Post-Traumatic Stress Disorder and the Risk of Erectile Dysfunction: A Nationwide Cohort Study in Taiwan

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Abstract

BACKGROUND: This study aimed to investigate the association between posttraumatic stress disorder and the risk of developing erectile dysfunction.

METHODS: In this population-based, retrospective cohort study, we used Taiwan's National Health Insurance Research Database to analyze the patients who were newly diagnosed with posttraumatic stress disorder (PTSD) between 2000 and 2013, with a 1:3 ratio by age, and index year matched in the non-PTSD comparison group, for the risk of erectile dysfunction.

RESULTS: In total, five out of 1,079 patients with PTSD developed erectile dysfunction, and three out of 3,237 patients in the non-PTSD group (47.58 vs 9.03 per 100,000 per person-year) developed erectile dysfunction. The Kaplan-Meier analysis showed that the PTSD cohort had a significantly higher risk of erectile dysfunction (log-rank, $p < 0.001$). The Cox regression analysis revealed that the study subjects were more likely to develop an injury (HR: 12.898, 95% CI=2.453- 67.811, $p = 0.003$) after adjusting for age, monthly income, urbanization level, geographic region, and comorbidities. Psychotropic medications in the patients with PTSD were not associated with the risk of erectile dysfunction.

CONCLUSIONS: Patients who suffered PTSD had a higher risk of developing erectile dysfunction.

Highlight

- Utilizing a nationwide, population-based database, the Longitudinal Health Insurance Database in 2000-2015 in Taiwan, which comprised of two million people, we conducted a study to clarify the association between post-traumatic stress disorder and erectile dysfunction.
- Post-traumatic stress disorder was associated with the risk of erectile dysfunction.
- Psychotropic medications in the subjects with PTSD were not associated with the risk of erectile dysfunction.

Introduction

As a devastating and debilitating mental illness that occurs after exposure to traumatic events, post-traumatic stress disorder (PTSD) involves a cluster of symptoms, such as intrusion, hyperarousal, avoiding stimuli associated with traumatic events, and negative alterations in cognition and mood (Stein et al., 2007; Yehuda, 2002). PTSD can also lead to negative impacts on quality of life and functional impairment in various domains, especially poorer relationship functioning, followed by sexual dysfunction (Cook et al., 2004; Danielsson et al., 2018; Pietrzak et al., 2009; Sayers et al., 2009). Hence, it should come as no surprise that patients with PTSD are at an increased risk of sexual dysfunction. However, erectile dysfunction (ED) in PTSD is often overlooked in clinical practices and receives little attention in the PTSD research, especially in Asian countries.

Several previous studies proved that veterans with sexual dysfunction have significantly more severe PTSD symptoms than those without sexual dysfunction (Nunnink et al., 2010). It has been suggested that comorbid mental and physical illness should be considered as an alternative explanation of the co-occurrence of sexual dysfunction and PTSD (Kotler et al., 2000; Letourneau et al., 1997), such as anxiety and depression (Ginzburg et al., 2010). Even though it is noteworthy that the percentage of sexual dysfunction is remarkably high in the PTSD patients (Cosgrove et al., 2002; Letourneau et al., 1997), some inconsistent results have existed between the symptom severity of PTSD and sexual dysfunction (Bentsen et al., 2015). Prevalence for sexual dysfunction among veterans with PTSD could be from 8% and 89% in different study sample sizes (Bentsen et al., 2015).

Few studies have investigated the correlation or rates of ED across PTSD populations (Arbanas, 2010; Badour et al., 2015), in which almost no literature addressed the longitudinal effects of sexual dysfunction. It is worth noting that one cross-sectional study in Turkey reported no association between the lifetime PTSD and ED (Evren et al., 2006). The previous studies have demonstrated that the prevalence of PTSD varied across countries and inadequate treatment is common (Alonso et al., 2018; Kessler et al., 2009), not to mention PTSD with sexual dysfunction. Co-occurring physical illnesses may also have a bidirectional relationship, as sexual health is linked to nearly every organ system. Sexual dysfunction often manifests from physical illnesses, including cardiovascular illness (e.g., stroke, coronary artery disease, and hypertension), diabetes mellitus, asthma and alcohol-related disease (Clayton and Ramamurthy, 2008). Moreover, prescription medications could stand for the probable mechanism that explains the co-occurrence

of ED and PTSD, such as serotonin reuptake inhibitors and benzodiazepines (Anticevic and Britvic, 2008; Fossey and Hamner, 1994).

There are only a few studies and systematic reviews examining the impact of PTSD on ED in the general population of Asian countries. Since the association between PTSD and ED has remained unclear, we conducted this study so as to investigate the association between PTSD and the risk of ED. We hypothesize that there is an increased risk of ED after PTSD, and we used the Taiwan National Health Insurance Research Database (NHIRD) to examine as to whether there is an association between PTSD and ED.

Methods

Data sources

The Taiwan National Health Insurance (NHI) program was launched in 1995 to provide a centralized health insurance for its citizens, and as of 2014 approximately 93% of the nation's medical care institutions were contracted, with an enrollment rate exceeding 99% of Taiwan's population (Ho Chan, 2010). The NHIRD is derived from the Taiwan NHI program, and all claims data are released by the Bureau of National Health Insurance for research purposes. The NHIRD uses the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) codes to record diagnoses (Chinese Hospital Association, 2000). The quality and validity of the NHIRD is adequate, and its data have been used in many published studies (Lin et al., 2014; Shen et al., 2013; Shih et al., 2014). In the present study, we used the data sets from the Registry for the one-million Longitudinal Health Insurance Database (LHID) which included comprehensive outpatient and inpatient information, such as demographic data, dates of clinical visits, diagnostic codes, and details of prescriptions, with regard to nearly 1 million beneficiaries over a 13-year period from the LHID in Taiwan (2000–2013).

Ethical approval

To protect patient privacy, patient identity data were scrambled cryptographically in the NHIRD. This study was approved by the Institutional Review Board of Tri-Service General Hospital (TSGHIRB-2-106-05-029), and the written informed consents were waived.

Study design and sampled participants

This study is of a retrospective, matched-cohort design. Patients with PTSD were selected from January 1, 2000 to December 31, 2013, according to the ICD-9-CM codes: 309.81. In addition, each enrolled patient was required to have made at least three outpatient visits within the one-year study period for adult males with PTSD according to these ICD-9-CM codes. The patients diagnosed with ED before 2000 or before the first visit for PTSD were excluded. In addition, all patients aged <20 years were also excluded. A total of 4,310 enrolled patients with the 1,079 subjects with PTSD and 3,237 in the age and index-year matched control group without PTSD in this study, in the 13 years of follow-up to December 31, 2013 (Figure S1).

Covariates

The covariates included age group (20–39 years, ≥40 years), geographic area of residence (north, center, south, west, and east of Taiwan), urbanization level of residence (levels 1–4), levels of hospitals as medical centers, regional hospitals,

and local hospitals, and monthly income (in New Taiwan Dollars [NT\$]: <18,000, 18,000–34,999, ≥35,000). Charlson Comorbidity Index (CCI) defined the comorbidity (Charlson et al., 2008; Charlson et al., 1987). The population and various indicators defined the urbanization levels. Level 1 was defined as a population of >1,250,000; level 2 was defined as a population between 500,000 and 1,249,999; and urbanization levels 3 and 4 were defined as a population between 149,999 and 499,999, and <149,999, respectively (Chang et al., 2014).

Comorbidity

Baseline comorbidities (in ICD-9-CM codes) included dementia, schizophrenia, anxiety disorder, bipolar disorder, depressive disorders, stroke, coronary artery diseases, hypertension, diabetes mellitus, asthma, and alcohol-related illness, with the reference from one previous study (Yang et al., 2018). Data on the usage of psychotropic medications, including antidepressants,

antipsychotics, and hypnotosedatives, were collected. The data of defined daily dose (DDD) were obtained from the WHO Collaborating Centre for Drug Statistics Methodology (<https://www.whooc.no/>), and the duration of the use of drugs was calculated by

dividing the cumulative doses by the DDD of drugs.

Main outcomes

All of the study participants were followed from the index date until the onset of erectile dysfunction, withdrawal from the NHI program, or the end of 2013. ED was divided into two subgroups: psychogenic ED and organic ED.

Statistical analysis

All statistical analyses were performed using the SPSS software V.22 (SPSS Inc., Chicago, Illinois, USA). χ^2 test and t-test were used to evaluate the distributions of the categorical and continuous variables, respectively. The Fisher's exact test for the categorical variables was used to statistically examine the differences between the two cohorts. The Cox regression model was used to determine the risk of psychiatric disorders, and the results were present as HR with a 95% CI. The difference in the cumulative incidence of psychiatric disorders between the study and control groups was estimated using the Kaplan-Meier method with the log-rank test. A two-tailed p value <0.05 was considered to indicate the statistical significance.

Results

Sample characteristics

Table 1 shows that the PTSD group had more anxiety, bipolar disorder, and depression, and less CAD and DM than the non-PTSD group. The PTSD group also tended to have lower CCI score, live in the northern and outlying islands of Taiwan, reside more in the regions of urbanization levels 2, and receive medical help from medical centers. There were no differences in the distribution of age and insurance premiums between these two groups.

Kaplan-Meier model for the cumulative risk of erectile dysfunction

At the end of the follow-up, five in the PTSD group (5 in 1079, 47.58 per 10⁵ person-years) and three in the non-PTSD group (3 in 3,237, 9.03 per 10⁵ person-years). The Kaplan-Meier analysis for the cumulative incidence of erectile dysfunction in the study and control groups is as shown in Figure 1 (log-rank test, p <0.001).

Hazard ratios analysis of ED in the patients with PTSD

In the Cox regression analysis model, the crude HR of the PTSD group was 14.766 (95% CI:3.426-63.635, p<0.001), and the adjusted HR of the PTSD in the development of ED was 12.898 (95% CI: 2.453-67.811, p=0.003), in comparison to the non-PTSD group, after adjustment for age, insurance premiums, comorbidities, antidepressants, sedatives/hypnotics, urban levels and regions in Taiwan, and the levels of hospitals the patients sought for medical care. Patients with comorbidities, as such anxiety (adjusted HR: 1.864, p=0.025), bipolar disorders (adjusted HR: 1.998, p=0.014), and depression (adjusted HR: 2.970, p=0.001), were associated with the risk of ED (Table 2). The patients using antidepressants, antipsychotics, and sedatives/hypnotics were not associated with the development of ED.

Subgroup analysis of ED in the patients with PTSD

Table 3 depicts that the PTSD cohort was associated with an increased risk of ED, in comparison to the non-PTSD cohort in the subgroup analysis. When compared with patients without anxiety, PTSD owned a significantly adjusted HR (7.804, p=0.014). Patients with anxiety, PTSD had more significant adjusted HR (18.191, p<0.001) as compared to the patients with anxiety but no PTSD; with a similar phenomenon in bipolar disorder (8.406 vs 13.978) and depression (7.975 vs 19.911).

Types of ED after PTSD

Table 4 reveals that the PTSD group was associated with an increased risk of developing overall ED 12.898 (95% CI: 2.453-67.811, $p=0.003$) and psychogenic ED 27.044 (95% CI: 2.731-267.795, $p<0.001$), but not organic ED.

Discussion

Association between PTSD and the risk of ED

Our results support the study hypothesis that patients with PTSD would have an increased risk of developing erectile dysfunction. The log-rank of the Cox regression model was significant ($p=0.003$). The adjusted HR was 12.898 (95% CI: 2.453-67.811, $p=0.003$). When compared with previous research about the association between PTSD and the risk of ED (Badour et al., 2015; Cosgrove et al., 2002; Kotler et al., 2000), this study focused on the longitudinal changes in general population of an Asian country. Previous nationwide cohort studies have reported that PTSD was associated with obstructive sleep apnea (Lin et al., 2019a), bronchial asthma (Hung et al., 2019), hypertension, DM, dyslipidemia (Lin et al., 2019b), osteoporosis (Huang et al., 2018), Parkinson's disease (Chan et al., 2017), dementia (Wang et al., 2016), and epilepsy (Chen et al., 2017). To the best of knowledge, this is the first study on the topic directly related to the association between PTSD and the risk of ED, in a nationwide, population-based cohort study, in an Asian country.

Comparison of this study to previous literatures

In our study, other psychiatric comorbidities, such as anxiety, depression and bipolar disorder, also contributed to the risk of developing erectile dysfunction; this is compatible with previous findings (Atlantis and Sullivan, 2012; Kotler et al., 2000). Sexual dysfunction is commonly reported adverse effects of antipsychotic and lithium, often prescribed for treatment of bipolar disorder patients (Elnazer et al., 2015; Montejo et al., 2010).

One study has shown the lifetime prevalence of PTSD ranges from 1.3 to 12.2%, and the one-year prevalence is 0.2 to 3.8% (Karam et al., 2014). Another previous study, using the NHIRD, has found that the one-year incidence of PTSD was 1.1% (Lin et al., 2014). In our study, the total incidence within the period of the 13-year follow up was around 0.31% (3,050 in 989,753), and while we excluded the 1,971 cases of PTSD which did not met the enrollment criteria of this study, the incidence was 0.11 % (1,079/989,753). Both were lower than the finding in the study of Lin et al., 2014. The discrepancy between the incidences in these two studies might well be related to the strict criteria we employed in the enrollment of the cases of PTSD, that is, each enrolled patient was required to have made at least three outpatient visits within the one-year study period for adult males with PTSD according to these ICD-9-CM codes 309.81.

Psychotropic medications and the risk of ED in patients with PTSD

In clinical practice guidelines, the most common psychotropic medications used in the patients with PTSD included selective serotonin reuptake inhibitors (SSRIs), serotonin norepinephrine reuptake inhibitors (SNRIs), other antidepressants, sedative-hypnotics, and antipsychotics (Ipser and Stein, 2012). Usage of psychotropic medications for PTSD were not associated with an increased risk of ED, after being adjusted by age, comorbidity, and other covariates. Previous studies had reported that antidepressants, antipsychotics and benzodiazepines were associated with ED (Montejo et al., 2015; Zainol et al., 2019) (Bala, 2018 #35; Zainol, 2019 #36). Therefore, more studies are needed to clarify the impact of these medications on the risk of ED in patients with PTSD.

Possible mechanisms for the increased risk of ED in patients with PTSD

There is an enormous amount of evidence indicating a multifactorial etiology of erectile dysfunction; either organic or non-organic, and a complex interaction exists in the psychological, interpersonal, social, cultural, physiological, and gender-influenced processes (Perelman, 2009; Reed et al., 2016). Several possible reasons could explain the underlying mechanism. PTSD itself can lead to a higher prevalence of erectile dysfunction, and also a higher prevalence of comorbidity exists among patients with PTSD (Arbanas, 2010). Besides, patients with PTSD are treated with psychotropic drugs which can cause side effects that could influence their sexual function (Harvey and Balon, 1995; Reisman, 2017).

Limitations

Despite recent researches that highlighted the relationship between ED and PTSD, finding an absolute causation and mechanism for a patient with ED suffering from PTSD is still challenging. The main limitation of this study is that the number of ED patient in this sample was rare, which might be related to underestimation of self-report, the stigmatization, and a lower percentage of doctor visits due to culture factors. The patients with ED may choose not to talk to the doctors due to embarrassment, discouragement, or disbelief of the treatment possibilities.

Conclusion

The patients with PTSD had a higher risk of developing erectile dysfunction than those without PTSD, as determined after adjustment for demographic data and medical and psychiatric comorbidities. Further study is therefore necessary to clarify the definite pathophysiology between PTSD and erectile dysfunction and to investigate as to whether prompt interventions for PTSD may reduce this risk.

Declarations

Declarations of interest: none

Author Contributions: SCW, NST, and YPL conceived, designed and conducted the study, performed the statistical analyses, analyzed and interpreted the data, and drafted the manuscript. WCC and CHC participated in its conception, design, assisted with the data collection and scoring of the behavioral measures, analyzed and interpreted the data, and were involved in drafting the manuscript and revised the manuscript critically for important intellectual content. SCW wrote the first draft. NST and YPL conducted the critical revision of the manuscript. All authors read and approved this manuscript.

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Data availability, in brief

Data are available from the National Health Insurance Research Database (NHIRD) published by Taiwan's National Health Insurance (NHI) Administration. Due to legal restrictions imposed by the government of Taiwan in relation to the "Personal Information Protection Act", data cannot be made publicly available. Requests for data can be sent as a formal proposal to the NHIRD (<https://dep.mohw.gov.tw/dos/np-2497-113.html>).

Conflict of interest: none

References

1. Alonso, J., Liu, Z., Evans-Lacko, S., Sadikova, E., Sampson, N., Chatterji, S., Abdulmalik, J., Aguilar-Gaxiola, S., Al-Hamzawi, A., Andrade, L.H., Bruffaerts, R., Cardoso, G., Cia, A., Florescu, S., de Girolamo, G., Gureje, O., Haro, J.M., He, Y., de Jonge, P., Karam, E.G., Kawakami, N., Kovess-Masfety, V., Lee, S., Levinson, D., Medina-Mora, M.E., Navarro-Mateu, F., Pennell, B.E., Piazza, M., Posada-Villa, J., Ten Have, M., Zarkov, Z., Kessler, R.C., Thornicroft, G., Collaborators, W.H.O.W.M.H.S., 2018. Treatment gap for anxiety disorders is global: Results of the World Mental Health Surveys in 21 countries. *Depress Anxiety* 35, 195-208.
2. Anticevic, V., Britvic, D., 2008. Sexual functioning in war veterans with posttraumatic stress disorder. *Croat Med J* 49, 499-505.
3. Arbanas, G., 2010. Does post-traumatic stress disorder carry a higher risk of sexual dysfunctions? *J Sex Med* 7, 1816-1821.
4. Atlantis, E., Sullivan, T., 2012. Bidirectional association between depression and sexual dysfunction: a systematic review and meta-analysis. *J Sex Med* 9, 1497-1507.
5. Badour, C.L., Gros, D.F., Szafranski, D.D., Acierno, R., 2015. Problems in sexual functioning among male OEF/OIF veterans seeking treatment for posttraumatic stress. *Compr Psychiatry* 58, 74-81.

6. Bentsen, I.L., Giraldi, A.G., Kristensen, E., Andersen, H.S., 2015. Systematic Review of Sexual Dysfunction Among Veterans with Post-Traumatic Stress Disorder. *Sex Med Rev* 3, 78-87.
7. Chan, Y.E., Bai, Y.M., Hsu, J.W., Huang, K.L., Su, T.P., Li, C.T., Lin, W.C., Pan, T.L., Chen, T.J., Tsai, S.J., Chen, M.H., 2017. Post-traumatic Stress Disorder and Risk of Parkinson Disease: A Nationwide Longitudinal Study. *The American journal of geriatric psychiatry : official journal of the American Association for Geriatric Psychiatry* 25, 917-923.
8. Chang, C.Y., Chen, W.L., Liou, Y.F., Ke, C.C., Lee, H.C., Huang, H.L., Ciou, L.P., Chou, C.C., Yang, M.C., Ho, S.Y., Lin, Y.R., 2014. Increased risk of major depression in the three years following a femoral neck fracture—a national population-based follow-up study. *PLoS One* 9, e89867.
9. Charlson, M.E., Charlson, R.E., Peterson, J.C., Marinopoulos, S.S., Briggs, W.M., Hollenberg, J.P., 2008. The Charlson comorbidity index is adapted to predict costs of chronic disease in primary care patients. *J Clin Epidemiol* 61, 1234-1240.
10. Charlson, M.E., Pompei, P., Ales, K.L., MacKenzie, C.R., 1987. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 40, 373-383.
11. Chen, Y.H., Wei, H.T., Bai, Y.M., Hsu, J.W., Huang, K.L., Su, T.P., Li, C.T., Lin, W.C., Wu, Y.H., Pan, T.L., Chen, T.J., Tsai, S.J., Chen, M.H., 2017. Risk of Epilepsy in Individuals With Posttraumatic Stress Disorder: A Nationwide Longitudinal Study. *Psychosomatic medicine* 79, 664-669.
12. Chinese Hospital Association, 2000. ICD-9-CM English-Chinese Dictionary. Taipei, Taiwan, Chinese Hospital Association Press.
13. Clayton, A., Ramamurthy, S., 2008. The impact of physical illness on sexual dysfunction. *Adv Psychosom Med* 29, 70-88.
14. Cook, J.M., Riggs, D.S., Thompson, R., Coyne, J.C., Sheikh, J.I., 2004. Posttraumatic stress disorder and current relationship functioning among World War II ex-prisoners of war. *J Fam Psychol* 18, 36-45.
15. Cosgrove, D.J., Gordon, Z., Bernie, J.E., Hami, S., Montoya, D., Stein, M.B., Monga, M., 2002. Sexual dysfunction in combat veterans with post-traumatic stress disorder. *Urology* 60, 881-884.
16. Danielsson, F.B., Schultz Larsen, M., Norgaard, B., Lauritsen, J.M., 2018. Quality of life and level of post-traumatic stress disorder among trauma patients: A comparative study between a regional and a university hospital. *Scand J Trauma Resusc Emerg Med* 26, 44.
17. Elnazer, H.Y., Sampson, A., Baldwin, D., 2015. Lithium and sexual dysfunction: an under-researched area. *Hum Psychopharmacol* 30, 66-69.
18. Evren, C., Can, S., Evren, B., Saatcioglu, O., Cakmak, D., 2006. Lifetime posttraumatic stress disorder in Turkish alcohol-dependent inpatients: relationship with depression, anxiety and erectile dysfunction. *Psychiatry Clin Neurosci* 60, 77-84.
19. Fossey, M.D., Hamner, M.B., 1994. Clonazepam-related sexual dysfunction in male veterans with PTSD. *Anxiety* 1, 233-236.
20. Ginzburg, K., Ein-Dor, T., Solomon, Z., 2010. Comorbidity of posttraumatic stress disorder, anxiety and depression: a 20-year longitudinal study of war veterans. *J Affect Disord* 123, 249-257.
21. Harvey, K.V., Balon, R., 1995. Clinical implications of antidepressant drug effects on sexual function. *Ann Clin Psychiatry* 7, 189-201.
22. Ho Chan, W.S., 2010. Taiwan's healthcare report 2010. *EPMA J* 1, 563-585.
23. Huang, W.S., Hsu, J.W., Huang, K.L., Bai, Y.M., Su, T.P., Li, C.T., Lin, W.C., Chen, T.J., Tsai, S.J., Liou, Y.J., Chen, M.H., 2018. Post-traumatic stress disorder and risk of osteoporosis: A nationwide longitudinal study. *Stress and health : journal of the International Society for the Investigation of Stress* 34, 440-445.
24. Hung, Y.H., Cheng, C.M., Lin, W.C., Bai, Y.M., Su, T.P., Li, C.T., Tsai, S.J., Pan, T.L., Chen, T.J., Chen, M.H., 2019. Post-traumatic stress disorder and asthma risk: A nationwide longitudinal study. *Psychiatry research* 276, 25-30.
25. Ipser, J.C., Stein, D.J., 2012. Evidence-based pharmacotherapy of post-traumatic stress disorder (PTSD). *Int J Neuropsychopharmacol* 15, 825-840.
26. Karam, E.G., Friedman, M.J., Hill, E.D., Kessler, R.C., McLaughlin, K.A., Petukhova, M., Sampson, L., Shahly, V., Angermeyer, M.C., Bromet, E.J., de Girolamo, G., de Graaf, R., Demyttenaere, K., Ferry, F., Florescu, S.E., Haro, J.M., He, Y., Karam, A.N., Kawakami, N., Kovess-Masfety, V., Medina-Mora, M.E., Browne, M.A., Posada-Villa, J.A., Shalev, A.Y., Stein, D.J., Viana, M.C., Zarkov, Z., Koenen, K.C., 2014. Cumulative traumas and risk thresholds: 12-month PTSD in the World Mental Health (WMH) surveys. *Depress Anxiety* 31, 130-142.

27. Kessler, R.C., Aguilar-Gaxiola, S., Alonso, J., Chatterji, S., Lee, S., Ormel, J., Ustun, T.B., Wang, P.S., 2009. The global burden of mental disorders: an update from the WHO World Mental Health (WMH) surveys. *Epidemiol Psichiatr Soc* 18, 23-33.
28. Kotler, M., Cohen, H., Aizenberg, D., Matar, M., Loewenthal, U., Kaplan, Z., Miodownik, H., Zemishlany, Z., 2000. Sexual dysfunction in male posttraumatic stress disorder patients. *Psychother Psychosom* 69, 309-315.
29. Letourneau, E.J., Schewe, P.A., Frueh, B.C., 1997. Preliminary evaluation of sexual problems in combat veterans with PTSD. *J Trauma Stress* 10, 125-132.
30. Lin, C.E., Chung, C.H., Chen, L.F., Chien, W.C., Chou, P.H., 2019a. The Impact of Antidepressants on the Risk of Developing Obstructive Sleep Apnea in Posttraumatic Stress Disorder: A Nationwide Cohort Study in Taiwan. *Journal of clinical sleep medicine : JCSM : official publication of the American Academy of Sleep Medicine* 15, 1233-1241.
31. Lin, C.E., Chung, C.H., Chen, L.F., You, C.H., Chien, W.C., Chou, P.H., 2019b. Risk of incident hypertension, diabetes, and dyslipidemia after first posttraumatic stress disorder diagnosis: A nationwide cohort study in Taiwan. *General hospital psychiatry* 58, 59-66.
32. Lin, K.H., Chu, P.C., Kuo, C.Y., Hwang, Y.H., Wu, S.C., Guo, Y.L., 2014. Psychiatric disorders after occupational injury among National Health Insurance enrollees in Taiwan. *Psychiatry Res* 219, 645-650.
33. Montejo, A.L., Majadas, S., Rico-Villademoros, F., Llorca, G., De La Gandara, J., Franco, M., Martin-Carrasco, M., Aguera, L., Prieto, N., Spanish Working Group for the Study of Psychotropic-Related Sexual, D., 2010. Frequency of sexual dysfunction in patients with a psychotic disorder receiving antipsychotics. *J Sex Med* 7, 3404-3413.
34. Montejo, A.L., Montejo, L., Navarro-Cremades, F., 2015. Sexual side-effects of antidepressant and antipsychotic drugs. *Curr Opin Psychiatry* 28, 418-423.
35. Nunnink, S.E., Goldwaser, G., Afari, N., Nievergelt, C.M., Baker, D.G., 2010. The role of emotional numbing in sexual functioning among veterans of the Iraq and Afghanistan wars. *Mil Med* 175, 424-428.
36. Perelman, M.A., 2009. The sexual tipping point: a mind/body model for sexual medicine. *J Sex Med* 6, 629-632.
37. Pietrzak, R.H., Goldstein, M.B., Malley, J.C., Johnson, D.C., Southwick, S.M., 2009. Subsyndromal posttraumatic stress disorder is associated with health and psychosocial difficulties in veterans of Operations Enduring Freedom and Iraqi Freedom. *Depress Anxiety* 26, 739-744.
38. Reed, G.M., Drescher, J., Krueger, R.B., Atalla, E., Cochran, S.D., First, M.B., Cohen-Kettenis, P.T., Arango-de Montis, I., Parish, S.J., Cottler, S., Briken, P., Saxena, S., 2016. Disorders related to sexuality and gender identity in the ICD-11: revising the ICD-10 classification based on current scientific evidence, best clinical practices, and human rights considerations. *World Psychiatry* 15, 205-221.
39. Reisman, Y., 2017. Sexual Consequences of Post-SSRI Syndrome. *Sex Med Rev* 5, 429-433.
40. Sayers, S.L., Farrow, V.A., Ross, J., Oslin, D.W., 2009. Family problems among recently returned military veterans referred for a mental health evaluation. *J Clin Psychiatry* 70, 163-170.
41. Shen, C.C., Tsai, S.J., Perng, C.L., Kuo, B.I., Yang, A.C., 2013. Risk of Parkinson disease after depression: a nationwide population-based study. *Neurology* 81, 1538-1544.
42. Shih, C.J., Chu, H., Chao, P.W., Lee, Y.J., Kuo, S.C., Li, S.Y., Tarng, D.C., Yang, C.Y., Yang, W.C., Ou, S.M., Chen, Y.T., 2014. Long-term clinical outcome of major adverse cardiac events in survivors of infective endocarditis: a nationwide population-based study. *Circulation* 130, 1684-1691.
43. Stein, D.J., Seedat, S., Iversen, A., Wessely, S., 2007. Post-traumatic stress disorder: medicine and politics. *Lancet* 369, 139-144.
44. Wang, T.Y., Wei, H.T., Liou, Y.J., Su, T.P., Bai, Y.M., Tsai, S.J., Yang, A.C., Chen, T.J., Tsai, C.F., Chen, M.H., 2016. Risk for developing dementia among patients with posttraumatic stress disorder: A nationwide longitudinal study. *Journal of affective disorders* 205, 306-310.
45. Yang, Y.J., Chien, W.C., Chung, C.H., Hong, K.T., Yu, Y.L., Hueng, D.Y., Chen, Y.H., Ma, H.I., Chang, H.A., Kao, Y.C., Yeh, H.W., Tzeng, N.S., 2018. Risk of Erectile Dysfunction After Traumatic Brain Injury: A Nationwide Population-Based Cohort study in Taiwan. *American journal of men's health* 12, 913-925.
46. Yehuda, R., 2002. Post-traumatic stress disorder. *N Engl J Med* 346, 108-114.
47. Zainol, M., Sidi, H., Kumar, J., Das, S., Ismail, S.B., Hatta, M.H., Baharuddin, N., Ravindran, A., 2019. Co-Morbid Erectile Dysfunction (ED) and Antidepressant Treatment in a Patient - A Management Challenge? *Curr Drug Targets* 20, 182-191.

Tables

Table 1. Characteristics of study at the baseline					
PTSD	With		Without		<i>P</i>
Variables	n	%	n	%	
Total	1,079	25.00	3,237	75.00	
Age (years)	36.05 ± 14.11		36.73 ± 14.28		0.174
Age group (years)					0.999
20-39	869	80.54	2,607	80.54	
≥40	210	19.46	630	19.46	
Insured premium (NT\$)					0.998
<18,000	967	89.62	2,901	89.62	
18,000-34,999	80	7.41	241	7.45	
≥35,000	32	2.97	95	2.93	
Dementia	3	0.28	4	0.12	0.337
Schizophrenia	40	3.71	144	4.45	0.338
Anxiety	68	6.30	5	0.15	<0.001
Bipolar disorder	123	11.40	15	0.46	<0.001
Depression	471	43.65	24	0.74	<0.001
Stroke	19	1.76	82	2.53	0.163
Coronary artery disease	7	0.65	97	3.00	<0.001
Hypertension	49	4.54	165	5.10	0.517
Diabetes mellitus	17	1.58	150	4.63	<0.001
Asthma	9	0.83	50	1.54	0.095
Alcohol-related disease	49	4.54	118	3.65	0.202
CCI					<0.001
0	1,029	95.37	2,794	86.31	
1	25	2.32	231	7.14	
2	11	1.02	70	2.16	
3	6	0.56	93	2.87	
≥4	8	0.74	49	1.51	
Antidepressants	959	88.88	246	6.98	<0.001
1-364 days	311	28.82	157	4.85	
≥365 days	648	60.06	69	2.13	
SSRI	892	82.67	153	4.72	<0.001
1-364 days	345	31.97	104	3.21	
≥365 days	547	50.70	49	1.51	
SNRI	937	86.84	136	4.20	<0.001

1-364 days	338	31.33	99	3.06	
≥365 days	599	55.51	37	1.14	
Other antidepressants	948	87.85	162	5.00	<0.001
1-364 days	375	34.75	112	3.46	
≥365 days	573	53.10	50	1.54	
Sedative / hypnotics	884	81.92	173	5.34	<0.001
1-364 days	431	39.94	95	2.93	
≥365 days	453	41.98	78	2.41	
Antipsychotics	839	77.76	137	4.23	<0.001
1-364 days	368	34.11	66	2.04	
≥365 days	471	43.65	71	2.19	
Residence of Taiwan					<0.001
Northern Taiwan	755	69.97	1,315	40.62	
Middle Taiwan	122	11.31	911	28.14	
Southern Taiwan	163	15.11	790	24.41	
Eastern Taiwan	28	2.59	209	6.46	
Outlets islands	11	1.02	12	0.37	
Urbanization level					<0.001
1 (The highest)	177	16.40	1,063	32.84	
2	776	71.92	1,362	42.08	
3	57	5.28	289	8.93	
4 (The lowest)	69	6.39	523	16.16	
Levels of hospitals					<0.001
Medical center	693	64.23	1,031	31.85	
Regional hospital	312	28.92	1,143	35.31	
Local hospital	74	6.86	1,063	32.84	
PTSD: posttraumatic stress disorder; P: Chi-square / Fisher exact test on category variables and t-test on continue variables; New Taiwan Dollars: NT\$; CCI: Charlson Comorbidity Index, stroke, coronary artery disease, Hypertension, diabetes mellitus and alcohol-related illness; SSRI: Selective Serotonin Reuptake Inhibitor; SNRI: Serotonin-Norepinephrine Reuptake Inhibitor					

Table 2. Hazard ratios analysis of ED in the patients with PTSD								
Variables	Crude HR	95% CI	95% CI	<i>P</i>	Adjusted HR	95% CI	95% CI	<i>P</i>
PTSD								
Without	Reference				Reference			
With	14.766	3.426	63.635	<0.001	12.898	2.453	67.811	0.003
Anxiety								
Without	Reference				Reference			
With	2.294	1.445	3.978	0.001	1.864	1.064	3.568	0.025
Bipolar disorder								
Without	Reference				Reference			
With	1.795	1.042	2.568	0.030	1.998	1.165	2.774	0.014
Depression								
Without	Reference				Reference			
With	4.030	2.457	7.198	<0.001	2.970	1.845	4.798	0.001
PTSD: posttraumatic stress disorder; HR: hazard ratio, CI: confidence interval, Crude Hazard Ratio								
Adjusted HR: Adjusted variables listed in the table 1								

Table 3. Factors of ED stratified by variables listed in the table by using multivariable Cox regression										
PTSD	With			Without			With vs. without (<i>Reference</i>)			
Stratified	Event	PYs	Rate (per 10 ⁵ PYs)	Event	PYs	Rate (per 10 ⁵ PYs)	Adjusted HR	95% CI	95% CI	<i>P</i>
Total	5	10,508.98	47.58	3	33,224.39	9.03	12.898	2.453	67.811	0.003
Age group (years)										
20-39	3	4,533.90	66.17	0	10,458.58	0.00	∞	-	-	0.995
≥40	2	5,975.08	33.47	3	22,765.80	13.18	6.245	1.198	32.687	0.002
Insured premium (NT\$)										
<18,000	5	10,375.92	48.19	3	32,687.78	9.18	12.898	2.453	67.811	0.003
18,000-34,999	0	129.16	0.00	0	402.26	0.00	-	-	-	-
≥35,000	0	3.89	0.00	0	134.34	0.00	-	-	-	-
Dementia										
Without	5	10,474.83	47.73	3	33,104.41	9.06	12.898	2.453	67.811	0.003
With	0	34.15	0.00	0	119.97	0.00	-	-	-	-
Schizophrenia										
Without	5	9,605.58	52.05	3	30,821.27	9.73	12.898	2.453	67.811	0.003
With	0	903.40	0.00	0	2,403.12	0.00	-	-	-	-
Anxiety										
Without	1	10,327.00	9.68	1	32,922.36	3.04	7.804	1.424	41.027	0.014
With	4	181.98	2,198.00	2	302.03	662.19	18.191	3.569	72.774	<0.001
Bipolar disorder										
Without	2	9,853.89	20.30	2	32,389.69	6.17	8.046	1.530	42.306	0.007
With	3	655.09	457.95	1	834.70	119.80	13.978	3.121	89.193	<0.001
Depression										
Without	1	9,699.42	10.31	1	31,603.57	3.16	7.975	1.517	41.995	0.012
With	4	809.56	494.10	2	1,620.82	123.39	19.911	3.697	101.454	<0.001
Stroke										
Without	5	9,852.17	50.75	3	31,397.33	9.55	12.898	2.453	67.811	0.003
With	0	656.81	0.00	0	1,827.05	0.00	-	-	-	-
Coronary artery disease										
Without	5	9,770.07	51.18	2	30,978.06	6.46	18.795	3.685	98.975	0.001
With	0	738.91	0.00	1	2,246.33	44.52	0.000	-	-	0.898
Hypertension										

Without	5	9,770.07	51.18	3	30,978.06	9.68	18.795	3.685	98.975	0.001
With	0	738.91	0.00	0	2,246.33	0.00	-	-	-	-
Diabetes mellitus										
Without	5	9,632.65	51.91	2	28,166.68	7.10	0.000	0.000	0.000	
With	0	876.33	0.00	1	5,057.71	19.77	0.000	-	-	
Asthma										
Without	5	10,481.74	47.70	3	32,871.27	9.13	18.795	3.685	98.975	0.001
With	0	27.24	0.00	0	353.12	0.00	-	-	-	-
Alcohol-related diseases										
Without	5	9,663.48	51.74	3	31,260.49	9.60	18.795	3.685	98.975	0.001
With	0	845.50	0.00	0	1,963.90	0.00	-	-	-	-
CCLR										
0	4	8,437.56	47.41	2	25,127.98	7.96	14.498	2.775	77.045	<0.001
1	1	1,208.07	82.78	0	3,296.20	0.00	∞	-	-	0.999
2	0	122.52	0.00	1	1,097.72	91.10	0.000	-	-	0.897
3	0	403.61	0.00	0	2,122.11	0.00	-	-	-	-
≥ 4	0	337.22	0.00	0	1,580.38	0.00	-	-	-	-
Antidepressants										
Without	0	1,248.79	0.00	1	29,780.20	3.36	0.000	-	-	0.986
1-364 days	2	4,054.91	49.32	0	1,779.27	0.00	∞	-	-	0.782
≥ 365 days	3	5,205.29	57.63	2	1,664.92	120.13	1.179	0.223	6.174	0.798
SSRI										
Without	4	1,379.70	289.92	2	29,897.01	6.69	106.254	20.174	559.784	<0.001
1-364 days	0	4,103.81	0.00	0	1,897.04	0.00	-	-	-	-
≥ 365 days	1	5,025.47	19.90	1	1,430.33	69.91	0.765	0.124	3.687	0.594
SNRI										
Without	4	1,349.01	296.51	2	29,901.12	6.69	108.513	20.634	570.501	<0.001
1-364 days	1	4,098.91	24.40	1	1,796.78	55.66	1.073	0.199	5.687	0.751
≥ 365 days	0	5,061.06	0.00	0	1,526.48	0.00	-	-	-	-
Other antidepressants										
Without	0	1,309.10	0.00	2	28,965.87	6.90	0.000	-	-	0.897
1-364 days	3	4,077.91	73.57	0	2,015.50	0.00	∞	-	-	0.989
≥ 365 days	2	5,121.97	39.05	1	2,243.01	44.58	2.114	0.408	11.277	0.735
Sedative / hypnotics										
Without	0	1,409.78	0.00	1	27,989.45	3.57	0.000	-	-	0.998

1-364 days	2	4,813.10	41.55	0	2,695.02	0.00	∞	-	-	0.975
≥ 365 days	3	4,286.10	69.99	2	2,539.92	78.74	2.176	0.414	11.438	0.762
Antipsychotics										
Without	0	1,698.91	0.00	1	28,750.12	3.48	0.000	-	-	0.897
1-364 days	2	4,340.11	46.08	1	2,245.78	44.53	2.533	0.482	13.601	0.513
≥ 365 days	3	4,469.96	67.11	1	2,228.48	44.87	3.661	0.689	19.265	0.772
Urbanization level										
1 (The highest)	2	3,141.06	63.67	2	9,110.76	21.95	7.101	1.354	37.301	0.021
2	3	4,877.23	61.51	0	14,053.73	0.00	∞	-	-	0.986
3	0	1,034.04	0.00	1	3,281.11	30.48	0.000	-	-	0.887
4 (The lowest)	0	1,456.64	0.00	0	6,778.79	0.00	-	-	-	-
Levels of hospitals										
Hospital center	3	3,498.68	85.75	2	10,247.28	19.52	10.789	2.049	56.535	<0.001
Regional hospital	2	4,968.42	40.25	0	15,631.31	0.00	∞	-	-	0.964
Local hospital	0	2,041.88	0.00	1	7,345.80	13.61	0.000	-	-	0.997
NT\$ = New Taiwan Dollars; PYs = Person-years; Adjusted HR = Adjusted Hazard ratio: Adjusted for the variables listed in Table 1.; CI = confidence interval; CCLR = Charlson Comorbidity Index; SSRI = Selective serotonin reuptake inhibitor; SNRI = Selective norepinephrine reuptake inhibitor										

Table 4. Factors of erectile dysfunction subgroup by using multivariable Cox regression				
PTSD	With vs. without (<i>Reference</i>)			
ED subgroup	Adjusted HR	95% CI	95% CI	<i>P</i>
Overall	12.898	2.453	67.811	0.003
Psychosexual ED (N=6)	27.044	2.731	267.795	<0.001
Organic ED (N=2)	0.000	-	-	0.998
ED: erectile disorder; PTSD: posttraumatic stress disorder; HR= hazard ratio, CI = confidence interval, Adjusted HR: Adjusted variables listed in Table 1.				

Figures

Figure 1

The flowchart of study sample selection

1

Figure 2

Kaplan-Meier for cumulative incidence of erectile dysfunction aged 20 and over stratified by post-traumatic stress disorder with log-rank test

Supplementary Files

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