Greater Prevalence and Incidence of Dementia in Older Veterans with Posttraumatic Stress Disorder

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OBJECTIVES: To explore the association between posttraumatic stress disorder (PTSD) and dementia in older veterans.

DESIGN: Administrative database study of individuals seen within one regional division of the Veterans Affairs healthcare network.

SETTING: Veterans Integrated Service Network 16.

PARTICIPANTS: Veterans aged 65 and older who had a diagnosis of PTSD or who were recipients of a Purple Heart (PH) and a comparison group of the same age with no PTSD diagnosis or PH were divided into four groups: those with PTSD and no PH (PTSD+/PH−, n = 3,660), those with PH and no PTSD (PTSD−/PH+, n = 1,503), those with PTSD and a PH (PTSD+/PH+, n = 153), and those without PTSD or a PH (PTSD−/PH−, n = 5,165).

MEASUREMENTS: Incidence and prevalence of dementia after controlling for confounding factors in multivariate logistic regression.

RESULTS: The PTSD+/PH− group had a significantly higher incidence and prevalence of dementia than the groups without PTSD with or without a PH. The prevalence and incidence of a dementia diagnosis remained two times as high in the PTSD+/PH− group as in the PTSD−/PH+ or PTSD−/PH− group after adjusting for the confounding variables. There were no statistically significant differences between the other groups.

CONCLUSION: The incidence and prevalence of dementia is greater in veterans with PTSD. It is unclear whether this is due to a common risk factor underlying PTSD and dementia or to PTSD being a risk factor for dementia. Regardless, this study suggests that veterans with PTSD should be screened more closely for dementia. Because PTSD is so common in veterans, this association has important implications for veteran care. J Am Geriatr Soc 58:1627–1633, 2010.

Key words: posttraumatic stress disorder; dementia; veterans

Exposure to life-threatening situations can cause posttraumatic stress disorder (PTSD), which includes symptom clusters of reexperiencing, avoidance, and hyperarousal. Its public health significance is increasing with the continued engagement in overseas conflicts. As many as 22% of veterans from Operation Enduring Freedom/Operation Iraqi Freedom (OEF/OIF) who used Veterans Affairs (VA) healthcare services between 2002 and 2008 were diagnosed with PTSD.2 Approximately 300,000 OEF/OIF veterans suffered from PTSD or depression in 2007.3

PTSD can have long-term consequences because it can be a chronic illness. According to one estimate, 9% to 15% of Vietnam veterans suffer from PTSD 15 years after military service. In another study, the PTSD rate was as high as 24% in older veterans (44–70) from World War II and the Korean and Vietnam wars who were seeking treatment.5 If this holds true for OEF/OIF veterans, the potential lifetime social and economic costs will be immense.

PTSD has also been conceptualized as a disorder of memory centered on the etiological traumatic event(s).6 Several investigators have found changes in attention, learning, memory, and executive functioning.7–10 Many risk factors for PTSD are also risk factors for dementia, including traumatic brain injury (TBI),11,12 low intelli-
Changes in the frontal and temporal lobes and reduced hippocampal volumes noted in some PTSD studies are commonly present in dementia. These observations led to the hypothesis that PTSD could be associated with a greater incidence and prevalence of dementia.

The goal of this study was to explore the association between PTSD and dementia in older veterans. A positive association would have broad implications for public policy and treatment.

METHODS

This study was conducted using administrative data from the Veterans Integrated Service Network (VISN) 16 Data Warehouse. It includes demographics, diagnostic codes (International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9) codes), laboratory test results, and information on medication use from all outpatient and inpatient encounters in 10 medical centers in the Veteran Affairs (VA) Healthcare Network of the south central region of the United States. The institutional review board of Baylor College of Medicine and affiliated hospitals approved the study.

Experimental Design

The study cohort included subjects aged 65 and older who had been seen at VA healthcare facilities within VISN 16 at least twice from October 1, 1997, to September 30, 1999, and who had a diagnosis of PTSD or were Purple Heart (PH) recipients (with or without PTSD). A comparison group matched according to age and sex that had had two or more VA visits from October 1, 1997, to September 30, 1999, but did not have a diagnosis of PTSD and had not received a PH was also created. A minimum of two VA visits was required, to increase the likelihood that patients were receiving ongoing medical care at the VA. See Figure 1 for more details.

Outpatient data files from fiscal year 1998 to 2008 (October 1, 1997, to September 30, 2008) were used in this study. Diagnoses of PTSD, dementia, and other physical comorbidities with known associations with dementia were obtained from outpatient encounters from October 1, 1997, to September 30, 2008.

Controlling for Demographics and Medical Comorbidities

Multiple medical conditions can alter the risk of dementia. Many of them, including dyslipidemia, hypertension (HTN), diabetes mellitus (DM), coronary artery disease (CAD), stroke, TBI, alcohol abuse and dependence and drug abuse and dependence, in addition to sex and race (whites vs nonwhites), were controlled for. The ICD-9 code for tobacco-use disorder was included in drug abuse and dependence. Some risk factors for dementia that are not included in the VA administrative databases, such as education or apolipoprotein E genotype, could not be controlled for.

Accounting for Combat-Related Trauma

Veterans wounded in combat receive the PH. Thus, PH status was used as a way of addressing combat exposure and combat-related trauma. TBI is an important subset of trauma, but it is not systematically separated from other forms of combat-related trauma in the VISN 16 database, although it was possible to identify subjects with head trauma using ICD-9 codes based on Guidelines for Surveillance of Central Nervous System Injury published by the Centers for Disease Control and Prevention.

Controlling for Increased Clinic Visits

It might be that the diagnosis of dementia is made more often in patients with PTSD because they see their physicians more frequently than those without PTSD. This could be especially true for veterans, because they have easy access to VA health care. To address this possibility, the number of VA primary care and mental health clinic visits was calculated for each group and statistically controlled for in the analyses. These clinic visits included visits to general medicine; women’s clinics; primary care, medicine; primary care, general psychiatry; and primary care, special psychiatry clinics. Multiple visits on the same day and to the same clinic were considered a single visit.

Detecting Dementia

To capture dementia patients whose treating physicians did not code, data were obtained regarding the use of cognitive medications used to treat dementia: acetyl cholinesterase inhibitors and memantine. In addition to classifying a patient as having dementia based on diagnosis codes, the analyses were also repeated using patients who had dementia diagnosis codes or cognitive medications as a proxy for dementia. See Appendix 1 for more details.

Figure 1. Approximate distribution of veterans aged 65 and older in the Veterans Integrated Service Network (VISN) 16 data warehouse. PTSD = posttraumatic stress disorder; PH = Purple Heart.
Statistical Analysis
Using the information on PTSD and PH status, subjects were categorized as belonging to one of four groups: with PTSD and no PH (PTSD+/PH–); with a PH and no PTSD (PTSD–/PH+); with PTSD and a PH (PTSD+/PH+); and a comparison group with neither PTSD nor a PH (PTSD–/PH–). In determining the incidence of dementia, all patients who had died and those who had a dementia diagnosis before September 30, 1999, were first excluded. Period prevalence was calculated using the entire period from October 1, 1997, to September 30, 2008.

Chi-square analysis was used to compare the groups for categorical variables, and analysis of variance was used for continuous variables. Multivariate logistic regression models based on generalized estimating equation methodology were used to assess the effect of various factors on the prevalence and incidence of dementia in all groups while controlling for confounding factors. Confounding factors were sex, race (white vs nonwhite) and some physical disorders considered to be risk factors for dementia, such as dyslipidemia, HTN, DM, CAD, stroke, TBI, alcohol abuse and dependence, and drug abuse and dependence. The number of primary care and mental health visits in the last 2 years was used to assess the effect of various factors on the incidence and prevalence of dementia in all groups while controlling for confounding factors. Multivariate logistic regression models based on generalized estimating equation methodology were used to assess the effect of various factors on the prevalence and incidence of dementia in all groups while controlling for confounding factors.

RESULTS
This study included 10,481 veterans. (3,660 in the PTSD+/PH– group, 1,503 in the PTSD–/PH+ group, 153 in the PTSD+/PH+ group, and 5,165 in the PTSD–/PH– group). Almost all were men (99.9%), with mean ages of 73.3 to 73.9 (SDs 4.6 to 5.2). Of patients for whom race was known, most were white (62–82% in all groups). The comparison group had more blacks (16.2%) and veterans of unknown race (20.5%) (Table 1).

Two risk factors for vascular disease differed between groups; HTN ranged from 58.1% to 76.5% (P<.001), and DM ranged from 25.4% to 34.6% (P<.001). The PTSD+ groups (13.3% and 13.1%) had a slightly higher stroke rate than the PTSD– groups (10.0% and 9.5%, P<.001), but there was no difference in the prevalence of CAD between groups (P=.11). Rates of TBI ranged from 0.8% in the comparison group to 3.3% in the PTSD+/PH+ group (P<.001), but rates were similar in the PTSD+/PH– and PTSD–/PH+ groups (2%).

There was a slightly higher prevalence of drug dependence and abuse in the PTSD+/PH– group (11.3%) than

Table 1. Comparison of Demographic and Clinical Characteristics and Number of Primary Care Visits of the Cohort and Control Groups

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>PTSD+/PH– n=3,660</th>
<th>PTSD–/PH+ n=1,503</th>
<th>PTSD+/PH+ n=153</th>
<th>PTSD–/PH– n=5,165</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age as of September 1999, mean ± SD</td>
<td>73.9 ± 5.3</td>
<td>73.7 ± 5.0</td>
<td>73.3 ± 4.7</td>
<td>73.8 ± 5.2</td>
<td>.27</td>
</tr>
<tr>
<td>Male, %</td>
<td>98.8</td>
<td>99.9</td>
<td>100</td>
<td>99.2</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Race, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>78.3</td>
<td>74.8</td>
<td>82.4</td>
<td>62.3</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>8.4</td>
<td>5.3</td>
<td>6.5</td>
<td>16.2</td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>0.4</td>
<td>0.1</td>
<td>0.7</td>
<td>0.4</td>
<td></td>
</tr>
<tr>
<td>American Indian</td>
<td>0.8</td>
<td>0.4</td>
<td>0.4</td>
<td>0.4</td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>0.7</td>
<td>0.5</td>
<td>2.0</td>
<td>0.3</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>11.5</td>
<td>18.9</td>
<td>8.5</td>
<td>20.5</td>
<td></td>
</tr>
<tr>
<td>Participants with comorbid conditions, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>35.1</td>
<td>40.2</td>
<td>50.3</td>
<td>24.8</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Hypertension</td>
<td>68.1</td>
<td>70.3</td>
<td>76.5</td>
<td>58.1</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>29.8</td>
<td>28.5</td>
<td>34.6</td>
<td>25.4</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>4.8</td>
<td>4.3</td>
<td>3.9</td>
<td>3.7</td>
<td>.11</td>
</tr>
<tr>
<td>Stroke</td>
<td>13.3</td>
<td>10.0</td>
<td>13.1</td>
<td>9.5</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Traumatic brain injury</td>
<td>2.0</td>
<td>2.0</td>
<td>3.3</td>
<td>0.8</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Alcohol abuse or dependence</td>
<td>3.8</td>
<td>1.0</td>
<td>1.3</td>
<td>1.6</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Drug abuse or dependence</td>
<td>11.3</td>
<td>7.2</td>
<td>8.5</td>
<td>7.8</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Number of primary care and mental health clinic visits from October 1997, to September 1999, mean ± SD</td>
<td>3.9 ± 3.8</td>
<td>2.0 ± 2.3</td>
<td>3.9 ± 3.2</td>
<td>2.1 ± 2.7</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Number of primary care and mental health clinic visits from October 1997, to September 2008, mean ± SD</td>
<td>14.5 ± 15.7</td>
<td>15.5 ± 14.7</td>
<td>23.0 ± 16.7</td>
<td>10.1 ± 13.0</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

*Data on race were missing for 1,773 patients.
†P-value for race is for the comparison between white and nonwhite.
‡After excluding those with dementia diagnosis before October 1, 1997.
PTSD = posttraumatic stress disorder; PH = Purple Heart; SD = standard deviation.
in the other groups (7.2–8.5%, \( P < .001 \)). There was also a difference in the rate of alcohol dependence and abuse between groups (3.8% for PTSD+/PH− vs 1.0–1.6% for the other groups; \( P < .001 \)).

The mean number of VA primary care and mental health visits was highest (3.9) in the PTSD+/PH− and PTSD+/PH+ groups from October 1, 1997, to September 30, 1999. It was similar (2.0 and 2.1) in the PTSD−/PH+ and comparison groups. The mean number of primary care and mental health clinic visits between October 1, 1997, and September 30, 2008, ranged from 10.1 to 23.0. PTSD+/PH+ patients had the most visits (23.0), followed by PTSD−/PH+ patients (15.5), PTSD+/PH− patients (14.5), and patients in the comparison group (10.1).

Prevalence of Dementia

The period prevalence of dementia in the PTSD+/PH− group was ascertained by dividing the number of veterans with any ICD-9 dementia diagnosis (\( n = 406 \)) during the 11-year interval of the study (1997–2008) by the total number in the group (\( n = 3,660 \)). The same was done for the other groups. The prevalence of dementia in the four groups differed significantly (11.1% for PTSD+/PH−, 7.2% for PTSD+/PH+, 5.9% for PTSD−/PH+, and 4.5% for the comparison group; \( P < .001 \)) (Table 2).

Adjusting for Demographics and Comorbid Illnesses

In multivariate analyses, the odds of a dementia diagnosis between October 1, 1997, and September 30, 2008, were two times as high in the PTSD+/PH− group as in the PTSD−/PH+ group (odds ratio (OR) = 2.0, 95% confidence interval (CI) = 1.6–2.5, \( P < .001 \)) or the comparison group (OR = 2.3, 95% CI = 2.0–2.7, \( P < .001 \)) but not significantly higher than the PTSD+/PH+ group (OR = 0.6, 95% CI = 0.3–1.2, \( P = .14 \)). The odds did not differ significantly when the PTSD−/PH− or PTSD−/PH+ groups were compared with the comparison group (OR = 1.2, 95% CI = 0.9–1.5, \( P = .20 \)) and OR = 1.4, 95% CI = 0.7–3.0, \( P = .38 \), respectively) or between the PTSD+/PH+ and PTSD−/PH+ groups (OR = 1.2, 95% CI = 0.6–2.2, \( P = .60 \)) (Table 3).

Incidence of Dementia

To determine the incidence of dementia, the number of patients with an ICD-9 diagnosis of dementia or those who had died (\( n = 1,044 \)) during the baseline period (1997–1999) was subtracted from the total number of veterans, and the annual development of dementia during the 9-year follow-up of the study was calculated (October 1, 1999–September 30, 2008), leaving 9,437 patients. There was a statistically significant difference between groups in the incidence of dementia (9.5% in the PTSD+/PH− group, 5.6% in the PTSD−/PH+ group, 6.8% in the PTSD+/PH+ group, and 4.0% in the comparison group; \( P < .001 \)) (Table 2).

Adjusting for Demographics, Comorbid Illnesses and Number of Primary Care and Mental Health Clinic Visits

In the multivariate analysis for incidence, number of primary care and mental health clinic visits before any subject had been diagnosed with dementia (October 1, 1997, to September 30, 1999) was also included. Patients in the PTSD+/PH− group had almost twice the odds of developing dementia of the PTSD−/PH+ group (OR = 1.7, 95% CI = 1.4–2.2, \( P < .001 \)) or comparison groups (OR = 2.2, 95% CI = 1.8–2.6, \( P < .001 \)) but not of the PTSD+/PH+ group (OR = 0.6, 95% CI = 0.4–1.1, \( P = .14 \)). As with the prevalence, there were no significant differences in incidence when the PTSD−/PH+ or PTSD+/PH+ groups were compared with the comparison group (OR = 1.2, 95% CI = 1.0–1.6, \( P = .09 \)) and OR = 1.4, 95% CI = 0.7–2.7, \( P = .31 \), respectively). There were also no significant differences between the PTSD+/PH+ and PTSD−/PH+ groups (OR = 1.1, 95% CI = 0.7–1.9, \( P = .67 \)) (Table 4).

Prevalence and Incidence of Dementia According to ICD-9 Codes and Cognitive Medications

A sensitivity analysis was performed to calculate the prevalence and incidence of dementia in which a dementia diagnosis was based on International Classification of Diseases, Ninth Revision, Clinical Modification codes only. Variables that were controlled for were sex, race, and comorbid illnesses, including diabetes mellitus, dyslipidemia, hypertension, coronary artery disease, stroke, traumatic brain injury, alcohol abuse and dependence, and drug abuse and dependence.

PTSD = posttraumatic stress disorder; PH = Purple Heart.

Table 2. Prevalence and Incidence of Dementia in All Groups*

<table>
<thead>
<tr>
<th>Results</th>
<th>PTSD+/PH−</th>
<th>PTSD−/PH+</th>
<th>PTSD+/PH+</th>
<th>PTSD−/PH−</th>
<th>All Groups</th>
<th>( P )-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>3,660</td>
<td>1,503</td>
<td>153</td>
<td>5,165</td>
<td>10,481</td>
<td></td>
</tr>
<tr>
<td>Prevalence, n (%)</td>
<td>406 (11.1)</td>
<td>88 (5.9)</td>
<td>11 (7.2)</td>
<td>231 (4.5)</td>
<td>736 (7.0)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Total</td>
<td>3,227</td>
<td>1,466</td>
<td>147</td>
<td>4,597</td>
<td>9,437</td>
<td></td>
</tr>
<tr>
<td>Incidence, n (%)</td>
<td>305 (9.5)</td>
<td>82 (5.6)</td>
<td>10 (6.8)</td>
<td>183 (4.0)</td>
<td>580 (6.2)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

* Dementia diagnosis was based on International Classification of Diseases, Ninth Revision, Clinical Modification codes only. To calculate incidence, all patients who had died or had a dementia diagnosis before October 1999 were excluded.

PTSD = posttraumatic stress disorder; PH = Purple Heart.

Table 3. Odds of Dementia Prevalence in All Groups After Controlling for Confounding Factors

<table>
<thead>
<tr>
<th>Group</th>
<th>Odds Ratio (95% Confidence Interval)</th>
<th>( P )-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTSD+/PH− vs PTSD−/PH−</td>
<td>2.3 (2.0–2.7)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>PTSD−/PH+ vs PTSD+/PH−</td>
<td>1.2 (0.9–1.5)</td>
<td>.20</td>
</tr>
<tr>
<td>PTSD+/PH+ vs PTSD−/PH−</td>
<td>1.4 (0.7–3.0)</td>
<td>.38</td>
</tr>
<tr>
<td>PTSD+/PH− vs PTSD+/PH+</td>
<td>2.0 (1.6–2.5)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>PTSD+/PH+ vs PTSD−/PH−</td>
<td>0.6 (0.3–1.2)</td>
<td>.15</td>
</tr>
<tr>
<td>PTSD+/PH+ vs PTSD+/PH+</td>
<td>1.2 (0.6–2.2)</td>
<td>.60</td>
</tr>
</tbody>
</table>

Dementia diagnosis was based on International Classification of Diseases, Ninth Revision, Clinical Modification codes only. Variables that were controlled for were sex, race, and comorbid illnesses, including diabetes mellitus, dyslipidemia, hypertension, coronary artery disease, stroke, traumatic brain injury, alcohol abuse and dependence, and drug abuse and dependence.

PTSD = posttraumatic stress disorder; PH = Purple Heart.
The prevalence and incidence of PTSD in the groups was 17.6% for PTSD and 9.3% in the comparison group; 

Some questions remain. For example, the duration of PTSD necessary to show cognitive changes is unclear. It is unclear whether the changes are static or progressive and why some studies have not shown cognitive changes.

Prior studies showing cognitive impairments in PTSD along with the dementia findings in the current study raise several significant questions about the natural history and pathophysiology of the development of dementia. One hypothesis is that the cognitive changes of PTSD are early markers of dementia (i.e., they progress to dementia decades later). A second hypothesis is that cognitive changes in PTSD may put veterans at risk for dementia. In that case, they develop clinical symptoms of dementia much earlier if they had PTSD-induced decreases in cognitive reserve. A third hypothesis is that PTSD and dementia share (an)other risk factor(s). An example might be low baseline cognitive reserves.

Most veterans with PTSD did not develop dementia during the 9-year follow-up period. It will be important to ascertain which veterans with PTSD are at greatest risk and to determine whether PTSD induced by other situations (e.g., rape) is also associated with greater risk.

Cognitive Changes Versus Dementia

One other group has reported similar findings of greater rates of dementia in persons with PTSD. Several studies have demonstrated cognitive changes in patients with PTSD. One found alterations in sustained attention and initial acquisition of information. A study of Holocaust survivors and elderly veterans with PTSD found impaired learning. A meta-analysis of 28 studies reported that verbal memory is the most impaired cognitive function in people with PTSD. War veterans appear to be more impaired than other groups. Several questions remain. For example, the duration of PTSD necessary to show cognitive changes is unclear. It is unclear whether the changes are static or progressive and why some studies have not shown cognitive changes.

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Neuroanatomical Changes with PTSD

Several studies have reported volume loss in the central nervous system of people with PTSD, although the areas have not been consistent, and not all studies have found them. In those reporting volume changes, some demonstrated frontal lobe volume loss and dysfunction. Using magnetic resonance spectroscopy, low neuronal density in the medial temporal lobes in combat-related PTSD has been suggested. There is also evidence of hippocampal dysfunction and smaller hippocampal volume in PTSD. Several studies have not replicated these findings, but if present, they could put veterans with PTSD at risk for dementia.

Risk Factors for PTSD and Dementia

Well-documented combat exposure and combat-related injuries were accounted for by having the PTSD group. Although it was possible to control for TBI through ICD-9 codes, it was also assumed that the PTSD group could have well represented veterans with significant, combat-related TBI, which would presumably increase the incidence of dementia in that group. However, it is also possible that other groups without a PH include veterans with significant TBI and other physical injuries. After removing those with PHs, the PTSD group still had a greater prevalence and incidence of dementia. This may suggest that PTSD is a greater risk factor for dementia than combat-related trauma.

PTSD is associated with a significantly greater number of primary care visits and could increase the opportunities for symptoms of dementia to be detected. Controlling for the number of primary care and mental health visits, along with sex, ethnicity, and comorbid illnesses, in a regression analysis made according to ICD-9 codes and use of cognitive medications. It might also include a few patients without dementia, such as those with mild cognitive impairment. This analysis produced similar results (data not shown). As expected, the period prevalence of dementia was higher in all groups than in previous analyses without cognitive medications, and a statistically significant difference remained in the prevalence of dementia between groups (21.0% in the PTSD group, 12.5% in the PTSD – PH group, 17.7% in the PTSD + PH group, and 9.3% in the comparison group; P < .001). There was also a significant difference in the incidence of dementia between groups (P < .001), even after excluding from the cohort all patients who had died, had an ICD-9 dementia diagnosis, or were taking cognitive medications. It might also include a few patients

Table 4. Odds of Dementia Incidence in All Groups After Controlling for All Confounding Factors, Including Primary Care Clinic Visits

<table>
<thead>
<tr>
<th>Group</th>
<th>Odds Ratio (95% Confidence Limits)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTSD + PH – vs PTSD – PH –</td>
<td>2.2 (1.8–2.6)</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>PTSD – PH + vs PTSD – PH –</td>
<td>1.2 (1.0–1.6)</td>
<td>.09</td>
</tr>
<tr>
<td>PTSD + PH + vs PTSD – PH –</td>
<td>1.4 (0.7–2.7)</td>
<td>.31</td>
</tr>
<tr>
<td>PTSD + PH – vs PTSD – PH +</td>
<td>1.7 (1.4–2.2)</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>PTSD + PH + vs PTSD + PH +</td>
<td>0.6 (0.4–1.1)</td>
<td>.13</td>
</tr>
<tr>
<td>PTSD + PH + vs PTSD – PH +</td>
<td>1.1 (0.7–1.9)</td>
<td>.67</td>
</tr>
</tbody>
</table>

Dementia diagnosis was based on International Classification of Diseases, Ninth Revision, Clinical Modification codes only. Variables that were controlled for were sex; race; comorbid illnesses, including diabetes mellitus, dyslipidemia, hypertension, coronary artery disease, stroke, traumatic brain injury, alcohol abuse and dependence, and drug abuse and dependence; and the number of primary care and mental health clinic visits between October 1, 1997, and September 30, 1999.

PTSD = posttraumatic stress disorder; PH = Purple Heart.

DISCUSSION

As hypothesized, the odds for a dementia diagnosis for patients with PTSD (PTSD + PH –) were two times as high as for those without PTSD (PTSD – PH –) or those with combat-related injuries without PTSD (PTSD – PH +). Results for prevalence and incidence do not appear to be due to differences in sex, combat-related trauma, greater health-service use, or comorbid physical disorders such as CAD, dyslipidemia, HTN, DM, stroke, TBI, alcohol use and dependence, or drug use and dependence.
analysis, did not change the finding that the odds for an ICD-9 dementia diagnosis or prescription of cognitive medications was greatest in the PTSD+/PH− group.

LIMITATIONS
Several limitations need to be considered before interpreting the results of this study. Some important variables that can affect cognition or dementia diagnosis could not be included, such as duration, severity, and treatment of PTSD; medication use; and apolipoprotein E status. In particular, education and premorbid intelligence were major confounders, but data on these variables were not available from the data warehouse. Data on race were missing for 1,773 individuals, and the distribution of race across the study groups was uneven. There were more blacks in the comparison group, although it has previously been shown that this group has a higher prevalence of dementia than white and Hispanic populations.28 Thus, it would have biased the study toward more dementia in the comparison group, the opposite of what was found. In addition, most subjects in this cohort were men, and results cannot be generalized to women. It was not possible to ascertain the type of dementia associated with PTSD. There may have been false-negative cases of PTSD, because it is known to be underdiagnosed in VA settings.29 In addition, the combat status of non-PH groups was not known, and not all combat injuries were documented with a PH during war or administratively accounted for at time of VA enrollment.

Another important limitation is the use of a VA administrative database, although all diagnoses were based on ICD-9 codes, and previous research has shown more than 96% agreement between these administrative files and written medical records.30 Low rates of substance-use disorders raise questions, especially in the PTSD group, because much higher rates are reported in other studies.31 This could be because of a survival phenomenon; those who had a substance-use disorder died at a younger age than those without a substance-use disorder in this cohort (mean age 71.5 vs 75.3, P < .001). In a recent regional study of 885 randomly selected VA primary care patients, 10.5% of those who met criteria for PTSD also met criteria for a substance-use disorder, whereas only 2.6% of those who were PTSD negative met criteria for a substance-use disorder. The average age of this sample was 61, 13 years younger than the current sample, again suggesting that the prevalence of substance-use disorders is lower in an older population because of higher mortality.29

CONCLUSIONS
Older veterans with PTSD had twice the incidence and prevalence of dementia diagnoses as those without, even after accounting for confounding illnesses, combat-related trauma, and number of primary care and mental health visits. The exact cause of this association is unclear. It could be that cognitive impairment in PTSD is an early marker of dementia, PTSD is an independent risk factor for dementia, or PTSD and dementia share a common risk factor such as low cognitive reserves. Similar studies need to be performed in the civilian population; to account for other important variables such as education, premorbid intelligence, and the apolipoprotein E genotype; or both to confirm this finding. Research is also needed to explore the causal relation between PTSD and dementia. It is essential to determine whether risk of dementia can be reduced by treating PTSD effectively. This could have enormous implications for veterans returning from OEF/OIF.

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