Depression Prevalence and Exposure to Organophosphate Esters in Aircraft Maintenance Workers

Jennifer E. Hardos; Lawrence W. Whitehead; Inkyu Han; Darrin K. Ott; D. Kim Waller

INTRODUCTION: Previous studies found that aircraft maintenance workers may be exposed to organophosphates in hydraulic fluid and engine oil. Studies have also illustrated a link between long-term low-level organophosphate pesticide exposure and depression.

METHODS: A questionnaire containing the Patient Health Questionnaire 8 depression screener was e-mailed to 52,080 aircraft maintenance workers (with $N = 4801$ complete responses) in a cross-sectional study to determine prevalence and severity of depression and descriptions of their occupational exposures.

RESULTS: There was no significant difference between reported depression prevalence and severity in similar exposure groups in which aircraft maintenance workers were exposed or may have been exposed to organophosphate esters compared to similar exposure groups in which they were not exposed. However, a dichotomous measure of the prevalence of depression was significantly associated with self-reported exposure levels from low (OR: 1.21) to moderate (OR: 1.68) to high exposure (OR: 2.70) and with each exposure route including contact (OR: 1.68), inhalation (OR: 2.52), and ingestion (OR: 2.55). A self-reported four-level measure of depression severity was also associated with a self-reported four-level measure of exposure.

DISCUSSION: Based on self-reported exposures and outcomes, an association is observed between organophosphate exposure and depression; however, we cannot assume that the associations we observed are causal because some workers may have been more likely to report exposure to organophosphate esters and also more likely to report depression. Future studies should consider using a larger sample size, better methods for characterizing crew chief exposures, and bioassays to measure dose rather than exposure.

KEYWORDS: engine oil, hydraulic fluid, aircraft maintenance, major depressive disorder.

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Aircraft turbine oils and hydraulic fluids often contain mixtures of tricresyl phosphate (TCP), tributyl phosphate (TBP), and triphenyl phosphate (TPP), which lubricate better than water and provide antiwear and anticorrosion properties at high temperatures.[17,20] These organophosphate esters act as cholinesterase inhibitors and interfere with normal nervous system functions.[1] The possibility has been raised that these chemicals are responsible for causing certain symptoms in aircrew. Engine bleed air is typically routed into the cockpit and cabin to pressurize or supply breathing air; this unfiltered air may contain heated or burned chemical components of turbine oil or hydraulic fluid.[8,21] It is believed to cause short-term effects like tremors, nausea, dizziness, and muscle weakness, and also long-term issues such as memory loss, fatigue, and sleep disorders with chronic exposure.[12] A less understood syndrome suspected in lower-level exposures is termed chronic organophosphate induced neuropsychiatric disorder, or COPIND. This condition involves neurological and behavioral symptoms, including personality change, mood destabilization, suicidal thoughts,

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and memory and attention impairment.[5] While there is significant research on cabin air contamination,[6,12,16] there is also concern regarding occupational exposures among individuals who work in aircraft maintenance because their exposure may exceed that of aircrew. Aircraft maintenance workers, known in the Air Force as aircraft maintainers, may be exposed to organophosphate esters via inhalation or dermal contact.[6] Some maintenance activities involve high pressure, high temperature, and the potential for spills, increasing the potential for generation of oil mists. Contact with fluids is also a concern because TCP produces the same health effects when absorbed through the skin, unlike TBP and TPP. As of yet, there has been no research conducted on U.S. military aircraft maintainers with respect to organophosphate ester exposure, although a search of chemicals authorized for use on Air Force bases revealed 3697 active authorizations for chemicals containing TCP, triorthocresyl phosphate, TBP, or TPP in Air Force units (data available from EESOH-MIS database to those with access).

Another recent issue is the rate of suicide among aircraft maintainers in the U.S. Air Force. According to 2011 testimony to the U.S. House of Representatives Committee on Armed Services, the aircraft maintenance field has one of the two highest suicide rates of any Air Force career field.[10] From 2009 to 2012, 22% of Air Force suicides were aircraft maintainers.[15] Available research suggests a link between pesticide-based cholinesterase inhibitors and depression.[5,14] Gulf War syndrome, which often includes depressive symptoms, has been postulated to have been caused by exposure to organophosphorus pesticides or nerve agents.[4] However, there is currently no research available on the association between exposure to organophosphates in turbine oils and hydraulic fluids and depression. This study sought to characterize the association between workplace exposure to organophosphate esters and prevalence of depression in aircraft maintenance workers.

METHODS

Subjects

Subjects were recruited using an e-mail list for the total population of active duty aircraft maintainers in the U.S. Air Force in November 2015. Thus, subjects were active duty Air Force aircraft maintainers with a 2AXXX Air Force Specialty Code (XXX indicating various codes for subspecialties), or job code, who consented to participate in a web-based survey. The 2AXXX subspecialties include those who work in propulsion, hydraulics, aerospace maintenance (e.g., crew chiefs), aerospace ground equipment, communications and navigation systems, avionics, nondestructive inspection, structural maintenance, metals technology, electrical and environmental systems, and aircraft egress systems. Prior to commencement, the study was approved by Institutional Review Boards at both the Air Force Research Laboratory and the University of Texas School of Public Health.

Procedure

A web-based health symptom and work history survey containing the Patient Health Questionnaire 8 (PHQ-8) depression questionnaire was administered to a cross-sectional sample of military personnel who were working in the aircraft maintenance field. Sample size calculations were completed prior to administering the survey and determined that 96 responses were needed to determine the prevalence of depression with a margin of error of 10% with a 95% confidence level. The questionnaire also asked about typical exposure routes and severity over the previous year, medication use, and personal protective equipment use habits. The survey was sent via e-mail to the entire population of 51,955 individuals who were working in aircraft maintenance at the start of the survey, November 1, 2013. The survey period lasted 3 wk from November to December 2013, with a reminder sent out halfway through the survey period to encourage participation. The population at the end of the survey was 52,080.[11] The PHQ-8 depression questionnaire was used because the alternative, i.e., the PHQ-9 questionnaire, contains a suicidal ideation question that the Institutional Review Board considered too sensitive to be asked without reporting individuals who responded affirmatively. However, the PHQ-8 questionnaire has been shown to be an acceptable measure of depression when the suicidal ideation question cannot be asked.[22]

Statistical Analysis

Responses were first assessed for study eligibility (**Fig. 1**). Survey results were analyzed using STATA to compute depression scores for respondents based on the standard PHQ scoring instructions.[18] Scores were associated with a categorical depression level (none, mild, moderate, moderately severe, severe) based on pre-established cut points. To compute a dichotomous measure of depression, a cut-point of 10 was used in accordance with similar studies of depression and in accordance with the convention in the literature on depression.[9,13]

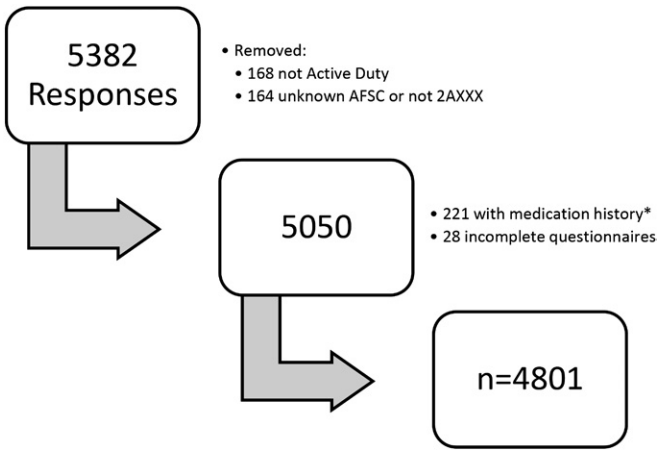

Fig. 1. Elimination of ineligible subjects from phase 2 survey respondents. *Atropine, scopolamine, amantadine (Symmetrel), bethanechol, tacrine (Cognex), Eserine, and physostigmine act on the cholinergic system. If a subject answered that he/she was taking one of these medications within the last year, he or she was excluded from the study.

Maintainers were grouped into similar exposure groups (SEGs) based on a review of their job descriptions, duties, and lists of chemical products authorized for use in their workplaces. The maintainers with jobs involving no expected exposure were grouped together in a separate SEG, while those involving expected exposures to organophosphates were grouped within SEGs describing their duties (hydraulics repair, engine maintenance, and crew chiefs). The "other" group—SEG 4—included workers in avionics, structural maintenance, metals technology, nondestructive inspection (X-ray of aircraft structure for cracks), communications/navigation, electronic warfare, and aerospace ground equipment maintenance. Maintainers in leadership positions were also included in the "other" category unless the individual had a propulsion- or hydraulic-specific leadership Air Force Specialty Code. Using a second grouping method, workers were also grouped by self-reported exposure route and exposure severity. Results were then analyzed to compute prevalence odds ratios for the association between exposure to organophosphates and depression. Odds ratios (OR) were computed separately for depression measured by job titles versus depression measured by exposure self-report on the questionnaire. Data were also analyzed to determine if exposed and unexposed workers differed in depression severity. A correlation test was performed to determine if any demographic variables were correlated. Additional logistic regressions were run to determine if any of the continuous variables of age, number of deployments, or years in the career field were independently associated with the dichotomous depression outcome. Age was separated by group according to the age groups that the Air Force uses to report demographics. The age groups used were 17–24, 25–34, 35–44, and 45+. Analysis was also performed involving the history of work in the hydraulics and propulsion fields, since some Air Force workers may switch career fields depending on Air Force staffing needs. Prevalence odds ratio was first examined for those who admitted to previous hydraulics or propulsion work but excluding all current hydraulics or propulsion workers.

RESULTS

Approximately 9.2% of the total maintenance worker population responded to the questionnaire. Participant age was similar for all SEGs, although slightly lower for hydraulic SEG respondents (**Table I**). This may be why they also had fewer years in their career field at the time of survey. Crew chiefs included fewer women than other groups, while the "other" SEG had the most women, at 8.1%. Crew chiefs also deployed more and had a larger percentage of workers who were single, divorced, or separated than the other groups. Compared to the entire population, the survey respondents were more likely to be women, more likely to be married, and more likely to be older.

The overall prevalence of any severity of depression in the respondents was 21.7% as measured by the PHQ-8 questionnaire. The exposed SEGs had a crude prevalence of 23% and the unexposed 20%, determined by self-reported depression. However, with the cut-point set at moderate or higher depression, the prevalence was 6.23%. Prevalence of a dichotomous depression variable was also investigated as a logistic regression using separate SEGs, with the "other" SEG as the reference. The propulsion and crew chief fields had a higher odds ratio than the unexposed; however, the *P*-values did not indicate significance. However, when exposure is separated by dichotomous self-reported exposure status (yes/no exposure), the prevalence OR is 2.67 [95% CI: (1.25,5.72); *P*-value = 0.011]. Prevalence odds ratios stratified by SEG were not statistically significant.

The only demographic variables with a high correlation were age and years in the career field, which is not a surprise because both are time related. Number of deployments, gender, and SEG were not highly correlated with each other or with age and time in field. This does not affect the interpretation of data. Statistical significance (*P*-value < 0.001) in logistic regression suggests that deployments may be important in prevalence of depression. Analysis of age shows a decreased or preventative odds of depression for the 45+ category [OR: 0.22; CI: (0.0295, 1.57); *P*-value = 0.129] but it is not significant.

Logistic regression of dichotomous depression outcome against marital status reveals that being legally separated is the only group with significantly elevated odds of depression [OR: 5.08; CI: (2.40,10.76); *P*-value < 0.001]. This fits with prior studies indicating that marital disruption increases depression risk.[2,3] Gender did not show a significant difference; however, the odds ratios [OR: 1.22; CI: (0.77,1.91); *P*-value = 0.395] were in line with the tendency for women to be more susceptible to depression.[23]

A multivariate model was run to determine which variables should be included in a final logistic regression. Marital status, gender, and SEG were categorical variables, while age, deployments, and years in the career field were continuous. Depression was a dichotomous dependent variable. Number of deployments [regression coeff: 0.09; CI: (0.04,0.15); *P*-value = 0.002] and marital status [legally separated coeff: 1.48; CI (0.71,2.26); *P*-value < 0.001] were determined to be associated with depression and included in the final model. The final model (**Table II**) demonstrated that none of the exposure SEGs based on phase 1 estimates were significantly related to depression prevalence. This indicates that the SEGs assigned do not have a higher prevalence of depression based on this survey.

Self-reported exposure routes were also investigated for association with the dichotomous depression outcome. Each perceived exposure pathway (air, ingestion, and dermal) was used as an independent variable in a logistic regression to compare with the presence or absence of depression (**Table III**). Likewise, workers were asked about their perceived exposure level, a categorical variable among all routes, that resulted in an increased association with depression as total exposure increased from low (OR: 1.21, 95% CI [0.78,1.88], *P*-value = 0.402) to moderate (OR: 1.68, 95% CI [1.09,2.58], *P*-value = 0.019) to high or frequent exposure (OR: 2.70, 95% CI [1.77,4.11], *P*-value = 0.000) after controlling for marital status and deployments.

Depression information was collected from a questionnaire designed to assess severity, so it was possible to also create a

Table I. Demographics of Participants in e-Mail Survey Stratified by Type of Work as Defined by SEG (Nov 2014).

DEMOGRAPHIC	2AXXX POPULATION*n (%)	OVERALL n (%) OR MEAN (95% CI)	SEG 1 PROPULSION n (%) OR MEAN (95% CI)	SEG 2 HYDRAULICS n (%) OR MEAN (95% CI)	SEG 3 CREW CHIEF n (%) OR MEAN (95% CI)	SEG 4 OTHER n (%) OR MEAN (95% CI)
Age	†	29.0 (28.9,29.2)	29.2 (28.7,29.8)	27.8 (26.9,28.6)	28.9 (28.6,29.2)	29.2 (28.9,29.5)
Gender						
Male	49,196 (94.5)	4503 (93.8)	437 (93.9)	171 (95)	1647 (96.3)	2248 (91.9)
Female	2884 (5.4)	298 (6.2)	28 (6.02)	9 (5)	64 (3.7)	197 (8.1)
Marital status						
Single	19,481‡ (37.4)	1417 (29.5)	127 (27.3)	63 (35)	500 (29.2)	727 (29.7)
Married	28,485 (54.7)	3038 (63.3)	309 (66.5)	108 (60)	1077 (62.9)	1544 (63.1)
Legally separated	†	39 (0.8)	4 (0.8)	0 (0)	19 (1.1)	16 (0.7)
Divorced	3114 (5.9)	307 (6.4)	25 (5.4)	9 (5)	115 (6.7)	158 (6.5)
Years in field	†	8.44 (8.27,8.61)	8.89 (8.36,9.42)	7.06 (6.21,7.91)	8.37 (8.09,8.64)	8.51 (8.25,8.76)
Deployments	†	1.38 (1.33,1.44)	1.22 (1.03,1.40)	1.33 (1.07,1.60)	1.51 (1.41,1.60)	1.33 (1.27,1.40)
Total	52,080	4801	465	180	1711	2445

* From Air Force Personnel Center data.[11]
† Data not available.
‡ Includes 26 widowed & 10 annulled.

categorical depression variable using a scale ranging from none, mild, moderate, moderately severe, to severe. A Chi-squared analysis comparing observed and expected frequencies of each depression severity level revealed no statistically significant relationship between SEG and depression severity. However, a Chi-squared analysis of depression severity and self-reported exposure level (**Table IV**) reveals a significant (P-value < 0.001) relationship between the exposure level variable and outcome, which is consistent with research on perceived exposure and symptoms.[5] This finding suggests a dose-response relationship between perceived exposure level to engine oil and hydraulic fluid and depression severity, although it does not establish that organophosphates are the constituents responsible for the depressive symptoms.

Prior work in the hydraulics or propulsion fields was not associated with an increase in depression prevalence [OR: 1.25; CI: (0.898,1.74); P-value = 0.185]. A second scenario involving those with no history vs. those with current or former hydraulics work results in no association as well [OR: 1.12; CI: (0.87,1.45); P-value = 0.379]. Further analyses controlling for marital status and deployments did not show an association between history of work and depression prevalence. When the depression severity cut-point of 4 was used to include the mild depression cases in the "depressed" category using the dichotomous depression variable, the prevalence odds ratios for depression and work history in hydraulics or propulsion were significant, so it is possible that the mild depression cases are more prevalent in those with a history of work in propulsion or hydraulics.

DISCUSSION

This study found no significant association between similar occupations and measures of depression (dichotomous and categorical). However, there was an association between self-reported exposure level and both depression prevalence and severity. Risk of depression was more than doubled for workers with any of the perceived exposure routes (ingestion, contact, and inhalation) as compared to those unexposed by each route. The disparity between the results for exposure measured by SEG and exposures measured by workers' self-report may suggest that SEGs misclassify some workers, since 89% of the workers who were "unexposed" based on their SEG reported occupational exposures to organophosphates. This could mean that there is no association, but it may also indicate that the SEGs were improperly assigned and there are exposed workers in the "other" category. This may be because they work in close proximity to workers using those chemicals or it could be because they use those chemicals themselves and the uses were overlooked or unrecorded in the paperwork that was reviewed for this study. It is also possible that the deployment rates, work hours, and intensity of work are different among the exposure groups, which may have produced disparities by gender and marital status.

Depression prevalence has never been assessed in maintainers, but results in this study are comparable to studies involving

Table II. Final Multivariate Model for Odds Ratio of Depression Prevalence by Occupation.

VARIABLE	OR (95% CI)	COEFF (95% CI)	*P*-VALUE
SEG			
1-Propulsion	1.13 (0.75,1.71)	0.12 (-0.28,0.54)	0.549
2-Hydraulics	0.98 (0.51,1.90)	-0.02 (-0.68,0.64)	0.957
3-Crew chiefs	1.19 (0.92,1.53)	0.17 (-0.08,0.43)	0.179
4-Other	1.00	-	-
Number of deployments	1.10 (1.04,1.16)	0.096 (0.04,0.15)	0.000
Marital status			
Single	1.00	-	-
Married	0.84 (0.64,1.099)	-0.17 (-0.44,0.09)	0.206
Divorced	0.97 (0.59,1.598)	-0.03 (-0.52,0.47)	0.912
Legally separated	4.31 (2.01,9.27)	1.46 (0697,2.23)	0.000

Table III. Prevalence of Depression by Self-Reported Exposure, Stratifying by Route of Exposure (Nov. 2014).

EXPOSURE TYPE (n)	ADJUSTED* PREVALENCE ODDS RATIO (95% CI)	*P*-VALUE
No contact (672)	1.00	-
Contact (4129)	1.68 (1.11,2.55)	0.015
No inhalation of oils or mists (2575)	1.00	-
Inhalation of oils or mists (2226)	2.52 (1.95,3.24)	0.000
No ingestion (4003)	1.00	-
Ingestion (798)	2.55 (1.97,3.30)	0.000
No inhalation of aircraft exhaust (1402)	1.00	-
Inhalation of exhaust (3399)	2.20 (1.59,3.04)	0.000

* Adjusted for marital status and number of deployments.

farm workers exposed to organophosphate pesticides.[5,14] Those studies used self-reported exposure rather than biological or exposure assessment, so the use of self-reported exposure may be an acceptable substitute when unable to accurately define SEG exposure.[5,14] However, it is important to note that interpretations must be made cautiously because a one-time questionnaire such as the one used in this study cannot establish temporality for the exposure and outcome.

To our knowledge, this is the first study of aircraft maintainers and depression. Access to active duty Air Force maintainers yields a population that works with a variety of airframes in a variety of locations, enabling a diverse cross-section of workers. In addition, the younger population of Air Force workers is a result of most Airmen joining the military as their first job, thus getting all of their training and exposure while employed with the same organization and limiting previous occupational exposure. Similarly, the use of only active duty personnel limits the age range and other variables that may confound the association between exposures and depression.

The nature of self-reported exposure must be kept in mind. It is possible that the workers who believe they are more exposed do so because they may be working longer hours or performing the more difficult tasks, which may also contribute to depression depending on whether workers view their increased responsibility and work load in a positive or negative light. Self-reported exposure may also correspond to self-reported depression simply because some respondents were more forthcoming with both work and personal information. Further, workers feeling and reporting depression symptoms may be more aware of other factors outside this study that may contribute or they may think contribute. Still, the odds ratio exceeding 2.6 is substantial as well as statistically significant. In addition, using self-reported exposure has been an accepted method for depression and organophosphate exposure studies in the past, so perceived exposure may be reliable in the absence of good exposure data.[5]

A cross-sectional study cannot establish temporality; therefore, this study cannot determine whether the exposure in the workplace preceded the onset of depression. However, the Air Force is unique in that it does not accept enlistees who have a history of major depressive disorder requiring more than 12 mo of outpatient mental health care or any history of inpatient care.[7] While enlistees can have a history of untreated depression, this rule at least minimizes the number of recruits who enter with a depression history. In addition, the PHQ-8 questionnaire only addresses depression symptoms within the previous 2 wk, so workers may have been diagnosed and treated in the past or are currently undergoing treatment.

Although in the workplace ingestion is usually considered a minor source of chemical exposure, approximately 17% of survey respondents perceived ingestion as a route of exposure. This could be because they acknowledge the risks of eating lunch without first washing their hands, or eating or drinking near chemicals in the workplace.

Bias may also exist in the questionnaire administration, since workers with higher exposure and depression may have more readily answered the survey questions or may have answered them differently. This type of selection bias is a particular concern since our response rate was low, i.e., 9%. In addition, depression can be a sensitive subject, especially among military personnel, and workers may not have been willing to admit they have symptoms. Workers who are busier at work may not be as likely to take the time to complete the survey, and these same workers may have higher exposures if they are busier performing work with organophosphate esters. This may have led to an underestimation of both depression and exposure. Military members are also accustomed to completing surveys, so some survey fatigue may have occurred if participants have recently been involved in other surveys. Regardless of the reason behind the low response rate, this may make it difficult to generalize this study to other populations.

Table IV. Analysis* of Severity of Depression by Self-Reported Exposure Level (Nov. 2014).

	FREQUENCY (*EXPECTED FREQUENCY*)				
DEPRESSION CATEGORY	NONE OR ALMOST NEVER	LOW OR SOMETIMES	MODERATE OR A FEW TIMES PER WEEK	HIGH OR FREQUENT	TOTAL
None	655 *(595.7)*	1262 *(1220.3)*	1069 *(1075.5)*	772 *(866.5)*	3758
Mild	77 *(117.9)*	224 *(241.6)*	216 *(212.9)*	227 *(171.5)*	744
Moderate	22 *(33.6)*	51 *(68.8)*	66 *(60.7)*	73 *(48.9)*	212
Moderately severe to severe	7 *(13.8)*	22 *(28.3)*	23 *(24.9)*	41 *(20.1)*	87
Total	761	1559	1374	1107	4801
	Pr = 0.000			Pearson $Chi^2(9) = 88.13$	

* Chi-squared analysis.

This is an initial study involving aircraft maintainers and depression, so the above limitations can be mitigated in future research by using improved study designs or larger populations. Recommendations for future research include personal air sampling to characterize exposure when aircraft engines are running in the vicinity of workers, including during engine test cell operations with high power, as those operations have been shown by other studies to be associated with the highest level of exposures.[6] More focused skin contact exposure analysis would aid in determining if skin contact poses a more serious threat to maintainers than inhalation exposure. Investigating the ingestion exposure patterns of workers may also help determine what role ingestion plays in total exposure to organophosphates. In addition, quantification of exposure for crew chiefs may be important, since respondents in this field admitted to exposures that may be similar to or higher than the propulsion and hydraulics workers. Collection of shiftwork history and sleep patterns, airframes worked on, and more extensive deployment history would enable more thorough investigation of other factors that may influence depression status or severity. In addition to extending this research to crew chiefs, it may be extended to pilots as well, as the cabin air systems may be supplemented by engine bleed air. There is recent research on tricresyl phosphate exposure in F-16 and F-22 pilots, but not on those who report symptoms or fume events.[19] Ultimately, a longitudinal study of maintenance workers to measure incidence of depression related temporally to exposure would be ideal.

No significant association was found between depression prevalence and assigned SEG, but there was a strong association between depression and self-reported exposure through each route (contact, inhalation, and ingestion) in normal work duties. A dose-response type of relationship was also demonstrated between perceived workplace exposure level and severity of depression.

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