Posttraumatic Stress Disorder and Incidence of Type-2 Diabetes: A Prospective Twin Study

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Abstract

Growing evidence has linked posttraumatic stress disorder (PTSD) to insulin resistance and type-2 diabetes, but most previous studies were cross-sectional. We examined the association between PTSD and incidence of diabetes in a prospective study of middle-aged male twins from the Vietnam Era Twin Registry. Lifetime PTSD was diagnosed at baseline with the Diagnostic Interview Schedule (DIS) according to *DSM-III-R* criteria. Subthreshold PTSD was defined by

meeting some, but not all, criteria for PTSD. A total of 4,340 respondents without self-reported diabetes at baseline were included. Of these, 658 reported a new diagnosis of treated diabetes over a median of 19.4 years of follow-up. At baseline, twins with PTSD showed more behavioral and metabolic risk factors such as overweight and hypertension. The age-adjusted cumulative incidence of diabetes was significantly higher in twins with PTSD (18.9%) than those without PTSD (14.4%), [odds ratio (OR)=1.4, 95% confidence interval (CI) 1.03-1.8], and intermediate in those with subthreshold PTSD (16.4%) (OR=1.2, 95% CI 0.9-1.5, p for trend=0.03). Adjustment for military, lifestyle and metabolic factors diminished the association. No significant association was found comparing twin pairs discordant for PTSD. In conclusion, PTSD was prospectively associated with a 40% increased risk of new-onset type-2 diabetes which was partially explained by a cluster of metabolic and behavioral risk factors known to influence insulin resistance. Shared biological or behavioral precursors which occur within families may lead to both PTSD and insulin resistance/diabetes. Thus, PTSD could be a marker of neuroendocrine and metabolic dysregulation which may lead to type-2 diabetes.

Keywords

Posttraumatic Stress Disorder; Diabetes; Twin Studies; Epidemiology; Stress

Objectives of the Study and Background

Posttraumatic stress disorder (PTSD) is a psychiatric condition that is common among Veterans and results from exposure to severe psychological stress, such as exposure to combat. Among Vietnam Veterans who served in the war zone, the lifetime prevalence is 15% to 19% (Dohrenwend et al., 2006; Thompson, Gottesman, & Zalewski, 2006). Reported prevalence estimates of PTSD are even higher in combat-exposed Veterans from the recent Iraq and Afghanistan wars (Hoge et al., 2004; Hoge, Terhakopian, Castro, Messer, & Engel, 2007).

Although the comorbidity of PTSD and other psychiatric disorders is well characterized, its impact on physical health is less well understood. Many studies have documented a higher prevalence of physical health problems among persons with PTSD, but most used cross-sectional designs and self-reported symptoms (Dedert, Calhoun, Watkins, Sherwood, & Beckham, 2010; Glaesmer, Brahler, Gundel, & Riedel-Heller, 2011; Schnurr & Jankowski, 1999). Evidence of a possible link between PTSD and type 2 diabetes—a growing public health problem and a major risk factor for cardiovascular disease and all-cause mortality (Danaei et al., 2011) —has received increased attention (Boyko et al., 2010; Goodwin & Davidson, 2005; Norman et al., 2006). PTSD has also been associated with the metabolic syndrome, a cluster of risk factors characterized by insulin resistance and elevated risk of diabetes (Heppner et al., 2009; Jin et al., 2009; Weiss et al., 2011). The mechanisms underlying these associations are ascribed to chronic perturbations of the hypothalamic-pituitary-adrenal (HPA) axis in those with PTSD, potentially leading to increased visceral adiposity, inflammation, and insulin resistance (Brunner et al., 2002; Chrousos, 2000; Friedman & McEwen, 2004). PTSD may also influence diabetes risk through adverse health behaviors, such as sedentary lifestyle, poor dietary habits, sleep problems, and excessive

alcohol consumption (Breslau, Davis, & Schultz, 2003). Finally, genetic and familial factors may play a role. Genetic predisposition is substantial for obesity and other metabolic syndrome risk factors (Diamond, 2003; Jowett et al., 2009), as well as health behaviors, such as physical inactivity and diet (Heitmann, Harris, Lissner, & Pedersen, 1999; Lauderdale et al., 1997). Therefore, shared genetic pathways could potentially confound the association between PTSD and diabetes, as previously described for depression and cardiovascular disease (Kendler, Gardner, Fiske, & Gatz, 2009; Vaccarino et al., 2009).

A major limitation of most previous studies linking PTSD to type-2 diabetes and other metabolic risk factors is their cross-sectional design, which limits the ability to demonstrate a temporal relationship between PTSD and diabetes. Using a prospective twin study design, this study examines the association between PTSD and the incidence of treated type-2 diabetes.

Materials and Methods

Setting

The Vietnam Era Twin (VET) Registry is the source of Vietnam-era Veterans for this study. The Registry was constructed from computerized military discharge records and is a national sample of male twin pairs from all branches who served on active duty during the Vietnam era (1964-1975). Members of the Registry were born from 1939 through 1957. The process of identifying twin pairs involved a matching algorithm based on last name, date of birth, and similar Social Security numbers. A military record search confirmed an individual was a member of a twin pair by matching parental names and place of birth. The Registry was assembled in the 1980s and has subsequently seen extensive use as a platform for genetic epidemiological studies of both physical and mental health. A complete description of the VET Registry has been published previously (Goldberg, Curran, Vitek, Henderson, & Boyko, 2002).

Design

A Twin Study of the Course and Consequences of PTSD in Vietnam Era Veterans [Veterans Administration (VA) Cooperative Studies Program (CSP) #569] is a prospective, observational study of physical and mental health among Veterans who are members of the VET Registry. The study used data collected at the Registry's inception that included socio-demographic data and military experience, as well as physical and mental health information collected in 1992 that included self-reported diabetes and PTSD. These measures constituted baseline data for the present study, and were combined with newly collected follow-up data from 2010 through 2012. In this analysis, we examined the association between PTSD assessed in 1992 and incident treated type-2 diabetes through 2012 among Veterans who were free of diabetes at the time PTSD was assessed.

Subjects

All members of the Registry who were known to be alive and had not withdrawn their Registry membership were recruited to participate in CSP #569. For these analyses, we restricted participants to those for whom PTSD was assessed in 1992 and who did not self-

report diabetes at that time. Informed consent was obtained from all participating Registry members, and the VA Central Institutional Review Board approved the study protocol.

Measures

Socio-demographic and Military Service Factors—Information on socio-demographic and military service factors were available from the military service records of members of the VET Registry. These data were abstracted at the time the VET Registry was established in the 1980s and included date of birth, race, marital status at enlistment, educational attainment at the time of enlistment, date of enlistment, branch of service, and rank at enlistment.

Extensive additional information was obtained through a series of Registry-wide surveys that were conducted from 1987 through 1992. Education and marital status were updated, and information on occupational status and family income was obtained. Combat exposure was measured by asking each Veteran whether he engaged in 18 specific combat activities such as receiving incoming fire, serving as a "tunnel rat," or checking enemy base camps, yielding a global index of combat exposure ranging from 0 to 18 (Janes, Goldberg, Eisen, & True, 1991).

Baseline Risk Factors and Medical Conditions—Registry-wide surveys conducted from 1987 through 1992 also provided extensive information about previous medical history and risk factors, including smoking history, alcohol consumption, anthropometric measurements, and dietary habits. Physical activity was determined by a series of questions about moderate everyday activities (6 questions) or intense sports-related physical activity (5 questions) (Lauderdale et al., 1997). Physical activity was classified as a 3-level ordinal variable of "no physical activity," "moderate physical activity" (engaged in at least one moderate every day activity, such as taking the stairs, walking for exercise, etc.), and "vigorous physical activity" (engaged regularly in at least one vigorous or sports-related activity for at least the last 3 months, such as biking, running, swimming, etc.). Alcohol consumption was addressed with a series of questions asking the respondent on how many days, during the past 2 weeks, he drank beer, wine or hard liquor, and on the days he drank, how many drinks he had per day. From these questions, an average of drinks per day was calculated. Diabetes at baseline was assessed with the question: "Do you have diabetes?" which was asked in a 1992 survey. Veterans answering either affirmatively to or not answering this question were excluded from the analysis. In the same survey, previous history of cardiovascular diseases was assessed by a series of questions asking whether the respondent was ever told by a doctor that he had angina pectoris, congestive heart failure, coronary heart disease, damaged heart valves, heart attack or myocardial infarction, heart murmur, phlebitis or thrombophlebitis, or stroke, or whether the respondent ever had balloon angioplasty or coronary artery bypass surgery.

Psychiatric Diagnoses—In 1992, twins who participated in a Registry-wide study were administered the Diagnostic Interview Schedule (DIS) for the assessment of psychiatric disorders according to *DSM-III-R* criteria. Surveys were conducted using trained interviewers and a computer-assisted telephone version of the DIS (Eisen et al., 2004). Both

lifetime and 12-month prevalence of PTSD, major depression, generalized anxiety disorder, and substance abuse disorder were assessed. In total, 8,169 Veterans were interviewed (3,516 twin pairs and 1,137 singletons), representing 79.7% of eligible twins who were still alive (Eisen et al., 2004). In addition to PTSD (meeting full diagnostic criteria), we examined subthreshold PTSD, defined as meeting both the A (exposure to traumatic stress) and B (re-experiencing symptoms) criteria and either the C (avoidance and numbing) or D (increased arousal) criteria. Lifetime PTSD diagnosis as of 1992 was the main exposure in our analysis.

Assessment of New-Onset Type-2 Diabetes—Between January 2010 and September 2012, Registry members were asked by questionnaire if they ever had a history of physician-diagnosed diabetes. A series of additional questions collected information on age at diagnosis and type of anti-diabetic treatment using a comprehensive list of generic and trade names for insulin and oral agents. If the Veteran responded positively to the medication treatment question and chose one or more anti-diabetic agents from a list provided, he was considered as having pharmaceutically-treated diabetes, which was the outcome used in this analysis. Given the age of the cohort, we assumed that all new diabetes cases were type-2. We validated this definition of diabetes against clinically-confirmed diabetes by comparison of all self-reported diabetes cases and a random sample of non-cases with health care provider checklists, and found an agreement of 97.5%.

Statistical Analysis

We examined baseline differences in socio-demographic, military service, and lifestyle factors according to PTSD status at baseline in 1992, the primary exposure, and according to whether participants developed diabetes through 2012, the primary outcome. We also compared baseline characteristics according to whether an individual completed the 2010-2012 mailed questionnaire in order to assess possible response bias. Formal testing for differences in response used Student's t and chi-squared tests.

Based on PTSD status in 1992 (no PTSD, subthreshold PTSD, and PTSD) we calculated the risk of incident diabetes through 2012. We used multivariate logistic regression to adjust for potential confounding factors that could influence the association between PTSD and type-2 diabetes. Odds ratios (ORs) and 95% confidence intervals (CI) were estimated for participants with PTSD and for those with subthreshold PTSD compared to those without PTSD. ORs can be interpreted as an estimate of relative-risks for uncommon outcomes, generally those occurring in less than 20% of the cohort (Zhang & Yu, 1998). For the within-pair twin analysis we used logistic regression to estimate the ORs for the association between PTSD and diabetes within twin pairs discordant for PTSD. We also performed a sensitivity analysis where all self-reported diabetes was considered, not just treated diabetes. In all analyses, significance levels were two-sided and set at p = 0.05. All analyses accounted for the clustered data structure represented by twin pairs using robust variance estimators. Data analyses were performed with Stata software version 13.1.

All incidence estimates, means, and ORs were weighted to account for potential non-response bias affecting the original distribution of socio-demographic and military service

factors in the VET Registry. Responses were weighted using a model-based reweighting approach (Rosenbaum, 1987). Briefly, this method fits a multivariable logistic regression model where the dependent variable (y_i) is defined as a binary outcome for responder and the reference population (1 if responder, 0 if reference) and the socio-demographic, military service variables, and lifestyle factors are the independent variables (x_i). Results from the fitted model are then used to generate inverse probability weights for response. This approach produces weighted estimates of parameters of interest, such as odds ratios, that account for all measured non-response differences from the living population of the VET Registry.

Results

Study Sample

Of 8,169 Veterans interviewed in the 1992 survey, 8,107 had valid psychiatric data. From these we excluded 1,261 Veterans for whom no diabetes data were available, and 100 who reported a history of diabetes in or before 1992, leaving 6,746 diabetes-free Veterans who were eligible for outcome assessment. From this pool, 629 (9%) Veterans were found to be deceased, 1,004 (15%) refused to participate in the follow-up survey, 196 (3%) never responded, 210 (3%) could not be located, 322 (5%) had withdrawn their membership from the registry, and 45 (1%) failed to answer the diabetes questions, leaving 4,340 Veterans (64%) for this analysis. **Figure 1** shows the construction of the sample for the current analysis.

Responders and non-responders were similar in most characteristics, except that non-responders tended more often to be non-white, not married, less educated and current smokers (**Supplemental e-Table1**). There were no differences in PTSD assessed in 1992 or other psychiatric diagnoses according to respondent status, nor were there differences in military service variables, including service in Southeast Asia, and cardiovascular risk factors, such as hypertension and BMI.

PTSD and Baseline Factors

In 1992, the prevalence of lifetime PTSD was higher among younger, unmarried, and less educated Veterans (**Table 1**). Those with PTSD were also more likely to be unemployed, to have served in the Army, and to have enlisted earlier. Veterans with PTSD tended to be less physically active, consume more alcohol, and smoke more. Overall they tended to have a higher rate of metabolic risk factors such as overweight and hypertension. In general, a gradation of association was noted for these risk factors, such that Veterans without PTSD had the lowest levels of risk factors, subthreshold PTSD intermediate levels, and full PTSD the highest levels. As expected, those with PTSD were more likely to have comorbid psychiatric diagnoses, such as major depression, generalized anxiety disorder, and substance abuse disorder.

PTSD and Incidence of Type-2 Diabetes

A total of 658 new diabetes diagnoses were reported over a median of 19.4 years of follow-up. The cumulative incidence of diabetes was higher in non-white, Hispanic, and less

educated Veterans (**supplemental e-Table 2**). As expected, those with higher BMI and hypertension at baseline were more likely to develop diabetes; however, there was no relationship between alcohol consumption, major depression, generalized anxiety disorder, and alcohol or drug abuse disorder in 1992 and diabetes onset through 2012.

The age-adjusted cumulative incidence of type-2 diabetes was significantly higher in Veterans with PTSD at baseline (18.9%) than in those without PTSD (14.4%, p=0.044), and somewhat intermediate in those with subthreshold PTSD (16.4%) (p for trend=0.027). The results were similar in Veterans who served in Southeast Asia and in those who did not (**Figure 2**). The age-adjusted OR for new-onset diabetes was 1.2 (95% CI: 0.9-1.5) for subthreshold PTSD and 1.4 (95% CI: 1.0-1.9) for PTSD meeting full diagnostic criteria (**Table 2**, model 1). Adjustment for military service factors and by demographic characteristics diminished these associations (model 2). Further adjustment for BMI and other cardiovascular and behavioral factors assessed at or before 1992, brought the OR estimate close to the null (model 3), while the addition of other psychiatric conditions to the model had no impact (model 4).

Table 3 shows the results of the twin-based within-pair analyses comparing brothers discordant for PTSD (370 pairs). In this analysis, no significant association was found between PTSD and diabetes onset.

When all self-reported diabetes was considered as the outcome, results remained similar, although they were slightly more significant. In the within-pair analysis, the unadjusted OR for subthreshold PTSD was 1.3 (95% CI: 0.9-1.8), and for PTSD it was 1.4 (95% CI: 0.9-2.1, p=0.08 for trend). The estimates were unchanged after adjusting for other factors although the confidence intervals became somewhat wider.

Discussion

In this prospective study of Vietnam-era Veterans, PTSD was associated with a 40% increased risk of new-onset type-2 diabetes which was largely explained by a cluster of metabolic and behavioral risk factors known to influence insulin resistance. It is possible that PTSD leads to hormonal and metabolic abnormalities that influences insulin resistance and, in turn, increase the risk of diabetes. Based on the analysis of PTSD-discordant twin pairs, familial factors shared by the twins play a role in these associations, and suggest that there are common biological or behavioral factors for both PTSD and insulin resistance/ diabetes.

This is the first prospective, long-term study to examine the association between a diagnosis of PTSD and incidence of treated diabetes mellitus. Although recent studies have reported an association between PTSD and diabetes (Boyko et al., 2010; Goodwin et al., 2005; Lukaschek et al., 2013; Norman et al., 2006), all except one (Boyko et al., 2010) were cross-sectional, and therefore limited in their ability to establish whether or not PTSD preceded the onset of diabetes. The only prospective study which found an association between PTSD and a self-report of physician-diagnosed diabetes (Boyko et al., 2010) is based on data from the Millennium Cohort Study that included 44,754 Veterans where PTSD was assessed by means of the PTSD Checklist, civilian scale. This is a young cohort (mean age

approximately 36 years old) followed for 3 years, among whom the rate of new-onset diabetes was very low (<0.01%) but baseline PTSD was associated with a 2-fold increase in risk of new diabetes. Thus, differences in the two study populations likely account for the divergent findings. In addition, self-reported diabetes included any reported diabetes, while we focused on diabetes treated pharmacologically.

Several studies have linked psychological stress and depression to visceral fat, insulin resistance, and other components of the metabolic syndrome (Brunner et al., 2002; Capuron et al., 2008; Chrousos, 2000; Vaccarino et al., 2008). Enduring dysregulation of the HPA axis has been implicated, such that stressful experiences activate the HPA axis leading to excessive cortisol production, central adiposity, insulin resistance, and associated metabolic abnormalities (Friedman et al., 2004). Indeed, HPA axis dysregulation with excess cortisol production has been reported in persons with glucose intolerance or diabetes (Andrews, Herlihy, Livingstone, Andrew, & Walker, 2002; Liu, Bravata, Cabaccan, Raff, & Ryzen, 2005). However, the neurobiology of PTSD is complex, particularly as it relates to stress response and metabolic risk, since lower, rather than higher, cortisol levels in plasma and urine have been associated with PTSD during basic conditions, likely due to enhanced negative feedback sensitivity of the glucocorticoid receptors (Bremner, Southwick, & Charney, 1999; Yehuda, 2002).

Our results are consistent with an important role of metabolic and lifestyle factors in the association between PTSD and type-2 diabetes. Veterans with PTSD had a higher prevalence of cardiometabolic risk factors at baseline, such as sedentary behavior, smoking, alcohol consumption, hypertension and overweight. When these factors were accounted for, the association between PTSD and incident diabetes was weakened. Although the direct role of these risk factors in the PTSD-diabetes association, or in affecting insulin resistance, cannot be discerned from our analysis, it is plausible that they are the consequences of PTSD (mediators) rather than PTSD being a consequence of these risk factors (potential confounders).

Within twin pairs, no association was found even in unadjusted analysis, suggesting that familial influences shared by the twins are important in this association. There could be shared environmental factors or health behaviors that influence diabetes risk, such as socioeconomic and lifestyle factors, many of which are acquired in childhood and are known to strongly predict adult behaviors (Case, Fertig, & Paxson, 2005; Lauderdale et al., 1997; Ortega, Ruiz, Castillo, & Sjostrom, 2008). It is also possible that common biological precursors lead to both PTSD and insulin resistance/diabetes. Thus, PTSD could be a marker of neuroendocrine and metabolic dysregulation which may lead to increased risk of diabetes. Future studies should focus on the elucidation of cardiometabolic pathways that are associated with PTSD and also increase the risk of insulin resistance and diabetes. As many of these factors may be modifiable, this research has important clinical and public health implications that are especially relevant to the physical and mental health of our Veteran population.

This study has a number of limitations. The gold standard for the presence of diabetes is 2 measures of fasting measure of glucose that exceed 125 mg/dL; this assessment was not

feasible. Instead we relied on self-report and a medication inventory to classify diabetes. We did a validation in a subsample and found an agreement of 97.5% between the definition of diabetes used in this analysis and clinically confirmed diabetes reported by health care providers. Although we have a good measure of clinically diagnosed diabetes, it likely underestimates the total burden of diabetes, since undiagnosed cases would not have been treated and therefore included. If PTSD status is associated with the likelihood of having diabetes diagnosed or treated among all those with diabetes, we may have failed to fully characterize the PTSD-diabetes association. However, when analyses were repeated with all self-reported diabetes as the outcome, conclusions did not change. Another limitation is that about 36% of eligible individuals at baseline were not included in this prospective analysis, primarily due to non-response. If the association between PTSD and diabetes were different in non-responders and responders, our findings would be biased. However, responders and non-responders were quite similar in their distribution of baseline risk factors and PTSD status, suggesting that bias due to non-response is unlikely in our results. Furthermore, we began our observation period in 1992, when PTSD status was assessed through the DIS, and excluded participants who reported diabetes prior to 1992. If diabetes in relationship with PTSD occurred earlier than 1992, we would have missed the association. Moreover, we were not able to provide insight into the temporal relationship at baseline between PTSD and cardiovascular and metabolic comorbidities associated with diabetes.

Another limitation is our lack of measures of insulin resistance, a major precursor and biological mechanism leading to diabetes. A direct measurement of either insulin action or insulin secretion would have been helpful in clarifying whether PTSD, directly or through other factors, affects the risk of diabetes by influencing insulin resistance. Additionally, we were unable to differentiate PTSD due to combat or to other types of trauma. Finally, our sample was all male and predominantly non-Hispanic whites; therefore, our findings are not generalizable to other demographic groups. Strengths of our study include the prospective design, the large sample size, and the availability of a clinical diagnosis of PTSD. In addition, the co-twin study design controls for potentially unmeasured confounding factors such as familial, genetic, and early environmental characteristics that may affect both the risk of PTSD and the risk of diabetes.

In conclusion, in a prospective study of Vietnam-era male Veterans, we found that PTSD was associated with a 40% increase in the risk of type-2 diabetes and with a cluster of metabolic and behavioral baseline risk factors that largely explained the association. Shared precursors to both PTSD and insulin resistance/diabetes may play a role in the link between PTSD and type-2 diabetes. Thus, PTSD could be a marker of hormonal and metabolic dysregulation which may lead to insulin resistance and increased risk of diabetes.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Highlights

- We examine whether PTSD is associated with incidence of type-2 diabetes.

- We use a longitudinal twin study design.

- PTSD is prospectively associated with a 40% increased risk of type-2 diabetes.

- Twins discordant for PTSD do not differ in their risk of diabetes.

- Common mechanisms may lead to both PTSD and insulin resistance/diabetes.
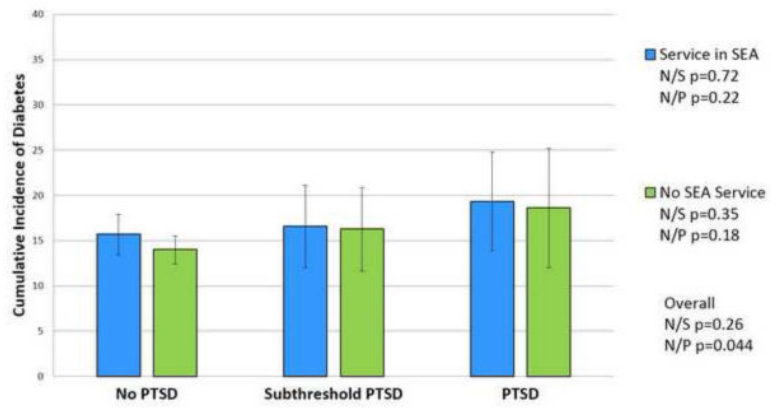
Figure 1.
Eligibility for Prospective Cohort Study of the Association of PTSD and Incident Diabetes
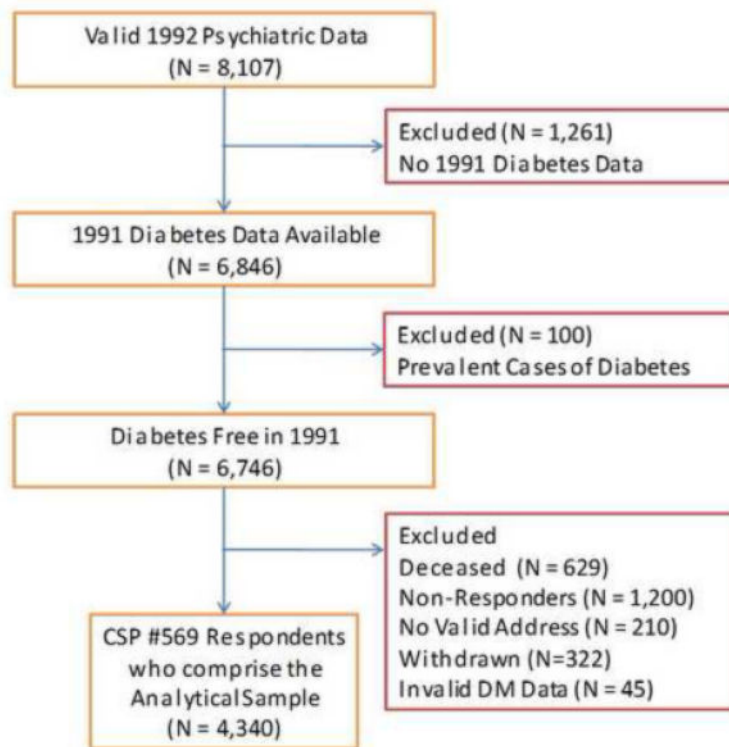
Figure 2.
Association of PTSD with Age-Adjusted Incident Diabetes According to Vietnam Theater
Service.

Footnotes to Figure 2:

N/S: No PTSD vs. Subthreshold PTSD

N/P: No PTSD vs. PTSD

No PTSD is defined as having no lifetime history of PTSD at the 1992 interview.

PTSD is defined as having a lifetime history of PTSD at the 1992 interview.

Subthreshold PTSD is defined as meeting both the A and B criteria and either the C or D
criteria for PTSD according to the DSM-IIIR.

All estimates are weighted for non-response.

Table 1

Demographic, Military Service, Lifestyle, Clinical and Psychiatric Factors by PTSD Status.

| | 1992 PTSD Diagnosis | | |
Factors at Baseline (1992)	No PTSD N=3,424	Subthreshold PTSD N=541	PTSD N=375
Demographic Factors			
Age			
39	18.6	20.4	21.8
40-41	19.0	19.2	22.9
42-43	33.5	33.9	35.4
44	28.9	26.5	19.9
White Race	91.0	90.7	90.1
Hispanic Ethnicity	2.6	2.5	4.1
Married/Partnered/Widowed	81.1	77.3	75.5
Education			
Less than H.S. Graduate	2.6	5.0	4.9
High School Graduate	30.8	30.9	29.5
Some College/Vocational	40.3	42.6	46.0
College Graduate or more	26.4	21.5	19.6
Employment Status			
Full Time	94.9	94.2	89.8
Part Time	1.1	1.7	3.4
Unemployed	4.0	4.1	6.8
Military Service Factors			
Branch of Service			
Army	49.0	52.3	55.3
Navy	26.0	20.6	19.8
Air Force	19.5	17.6	12.8
Marines	5.5	9.5	12.1
Enlistment year			
1967	33.5	37.0	35.2
1968-69	33.1	33.9	33.1
1970	33.3	29.1	31.7
Officer Military Rank at Enlistment	3.6	1.7	1.4
Service in Southeast Asia	34.8	49.8	61.3
Lifestyle and Cardiovascular Risk Factors			
Cigarette Smoking			
Current	30.0	37.2	45.8
Former	33.3	37.6	31.5
Never	36.7	25.2	22.7
Alcohol Consumption			
Never Drinker	6.7	5.7	5.3

Factors at Baseline (1992)	1992 PTSD Diagnosis		
	No PTSD N=3,424	Subthreshold PTSD N=541	PTSD N=375
Former Drinker	31.3	33.2	36.9
<2 per day	47.4	41.4	39.7
2 per day	14.6	19.7	18.0
Physical Activity			
No Physical Activity	11.0	10.0	7.9
Moderate Physical Activity	63.5	63.0	65.8
Vigorous Physical Activity	25.5	27.0	26.3
BMI			
< 25	40.6	43.4	35,4
25 – 30	48.1	44.9	53.3
> 30	11.3	11.7	11.3
Hypertension	17.1	19.3	23.4
Cardiovascular Disease	11.3	10.9	17.4
Psychiatric Conditions			
Major Depressive Disorder	5.5	13.3	32.7
Generalized Anxiety Disorder	0.9	3.1	10.6
Alcohol Use Disorder	48.6	62.8	72.2
Substance Use Disorder	6.3	12.5	27.1

All data weighed for non-response.

Table 2

Association of PTSD with Incident Diabetes Among VET Registry Members, Unadjusted and Adjusted for Demographic, Military Service, Lifestyle, Clinical, and Psychiatric Factors

Models	Incident Diabetes						
	No PTSD n=3,424		Subthreshold PTSD n=541		PTSD n=375		P for Trend
	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)	
Model 1: **Adjusted for Age**	1.0	(ref)	1.2	(0.9 – 1.5)	1.4	(1.03 – 1.8)	0.027
Model 2: **Adjusted for Demographic and Military Service Factors** [*]	1.0	(ref)	1.1	(0.8 – 1.4)	1.2	(0.9 – 1.7)	0.16
Model 3: **Adjusted for All Above Plus Lifestyle and Cardiovascular Risk Factors**[†]	1.0	(ref)	1.1	(0.8 – 1.5)	1.1	(0.8 – 1.5)	0.41
Model 4: **Adjusted for All Above Plus Psychiatric Conditions**[‡]	1.0	(ref)	1.2	(0.9 – 1.5)	1.2	(0.9 – 1.7)	0.16

All data weighed for non-response.

No PTSD is defined as having no lifetime history of PTSD at the 1992 interview.

PTSD is defined as having a lifetime history of PTSD at the 1992 interview.

Subthreshold PTSD is defined as meeting both the A and B criteria and either the C or D criteria for PTSD according to the DSM-IIIR.

[*] The model adjusted demographic and military service factors including age, race, ethnicity, marital status, education, branch of service, enlistment year, service in Southeast Asia, and military rank at enlistment.

[†] In addition to the factors above, the model adjusted for baseline (1992) lifestyle and clinical factors including cigarette smoking, alcohol use, physical activity, BMI, hypertension, hypercholesterolemia, and history of cardiovascular disease.

[‡] In addition to the factors above, the model adjusted for baseline (1992) psychiatric factors including depression, generalized anxiety disorder, and alcohol or drug abuse disorder.

Table 3

Association of PTSD with Incident Diabetes Among VET Registry Twin Pairs Discordant for PTSD. Unadjusted and Adjusted for Selected Demographic, Military Service and Lifestyle Factors.

	Incident Diabetes						
Models	**No PTSD n=3,424**		**Subthreshold PTSD n=541**		**PTSD n=375**		**P for Trend**
	OR	**(95% CI)**	**OR**	**(95% CI)**	**OR**	**(95% CI)**	
Model 1: **Adjusted for Age**	1. 0	(ref)	1. 2	(0.8 – 1.7)	1. 0	(0.6 – 1.7)	0.68
Model 2: **Adjusted for Demographic and Military Service Factors** [*]	1. 0	(ref)	1. 2	(0.8 – 1.8)	1. 0	(0.6 – 1.7)	0.83
Model 3: **Adjusted for Selected Demographic, Military Service and Lifestyle Factors** [†]	1. 0	(ref)	1. 2	(0.8 – 1.8)	1. 0	(0.6 – 1.8)	0.75

All data weighed for non-response.

No PTSD is defined as having no lifetime history of PTSD at the 1992 interview.

PTSD is defined as having a lifetime history of PTSD at the 1992 interview.

Subthreshold PTSD is defined as meeting both the A and B criteria and either the C or D criteria for PTSD according to the DSM-IIIR.

Model 1 includes 370 twin pairs; Model 2 includes 352 twin pairs; and Model 3 includes334 twin pairs.

[*] The model adjusted for demographic and military service factors including age, race, ethnicity, marital status, education, branch of service, enlistment year, service in Southeast Asia, and military rank at enlistment.

[†] The model adjusted for selected demographic, military service and lifestyle factors including age, race, ethnicity, education, military rank at enlistment, service in Southeast Asia, physical activity, and BMI.