symptoms among farmers.

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Keywords

Farmers; organic solvent exposure; depressive symptoms; CES-D; epidemiology

INTRODUCTION

In 1983, the National Institute for Occupational Safety and Health (NIOSH) classified neurotoxic disorders among the ten leading causes of work-related disease (NIOSH 1988). Despite such recognition, neurotoxicity continues to be an important occupational health problem among working people for a number of reasons, including (i) the large number of industrial chemicals characterized by neurotoxic properties; (ii) the vulnerability of nervous system tissue to injury; (iii) the large number of workers exposed to neurotoxic substances; and (iv) the importance of a healthy nervous system for purposeful daily functioning and overall quality of life. Furthermore, chronic central nervous system (CNS) impairment is also a risk factor for acute workplace injuries (NIOSH 1988). The agricultural industry provides workers with opportunity for exposure to various neurotoxic substances, including pesticides and organic solvents (Bunn et al. 2009; Monat-Descamps and Deschamps 2012). Although pesticides have been studied among agricultural producers, there is little research that focuses on neurological effects, including depressive symptoms, of exposure to organic solvents among them.

Farmers are known to experience higher rates of depression and anxiety in comparison to non-farmers (Browning et al. 2008; Hounsome et al. 2012; Torske et al. 2016a; Torske et al. 2016b). Estimates of depression prevalence among farmers have ranged from 8% to 20%, compared to a national prevalence of approximately 8% (Beseler et al. 2008; CDC 2012). Exposure to neurotoxic substances, one potential risk factor for mood disorder, can be mitigated with appropriate engineering controls, work practices, and use of personal protective equipment.

Organic solvents are found in many commercially available products including paints, varnishes, lacquers, stains, glues, adhesives, fuels, and cleaning/degreasing agents (NIOSH 1987; NIOSH 1988). Due to their lipid-solubility, solvents are readily absorbed following dermal and respiratory exposure and cross the blood-brain barrier. Both organic solvents and their metabolites (which can have greater toxicity than their parent compounds), accumulate in lipid-rich tissues such as those found in the nervous system (ATSDR 1995; NIOSH 1987). Long-term occupational exposure to organic solvents has been associated with cognitive impairment and adverse effects on mood (Monat-Descamps and Deschamps 2012; van der Hoek et al. 2000; van Valen et al. 2009; Visser et al. 2011). Workers who are regularly exposed to organic solvents have also been shown to be at a higher risk of CNS disorders than similar but otherwise unexposed workers (NIOSH 1987).

Studies of neurotoxic effects of chemical exposures among farmers have focused on mainly pesticide exposure (Beseler and Stallones 2003; Freire and Koifman 2013; Starks et al. 2012a; Starks et al. 2012b; Starks et al. 2012c). Furthermore, some studies have linked pesticide use and depression in agricultural populations (Beard et al. 2013; Beard et al. 2014; Beseler and Stallones 2008; Beseler et al. 2008). However, maintenance and repair of farm buildings, machinery, and equipment are common tasks performed by farmers, often requiring the use of solvent-based products (e.g., paints, adhesives, degreasers, lubricants, pesticide additives) (Amshoff and Reed 2005; Bunn et al. 2009; Wu et al. 2003). Furthermore, in the era of highly mechanized agriculture, farmers are regularly exposed to internal combustion engine fuels. While studies of solvent exposures among agricultural workers have examined a few health outcomes (Coble et al. 2003; Hoppin et al. 2004), those focusing on neurotoxic effects of solvent exposures are infrequent (Cole et al. 1997).

While research on the effects of solvent exposure among agricultural workers is limited, the neurotoxic manifestations of solvent exposure have been studied among workers in other occupations (Furu et al. 2012). However, these studies of neurological effects, particularly of mood and depressive symptoms, among non-agricultural populations have shown inconsistent results (Bowler et al. 2001; Escalona et al. 1995; Nordling Nilson et al. 2010; Satoh et al. 1996; Saygun et al. 2012).

The aim of the current cross-sectional analysis was to examine associations between questionnaire-based metrics of organic solvent exposure and a well-established measure of depressive symptoms (the Center for Epidemiologic Studies Depression Scale (CES-D)) (Radloff 1977). These results may provide insight into an additional risk factor for mood disorders among members of this vulnerable population.

METHODS

We studied associations between self-reported organic solvent use and CES-D scores among a subsample of participants enrolled in the AHS, a large prospective study of licensed pesticide applicators in Iowa and North Carolina (Alavanja et al. 1996). Between 1993 and 1997, 52,394 private applicators enrolled in the AHS by completing a self-administered questionnaire at the time of state-based pesticide licensing and certification and a second self-administered questionnaire within one month of enrollment. Two follow-up phone interviews were subsequently administered to AHS participants between 1999–2003 and 2005–2010. AHS questionnaires and interviews collected information on demographic/lifestyle characteristics, pesticide exposure, other occupational behaviors/exposures, and health conditions. Copies of AHS questionnaires are available online (AHS 2016).

Study participants

A detailed description of participant sampling methods has been published previously (Starks et al. 2012b) and is described here briefly. Private pesticide applicators were invited to participate in the present neurobehavioral study if they had completed all previous AHS questionnaires and interviews, resided in Iowa or North Carolina, and lived within approximately 150 miles of the testing facilities. AHS participants were ineligible for inclusion in the current study if they had previously reported stroke, amyotrophic lateral sclerosis, multiple sclerosis, Parkinson’s disease, retinal or macular degeneration, hypothyroidism or diabetes or if they reported drinking 42 or more alcoholic beverages per week. The sample was limited to participants who were farming at the time of AHS enrollment. We also excluded women because they represented less than 1% of licensed pesticide applicators in the AHS cohort. A total of 1,807 male AHS participants were initially eligible to participate in the present study of which 759 (42%) agreed to participate and were scheduled for neurobehavioral testing. Of these, 58 participants either cancelled or failed to attend their scheduled appointment. In total, 701 individuals were available to participate for an overall response rate of 39 percent. Of these, 692 completed the CES-D.

Testing was conducted between November 2006 and March 2008. The study was approved by all relevant Institutional Review Boards. Written informed consent was obtained from all individual participants included in the study.

Outcome Measure

Information on depressive symptoms was collected using the CES-D, a widely-used self-report scale designed to evaluate current level of depressive symptomology related to depressed affect, positive affect, somatic and retarded activity, and interpersonal relations (Radloff 1977). The scale has consistently demonstrated high validity, reliability, and internal consistency. When completing the CES-D, which was computer-administered in a private room, participants were asked to "please indicate how often you've felt this way during the past week" for each of 20 items representing personal feelings or behaviors. The frequency of the experience was captured on a Likert scale with 0 representing "rarely" or "none" of the time and 3 representing "most" or "all of the time" (5-7 days). CES-D summary scores range can range from 0 to 60 with higher scores indicating greater levels of depressive symptoms. Because of the tendency for CES-D score distributions to be right skewed, $\log_{10}$-transformed CES-D score values were used in all linear regression models to normalize residuals. In addition, because a CES-D score of 16 or higher is considered indicative of a high risk for clinical depression or need for treatment (Radloff 1977; Stallones and Beseler 2002), a dichotomous depression variable was created (i.e., a score of below 16 indicated low-risk for depression and a score of 16 or above indicated high-risk for depression) for use in logistic regression analyses.

Organic Solvent Exposure Assessment

Organic solvent exposure was assessed at the time of CES-D testing with an investigator-administered questionnaire designed to ascertain ever-use and years of use (from start and stop dates) of six common organic solvents: gasoline, paint/lacquer thinner, turpentine, benzene, toluene, and petroleum distillates. Specifically, the question was phrased: "Have you ever worked with or been exposed to any of the following chemicals for 8 hours a week or more in a past job, your present job, or at home (i.e. hobbies)." Two summary variables were created from these solvent use questions: ever-use of any organic solvent and total years of use of any organic solvent. From the total years of use of each organic solvent variable, categories of years of use were created based on the median number of years of use among those reporting ever-use of the solvent. This categorization strategy resulted in a three level categorical variable with categories of never-use (referent), years of use at or below the median (i.e., "short duration"), and years of use above the median (i.e., "long duration"). The number of respondents specifically reporting use of benzene, toluene, and turpentine was not large enough to be included in individual analysis of these solvents (N=18, 11, and 5, respectively). Three dichotomous solvent exposure variables collected at the time of AHS enrollment were also included in the analyses: ever-use of solvent additives when personally mixing pesticides; ever-use of gasoline to clean hands or equipment; and ever-use of other solvents for general cleaning purposes. Thus, in total, seven ever-use variables and four categorical years of use variables were included in the analyses.

Statistical Analysis

Covariates considered for potential confounding of the association between metrics of organic solvent exposure and CES-D scores were state of residence (NC and IA), age in years, education, marital status, smoking status, alcohol use, co-exposures (i.e., $\log_{10}$-transformed cumulative organophosphate exposure or $\log_{10}$-transformed cumulative all-pesticide exposure, ever exposure to welding, and ever exposure to soldering), and head injury. Personal protective equipment (PPE) was included as a marker of general safety practices using information from AHS questions related to PPE use during pesticide handling. High pesticide exposure events (HPEE), or incidents while using any pesticide which caused an unusually high personal exposure (Alavanja et al. 1999), were likewise considered for potential confounding.

Univariate analyses were used to explore the distribution of CES-D scores (both as continuous and high- vs. low-risk dichotomous variables), solvent exposure metrics, and covariates across the entire sample with frequencies and percentages or means/medians and standard deviations/ranges reported.

Crude and multivariable (i.e., adjusted) beta coefficients with standard errors and p-values were estimated for the linear relationships between each solvent variable and $\log_{10}$ CES-D score. A standard procedure was used to select covariates for inclusion in the multivariable models. First, linear regression analyses were used to examine bivariate associations between each candidate covariate and the $\log_{10}$-transformed CES-D score. Covariates that were individually associated with the $\log_{10}$-transformed CES-D score with a p-value of less than 0.20 were then included simultaneously in an initial multiple linear regression model. Variables associated with $\log_{10}$ CES-D score with a p-value of 0.20 or greater were then removed sequentially until only those with $p<0.20$ remained. The covariates retained in this reduced model were subsequently included in all multivariable linear regression models of associations between organic solvent exposure variables and $\log_{10}$ CES-D scores. The few participants with missing values for variables were excluded from multivariable models. Similarly, logistic regression methods were used to examine associations between metrics of organic solvent exposure and the dichotomous depression outcome variable (i.e., high-risk vs. low-risk). A method analogous to the linear regression base model selection procedure was repeated for the logistic regression analyses. Crude and multivariable odds ratios (ORs) with 95% confidence intervals (CIs) were estimated for the relationships between each solvent exposure and the dichotomized depression risk status. Lastly, tests for linear trend were performed for the categorical exposure variables to characterize possible exposure-response relationships between levels of exposure duration and CES-D results in both the linear and logistic analyses.

All statistical analyses were conducted using SAS software (versions 9.3 and 9.4; SAS Institute Inc., Cary, NC).

RESULTS

The demographic characteristics of all farmers who participated in the study are provided in Table 1. By design, approximately half of participants were from Iowa (51%) and half from North Carolina (49%). The mean age was 61 years (SD=11.6) and 50% of the sample had at least a high school education. A large majority of participants were married or living as married (88%). A majority of the participants were never smokers (58%), reported drinking zero alcoholic drinks per week (57%), reported using PPE for pesticide use (86%), and had not experienced a head injury (76%). With regard to co-exposures, the geometric mean lifetime exposure to all organophosphate pesticides was 195.28 days (GSD=4.0) (with n=673 reporting ever-use of an organophosphate pesticide) and 988.69 days (GSD=2.9) for all pesticides (ever-use n=691); 77% of participants had not experienced a high pesticide exposure event (HPEE), 19% reported welding exposure, and 5% reported soldering.

The mean CES-D score was 6.5 (SD=6.4; median=5; range=0 – 44). When applying the threshold of a score of less than 16 vs. 16 or greater, 92% (n=634) of the sample met criteria for low-risk of depression and 8% (n=58) met criteria for high-risk of depression.

Forty-one percent of the sample reported some solvent exposure (Table 2), with gasoline exposure most common (32%), followed by petroleum distillates (25%), and paint thinner (11%). Exposures to benzene, toluene, and turpentine were each reported by less than 3% of the sample and were not included in solvent-specific analyses. At enrollment, 10% of participants reported using solvent additives when mixing pesticides, 40% reported using gasoline to clean hands or equipment, and 28% reported using other solvents for general cleaning purposes.

Crude and adjusted associations between solvent exposure variables and continuous CES-D scores were comparable (linear regression results, Table 3). All estimates revealed a positive association between both ever-use and duration of use and depressive symptoms ascertained with the CES-D. After adjusting for age, state, marital status, and HPEE, statistically significant ($p<0.05$) associations were observed between CES-D score and ever-use of any solvents, long duration of any solvent exposure, ever-use of gasoline, ever-use of petroleum distillates, and short duration of petroleum distillate exposure. Neither the crude nor adjusted associations between the three solvent-use measures collected at enrollment (i.e., “using solvent additives when mixing pesticides”, “using gasoline to clean hands or equipment”, and “using other solvents to clean”) and CES-D score were statistically significant (Table 3).

Results from the logistic regression analysis (Table 3) showed fewer statistically significant associations between metrics of solvent exposure and the dichotomized CES-D outcome than were observed between metrics of solvent exposure and the continuous CES-D variable. Although many associations were not statistically significant, nearly all were positive (i.e., OR>1.0). After controlling for age, marital status, smoking, alcohol use, lifetime organophosphate pesticide use, and HPEE, participants reporting ever-use of any solvent had 1.79 times greater odds of being categorized as high-risk for depression than participants reporting never-use (95% CI: 1.02-3.13).

Results of the tests for trend (Table 3) are consistent with an exposure-response relationship between solvent exposure duration and CES-D score, particularly for duration of exposure to any solvent and duration of exposure to gasoline.

DISCUSSION

Metrics of exposure to any solvent, gasoline, and petroleum distillates were associated with CES-D score. Overall, similar associations were observed when CES-D was analyzed as a continuous measure than as a binary categorical measure although, as expected, the categorical results were not as statistically robust.

Although associations between solvent exposure and mental health outcomes have not been studied among agricultural workers, one study of a rural Ecuadorian population in which approximately 67% of the sample were farmers found no association between general solvent use and results obtained with the Profile of Mood States scale, although associations with other neurobehavioral outcomes were demonstrated (Cole et al. 1997). The current study, however, found several associations between more specific solvent use measures and depressive symptoms among members of an all-farming sample. Although some studies in other industries have found null effects (Satoh et al. 1996; Saygun et al. 2012), there is evidence supporting associations between solvent exposure and impaired mental health as measured by a variety of scales (Bowler et al. 2001; Escalona et al. 1995; Nordling Nilson et al. 2010).

Overall, the results of the current study support the conclusion that exposure to organic solvents is associated with adverse effects on depressive symptoms among farmers. First, virtually all estimates of association were positive, regardless of statistical significance. Second, exposure-response relationships were observed for several solvents. Third, as described above, studies of solvent exposure conducted in other industries support this conclusion. Although the effects of exposure on CES-D score were modest, it is important to recognize that such exposures potentially represent modifiable risk factors for depression and an opportunity for early intervention among farmers, who are known to be at increased risk for depression.

There were several strengths to the current study. First, the relatively large sample size of farmers representing various farming practices and commodities allowed for greater statistical power and assessment of exposure-effect gradients. Second, because the CES-D can be analyzed as a continuous measure, this study may have more statistical power to identify subtle mood effects of solvent exposure in comparison to studies using clinically-diagnosed depression as the health outcome (Burbacher 1993). Third, a widely-used, valid, reliable, and consistent metric (the CES-D) was used to assess depressive symptoms allowing for comparison to other studies using this instrument (Letz et al. 2003; Letz et al. 1996; Radloff 1977). Fourth, exposure assessment using questionnaires can better characterize long-term cumulative or low-level exposures than can environmental sampling or biomarker data capturing exposure information at only one given point in time. In addition, task-based exposure measures (i.e., use of individual solvents, mixing solvents with pesticides and use of gasoline/solvents to clean) may better characterize all potential routes of exposure, including inhalation and dermal absorption of solvents, than traditional measures of solvent concentrations in breathing zone air.

There are also limitations to the current study. The analysis used a cross-sectional design among farmers who had been working in agriculture for many decades. Baseline depressive symptomology was unavailable and CES-D results were obtained at the same time as a majority of the solvent exposure measures. Although it is possible that farmers experiencing depression might have over-reported exposure in comparison to those not experiencing depression, we have no basis to believe that such differential error occurred. Such exposure information error would bias the observed associations away from the null.

Because exposure information was self-reported, error (misclassification) in exposure estimation may have occurred due to poor recall, which could bias results toward the null. Although the validity of self-reported estimates of solvent exposure is not known, several studies have shown that recall of pesticide use among farmers does agree with both expert judgment and biological sampling (Blair et al. 2002; Engel et al. 2001; Fritschi et al. 1996; Hoppin et al. 2002). Thus, there is reason to believe that members of this study population are able to provide valid estimates of past occupational exposures.

Another limitation of the current study is the potential for some minimal exposure (and health effect) among those categorized as “never” exposed. In particular, solvent exposure of less than eight hours of use per week was defined as non-use. Thus, participants who may have used solvents for shorter durations were defined as never exposed, although they may still have had some exposure and some health effects. This potential misclassification would result in an attenuation of the strength of the observed effects in comparison to the true effects of organic solvent exposure.

There is minimal risk for differential error in outcome estimation because the CES-D was administered by trained personnel blinded to participant exposure status. However, the CES-D scale assesses depressive symptoms experienced over a seven-day period (i.e., current mood state); and depressed mood is not static over time (Beseler and Stallones 2008; Nordling Nilson et al. 2010; Radloff 1977). On the other hand, previous research has found associations between CES-D results and pesticide poisoning experienced up to three years before (Beseler and Stallones 2008). We believe that the potential for some depressive effects to have been missed by the limited CES-D time window would occur equally across solvent exposure strata and not create the appearance of an association if one did not truly exist, and would otherwise weaken observed associations.

Selection bias may have affected the current study sample. While participation from Iowa and North Carolina does present a broad range of farm and personal characteristics, only those persons pursuing restricted-use pesticide certification were enrolled and only those residing within 150 miles of neurobehavioral testing facilities were eligible. Therefore, farmers who do not use pesticides, live in more rural/remote areas, or are financially disadvantaged and have no reliable means of transportation may not have been included in the sample. Work practices leading to lower exposures to a wide range of occupational hazards may have been more common in this population relative to other occupational groups because of the training/testing in safe handling of pesticides required to obtain a license to use restricted-use pesticides, which was the basis for recruiting AHS participants (Alavanja et al. 1996). Therefore, solvent exposure per unit time of solvent use may be lower among workers licensed to use pesticides than those without such licensing.

Additionally, a healthy worker effect must be considered in interpreting results, as those with moderate-to-severe depression or adverse neurological symptoms may not be working or may not have completed all phases of the AHS (i.e., remained enrolled for at least 10 years), and subsequently been ineligible for participation in the parent study. In addition, because of the long duration of exposure, it is possible that the persons most affected by exposure were unable to participate in the study. Such selective-survival would result in an attenuation of observed associations in comparison to true associations. However, a previous study of this population found that participants reporting depression at enrollment were equally likely to drop out by the first follow-up as non-depressed participants, suggesting loss to follow-up during this time period was minimally selective (Montgomery et al. 2010). Lastly, though the response rate for the current study was modest (39%), a previously published study documented that participants of the current study were comparable to non-participants across many demographic characteristics (Starks et al. 2012a).

Employing a large number of statistical tests may result in the observation of significant associations due to chance alone (alpha error). Statistical adjustments were not made when analyzing the results of the current study. However, as discussed previously, because virtually all associations, both significant and non-significant, were positive (i.e., greater exposure was associated with greater adverse effect), and because several statistically significant tests for liner trend were also observed, it is very unlikely that the effects observed were due to chance alone.

In conclusion, the results of the current analysis demonstrate an association between organic solvent exposure and depressive symptoms. Depression is a major adverse health effect among agricultural producers. Occupational exposure to organic solvents is a modifiable risk factor. Consequently, the results of the current study justify additional efforts to limit occupational exposure to organic solvents (primary prevention) and may also justify greater scrutiny of possible exposure to neurotoxicants among persons either who have mild depressive symptoms or who are diagnosed with clinically overt depression.

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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Table 1

Demographic characteristics

	n	%
State		
Iowa	354	51.16
North Carolina	338	48.84
Education		
<High School	348	50.29
High School+	344	49.71
Marital status[a]		
Married	612	88.44
Single/Divorced/Widowed	77	11.13
Smoking		
Never	400	57.80
Current	46	6.65
Past	246	35.55
Alcohol use		
0 drinks/week	397	57.37
1-7 drinks/week	226	32.66
>7 drinks/week	69	9.97
Personal protective equipment (PPE)		
No	96	13.87
Yes	596	86.13
Head injury		
No	528	76.30
Yes- No loss of consciousness	70	10.12
Yes- Loss of consciousness	94	13.58
Welding exposure		
No	558	80.64
Yes	134	19.36
Soldering exposure		
No	657	94.94
Yes	35	5.06
High pesticide exposure event (HPEE)		
No	533	77.02
Yes	159	22.98
	Mean	**SD**

	n	%
Age	61.21	11.64
Cumulative lifetime days of organophosphate pesticide exposure[b]	195.28	4.02
Cumulative lifetime days of total pesticide exposure[b]	988.69	2.94

SD: Standard deviation

[a]Missing values n=3

[b]Geometric mean and geometric standard deviation for ever-use values; n=673 for cumulative organophosphate pesticide exposure; n=691 for cumulative total pesticide exposure

Table 2

Solvent exposure duration categories

	n	%
Any solvents		
Never use	411	59.39
Ever use	281	40.61
Short duration (1–36 years)	143	20.66
Long duration (>36 years)	138	19.94
Gasoline		
Never use	475	68.64
Ever use	217	31.36
Short duration (1–21 years)	111	16.04
Long duration (>21 years)	106	15.32
Paint thinner		
Never use	616	89.02
Ever use	76	10.98
Short duration (1–17 years)	39	5.64
Long duration (>17 years)	37	5.35
Petroleum distillates		
Never use	520	75.14
Ever use	172	24.86
Short duration (1–30.5 years)	84	12.14
Long duration (>30.5 years)	88	12.72
Solvents in pesticides	72	10.40
Gasoline to clean[a]	278	40.17
Solvents to clean[a]	190	27.46

SD: Standard deviation

[a]Missing values n<17

Table 3

Relationship between solvent exposures and CES-D score (n=692)

	Linear regression results (log_{10}-transformed CES-D score)						Logistic regression results (CES-D score of 16+ vs. <16)			
	Crude			Adjusted[a]			Crude		Adjusted[b]	
	Beta (SE)	p-value	p for trend	Beta (SE)	p-value	p for trend	OR (95% CI)	p for trend	OR (95% CI)	p for trend
Any solvents										
Ever vs. never	**0.08 (0.03)**	**0.01**		**0.07 (0.03)**	**0.04**		**1.90 (1.11, 3.27)**		**1.79 (1.02, 3.13)**	
Never use	Ref.		**0.01**	Ref.		**0.03**	Ref.	**0.03**	Ref.	**0.05**
Short duration (1–36 years)	0.06 (0.04)	0.12		0.05 (0.04)	0.24		1.87 (0.97, 3.59)		1.70 (0.86, 3.34)	
Long duration (>36 years)	**0.10 (0.04)**	**0.01**		**0.09 (0.04)**	**0.03**		**1.94 (1.01, 3.74)**		1.90 (0.95, 3.80)	
Gasoline										
Ever vs. never	**0.08 (0.03)**	**0.01**		**0.07 (0.04)**	**0.04**		1.61 (0.93, 2.79)		1.52 (0.86, 2.70)	
Never use	Ref.		**0.01**	Ref.		**0.05**	Ref.	0.07	Ref.	0.10
Short duration (1–21 years)	0.08 (0.04)	0.06		0.07 (0.04)	0.14		1.43 (0.70, 2.91)		1.28 (0.61, 2.67)	
Long duration (>21 years)	**0.09 (0.04)**	**0.04**		0.08 (0.04)	0.07		1.81 (0.92, 3.57)		1.82 (0.89, 3.69)	
Paint thinner										
Ever vs. never	0.07 (0.05)	0.15		0.06 (0.05)	0.18		1.55 (0.73, 3.31)		1.47 (0.68, 3.21)	
Never use	Ref.		0.13	Ref.		0.17	Ref.	0.13	Ref.	0.19
Short duration (1–17 years)	0.05 (0.07)	0.42		0.05 (0.07)	0.45		0.96 (0.29, 3.25)		0.94 (0.27, 3.26)	
Long duration (>17 years)	0.09 (0.07)	0.19		0.08 (0.07)	0.23		2.24 (0.89, 5.63)		2.06 (0.79, 5.35)	
Petroleum distillates										
Ever vs. never	**0.09 (0.03)**	**0.01**		**0.08 (0.04)**	**0.03**		1.53 (0.86, 2.73)		1.34 (0.73, 2.45)	
Never use	Ref.		**0.02**	Ref.		0.06	Ref.	0.41	Ref.	0.79
Short duration (1–30.5 years)	**0.11 (0.05)**	**0.02**		**0.10 (0.05)**	**0.04**		**2.06 (1.03, 4.11)**		1.90 (0.92, 3.92)	
Long duration (>30.5 years)	0.08 (0.05)	0.09		0.07 (0.05)	0.16		1.07 (0.46, 2.47)		0.87 (0.36, 2.08)	
Solvents in pesticides (yes vs. no)	0.00 (0.05)	>0.99	–	0.03 (0.05)	0.59	–	1.67 (0.78, 3.55)	–	2.22 (0.99, 4.94)	–

	Linear regression results (log_{10}-transformed CES-D score)						Logistic regression results (CES-D score of 16+ vs. <16)			
	Crude			Adjusted[a]			Crude		Adjusted[b]	
	Beta (SE)	p-value	p for trend	Beta (SE)	p-value	p for trend	OR (95% CI)	p for trend	OR (95% CI)	p for trend
Gasoline to clean (yes vs. no)	0.03 (0.03)	0.36	–	0.03 (0.03)	0.37	–	1.36 (0.77, 2.39)	–	1.48 (0.83, 2.67)	–
Solvents to clean (yes vs. no)	0.02 (0.03)	0.63	–	0.00 (0.03)	0.89	–	1.28 (0.70, 2.34)	–	1.19 (0.64, 2.22)	–

SE: Standard error; Ref.: Referent; OR: Odds ratio

[a] Adjusted for state, age, marital status, and HPEE

[b] Adjusted for age, marital status, smoking, alcohol use, lifetime organophosphate pesticide exposure, and HPEE

Bolded if $p < 0.05$