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Risk for Incident Hypertension Associated with PTSD in Military Veterans, and The Effect of PTSD Treatment

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Abstract

Objective—PTSD increases cardiovascular disease and cardiovascular mortality risk. Neither the prospective relationship of PTSD to incident hypertension risk, nor the effect of PTSD treatment on hypertension risk has been established.

Methods—Data from a nationally representative sample of 194,319 veterans were drawn from the Veterans Administration roster of United States service men and women. This included veterans whose end of last deployment was from September 2001 – July 2010, and whose first VA medical visit was from October 1, 2001 – January 1, 2009. Incident hypertension was modeled as 3 events: 1) a new diagnosis of hypertension; and/or 2) a new prescription for anti-hypertensive medication; and/or 3) a clinic BP reading in the hypertensive range (≥140mmHg/90mmHg, systolic/diastolic). PTSD diagnosis was the main predictor. PTSD treatment was defined as, 1) at least 8 individual psychotherapy sessions of ≥ 50min during any consecutive 6 months and/or 2) a prescription for SSRI medication.

Results—Over a median 2.4 year follow-up, the incident hypertension risk independently associated with PTSD ranged from HR=1.12 (95% CI 1.08 – 1.17, p<0.0001) to HR=1.30 (95% CI 1.26 – 1.34, p<0.0001). The interaction of PTSD and treatment revealed that treatment reduced the PTSD associated hypertension risk (e.g., from HR=1.44 [95% CI 1.38 – 1.50, p<0.0001] for those untreated, to HR=1.20 [95% CI 1.15 – 1.25, p<0.0001] for those treated).

Conclusions—These results indicate that reducing the long term health impact of PTSD and the associated costs, may require very early surveillance and treatment.

Keywords

Hypertension; PTSD; Veterans

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INTRODUCTION

Post-traumatic stress disorder (PTSD), a disabling condition that develops consequent to trauma, is defined in part by hyperarousal, avoidance, and re-experience of trauma[1]. It is the most commonly diagnosed mental health disorder in veterans with combat exposure[2–3], with a prevalence in men and women of over 20%[2], and a significant impact on quality of life and physical health domains[2,4–5]. PTSD is often accompanied by elevated resting heart rate and blood pressure (BP), an exaggerated HR and BP response to stressful stimuli under laboratory conditions[6], and alterations of autonomic[7–9] and HPA axis[10] regulation, processes that can contribute to eventual cardiovascular system damage[11]. Wide ranging cross-sectional and prospective studies[12–25] of individuals with a diagnosis of PTSD and those with elevated PTSD symptoms not sufficient to meet diagnostic criteria, reveal a higher prevalence of cardiovascular disease (CVD) and, as we reported in a recent meta-analysis[26], greater risk for early CVD events or CVD-specific mortality that is independent of traditional risk factors. With this evidence, researchers are stating that it is time to develop and test interventions targeted to reduction of CVD risk associated with PTSD[27].

PTSD has also been linked to hypertension, a major risk factor for CVD and stroke, which together impose a more than $69 billion annual financial burden in the US. In a small convenience sample of US military veterans[28], the resting systolic/diastolic BP were 11/9mmHg higher among those with vs. without PTSD. The National Comorbidity Study reported in multivariate analyses a 2-fold greater *prevalence* of hypertension among those with vs. without PTSD[15], with similar cross-sectional findings in a registry of over 300,000 veterans[29]. A relatively small *prospective* study of veterans who sought primary care treatment found that PTSD increased the odds of a range of medical and mental health conditions over a median 4.5 years, including a hypertension diagnosis by 38%[30]. While these studies provide a signal that PTSD is independently related to hypertension risk, with the exception of one small regional study, the analyses are all cross-sectional. Furthermore, these findings do not provide any information regarding the effect that PTSD treatment has on the relationship between PTSD and hypertension, a critical question if efforts to reduce hypertension and CVD risk associated with PTSD are to be mounted.

In the current study we used data from a large national registry of almost 300,000 veterans deployed from September 11, 2001 – January 1, 2009, to investigate the prospective relationship of PTSD to incident hypertension. We furthermore tested whether treatment for PTSD was associated with attenuation of the effect of PTSD on incident hypertension risk.

METHODS

Data Sources and Study Population

The sample was selected from the list of Veterans obtained from the VA roster of Operations Iraqi Freedom, Enduring Freedom, and New Dawn (OIF/OEF/OND), provided by Defense Manpower Data Center—Contingency Tracking System Deployment File as part of the Women Veterans Cohort Study[c.f., 31]. The roster includes information on sex, date of birth, race, and deployment start and end dates. For the current analyses, we included Veterans who were engaged in OIF/OEF/OND, and 1) whose end of last deployment was between

September 2001 and July 2010, 2) whose first VA medical visit was between October 1, 2001 and January 1, 2009, and 3) who had at least 2 medical visits with a BP measurement during the period of observation after their last deployment end date. The initial sample thus included 274,679 Veterans. The institutional review boards at the parent organizations (Yale University, VA Connecticut Healthcare System) approved the cohort study on which the current data analyses are based.

Information on eligible medical visits, International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) codes recorded in the VA database and used to determine medical and psychiatric conditions, body mass index (BMI), CPT codes to determine the services delivered at each eligible medical visit, clinic BP readings, and medication prescriptions, were ascertained from the VA Corporate Data Warehouse. ICD-9-CM codes from outpatient visits were mapped to validated diagnostic groupings in order to determine a diagnosis of PTSD (ICD-9-CM 309.81), major depression (ICD-9-CM 296.2–3), and alcohol/substance use disorder (ICD-9-CM 291–292; 303–305)[c.f.,32]. A Veteran was considered to have PTSD, depression, and/or substance use disorder if codes occurred on two or more outpatient visits, or one or more inpatient visit. This methodology has been used for the identification of psychiatric disorders in administrative data[c.f.,33] and for identification of HIV in Medicaid data[c.f.,34]. In addition, incident hypertension was defined using information in the VA database, with three distinct events ascertained: 1) a new diagnosis of hypertension in the problem list (ICD-9-CM 401); and/or 2) a new prescription for anti-hypertensive medication, including ACE inhibitors (e.g., Lisinopril, captopril), angiotensin receptor blockers (e.g., losartan), beta-blockers (e.g., atenolol, propranolol), calcium channel blockers (e.g., amlodipine), and diuretics (e.g., hydrochlorothiazide) – the anti-hypertensive medications clonidine and prazosin were not included in this classification as they are also used for treating aspects of PTSD; and/or 3) an entry in the record of a clinic BP in the hypertensive range (≥140mmHg/90mmHg, systolic/diastolic).

Receipt of standard of care treatment for PTSD was defined as, 1) CPT codes indicating at least 8 individual psychotherapy sessions of ≥ 50 min duration (CPT 90834, 90837) over any consecutive 6 months during the period of observation, and/or 2) a prescription for SSRI medications recorded in the VA database.

BP measurements that had implausible systolic values (<70mmHg or >240mmHg) or diastolic values (<35mmHg or >140mmHg) were removed (0.06% BP measures removed, leaving n=274,659 veterans). If there were two or more BP recordings on the same day, the BP measurement with the lowest systolic value was retained. Veterans who before or on the day of first BP measurement, 1) were diagnosed with hypertension (n=3,741 – 1%), 2) received a prescription for antihypertensive medication (n=8,725–3%), or 3) had their first BP in the hypertensive range (n=53,404 – 19%) were removed from analysis. From the 216,118 veterans remaining, we further excluded those for whom the pre-specified covariates of sex, race/ethnicity, or baseline BMI were missing (n=21,799 – 10%). This left a total N=194,319 for analysis.

Statistical Analysis

Descriptive statistics were used to summarize the characteristics of the sample. We report overall group statistics, and by PTSD and treatment status (see Table 1). The prospective contribution of PTSD, of treatment, and of the interaction of these variables to risk for incident hypertension was tested using Cox proportional hazards regression. Time zero (baseline) was the time of the first available BP measurement for each Veteran. We separately analyzed the time to the following three events:

earliest occurrence of hypertension diagnosis (Event 1);

earliest occurrence of hypertension diagnosis and/or antihypertensive medication prescription (Event 2);

earliest occurrence of hypertension diagnosis, and/or antihypertensive medication prescription, and/or BP measurement in the hypertensive range (Event 3).

Veterans who did not experience any of these events were censored on the date of their last recorded BP measurement.

The main predictor of interest was PTSD status, which was treated as a binary time-dependent variable valued 0 prior to PTSD diagnosis and 1 after diagnosis. Veterans who did not receive a PTSD diagnosis during the period of observation had the PTSD variable of 0 throughout. The models also included a binary time-dependent variable for PTSD treatment, with value 1 after treatment was received (earliest 6 month period with ≥ 8 individual psychotherapy CPT codes or first SSRI prescription) and value 0 otherwise. Other predictors included in the regression analyses were sex, race/ethnicity (White, Black, Hispanic, or Other), age at baseline, baseline systolic/diastolic BP, baseline BMI (closest BMI within 90 days of baseline) and baseline smoking (indication in the VA database of positive smoking status within 180 days of baseline). Veterans endorsing both White and Hispanic were coded as Hispanic; Veterans who endorsed both Black and Hispanic were coded as Black. We also adjusted for a diagnosis of major depression and of substance use disorder (alcohol or drug abuse), both as time-dependent variables valued 0 prior to diagnosis and 1 after diagnosis. Furthermore, we anticipated that veterans with mental health disorders may have had higher use of medical services (such as primary care), which could lead to ascertainment bias if these Veterans had more frequent assessment of BP. Therefore, we additionally adjusted the models for a time-dependent covariate representing each Veteran's number of days with a BP measurement during 90 day intervals.

We fit models with main effects for all the variables described. We then investigated if the association of PTSD with hypertension depends on whether treatment was received by adding a PTSD by treatment interaction term to the models. To test for sex differences in this association, we further included the two and three way interactions of sex with PTSD and treatment. To simplify the interpretation of results, we removed interaction terms that were not statistically significant at the 0.05 level from the final models.

RESULTS

Study Sample

The final sample of 194,319 Veterans was 85% male and 65% White, with a median age at baseline of 27.9 years (IQR=24.4–37.6). Median follow-up was 2.4 years (IQR=1.3–3.8 years). At baseline, 43% were overweight (BMI>25kg/m^2) and 28% obese (BMI>30kg/m^2); 32% were smokers. During the period of observation 11% received a diagnosis of major depression, and 13% received a diagnosis of substance use/abuse disorder. Also during the time of observation, 36% (n=69,583) received a diagnosis of PTSD; psychotherapy was received by 6% (13% with PTSD, 1% without), and SSRI medication was prescribed to 38% (74% with PTSD, 17% without). Because most veterans who received psychotherapy also received SSRI medication (81%), these were combined into a single “Treatment” term for analyses (see Table 1).

PTSD and Incident Hypertension

Of the total sample, 10% received a diagnosis of hypertension (event 1, N=19,420), with an additional 8% being prescribed an antihypertensive medication (event 2, cumulative 17%, N=33,030) and an additional 27% evidencing BP in the hypertensive range (event 3, cumulative 45%, N=87,450). In the Cox models with main effects only, PTSD was associated with a HR of 1.12 (95%CI 1.08–1.17, p<0.0001) for event 1, 1.30 (95%CI 1.26–1.34, p<0.0001) for event 2 (which by definition included event 1), and 1.27 (95%CI 1.25–1.30, p<0.0001) for experiencing event 3 (which by definition included events 1 and 2). In addition, treatment was associated with a HR of 1.18 (95%CI 1.14–1.23, p<0.0001), 1.46 (95%CI 1.42–1.51, p<0.0001), and 1.32 (95%CI 1.30–1.34, p<0.0001) for events 1, 2, and 3, respectively.

In the Cox models that considered interactions of PTSD, treatment, and sex, the PTSD by treatment interaction was significant (p<0.0001) for events 1, 2, and 3 (see Table 2), while the PTSD by sex interaction was significant only for event 3 (p=.010; see Table 2). Among Veterans with PTSD who did not receive treatment during the period of observation, the HR for the effect of PTSD on event 1 was 1.24 (95% CI 1.17–1.31, p<0.0001), while for those who *did* receive treatment, the corresponding HR for the effect of PTSD was lower and no longer statistically significant (HR= 1.03, 95% CI 0.97–1.08, p=0.347). Similarly for event 2, the effect of PTSD was significantly lower among Veterans who received treatment during the period of observation (HR=1.20, 95% CI 1.15–1.25, p<0.0001) than among Veterans who did not (HR=1.44, 95% CI 1.38–1.50, p<0.0001).

In the Cox model for event 3, the HR associated with PTSD was significantly higher in females than in males. Table 2 presents, separately for males and females, the effect of PTSD on event 3 by treatment status. As was the case for events 1 and 2 in the full cohort, the effect of PTSD for event 3 was significantly lower among Veterans who received PTSD treatment (HR=1.13, 95% CI 1.10–1.16, p<0.0001 for males, HR=1.21, 95% CI 1.15–1.27, p<0.0001, for females) than among Veterans who did not (HR=1.37, 95% CI 1.33–1.40, p<0.0001, for males, HR=1.46, 95% CI 1.39–1.54, p<0.0001, for females).

DISCUSSION

In this nationally representative sample of almost 200,000 OIF/OEF/OND Veterans who received care through the VA during the period of observation, a diagnosis of PTSD left untreated was associated with a 24–46% greater risk of incident hypertension. This finding held for both male and female Veterans, with females showing a slightly higher risk for early BP elevation into the hypertensive range. The finding that females had a higher risk for early BP in the hypertensive range but not for receipt of an anti-hypertensive medication or a hypertension diagnosis may indicate that women are less likely to receive a hypertension diagnosis and/or antihypertensive medication than men even when their BP is in the hypertensive range – e.g., even with this hypertensive BP they did not receive medication or diagnosis. This finding is consistent with literature concerning other CVD risk factors[35]. The overall findings in a nationwide Veteran cohort substantially extend beyond the prior research concerning PTSD and hypertension risk, which has largely been cross-sectional[15,29].

In the current study, we observed an overall hypertension incidence over a median 2.4 year follow-up that ranged from 10% to 45%, depending on how hypertension was defined, all in a young sample (average age of 27.9 years, IQR of 24.4–37.6 years). This incidence in a young group of individuals, observed soon after separation from military service is alarming, occurring much earlier than typically observed in the general US population or western societies[37,38], and much greater than reported in other studies of military veterans. For example the Millennium Cohort Study of approximately 55,000 active duty and Reserve/National Guard members reported a 33% increased odds (95% CI 1.07–1.65) of *self-reported* hypertension at 3-year follow-up among individuals with multiple combat exposures vs. those who were not deployed to conflict zones however, the contribution specifically of psychiatric disorders such as PTSD, depression, and substance use was not ascertained[36]. Furthermore, self-reported hypertension was observed in only 6.1% of those with multiple combat exposures and 7.3% in those who were not deployed. Thus, the results of the present study indicate that efforts to reduce the long term health impact of PTSD in military Veterans - and the associated costs in quality of life and healthcare dollars - may require very early surveillance, and the testing of treatment algorithms that involve lower thresholds for anti-hypertensive treatment.

The current report is also the first showing that treatment, a VA imperative[39] and here defined by SSRI prescription and/or receipt of individual psychotherapy, may affect PTSD associated hypertension risk. This finding while not previously reported, is more complicated, since as a main effect, treatment was associated with elevated hypertension risk, and indeed, the event rate per 1000 person years was higher in the groups (with and without PTSD) that received treatment. In a previous follow-up of Australian Gulf War Veterans[40], it was reported that only current PTSD (e.g., at the time of the assessment) was associated with incident hypertension, in comparison to having a trauma history and no current PTSD. The authors concluded that Veterans who no longer met criteria for PTSD presumably also did not continue to evidence the physiological dysregulation that characterizes this diagnosis. Theories that outline a causal path from PTSD to physical disease point to dysregulation in hypothalamic pituitary-adrenocortical and sympathetic-

adrenal-medullary stress axes[41,42]. Ongoing dysregulation in these pathways can disrupt regulation of BP, inflammation, and associated gene expression[c.f.,43]. There may also be a concomitant down-regulation of vagal input to relevant processes, including regulation of both acute and chronic hemodynamics and inflammatory processes[44,45]. The mitigation of PTSD by treatment - or the passage of time[46,47] - may promote a return of these key biological processes to a more normal state, and thus a reduction of incident hypertension risk. Longer term follow-up of the OIF/OEF/OND cohort will be required to ascertain whether a history of PTSD in remission truly normalizes incident hypertension risk or defines an additional at risk group, when compared to individuals with no history of PTSD.

While the prospective finding in this nationally representative sample of OIF/OEF/OND Veterans seeking care through the VA of both increased incident hypertension risk attributable to PTSD and of PTSD associated risk mitigation with treatment make important new contributions to the literature, the current report also has several limitations. The findings rely on administrative data, thus the accuracy of some data - particularly BP measurements - may be questioned. Clinic BP measurement within VA is largely accomplished with the use of automated devices, with the patient seated, and the displayed BP entered in the EMR. These BPs are then used for clinical decision making. While we cannot confirm the approach used in every VHA facility from which data were drawn, the consistency of finding for all 3 defined outcomes – diagnosis, medication prescription, *and/or* BP elevated above the hypertensive range – tempers this concern. There may also be misclassification in the study measures for PTSD and for hypertension, along with measures of other Veteran characteristics. Yet, the findings hold when hypertension is defined by diagnosis – an ICD-9 code on which billing is based - and/or prescription of anti-hypertensive medication, which also has billing implications. We have adjusted the analysis for known demographic, clinical, lifestyle and access-related factors that were assessed and could potentially bias the association between PTSD and hypertension.

There may also be selection/ascertainment bias related to seeking VA care based on PTSD symptoms. Despite analytic control, the possibility of ascertainment bias or residual confounding from known or unknown factors remains. It may also be that Veterans with more severe PTSD and/or hypertensive symptoms come to VA for care, and thus the findings may not generalize to Veterans who receive care elsewhere, or to members of the general population that experience trauma and subsequently develop PTSD. Yet, approximately 50% of OIF/OEF/OND Veterans have registered with the VA, and of these, over 80% have at least 1 medical visit on record. Thus, a large proportion is represented by these data. Finally, it is not possible to ascertain the extent to which the diagnosis of PTSD is based on a brief screen, self-report instrument, or diagnostic interview. Thus, the observed incidence may be higher - or lower - than would be determined with proper assessment.

The findings regarding treatment – SSRI medication and/or psychotherapy – are also conflicting, showing a lowering of PTSD associated hypertension risk, yet also showing an independent elevation of risk as a main effect, and a higher event rate for those receiving treatment. These observational data were not comprehensive, in that PTSD symptom severity was not available, and thus those receiving treatment may have had more severe PTSD and thus the highest risk for incident hypertension - e.g., PTSD treatment as defined

here may have been a proxy for severity. In addition, key life-style factors[48,49] such as physical activity, diet, and sleep, each known to increase hypertension risk were not available. Furthermore, 17% of the overall sample without PTSD received treatment as defined by the study - almost all SSRI medication, perhaps for chronic pain - and there is evidence of an association between use of SSRI medications and hypertension[50], and of chronic pain and hypertension[51]. The effect of treatment on PTSD associated hypertension risk was not specifically tested in a randomized clinical trial, and the definition of treatment was imprecise, in that we were unable to determine whether individual psychotherapy received was evidence-based for PTSD[50], or whether prescription of SSRI medication was for PTSD vs. other factors such as co-morbid depression. The question of whether PTSD treatment affects PTSD associated hypertension risk will be critical to ascertain, so as to inform best approaches for CVD risk reduction among individuals with PTSD.

Given the VA imperative to provide PTSD treatment[52], it may not be possible to conduct a randomized clinical trial testing the effect of PTSD treatment on the associated incident hypertension risk, as this would entail withholding PTSD treatment for a period sufficient for new onset hypertension to be observed. A clinical trial that compares two different forms of PTSD therapy – e.g., pharmacotherapy vs. exposure therapy or cognitive reprocessing therapy, using variables such as daytime and night time average ambulatory BP, BP reactivity observed under controlled conditions during exposure to stressful tasks and/or PTSD relevant stimuli, and BP elevations during exposure to ecological stressors observed during ambulatory monitoring[53,54], may provide useful surrogate endpoints for such a trial.

Conclusions

We observed a 24%–46% greater risk for incident hypertension associated with untreated PTSD in a large, nationally representative sample of almost 200,000 Veterans of OIF/OEF/OND military conflicts. This PTSD associated risk was substantially lower among those Veterans who received PTSD treatment, though these findings were somewhat conflicting. Therefore, the effect of PTSD treatment on subsequent hypertension risk should be studied in randomized clinical trials using surrogate endpoints (e.g., ambulatory BP), that would provide for more immediate effects that do not entail withholding of treatment. Furthermore, efforts to reduce the long term health impact of PTSD and the associated costs in healthcare dollars may require early surveillance and the testing of treatment algorithms involving lower thresholds for anti-hypertensive treatment.

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Acronyms

PTSD	post-traumatic stress disorder
OIF/OEF/OND	Operations Iraqi Freedom/Enduring Freedom/New Dawn

BP	blood pressure
CVD	cardiovascular disease
VA	Veterans Administration
ICD-9-CM	International Classification of Diseases, 9th Revision, Clinical Modification
BMI	body mass index
SSRI	selective serotonin reuptake inhibitor
IQR	interquartile range
HR	hazard ratio

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Table 1

Characteristics of the Study Cohort

	No PTSD No Treatment (N=103,045)	No PTSD Treatment (N=21,691)	PTSD No Treatment (N=16,390)	PTSD Treatment (N=53,193)	Overall Sample (N=194,319)
Men	87122 (85%)	16229 (75%)	14906 (91%)	46511 (87%)	164768 (85%)
Race :					
Black	18083 (18%)	3257 (15%)	2728 (17%)	8823 (17%)	32891 (17%)
Hispanic	13316 (13%)	2746 (13%)	2112 (13%)	6319 (12%)	24493 (13%)
Other	7304 (7%)	1533 (7%)	695 (4%)	2023 (4%)	11555 (6%)
White	64342 (62%)	14155 (65%)	10855 (66%)	36028 (68%)	125380 (65%)
Median Age @ baseline (IQR)	28.2 [24.5;39.1]	28.1 [24.6; 37.3]	26.9 [24.0;34.8]	27.7 [24.3; 35.8]	27.9 [24.4;37.6]
Baseline BMI (kg/m^2)					
Median [IQR]	27.3 [24.6;30.4]	27.2 [24.3; 30.4]	27.4 [24.6; 30.5]	27.5 [24.5; 30.7]	27.4 [24.5;30.5]
<25 kg/m^2	29202 (28%)	6687 (31%)	4580 (28%)	15100 (28%)	55569 (29%)
25–30 kg/m^2	45452 (44%)	9013 (42%)	7141 (44%)	22258 (42%)	83864 (43%)
≥30 kg/m^2	28391 (28%)	5991 (28%)	4669 (28%)	15835 (30%)	54886 (28%)
Baseline BP					
<120/80	36413 (35%)	8098 (37%)	5441 (33%)	17475 (33%)	67427 (35%)
Median SBP [IQR]	122 [114; 130]	122 [114; 129]	123 [115; 130]	123 [115; 130]	122 [115; 130]
Median DBP [IQR]	74 [68; 80]	74 [68; 80]	74 [68; 80]	74 [68; 80]	74 [68; 80]
Baseline smoking	27151 (26%)	7607 (35%)	5796 (35%)	21954 (41%)	62508 (32%)
Major depression	969 (1%)	4674 (22%)	1112 (7%)	14014 (26%)	20769 (11%)
Substance use disorder	3704 (4%)	3346 (15%)	2485 (15%)	15655 (29%)	25190 (13%)
Type of Treatment Received					
Psychotherapy		1560 (1%)		9267 (13%)	10827 (6%)

	No PTSD No Treatment (N=103,045)	No PTSD Treatment (N=21,691)	PTSD No Treatment (N=16,390)	PTSD Treatment (N=53,193)	Overall Sample (N=194,319)
SSRI		21138 (17%)		51732 (74%)	72870 (38%)
Hypertension Events per 1000 Person Years *					
Event 1	37.5	40.9	39.1	42.2	39.7
Event 2	68.1	88.0	79.0	101.2	77.3
Event 3	235.3	299.6	308.4	329.5	261.1

Note: IQR=Interquartile Range; BMI=body mass index; BP=blood pressure; SBP=systolic blood pressure; DBP=diastolic blood pressure; SSRI=selective serotonin reuptake inhibitor.

*Events per 1000 person years provides an index of the incidence of new events that happen over time and accommodates the variable length of follow-up per individual. It provides a metric for comparison between sub-groups and event types within this sample, and a metric for comparison to other samples.

Table 2

Adjusted hazard ratios (HR) for the effect of PTSD on hypertension Events 1, 2, and 3 by treatment status (n=194,319)

Event		Treatment Status	HR for Effect of PTSD	95% CI for HR	p-value
1	Overall*	No Treatment	1.24	1.17, 1.31	<.0001
		Treatment	1.03	0.97, 1.08	0.347
2	Overall*	No Treatment	1.44	1.38, 1.50	<.0001
		Treatment	1.20	1.15, 1.25	<.0001
3	Overall*	No Treatment	1.38	1.34, 1.41	<.0001
		Treatment	1.14	1.11, 1.17	<.0001
	Men+	No Treatment	1.37	1.33, 1.40	<.0001
		Treatment	1.13	1.10, 1.16	<.0001
	Women+	No Treatment	1.46	1.39, 1.54	<.0001
		Treatment	1.21	1.15, 1.27	<.0001

*HR estimates were obtained from multivariable Cox models including as predictors PTSD, treatment, the PTSD*treatment interaction, race, gender, baseline age, BMI, smoking, systolic and diastolic BP, number of days with BP measurements, major depression and substance use disorder.

+HR estimates from multivariable Cox model that additionally includes the PTSD*gender interaction.