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Clinically Meaningful PTSD Improvement and Incident Hypertension, Hyperlipidemia and Weight Loss

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Abstract

Objective: PTSD is associated with increased risk for cardiometabolic disease. Clinically meaningful PTSD improvement is associated with a lower risk for diabetes, but it is not known if

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similar associations exist for incident hypertension, hyperlipidemia, and clinically relevant weight loss (i.e. ≥5% loss).

Methods: Medical record data from Veterans Health Affairs patients with clinic encounters between fiscal year (FY) 2008 to 2015 were used to identify patients with worsening/no PTSD improvement (i.e. PTSD checklist (PCL) score decrease < 10), small (10–19 point PCL decrease) and large (≥20 point PCL decrease) PTSD improvement. To estimate the association between degree of PTSD improvement and incident hypertension (n=979), incident hyperlipidemia (n=1,139) and incident ≥5% weight loss (1,330), we computed Cox proportional hazard models, controlling for confounding using inverse probability of exposure weighting (IPEW).

Results: Overall, patients were about 40 years of age, 80% male and 65% white. Worsening/no PCL change occurred in about 60%, small improvement in 20% and large improvement in 20%. After weighting data, compared to worsening/no change, both small and large PTSD improvements were associated, albeit not significantly, with lower risks for hypertension (HR=0.68; 95%CI:0.46–1.01 and HR=0.79; 95%CI:0.53–1.18, respectively). In weighted data, PTSD improvement was not associated with incident hyperlipidemia or ≥5% weight loss.

Conclusions: We observed limited evidence for an association between PTSD improvement and decreased hypertension risk. PCL decreases were not associated with hyperlipidemia or ≥5% weight loss. Further studies that measure potential physical health benefits of change in specific PTSD symptoms are needed.

Keywords

Posttraumatic stress disorder; hypertension; hyperlipidemia; obesity; epidemiology

INTRODUCTION

Posttraumatic stress disorder (PTSD) has been associated with metabolic disease (Cohen, Marmar, Ren, Bertenthal, & Seal, 2009; Schnurr & Green, 2004; Talbot et al., 2015) and metabolic syndrome (Heppner et al., 2009; S. Rosenbaum et al., 2015). PTSD likely leads to type 2 diabetes (T2D), weight gain, hypertension and hyperlipidemia through multifactorial processes which include physiological abnormalities related to allostatic load and stress regulation (Friedman & McEwen, 2004) and poor health behaviors such as sedentary lifestyle, heavy smoking and alcohol consumption, and poor diet (Schnurr & Green, 2004).

Most, but not all, (Tsai & Shen, 2017) cross-sectional studies indicate PTSD is associated with prevalent hypertension (Burg et al., 2017; Kibler, Joshi, & Ma, 2009; Paulus, Argo, & Egge, 2013). There are few longitudinal studies of PTSD and incident hypertension. Among combat injured Veterans, PTSD was associated with a near two-fold increased risk for hypertension (Howard et al., 2018) and the prospective Nurses' Health Study revealed an increasing risk for hypertension with increasing number of PTSD symptoms (Sumner et al., 2016) in models that adjusted for family history and sociodemographics; however, no association was observed after further control for obesity, smoking, alcohol use, antidepressants and other confounding variables. Similarly no association was observed between PTSD and hypertension in a prospective veteran cohort (Schnurr, Spiro, & Paris, 2000).

Compared to Veterans with trauma and no PTSD, those with PTSD were 49% more likely to have high cholesterol (El-Gabalawy, Blaney, Tsai, Sumner, & Pietrzak, 2018) and in two smaller, cross-sectional studies in civilians, PTSD compared to no PTSD was associated with higher total serum cholesterol (Maia et al., 2008; Talbot et al., 2015). Analysis of National Health and Nutrition Examination study data found PTSD was associated with twice the prevalence of hypercholesterolemia after controlling for depression (Tsai & Shen, 2017).

Longitudinal studies indicate PTSD is associated with increased risk of weight gain in veterans (Buta et al., 2018; LeardMann et al., 2015) and non-veteran cohorts (Kubzansky et al., 2014; Pagoto et al., 2012; Perkonigg, Owashi, Stein, Kirschbaum, & Wittchen, 2009). Over a 3-year observation period, in a cohort of nearly 500,000 veterans, those with PTSD compared to patients without PTSD, were more likely to be overweight/obese and gaining weight, vs. remaining overweight at a stable level (Maguen et al., 2013).

It is not known if clinically significant improvements in PTSD are associated with reduced risk for these poor health outcomes. A few exceptions include evidence that adequate PTSD treatment is associated with reduced blood pressure (Burg et al., 2017; Schubert et al., 2019). In addition, a large retrospective cohort study revealed that veterans with PTSD who did vs. did not have clinically meaningful reduction in PTSD Checklist scores were 50% less likely to develop T2D (Scherrer et al., 2019).

We sought to expand knowledge about the link between PTSD improvement and cardiovascular risk factors. To our knowledge there is no existing literature which has measured the association between PTSD symptom decrease and risk for hypertension, hyperlipidemia or clinically relevant weight loss which is defined as ≥5% weight loss (Jensen et al., 2014). We use ≥5% weight loss because this threshold is applied in evaluating the VHA's weight management program as it is associated with reduction in obesity related disease (Littman, Boyko, McDonell, & Fihn, 2012). Our goals were not to determine the effect of PTSD psychotherapy. Rather, we sought to determine the association between the magnitude of PTSD symptom reduction (either through treatment or spontaneous remission) and these chronic health problems.

In Veterans Health Affairs (VHA) patients with PTSD we created a categorical variable to measure worsening/no PTSD improvement, small PTSD improvement and large PTSD improvement. We tested the hypotheses that patients with small and large PTSD improvement, compared to those with worsening/no PTSD improvement, would have a significantly lower risk for incident hypertension and incident hyperlipidemia. In addition, we hypothesized that compared to patients with worsening/no PTSD improvement, those with small and large PTSD improvement would have an increased likelihood of ≥5% weight loss.

METHODS

The study was approved by the Harry S. Truman Memorial Veterans' Hospital, Columbia Missouri and the Saint Louis University Institutional Review Boards. Data were obtained

from VHA patient medical records from fiscal years (FY) 2008 to FY2015, which contain diagnostic codes, type of clinic encounter (e.g. primary care, PTSD psychotherapy, physical therapy, etc.), dispensed medications and fill dates, laboratory results, vital sign and demographic measures.

MEASURES

Exposure variable: Detailed variable definitions are shown in e-Table 1. The PTSD Checklist (PCL) score was used to measure PTSD severity and improvement. The PCL is used to screen for PTSD, assist in making a PTSD diagnoses and to monitor PTSD symptom changes (www.ptsd.va.gov). We did not distinguish whether scores were from the military or civilian PCL version or versions specific to a traumatic event. The military PCL and civilian PCL differ the by types of traumatic events queried. The PCL includes 17 questions about PTSD symptoms per DSM-IV criteria. Each item is scored on a 1 to 5 scale with 1 = 'not at all' to 5='extremely. Summing scores results in a range from 17 to 85. The PCL has good internal consistency, test-retest reliability, and convergent validity (Blanchard, Jones-Alexander, Buckley, & Forneris, 1996; Ruggiero, Del Ben, Scotti, & Rabalais, 2003).

PCL scores were obtained from administrative data and manually chart abstracted by Abt Associates' (www.abtassociates.com) trained medical chart abstractors. Abt Associates abstracted 22,287 valid PCL scores from a random sample of 5,916 patients with PTSD diagnosed between FY2008 and FY2012. After adding administrative data and removing duplicate scores, 26,631 valid PCL values for 4,441 (out of 5,916) PTSD patients were available from encounters between FY2008 to FY2015.

PTSD was defined by two outpatient ICD-9 codes in the same 12 months or 1 inpatient code for PTSD. This diagnostic algorithm has good agreement (79.4%) with the Structured Clinical Interview for DSM-IV lifetime diagnosis for PTSD (Holowka et al., 2014), and has 82% positive predictive value when compared to a PCL score ≥50 (Gravely et al., 2011).

We defined an exposure year in which patients were classified into three PCL change exposure groups defined as large PTSD improvement (≥20 point PCL decrease), small PTSD improvement (10–19 point PCL decrease), and worsening/no change in PTSD (< 10 point PCL decrease). A 10–20 point decrease on the PCL is considered clinically meaningful improvement (Monson et al., 2008). We used the 20 point cutoff for a large decrease to enhance our ability to detect an association between PTSD improvement and each health outcome (Salas et al., 2020; Scherrer et al., 2019). The exposure year was the 12-month period after a patient's first visit with a PCL ≥50 in FY2008 to FY2012, which is the threshold for probable PTSD (Monson et al., 2008; "Using the PTSD Checklist (PCL)," National Center for PTSD 2012). Change in PCL scores was measured by the difference in the last PCL in the exposure year that was at least 8 weeks after the first PCL≥50. We used a 12 month period to measure change because this is a sufficient amount of time for patients to complete minimally adequate duration of psychotherapy, i.e. 9 or more sessions in 15 weeks. In addition the 12 month period allowed us to identify a sufficient number of subjects with repeated PCL values to measure change in PTSD severity.

Outcome variables: Incident hypertension was defined by ICD-9 code 401.x or a new fill for an anti-hypertensive medication with the exception of prazosin and clonidine (Burg et al., 2017). Incident hyperlipidemia was defined by ICD-9 codes 272.0, 272.1, 272.2 or 272.4 or a new fill for an anti-lipemic medication. Incident ≥5% weight loss was defined by the difference between index weight (the last available weight in the year prior to index) and the first weight value >90 days after start of follow-up that indicated a ≥5% decrease.

Covariates: Sociodemographic variables included age (continuous), gender (male vs. female), race (white, black, other), marital status (married vs. else) and access to only VHA health insurance vs. other forms of health insurance. A 'missing' category was included for demographic variables to retain all cases. Age, gender, marital status, and insurance were missing in 0% of cases. About 5% of the sample was missing race.

We created a high primary health care utilization variable, which is the top quartile of average outpatient visits per month (vs. the lowest 75th percentile), to control for detection bias. Psychiatric and behavioral comorbidities were coded as binary indicators (yes vs. no) and included depression, anxiety disorders, sleep disorder, alcohol abuse/dependence, drug abuse/dependence and smoking status. We also included binary (yes vs. no) variables indicating sustained use of atypical antipsychotics, specific antidepressants (mirtazapine and bupropion), and TCA and SNRI antidepressant classes because they are associated with changes in weight (Gafoor, Booth, & Gulliford, 2018; Spertus, Horvitz-Lennon, Abing, & Normand, 2018). Binary indicators for physical comorbidities included hypertension, hyperlipidemia and obesity. The latter were included as covariates when not modeled as the outcome. All covariates were measured between FY2008 up to index date. We also included binary (yes vs no) psychiatric treatment variables to describe minimally adequate PTSD psychotherapy, measured only in the exposure year, and acute phase (12 weeks of antidepressant medication (ADM)) therapy, measured from FY2008 to index date. We controlled for severity of the first PCL value by including a severe (≥70) vs. moderate (50–69) PTSD indicator. Finally, for the weight loss sample, we controlled for baseline BMI (normal < 25.0, overweight 25.0- < 30.0, obese ≥30.0).

ELIGIBILITY

In this retrospective cohort design, we randomly selected 5,916 patients, (a sample size for which chart abstraction of PCL scores was feasible), from a parent sample of 17,476 patients aged 18–70 years who had at least two PTSD specialty clinic encounters and a diagnosis of PTSD between FY2008 to FY2012. We compared the parent and random sample on age, gender, marital status, race, and insurance distributions and found they were similar in both samples.

The observation period began in FY2008 because the VHA began implementing evidence based PTSD treatment at that time. We used FY2008 to FY2013 to measure change in PCL scores. Because data were available up to FY2015, all subjects had at least two years and a maximum of seven years follow-up for the outcome to occur after PCL change. See e-Figure for an illustration of the retrospective cohort design.

Index, (i.e. baseline), date was the end of the exposure year; thus, the exposure year could occur anytime between FY2008 and FY2013 and the index date could occur between FY2009 to FY2013 (see e-Figure). Follow-up time was measured as days from index to incident hypertension, incident hyperlipidemia or incident ≥5% weight loss, or until censor date, which is the last clinic encounter if there was no incident condition.

Three separate samples were created for each outcome. In the year prior to index (i.e. in the exposure year), the hypertension sample had no ICD-9 code for hypertension and no anti-hypertension medication while the hyperlipidemia sample had no ICD-9 codes for hyperlipidemia and no anti-lipemic medication. The sample to model ≥5% weight loss must have had a weight in the year before index and a second weight value >90 days after index. Because T2D is highly correlated with each outcome all samples were free of T2D at index.

As shown in Figure 1, after applying eligibility criteria, 979 patients with PTSD were eligible for the incident hypertension sample; 1,139 with PTSD were eligible for the incident hyperlipidemia sample; and 1,330 with PTSD were eligible for the incident ≥5% weight loss sample.

Analytic Approach

Propensity score methods: Propensity scores (PS) and inverse probability of exposure weighting (IPEW) balanced the distribution of covariates listed in Table 2 between the three PTSD improvement groups. Balancing the distribution of covariates controls for potential confounding (P. R. Rosenbaum & Rubin, 1983). The PS is the probability of worsening/no PTSD change, a small PTSD improvement and a large PTSD improvement, conditional on covariates, calculated from a multinomial logistic regression model. After obtaining the PS, stabilized weights were calculated for each patient using standard approaches (Austin & Stuart, 2015; Curtis, Hammill, Eisenstein, Kramer, & Anstrom, 2007; Harder, Stuart, & Anthony, 2010; Xu et al., 2010). Stabilized weights should have a mean close to one and a maximum <10 for well-specified PS models, and any weights ≥10 should be trimmed (Sturmer, Wyss, Glynn, & Brookhart, 2014). After applying IPEW, a pseudo-population is created where covariates are balanced between PCL change groups, evidenced by a standardized mean difference (SMD%)<10% (Austin & Stuart, 2015).

Primary analyses: SAS v9.4 (SAS Institute, Cary, NC) was used for all analyses at an alpha level of 0.05. Descriptive analyses used chi-square tests for categorical variables and one-way ANOVA for continuous variables to measure the association of the PCL change groups with each covariate. Poisson regression models calculated outcome incidence rates per 1000 person-years (PY).

Crude (unweighted) and weighted Cox proportional hazards models measured the association between the change in PCL scores and each outcome with worsening/no PCL change as the referent group. Associations were expressed as hazard ratios (HR) and 95% confidence intervals. Robust, sandwich-type variance estimators were used to calculate confidence intervals and p-values in weighted models. The proportional hazards assumption in each model was tested by examining a time dependent interaction term of PCL exposure group and log follow-up time, where a significant ($p<0.05$) interaction term indicates

different hazards over time. The assumption was met for all models (p-value range: 0.10 to 0.85).

Sensitivity analyses: Allowing patients to have baseline obesity may reduce our ability to detect an association between PCL change and incident hypertension and hyperlipidemia. We conducted sensitivity analyses by requiring patients to be free of obesity and free of hypertension and T2D at baseline for models of incident hypertension and free of obesity, hyperlipidemia and T2D in models of incident hyperlipidemia.

RESULTS

Patient characteristics by each sample are shown in Table 1. In the 3 samples combined, about 60% experienced worsening/no PTSD improvement, 20% had a small PTSD improvement and 20% had a large PTSD improvement. Patients were approximately 40 years of age, 80% male, and two-thirds white.

Across the three patient samples, the first, average PCL score was around 64 while last PCL score was around 56. About 30% of each sample had a severe (≥70) initial PCL. The prevalence of depression, anxiety, sleep disorder, minimally adequate duration of PTSD psychotherapy and acute phase antidepressant treatment were slightly higher in the ≥5% weight loss sample. The prevalence of other covariates were similar in the three samples.

Table 2 shows the distribution of covariates across the 3-group PTSD improvement variable in each sample. In the hypertension sample, those with a large PTSD improvement were older (average age: 40.1) compared to those with a small PTSD improvement (average age: 37.6) and worsening/no change (average age: 37.5). Patients with a large PTSD improvement had the highest prevalence of VHA only insurance followed by those with worsening/no PTSD change and those with a small PTSD improvement. Minimally adequate duration of PTSD psychotherapy was most prevalent in the large PTSD improvement group (60.1%), followed by the small PTSD improvement (43.8%) and worsening/no change PTSD group (35.7%). The prevalence of acute phase ADM treatment was largest in the no change group (74.0%) and lowest in the large PTSD improvement group (61.9%). Other anxiety, alcohol and drug abuse/dependence, and atypical antipsychotic use were also related to magnitude of PTSD improvement.

In the hyperlipidemia sample, the large PTSD improvement group had the lowest prevalence of males (75.5%) compared to the worsening/no change (83.0%) and small PTSD improvement (84.9%) groups. Minimally adequate duration of PTSD psychotherapy was most prevalent in the large improvement (55.8%) group and least prevalent in the worsening/no change (36.8%) group. Conversely, acute phase ADM treatment was most prevalent in the worsening/no change group (74.7%) and least in the large improvement (66.1%) group. Other anxiety and hypertension were also most prevalent in the worsening/no change group. See Table 2.

In the weight loss sample, the prevalence of an initial severe PCL was largest in patients who had large (36.3%) and small (34.1%) PTSD improvement compared to worsening/no change (28.9%). Minimally adequate duration of PTSD psychotherapy and acute phase ADM

treatment followed similar patterns as both the hypertension and hyperlipidemia samples. Other anxiety and drug abuse/dependence was least prevalent in the small PTSD improvement group, and other anxiety was most prevalent in the worsening/no change group while drug abuse/dependence was most prevalent in the large PTSD improvement group. See Table 2.

Table 3 shows cumulative incidence (%) and incidence rate per 1000 person-years (PY) overall and by PTSD improvement group in each sample. For hypertension, there were 225 events (23.0%), hypertension rate was 70.9/1000PY, and median follow-up time was 3.3 years (IQR: 2.1 to 4.5). For hyperlipidemia, there were 281 events (24.7%), an overall hyperlipidemia rate of 77.0/1000PY, and median follow-up time of 3.2 years (IQR: 2.1 to 4.4). Finally, there were 553 weight loss events (41.6%), with a rate of 156.9/1000PY and median follow-up time of 2.6 years (IQR: 1.4 to 3.8).

Relative to worsening/no change, patients with small and large PTSD improvement had lower hypertension incidence rates. Hyperlipidemia incidence rates were similar across PTSD improvement groups. Incidence of ≥5% weight loss was similar between the worsening/no change and small PTSD improvement groups and was lower among the large PTSD improvement group.

E-Table 2 shows IPEW results. IPEW balanced all covariates (SMD<10%) between the PCL change groups in each sample. There were no extreme weights (i.e. no weights were trimmed) in any sample. For the hypertension sample, stabilized weights ranged from 0.37 to 6.10 with a mean=1.00 (SD±0.41). In the hyperlipidemia sample, weights ranged from 0.37 to 3.59, mean=1.00 (SD±0.33). And finally, in the weight loss sample, weights ranged from 0.32 to 4.51, mean=1.00 (SD±0.35).

Table 4 shows results of unweighted and weighted Cox proportional hazard models. Results of crude, unweighted analysis revealed that, a small PTSD improvement compared to worsening/no change was associated with a significantly lower risk for hypertension (HR=0.66; 95% CI=0.46–0.95). A large PTSD improvement compared to worsening/no change showed a similar, yet non-significant trend toward lower risk (HR=0.74; 95% CI=0.53–1.04). After weighting data, the hazard ratios were largely unchanged but were not statistically significant due to broad confidence intervals. For both hyperlipidemia and weight loss, crude and weighted models showed no association between degree of PTSD improvement and incident hyperlipidemia or incident ≥5% weight loss.

Sensitivity Analysis

For the hypertension and hyperlipidemia samples, weighted models were run in a subset of patients without a history of obesity at baseline. In patients free of obesity, T2D, and hypertension at index (n=543), degree of PTSD improvement was not significantly associated with incident hypertension. Compared to worsening/no change, a small PTSD improvement was not significantly associated with incident hypertension (HR=0.69; 95%CI:0.40–1.20); nor was a large PTSD improvement (HR=0.79; 95%CI:0.45–1.38).

In a subsample free of obesity, T2D, and hyperlipidemia at index (n=622), weighted models showed no association between degree of PTSD improvement and incident hyperlipidemia. Results showed that compared to worsening/no change in PCL, there was no association between a small PTSD improvement (HR=1.03; 95%CI: 0.61–1.71) or a large PTSD improvement, (HR=0.93; 95%CI: 0.56–1.56) with incident hyperlipidemia.

DISCUSSION

In a cohort of VHA patients with PTSD, we found no association between small and large PTSD improvement and incident hyperlipidemia or likelihood of ≥5% weight loss. Although not statistically significant, after balancing covariates, we observed a small PTSD improvement and a large PTSD improvement were associated with a 32% and 21% lower risk for hypertension, respectively, as compared to worsening/no improvement.

The pattern of incidence rates and hazard ratios suggest PTSD improvement is likely associated with a lower risk for hypertension but unrelated to risk for hyperlipidemia and clinically relevant weight loss. Even though our point estimates are not statistically significant, our results are consistent with the idea that PTSD improvement has a different relationship with risk for hypertension as compared to risk for hyperlipidemia and weight gain. If confirmed in other samples, a unique relationship between PTSD improvement and decreased hypertension risk could be due to normalization of blood pressure following PTSD symptom reduction and alleviation of chronic stress. The current results interpreted in the context of our previous observation that clinically meaningful PTSD symptom decrease is associated with a 49% lower risk for T2D (Scherrer et al., 2019) raises the possibility that hyperglycemia and blood pressure are more sensitive and change more rapidly following large reductions in chronic stress associated with PTSD improvement. In contrast, PTSD may have no direct relationship with hyperlipidemia and substantial weight gain because these conditions take longer to develop, risk factors may be present prior to PTSD treatment and reducing risk may be dependent on long-term lifestyle change. Both physiological changes and behavioral factors likely contribute to links between PTSD and metabolic disease. We speculate that normalization of cortisol could be more strongly associated with hypertension versus hyperlipidemia and weight loss. Sustained lifestyle changes such as exercise and diet that lead to weight loss and improved cholesterol may require interventions paired with PTSD treatment.

Another possibility is that different PTSD phenotypes, with and without successful treatment, have different relative risks for hypertension, hyperlipidemia, weight gain and T2D. A large prospective cohort study in patients free of these conditions is needed. Such a study should include measuring specific PTSD symptoms and involve an intervention using evidence based PTSD treatment to establish which health outcomes are mitigated following large reductions in specific PTSD symptoms.

Our results are consistent with previous studies indicating PTSD treatment is associated with reduced risk for hypertension (Burg et al., 2017; Schubert et al., 2019). We are not aware of existing research designed to determine whether PTSD improvement is associated with incident hyperlipidemia. Except for one small study demonstrating PTSD symptom

reduction was correlated with weight loss among persons involved in a commercial diet plan (Johannessen & Berntsen, 2013), we are not aware of research reporting on the association between PTSD symptom change and clinically relevant weight loss.

Limitations:

Our results should be interpreted in the context of several limitations. Retrospective cohort designs are vulnerable to unmeasured confounding. We believe this study has controlled for potential confounding by balancing covariates across level of PTSD improvement, but it is possible that residual confounding exists. Measures of social support, lifestyle, diet and exercise, and individual PTSD symptoms were not available and could confound the current findings. It is possible that some outcomes were misclassified. Classifying patients with undiagnosed hypertension or undiagnosed hyperlipidemia as unaffected could bias results to the null hypothesis. However, these conditions are screened in routine annual physicals which limits the chance that they are undetected. We did not have sufficient sample size to create a cohort free of both hypertension and hyperlipidemia that would allow for precise confidence intervals and it remains unknown if PTSD improvement is associated with lower risk for these conditions in patients who are initially healthy. Our cohort was mostly male and all were veterans; therefore, results may not generalize to predominately female patient populations and to non-veteran populations. Last, we lacked a large enough sample to determine if Asian or Hispanic race/ethnicity influenced results.

Conclusions:

The present study provides modest evidence for secondary benefits of PTSD improvement that mitigate risk for hypertension. Similar conclusions regarding hyperlipidemia and weight gain are not supported. Prospective, intervention studies that measure dietary habits and individual PTSD symptoms in patients free of all cardiometabolic risk factors are warranted.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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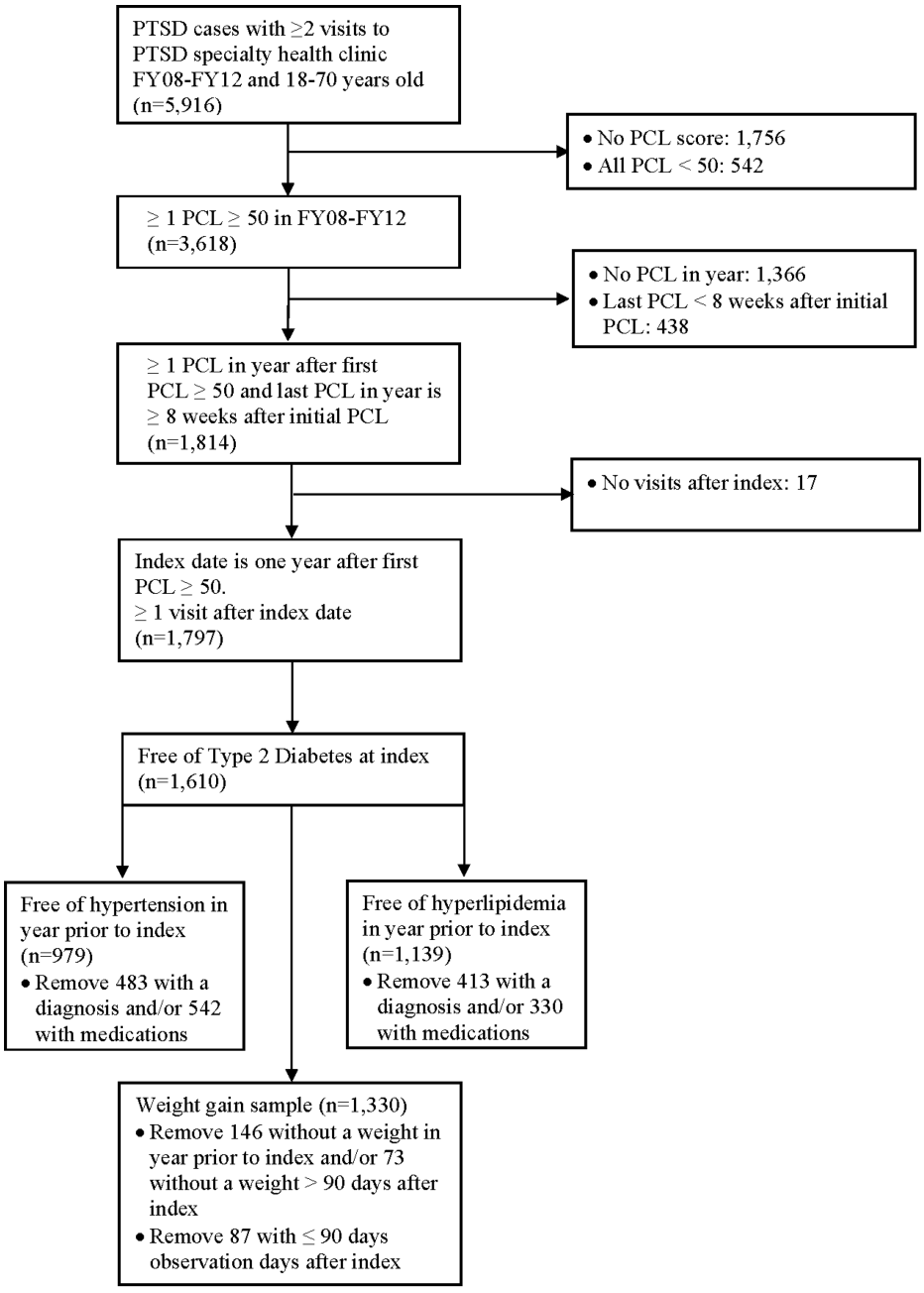

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Figure 1.
Sample selection process - PTSD cases

Table 1.

Overall sample characteristics, veterans with PTSD age 18–70 years

Variable, n(%) or mean (±sd)	Incident hypertension sample (n=979)	Incident hyperlipidemia sample (n=1,139)	Weight loss sample (n=1,330)
PCL change[^]			
Worsening/no change	558 (57.0)	688 (60.4)	800 (60.1)
Small improvement	203 (20.7)	218 (19.1)	252 (18.9)
Large improvement	218 (22.3)	233 (20.5)	278 (20.9)
Age (years), mean (±sd)	38.1 (±11.8)	38.6 (±12.2)	42.6 (±13.6)
Male gender, n(%)	799 (81.6)	932 (81.8)	1115 (83.8)
Race, n(%)			
White	666 (68.0)	751 (65.9)	870 (65.4)
Black	186 (19.0)	241 (21.2)	307 (23.1)
Other	76 (7.8)	89 (7.8)	103 (7.7)
Missing	51 (5.2)	58 (5.1)	50 (3.8)
Married, n(%)	396 (40.5)	465 (40.8)	599 (45.0)
VHA only insurance, n(%)	673 (68.7)	800 (70.2)	866 (65.1)
High primary HCU, n(%)	245 (25.0)	280 (24.6)	334 (25.1)
First PCL severe (≥70), n(%)	286 (29.2)	355 (31.2)	418 (31.4)
First PCL, mean (±sd)	64.3 (±9.0)	64.5 (±9.2)	64.7 (±9.1)
Last PCL, mean (±sd)	55.2 (±16.1)	56.4 (±16.0)	56.5 (±15.8)
Psychiatric comorbidities and treatments[a]			
Depression, n(%)	691 (70.6)	803 (70.5)	989 (74.4)
Other anxiety, n(%)[b]	234 (23.9)	295 (25.9)	363 (27.3)
Sleep disorder, n(%)	401 (41.0)	489 (42.9)	634 (47.7)
Alcohol abuse/dependence, n(%)	370 (37.8)	456 (40.0)	531 (39.9)
Drug abuse/dependence, n(%)	228 (23.3)	283 (24.8)	337 (25.3)
Smoking, n(%)[c]	516 (52.7)	602 (52.8)	686 (51.6)
Adequate PTSD psychotherapy, n(%)[d]	419 (42.8)	479 (42.0)	623 (46.8)
Adequate ADM treatment, n(%)[e]	689 (70.4)	819 (71.9)	1007 (75.7)
Atypical antipsychotic, n(%)[f]	212 (21.7)	253 (22.2)	337 (25.3)
ADM – TCA, n(%)[f]	97 (9.9)	114 (10.0)	159 (11.9)
ADM – SNRI, n(%)[f]	93 (9.5)	119 (10.5)	156 (11.7)
ADM – Mirtazapine, n(%)[f]	125 (12.8)	168 (14.8)	198 (14.9)
ADM - Bupropion, n(%)[f]	199 (20.3)	239 (21.0)	289 (21.7)
Physical comorbidities[a]			
Hypertension, n(%)	-	283 (24.9)	496 (37.3)

Variable, n(%) or mean (±sd)	Incident hypertension sample (n=979)	Incident hyperlipidemia sample (n=1,139)	Weight loss sample (n=1,330)
Hyperlipidemia, n(%)	224 (22.9)	-	491 (36.9)
Obesity, n(%) [g]	436 (44.5)	517 (45.4)	-
Baseline BMI category, n(%)	-	-	
Normal (< 25.0)	-	-	273 (20.5)
Overweight (25.0 – < 30.0)	-	-	488 (36.7)
Obese (≥ 30)	-	-	569 (42.8)

HCU=healthcare utilization; ADM=antidepressant; PTSD=Posttraumatic stress disorder; PCL=PTSD checklist.

[^] PCL change: no/worsening is <10 point PCL decrease, small improvement is 10–19 point PCL decrease, large improvement is ≥20 point PCL decrease

[a] Comorbidities occur from start of FY2008 to index date

[b] Composite of panic disorder, obsessive compulsive disorder, social phobia, generalized anxiety disorder, anxiety not otherwise specified

[c] Current smoker in health factors or ICD-9-CM code

[d] Measured from first PCL to index date (exposure year). Presence of at least 9 psychotherapy visits in any 15 week period

[e] At least 12 weeks of continuous ADM fills prior to index date

[f] Sustained use – at least 2 fills in any 6-month period prior to index

[g] BMI≥30 or ICD-9-CM code

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Table 2.

Sample characteristics overall and by degree of PTSD improvement[^] for each analytic sample, veterans age 18–70 years with PTSD

	Hypertension sample (n=979)			Hyperlipidemia sample (n=1,139)			Weight loss sample (n=1,330)		
Variable, n(%) or mean (±sd)	**Worsening/no change (n=558)**	**Small PTSD improvement (n=203)**	**Large PTSD improvement (n=218)**	**Worsening/no change (n=688)**	**Small PTSD improvement (n=218)**	**Large PTSD improvement (n=233)**	**Worsening/no change (n=800)**	**Small PTSD improvement (n=252)**	**Large PTSD improvement (n=278)**
Age (years), mean (±sd)	37.5 (±11.3)	37.6 (±12.0)	40.1 (±12.8)*	38.5 (±12.1)	37.6 (±12.6)	39.8 (±12.0)	42.2 (±13.5)	42.6 (±13.6)	43.7 (±13.7)
Male gender, n(%)	462 (82.8)	166 (81.8)	171 (78.4)	571 (83.0)	185 (84.9)	176 (75.5)*	680 (85.0)	213 (84.5)	222 (79.9)
Race, n(%)									
White	373 (66.8)	133 (65.5)	160 (73.4)	444 (64.5)	146 (67.0)	161 (69.1)	520 (65.0)	155 (61.5)	195 (70.1)
Black	109 (19.5)	38 (18.7)	39 (17.9)	149 (21.7)	44 (20.2)	48 (20.6)	186 (23.2)	61 (24.2)	60 (21.6)
Other	47 (8.4)	18 (8.9)	11 (5.1)	61 (8.9)	14 (6.4)	14 (6.0)	59 (7.4)	28 (11.1)	16 (5.8)
Missing	29 (5.2)	14 (6.9)	8 (3.7)	34 (4.9)	14 (6.4)	10 (4.3)	35 (4.4)	8 (3.2)	7 (2.5)
Married, n(%)	226 (40.5)	80 (39.4)	90 (41.3)	284 (41.3)	84 (38.5)	97 (41.6)	359 (44.9)	112 (44.4)	128 (46.0)
VHA only insurance, n(%)	388 (69.5)	126 (62.1)	159 (72.9)*	484 (70.3)	144 (66.1)	172 (73.8)	527 (65.9)	150 (59.5)	189 (68.0)
High primary HCU, n(%)	147 (26.3)	51 (25.1)	47 (21.6)	176 (25.6)	56 (25.7)	48 (20.6)	204 (25.5)	67 (26.6)	63 (22.7)
First PCL severe (≥70), n(%)	151 (27.1)	65 (32.0)	70 (32.1)	205 (29.8)	72 (33.0)	78 (33.5)	231 (28.9)	86 (34.1)	101 (36.3)*
Depression, n(%)	406 (72.8)	137 (67.5)	148 (67.9)	494 (71.8)	146 (67.0)	163 (70.0)	604 (75.5)	183 (72.6)	202 (72.7)
Other anxiety, n(%)[b]	155 (27.8)	31 (15.3)	48 (22.0)**	198 (28.8)	41 (18.8)	56 (24.0)*	244 (30.5)	46 (18.3)	73 (26.3)***
Sleep disorder, n(%)	229 (51.0)	89 (43.8)	83 (38.1)	300 (43.6)	91 (41.7)	98 (42.1)	383 (47.9)	119 (47.2)	132 (47.5)
Alcohol abuse/ dependence, n(%)	236 (42.3)	62 (30.5)	72 (33.0)**	294 (42.7)	79 (36.2)	83 (35.6)	334 (41.8)	89 (35.3)	108 (38.8)
Drug abuse/ dependence, n(%)	141 (25.3)	34 (16.8)	53 (24.3)*	179 (26.0)	44 (20.2)	60 (25.8)	206 (25.8)	48 (19.1)	83 (29.9)*
Smoking, n(%) [c]	299 (53.6)	101 (49.7)	116 (53.2)	367 (53.3)	113 (51.8)	122 (52.4)	403 (50.4)	134 (53.2)	149 (53.6)
Adequate PTSD psychotherapy, n(%) [d]	199 (35.7)	89 (43.8)	131 (60.1)***	253 (36.8)	96 (44.0)	130 (55.8)***	334 (41.8)	129 (51.2)	160 (57.6)***

	Hypertension sample (n=979)			Hyperlipidemia sample (n=1,139)			Weight loss sample (n=1,330)		
Variable, n(%) or mean (±sd)	**Worsening/no change (n=558)**	**Small PTSD improvement (n=203)**	**Large PTSD improvement (n=218)**	**Worsening/no change (n=688)**	**Small PTSD improvement (n=218)**	**Large PTSD improvement (n=233)**	**Worsening/no change (n=800)**	**Small PTSD improvement (n=252)**	**Large PTSD improvement (n=278)**
Adequate ADM treatment, n(%) [e]	413 (74.0)	141 (69.5)	135 (61.9) **	514 (74.7)	151 (69.3)	154 (66.1) *	623 (77.9)	193 (76.6)	191 (68.7) **
Atypical antipsychotic, n(%) [f]	132 (23.7)	46 (22.7)	34 (15.6) *	166 (24.1)	48 (22.0)	39 (16.7)	218 (27.2)	56 (22.2)	63 (22.7)
ADM – TCA, n(%) [f]	60 (10.7)	18 (8.9)	19 (8.7)	78 (11.3)	19 (8.7)	17 (7.3)	100 (12.5)	31 (12.3)	28 (10.1)
ADM – SNRI, n(%) [f]	61 (10.9)	17 (8.4)	15 (6.9)	78 (11.3)	18 (8.3)	23 (9.9)	98 (12.3)	28 (11.1)	30 (10.8)
ADM – Mirtazapine, n(%) [f]	79 (14.2)	21 (10.3)	25 (11.5)	105 (15.3)	27 (12.4)	36 (15.5)	122 (15.3)	34 (13.5)	42 (15.1)
ADM - Bupropion, n(%) [f]	122 (21.9)	35 (17.2)	42 (19.3)	148 (21.5)	41 (18.8)	50 (21.5)	171 (21.4)	50 (19.8)	68 (24.5)
Hypertension, n(%)	-	-	-	189 (27.5)	43 (19.7)	51 (21.9) *	306 (38.2)	94 (37.3)	96 (34.5)
Hyperlipidemia, n(%)	127 (22.8)	48 (23.6)	49 (22.5)	-	-	-	285 (35.6)	104 (41.3)	102 (36.7)
Obesity, n(%) [g]	246 (44.1)	91 (44.8)	99 (45.4)	319 (46.4)	90 (41.3)	108 (46.4)	-	-	-
Baseline BMI category, n(%)	-	-	-	-	-	-			
Normal (< 25.0)	-	-	-	-	-	-	165 (20.6)	48 (19.1)	60 (21.6)
Overweight (25.0 – < 30.0)	-	-	-	-	-	-	283 (35.4)	98 (38.9)	107 (38.5)
Obese (≥ 30)	-	-	-	-	-	-	352 (44.0)	106 (42.1)	111 (39.9)

PTSD=posttraumatic stress disorder; PCL=PTSD checklist (range: 17–85); HCU=healthcare utilization; ADM=antidepressant

*** p<0.001

** p<0.01

* p<0.05

^ PCL change: no/worsening is <10 point PCL decrease, small improvement is 10–19 point PCL decrease, large improvement is ≥20 point PCL decrease

[a] Comorbidities occur from start of FY2008 to index date

[b] Composite of panic disorder, obsessive compulsive disorder, social phobia, generalized anxiety disorder, anxiety not otherwise specified

[c] Current smoker in health factors or ICD-9-CM code

[d] Measured from first PCL to index date (exposure year). Presence of at least 9 psychotherapy visits in any 15 week period

[e] At least 12 weeks of continuous ADM fills prior to index date

[f] Sustained use – at least 2 fills in any 6 month period prior to index

[g] BMI≥30 or ICD-9-CM code

Table 3.

Cumulative incidence and incidence rate per 1000 person-years of hypertension, hyperlipidemia and ≥5% weight loss outcomes in patients with PTSD who have worsening/no improvement, small improvement or large PTSD improvement[a]

Hypertension	**Total n**	**Cumulative incidence Events (%)**	**Incidence rate per 1000PY**
Overall	*979*	*225 (23.0%)*	*70.9/1000PY*
PCL Change			
Worsening/No change	558	146 (26.2%)	81.3/1000PY
Small improvement	203	36 (17.7%)	53.4/1000PY
Large improvement	218	43 (19.7%)	61.3/1000PY
Hyperlipidemia	**Total n**	**Events (%)**	**Incidence rate per 1000PY**
Overall	*1,139*	*281 (24.7%)*	*77.0/1000PY*
PCL Change			
Worsening/No change	688	173 (25.1)	77.3/1000PY
Small improvement	218	50 (22.9)	71.5/1000PY
Large improvement	233	58 (24.9%)	81.3/1000PY
≥5% weight loss	**Total n**	**Events (%)**	**Incidence rate per 1000PY**
Overall	*1,330*	*553 (41.6%)*	*156.9/1000PY*
PCL Change			
Worsening/No change	800	341 (42.6%	160.5/1000PY
Small improvement	252	106 (42.1%)	158.9/1000PY
Large improvement	278	106 (38.1%)	144.7/1000PY

a. no/worsening is <10 point PTSD Checklist decrease, small improvement is 10–19 point PCL decrease, large improvement is ≥20 point PCL decrease

PY=person-years; PCL=PTSD checklist

Table 4.

Results from Cox proportional hazards models estimating the association of worsening/no PTSD improvement, small PTSD improvement and large PTSD improvement[a] and incident hypertension, hyperlipidemia and ≥5% weight loss among veterans age 18–70 years

	hypertension		hyperlipidemia		≥5% weight loss	
	Model 1 Unweighted	Model 2 Weighted [b]	Model 1 Unweighted	Model 2 Weighted [b]	Model 1 Unweighted	Model 2 Weighted [b]
	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)
PCL Change						
No change	1.00	1.00	1.00	1.00	1.00	1.00
Small decrease	**0.66 (0.46–0.95)**	0.68 (0.46–1.01)	0.92 (0.67–1.26)	1.10 (0.78–1.55)	0.98 (0.79–1.22)	1.07 (0.85–1.36)
Large decrease	0.74 (0.53–1.04)	0.79 (0.53–1.18)	1.04 (0.77–1.40)	1.01 (0.73–1.39)	0.90 (0.72–1.12)	0.95 (0.74–1.22)

HR=hazard ratio; CI=confidence interval; NIM=not in model; HCU=healthcare utilization, ADM=antidepressant

Bold text indicates significant hazard ratio

a. no/worsening is <10 point PTSD Checklist decrease, small improvement is 10–19 point PCL decrease, large improvement is ≥20 point PCL decrease

b. Weighted by inverse probability of exposure weighting