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

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Primary research

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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 hypnosedatives, were collected. The data of defined daily dose (DDD) were obtained from the WHO Collaborating Centre for Drug Statistics Methodology (https://www.whocc.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). χ² 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 sough 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 as 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 meet 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). 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

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Table 1. Characteristics of study at the baseline

| Variables                        | With        |          | Without    |          |     P  |
|----------------------------------|-------------|----------|------------|----------|--------|
|                                  | n           | %        | n          | %        |        |
| Total                            | 1,079       | 25.00    | 3,237      | 75.00    | 0.174  |
| 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 \\
\geq 365 days & 599 & 55.51 & 37 & 1.14 \\
**Other antidepressants** & 948 & 87.85 & 162 & 5.00 \textless 0.001 \\
1-364 days & 375 & 34.75 & 112 & 3.46 \\
\geq 365 days & 573 & 53.10 & 50 & 1.54 \\
**Sedative / hypnotics** & 884 & 81.92 & 173 & 5.34 \textless 0.001 \\
1-364 days & 431 & 39.94 & 95 & 2.93 \\
\geq 365 days & 453 & 41.98 & 78 & 2.41 \\
**Antipsychotics** & 839 & 77.76 & 137 & 4.23 \textless 0.001 \\
1-364 days & 368 & 34.11 & 66 & 2.04 \\
\geq 365 days & 471 & 43.65 & 71 & 2.19 \\
\textbf{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 \\
\textbf{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 \\
\textbf{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 \\
\textbf{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}
| Variables          | Crude HR | 95% CI | 95% CI | P   | Adjusted HR | 95% CI | 95% CI | P   |
|--------------------|----------|--------|--------|-----|-------------|--------|--------|-----|
| 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
| Stratified | Event | PYs     | Rate (per 10^5 PYs) | Event | PYs     | Rate (per 10^5 PYs) | Adjusted HR | 95% CI      | 95% CI      | P       |
|------------|-------|---------|---------------------|-------|---------|---------------------|-------------|-------------|-------------|---------|
| **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  | 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  | -      | -     | -      | -      |
| CCL/R               |         |    |          |       |   |           |      |        |       |        |       |
| 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  |
### Table 4. Factors of erectile dysfunction subgroup by using multivariable Cox regression

| PTSD          | With vs. without (Reference) |
|---------------|-----------------------------|
| **PTSD**      | **Adjusted HR** | **95% CI** | **95% CI** | **P** |
| **ED subgroup** |                |          |          |      |
| 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.
Figure 1

The flowchart of study sample selection
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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- TableS1.docx