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Research paper

Posttraumatic stress disorder, cardiovascular disease outcomes and the modifying role of socioeconomic status

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ABSTRACT

Introduction: Substantial evidence indicates that post-traumatic stress disorder (PTSD) is associated with an increased incidence of cardiovascular disease (CVD), and differential PTSD-CVD association by socioeconomic status had been suggested. However, there are inadequate evidence on differential association. This study investigated sociodemographic heterogeneity in the association between PTSD and CVD.

Methods: A total of 53,749 patients diagnosed with PTSD in 2004–2018 were recruited from Korean National Health Insurance Database. Date of first diagnosis of PTSD was set as an index date. We recruited 3 controls per each patient, matched by age and sex (N = 161,247). Monthly insurance premiums were used as a surrogate variable for socioeconomic status. Cox proportional hazard model was used to estimate the hazard of incident coronary artery disease, incident stroke, and cardiovascular mortality. We stratified participants by age, sex, and insurance premium to test heterogeneities in the association.

Results: PTSD was associated with increased risk for coronary artery disease, hemorrhagic stroke, and cardiovascular mortality. Elevation in risk of cardiovascular disease was more prominent in younger individuals. PTSD increased the risk of coronary artery disease and ischemic stroke more in individuals with lower SES, especially in men.

Limitations: Insurance premium might not fully represent socioeconomic status of individual. Misclassification or misdiagnosis of PTSD by might have introduced biases.

Conclusions: PTSD was associated with increased incidence of CVD, particularly in male patients with low SES. For PTSD patients with lower SES, preventive measures against cardiovascular disease would be able to decrease the disease burden of cardiovascular comorbidity in PTSD.

1. Introduction

A large body of literature has suggested a link between post-traumatic stress disorder (PTSD) and the onset of cardiovascular disease (CVD) (Hageman et al., 2001; Koenen et al., 2017b; O'Donnell et al., 2021). It has also been reported that patients with PTSD have a higher risk of stroke (Byers et al., 2014; Nelson et al., 2020), ischemic heart disease (Song et al., 2019; Sumner et al., 2015), and cardiovascular mortality (Ebrahimi et al., 2021; Song et al., 2019). The mechanisms underlying the observed association are unclear; U.S.-based studies have shown conflicting findings as to whether the observed association is eliminated after adjustment for CVD risk factors (Scherrer et al., 2019) or whether the observed association persists (Sumner et al., 2015).

Studies included in systematic reviews of this literature are characterized by a significant degree of heterogeneity (Emdin et al., 2016; Roy et al., 2015). This differential vulnerability to PTSD might be attributed, in part, to differences in socioeconomic status (SES) or the age and sex profiles of study participants. A sizeable literature suggests that SES may moderate the adverse health effects of external stressors (Brunner, 1997; Diderichsen et al., 2019; Dohrenwend, 1973). Kessler (1979) and

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Table 1
Characteristics of Korean patients diagnosed with post-traumatic stress disorder in 2004–2018 (N = 53,749) and their matched controls (N = 161,247).

	Men			Women		
	Case (N = 19,030)	Control (N = 57,090)	p-value	Case (N = 34,719)	Control (N = 104,157)	p-value
Age at index date, Mean (SD)	**49.88 (11.30)**	**50.31 (11.54)**	**<0.001**	**49.86 (11.30)**	**49.71 (11.27)**	**0.032**
Follow-up years, mean (SD)						
Until any major cardiovascular events	**5.99 (4.13)**	**6.45 (4.08)**	**<0.001**	**6.64 (4.17)**	**6.70 (4.12)**	**0.021**
Until coronary artery disease	**6.22 (4.15)**	**6.58 (4.10)**	**<0.001**	**6.64 (4.17)**	**6.80 (4.13)**	**<0.001**
Until stroke	6.12 (4.16)	6.57 (4.10)	<0.001	6.75 (4.18)	6.76 (4.12)	0.701
Until ischemic stroke	6.19 (4.16)	6.60 (4.10)	<0.001	6.75 (4.18)	6.79 (4.13)	0.124
Until hemorrhagic stroke	**6.69 (4.11)**	**6.32 (4.18)**	**<0.001**	**6.75 (4.18)**	**6.86 (4.13)**	**<0.001**
Until cardiovascular mortality	**6.71 (4.12)**	**6.38 (4.18)**	**<0.001**	**6.75 (4.18)**	**6.88 (4.14)**	**<0.001**
Systolic blood pressure, mmHg, mean (SD)	**124.52 (15.10)**	**126.08 (15.71)**	**<0.001**	**118.23 (16.00)**	**119.78 (16.43)**	**<0.001**
Fasting blood glucose, mg/dL, mean (SD)	99.58 (33.11)	99.19 (30.78)	0.138	94.28 (24.39)	94.24 (23.64)	0.787
Total serum cholesterol, mg/dL, mean (SD)	**194.81 (43.18)**	**195.58 (42.63)**	**0.031**	194.95 (45.23)	195.02 (42.37)	0.793
Cigarette smoking, N (%)			0.053			**<0.001**
Nonsmoker	6546 (24.76)	19,889 (34.84)		**30,365 (87.46)**	**94,651 (90.87)**	
Former smoker	3154 (16.57)	9720 (17.03)		**1014 (2.92)**	**2125 (2.04)**	
Current smoker	9137 (48.01)	26,987 (47.27)		**2562 (7.38)**	**4895 (4.70)**	
N/A	193 (1.01)	494 (0.87)		**778 (2.24)**	**2486 (2.39)**	
Alcohol consumption N (%)			**<0.001**			0.643
Current drinker	**12,125 (63.72)**	**38,596 (67.61)**		10,662 (30.71)	32,124 (30.84)	
Nondrinker or former drinker	**6905 (36.28)**	**18,494 (32.39)**		24,057 (69.29)	72,033 (69.16)	
Monthly insurance premium, N (%)			**<0.001**			**<0.001**
0 (Medicaid recipient)	**549 (2.88)**	**917 (1.61)**		**1394 (4.02)**	**2185 (2.10)**	
≤20p (1–17,001)	**4097 (21.53)**	**11,108 (19.46)**		**7882 (22.70)**	**24,023 (23.06)**	
20–40p (17,001–27,300)	**3664 (19.25)**	**10,879 (19.06)**		**6166 (17.76)**	**18,678 (17.93)**	
40–60p (27,301–41,000)	**3944 (20.73)**	**12,113 (21.22)**		**6688 (19.26)**	**20,773 (19.94)**	
60–80p (41,001–56,950)	**3579 (18.81)**	**11,429 (20.02)**		**6326 (18.22)**	**19,846 (19.05)**	
≥80p (56,951–)	**3197 (16.80)**	**10,644 (18.64)**		**6263 (18.04)**	**18,652 (17.91)**	
Psychiatric comorbidities, N (%)						
Psychotic symptoms and/or psychosis	**1589 (8.35)**	**1045 (1.83)**	**<0.001**	**2216 (6.38)**	**1827 (1.32)**	**<0.001**
Manic episodes and/or bipolar disorders	**2670 (14.03)**	**1334 (2.34)**	**<0.001**	**4143 (11.93)**	**2664 (2.56)**	**<0.001**
Depressive symptoms and/or disorders	**11,109 (58.38)**	**11,407 (19.98)**	**<0.001**	**22,995 (66.23)**	**32,230 (30.94)**	**<0.001**
Anxiety symptoms and/or disorders	**6398 (33.62)**	**6093 (10.67)**	**<0.001**	**14,364 (41.37)**	**18,772 (18.02)**	**<0.001**
Cardiovascular diseases, N (%)						
Coronary artery disease[a]	**878 (4.61)**	**2118 (3.71)**	**<0.001**	**918 (2.64)**	**2039 (1.96)**	**<0.001**
Ischemic stroke[b]	**758 (3.98)**	**1471 (2.58)**	**<0.001**	**1051 (3.03)**	**1990 (1.91)**	**<0.001**
Hemorrhagic stroke[b]	**266 (1.40)**	**435 (0.76)**	**<0.001**	**534 (1.54)**	**537 (0.52)**	**<0.001**
Cardiovascular mortality	**151 (0.79)**	**323 (0.57)**	**<0.001**	**175 (0.50)**	**318 (0.31)**	**<0.001**
All-cause deaths, N (%)	**1221 (6.42)**	**2651 (4.64)**	**<0.001**	**1054 (3.04)**	**1939 (1.86)**	**<0.001**

Values with a p-value less than 0.05 were considered to be statistically significant and bolded. SD, standard deviation; IU, international unit.
[a] 1) Diagnosed with myocardial infarction or 2) diagnosed with coronary artery diseases and underwent revascularization.
[b] Diagnosed with stroke and underwent radiologic study of the brain (CT/MRI).

Grzywacz et al. (2004) suggested differences in exposure and susceptibility to stressors, indicating that individuals with lower SES are more susceptible to health effects of stressors. Later, Mock & Arai analysed data from the 2005 Canadian Community Health Survey and concluded that higher socioeconomic status acts as a buffer to chronic health effects of childhood trauma (Mock and Arai, 2011). However, these evidences might not be able to be directly applied to PTSD-CVD association, as they mostly focus on stressors, distress and traumatic events rather than the disease entity of PTSD. Although traumatic events and distress are important prerequisites of PTSD, PTSD is a complex term that encompasses both preceding psychiatric trauma and its consequent neurobiological reaction (Cowell et al., 2017; Hamblen et al., 2019; Ross et al., 2017; Rutten et al., 2013). As it is, differential health effects of PTSD by SES are still to be tested and evidence that support the heterogeneity are yet to be investigated. To address these gaps in the literature, we used a national representative longitudinal database to estimate the association between PTSD and CVD risk, and to assess the extent to which socioeconomic disparities conditioned these associations.

2. Methods

2.1. Patient enrollment

Medical service utilization data of patients with PTSD, who received medical services during 2004–2018, were obtained from the Korean National Health Insurance Database (NHID), which is an administrative database constructed by the National Health Insurance System (NHIS) of South Korea. It covers roughly 98 % of the South Korean population, making it one of the most representative nationwide cohort databases (Kwon, 2009).

Patients with at least one insurance claim record with an ICD-10 diagnostic code for PTSD (F43.1) during 2004–2018 were recruited from NHID (N = 109,235).We excluded patients with erroneous data for insurance qualification (N = 5), patients aged 29 years or younger or 80 years or older at the time of their PTSD diagnosis (N = 43,909), those who did not receive NHIS health check-up (N = 9629), and those diagnosed with major cardiovascular diseases before PTSD diagnosis (N = 1943), leaving 53,749 patients with PTSD for in the analytic sample (19,030 men and 34,719 women; Supplementary Material 1). The first date of PTSD diagnosis was set as the index date. We selected 3 controls per patient, matched by age and sex (N = 161,247). Up to five years of age difference was accepted during the matching procedure. For selected controls, index date was set as index date of matched PTSD patients.

2.2. Outcome: major cardiovascular events

Incident major cardiovascular events (coronary artery disease, ischemic stroke, hemorrhagic stroke and cardiovascular mortality) were set as primary end points. Patients with one or more ICD-10 diagnostic codes for myocardial infarction or ischemic heart disease with revascularization were defined as coronary artery disease cases. Patients with

Table 2
Hazard ratios (HRs) and their 95 % confidence intervals (CIs) of post-traumatic stress disorder for cardiovascular diseases.

	Unadjusted model	Fully adjusted model	e-value for hazard ratio	e-value for confidence interval
Total participants				
Coronary artery disease	**1.20 (1.14–1.27)*****	**1.11 (1.04–1.17)*****	1.46	1.24
Stroke	**1.53 (1.44–1.63)*****	**1.18 (1.03–1.20)****	1.64	1.21
Ischemic stroke	**1.39 (1.29–1.49)*****	1.05 (0.96–1.14)	1.28	1.00
Hemorrhagic stroke	**1.84 (1.69–2.01)*****	**1.64 (1.49–1.80)*****	2.66	2.34
Cardiovascular mortality	**1.27 (1.15–1.41)*****	**1.42 (1.26–1.58)*****	2.19	1.83
Men				
Coronary artery disease	**1.20 (1.11–1.30)*****	**1.09 (1.00–1.19)***	1.40	1.00
Stroke	**1.68 (1.57–1.81)*****	**1.30 (1.19–1.40)*****	1.92	1.67
Ischemic stroke	**1.58 (1.46–1.72)*****	**1.19 (1.09–1.31)*****	1.67	1.40
Hemorrhagic stroke	**1.92 (1.68–2.19)*****	**1.56 (1.33–1.83)*****	2.49	1.99
Cardiovascular mortality	**1.35 (1.15–1.58)*****	**1.35 (1.12–1.62)*****	2.04	1.49
Women				
Coronary artery disease	**1.20 (1.12–1.30)*****	**1.12 (1.04–1.21)****	1.49	1.24
Stroke	**1.45 (1.34–1.57)*****	**1.17 (1.05–1.30)****	1.62	1.28
Ischemic stroke	**1.23 (1.12–1.35)*****	0.99 (0.89–1.10)	1.11	1.00
Hemorrhagic stroke	**1.80 (1.60–2.01)*****	**1.69 (1.49–1.90)*****	2.77	2.34
Cardiovascular mortality	**1.22 (1.06–1.39)*****	**1.42 (1.22–1.64)*****	2.19	1.74

Fully adjusted models are adjusted for body mass index, systolic blood pressure, diastolic blood pressure, total cholesterol, fasting glucose, psychotic disorder, manic episodes/bipolar disorders, depressive symptoms/disorders and anxiety-related disorders, current smoking status, current alcohol consumption status and monthly insurance premium.
* p-value <0.05.
** p-value <0.01.
*** p-value <0.001.

one or more ICD-10 diagnostic codes for stroke with brain CT/MRI records were defined as stroke cases. Among patients with stroke, patients with ICD-10 code 'I63' were defined as ischemic stroke cases, and those with ICD-10 code 'I60-I62' were defined as hemorrhagic stroke cases. Patients with mortality records that were linked to ICD-10 diagnostic codes for CVD ('I' codes) were defined as cardiovascular mortality cases. The first date of diagnosis record with corresponding ICD-10 codes for CVD was defined as the date of diagnosis. Corresponding diagnostic codes and insurance claim codes for outcome definitions are presented in Supplementary Material 2–3.

2.3. Covariates

Both concurrent medical and psychiatric conditions at the index date were included as comorbidities. Systolic blood pressure, diastolic blood pressure, fasting blood glucose, total serum cholesterol, serum aspartate aminotransferase, serum alanine aminotransferase and serum γ-glutamyl transferase were measured during national medical check-up at designated medical institutions. Psychotic disorders, manic episodes/bipolar disorders, depressive symptoms/disorders and anxiety and related disorders were included as psychiatric comorbidities. Additionally, cigarette smoking and alcohol consumption status were included as covariates. The ICD-10 diagnostic codes corresponding to these conditions are listed in Supplemental Material 2.

Monthly insurance premiums were used as a surrogate variable for SES of participants. Based on the National Health Insurance Act, NHIS premiums for each individual is calculated based on their employment status, monthly income, and their household characteristics, and therefore is a comprehensive surrogate variable for socioeconomic status (Khang et al., 2010). NHIS premiums are widely used in the epidemiologic literature as a proxy for SES. Information on the mean monthly insurance premium was collected from the NHID, and quintile values of the mean monthly insurance premiums of all participants included in the final analysis were used to categorize the participants. Medicaid recipients who did not pay any insurance premium were classified as a separate subgroup.

2.4. Statistical analyses

Characteristics of male and female PTSD patients at the time of PTSD diagnosis were described, along with the characteristics of their matched controls. We used *t*-test for comparing continuous variables and chi-square test for comparing categorical variables. For patients with CVDs, the follow-up period was censored at the first date of CVD diagnosis, including cardiovascular mortality. For other participants, follow-up period was censored at the date of the last insurance claim or date of death. Cox regression models were fitted to the data to estimate the hazard ratio (HR) associated with PTSD for incident coronary artery disease, incident stroke, and cardiovascular mortality, with mortality by causes other than CVD considered as competing risks. For incident stroke, the HRs for all strokes, ischemic strokes, and hemorrhagic strokes were estimated separately. We additionally estimated e-value for each estimated hazard ratio. For sensitivity analysis, we selected 'vasomotor and allergic rhinitis' (ICD-10 diagnostic code: J30) as a negative outcome control/falsification outcome to provide additional evidence for the specificity of the exposure-outcome association (Lipsitch et al., 2010; Prasad and Jena, 2013). To investigate socioeconomic heterogeneity in the association between PTSD and CVD, we conducted analyses stratified by monthly insurance premium and sex. All analyses were conducted using SAS software, version 9.4 (SAS Institute Inc., Cary, NC, USA).

2.5. Ethics approval

The study protocols were approved by the Institutional Review Board of Yonsei University Health System, Seoul, Korea (approval number Y-2019-0042). Informed consent was waived for this study, as NHID data used in this study were deidentified. All procedures contributing to this work complied with the ethical standards of the relevant national and institutional committees on human experimentation and with the 1975 Declaration of Helsinki, which was revised in 2008.

3. Results

3.1. Characteristics of participants

The analysis cohort included 253,512 individuals with a total of 1,663,038 person-years of follow-up. The mean duration of follow-up until any major cardiovascular event was 6.56 years (standard deviation [SD] 4.12). In the sample of men, the average duration of follow-up until major cardiovascular event was 5.99 years (SD 4.13) for PTSD patients and 6.45 years (SD 4.08) for controls. In the sample of women, the average duration of follow-up was 6.64 years (SD 4.17) for PTSD patients and 6.70 years (SD 4.12) for controls.

The mean age at the time of PTSD diagnosis was 49.88 years (SD 11.30) for men and 49.86 years (SD 11.30) for women. The proportion

Table 3
Hazard ratios and their 95 % confidence intervals of post-traumatic stress disorder for cardiovascular diseases by insurance premium subgroups.

Insurance premium percentile	0p	1–20p	21–40p	41–60p	61–80p	≥81p	P for trend
Total							
Coronary artery disease	1.15 (0.88–1.50)	**1.21 (1.05–1.39)** **	**1.13 (1.00–1.29)** *	1.11 (0.96–1.27)	1.09 (0.96–1.24)	0.99 (0.86–1.14)	**0.027**
Stroke	**1.45 (1.17–1.79)** ***	**1.14 (1.01–1.29)** *	1.06 (0.95–1.19)	1.05 (0.93–1.19)	1.01 (0.90–1.13)	**0.85 (0.75–0.97)** *	**0.011**
Ischemic stroke	**1.41 (1.10–1.79)** **	0.97 (0.84–1.13)	0.92 (0.81–1.05)	0.94 (0.82–1.09)	**0.84 (0.74–0.96)** *	**0.74 (0.64–0.86)** ***	**0.028**
Hemorrhagic stroke	**1.69 (1.07–2.68)** *	**1.91 (1.51–2.41)** ***	**1.70 (1.37–2.10)** ***	**1.66 (1.32–2.08)** ***	**1.64 (1.32–2.02)** ***	**1.38 (1.09–1.75)** **	0.082
Cardiovascular mortality	1.33 (0.88–2.02)	**1.51 (1.14–2.01)** **	**1.70 (1.32–2.18)** ***	**1.46 (1.11–1.92)** **	**1.48 (1.15–1.91)** **	1.10 (0.83–1.46)	0.440
Men							
Coronary artery disease	1.23 (0.79–1.91)	1.06 (0.86–1.32)	1.17 (0.97–1.40)	1.16 (0.95–1.42)	1.13 (0.94–1.36)	0.93 (0.75–1.16)	0.155
Stroke	**1.87 (1.31–2.68)** ***	**1.48 (1.22–1.80)** ***	**1.22 (1.03–1.46)** *	**1.27 (1.05–1.54)** *	**1.32 (1.10–1.59)** **	1.05 (0.85–1.29)	**0.029**
Ischemic stroke	**1.83 (1.21–2.76)** **	**1.36 (1.09–1.70)** **	1.09 (0.89–1.33)	1.23 (0.99–1.53)	1.17 (0.95–1.44)	1.02 (0.79–1.30)	**0.046**
Hemorrhagic stroke	2.21 (0.99–4.94)	**2.01 (1.37–2.94)** ***	**1.62 (1.14–2.32)** **	1.19 (0.80–1.76)	**1.63 (1.17–2.29)** **	1.28 (0.86–1.91)	**0.039**
Cardiovascular mortality	1.46 (0.63–3.38)	**1.87 (1.19–2.94)** **	1.50 (0.98–2.30)	1.09 (0.70–1.69)	1.39 (0.92–2.11)	0.97 (0.61–1.55)	0.109
Women							
Coronary artery disease	1.09 (0.77–1.54)	**1.35 (1.12–1.63)** **	1.12 (0.94–1.34)	1.08 (0.89–1.31)	1.07 (0.90–1.29)	1.01 (0.84–1.22)	0.229
Stroke	1.21 (0.92–1.58)	0.94 (0.80–1.11)	0.94 (0.81–1.10)	0.93 (0.79–1.08)	**0.85 (0.73–0.98)** *	**0.76 (0.64–0.89)** ***	**0.015**
Ischemic stroke	1.14 (0.83–1.56)	**0.75 (0.61–0.92)** **	**0.79 (0.66–0.95)** *	**0.78 (0.65–0.94)** *	**0.67 (0.56–0.80)** ***	**0.60 (0.49–0.73)** ***	**0.035**
Hemorrhagic stroke	1.43 (0.79–2.59)	**1.82 (1.34–2.47)** ***	**1.72 (1.30–2.26)** ***	**1.95 (1.46–2.60)** ***	**1.69 (1.28–2.23)** ***	**1.46 (1.09–1.98)** *	0.996
Cardiovascular mortality	1.16 (0.69–1.95)	1.20 (0.87–1.78)	**1.75 (1.27–2.41)** ***	**1.77 (1.22–2.55)** **	**1.50 (1.08–2.09)** *	1.07 (0.73–1.57)	0.878

All estimates were from models adjusted for comorbidities listed in Charlson comorbidity index, psychiatric comorbidities, hypertension, and dyslipidemia. P: percentile.

of Medicaid recipients was higher among patients with PTSD than among controls (men: 549 (2.88 %) vs. 917 (1.61 %), $p < 0.001$; women: 1394 (4.02 %) vs. 2185 (2.10 %), $p < 0.001$; Table 1), suggesting that lower SES is associated with PTSD.

Psychiatric comorbidities at the index date, including psychotic disorders, manic episodes/bipolar disorders, depressive symptoms/disorders, and anxiety symptoms/disorders, were more prevalent in patients with PTSD than in matched controls. Incident coronary artery disease, ischemic stroke, and hemorrhagic stroke and cardiovascular mortality were more common in PTSD patients than in their controls (Table 1).

3.2. Association between PTSD and CVD

PTSD was associated with an increased risk of coronary artery disease (HR = 1.11, 95 % CI 1.04–1.17, e-value = 1.46 [CI 1.24]), hemorrhagic stroke (HR = 1.64, 95 % CI 1.49–1.80, e-value = 2.66 [CI 2.34]), and cardiovascular mortality (HR = 1.42, 95 % CI 1.26–1.58, e-value = 2.19 [CI 1.83]). In contrast, ischemic stroke was not associated with PTSD (HR = 1.05, 95 % CI 0.96–1.14, e-value = 1.21 [CI 1.00]). Among men, PTSD was associated with an increased risk of coronary artery disease (HR = 1.09, 95 % CI 1.00–1.19, e-value = 1.40 [CI 1.00]), ischemic stroke (HR = 1.19, 95 % CI 1.09–1.40, e-value = 1.67 [CI 1.40]), hemorrhagic stroke (HR = 1.56, 95 % CI 1.33–1.83, e-value = 2.49 [CI 1.99]), and cardiovascular mortality (HR = 1.35, 95 % CI 1.12–1.62, e-value = 2.04 [CI 1.49]). Among women, PTSD was associated with an increased risk of coronary artery disease (HR = 1.12, 95 % CI 1.04–1.21, e-value = 1.49 [CI 1.24]), hemorrhagic stroke (HR = 1.69, 95 % CI 1.49–1.90, e-value = 2.77 [CI 2.34]), and cardiovascular mortality (HR = 1.42, 95 % CI 1.22–1.64, e-value = 2.19 [CI 1.74]; Table 2). Female patients with PTSD had lower risk of ischemic stroke compared to their matched controls (HR = 0.90, 95 % CI 0.83–0.95, e-value = 1.46 [CI 1.29]). In the negative control analysis, PTSD did not have an increased risk of allergic rhinitis (HR = 0.89, 95 % CI 0.61–1.30, e-value = 1.50 [CI 1.00]), indicating that PTSD-CVD association is not likely to have been detected by chance.

3.3. Heterogeneous association between PTSD and CVD by SES

Subgroup analyses on insurance premium showed probable socioeconomic heterogeneities in association between PTSD and CVD. For coronary artery disease (p-value for trend = 0.027) and ischemic stroke (p-value for trend = 0.028), PTSD-CVD association was stronger in subgroups with lower insurance premium. This trend was more apparent in men than in women. PTSD-hemorrhagic stroke association (p-value for trend = 0.082) and PTSD-cardiovascular mortality association (p-value for trend = 0.440) was not modified by socioeconomic status (Table 3, Figs. 1–2).

4. Discussion

In this longitudinal analysis of Korean population-based national health insurance data, we identified associations between PTSD and the CVD outcomes of coronary artery disease, hemorrhagic stroke, and cardiovascular mortality. We also found that PTSD was associated with increased risk of ischemic stroke among men, but not among women. These estimated associations were larger in magnitude among people with lower SES, especially in male patients with PTSD.

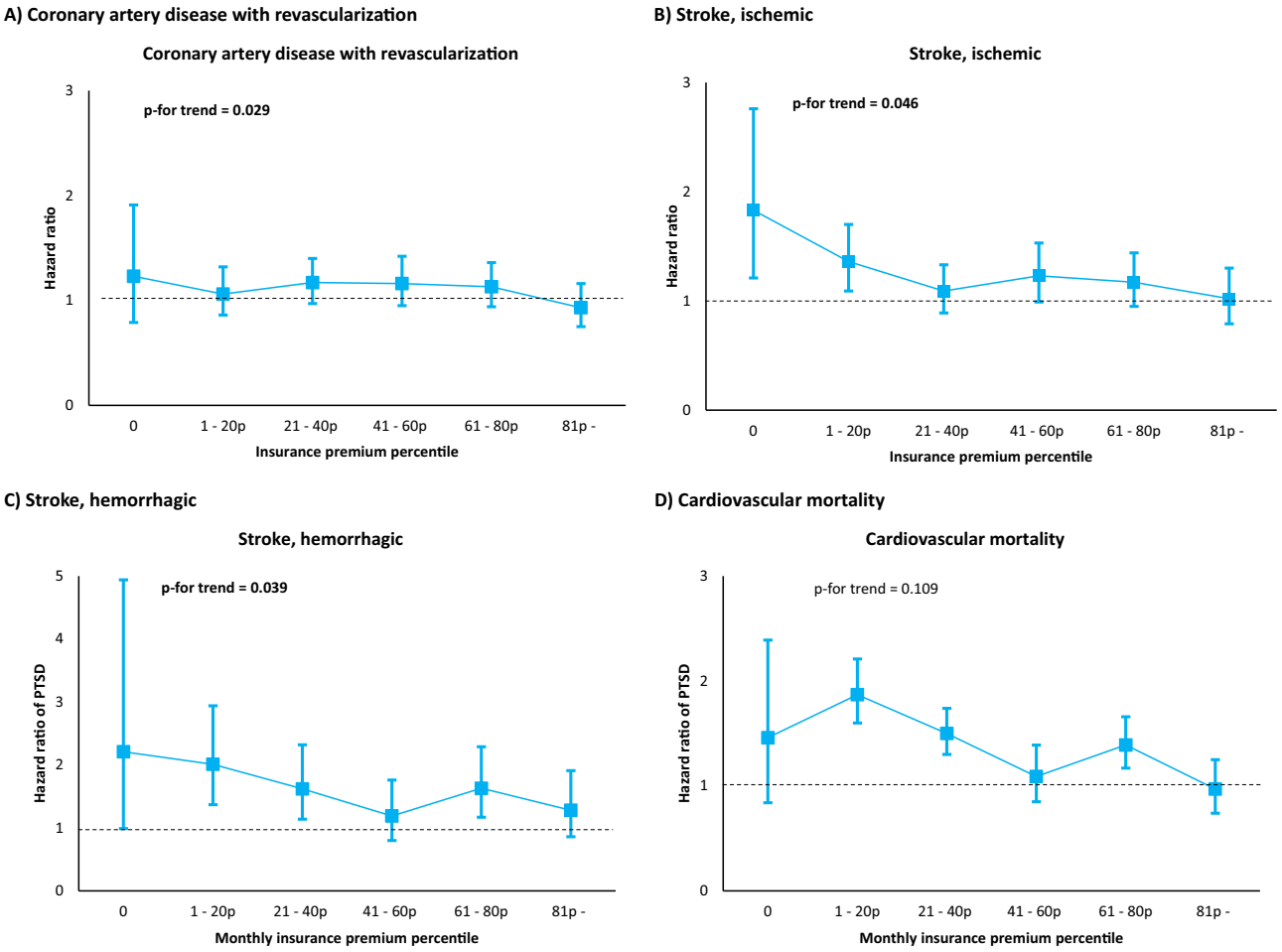

Fig. 1. Hazard ratios of PTSD on major cardiovascular disease in men by insurance premium subgroup. PTSD-CVD association was more prominent in patients with lower socioeconomic status.

In addition to the primary finding of an association between PTSD and CVD outcomes, the results also showed that the adverse cardiovascular health effects of PTSD are most pronounced among individuals in the lowest SES subgroups. It has also been theorized that people with higher SES may have certain coping strategies available to them, such as greater material resources, that could increase their mental and physical resilience to external stressors (Lazzarino et al., 2013; Smith, 1996). This finding was consistent with those described in a cross-sectional study on African Americans (Islam et al., 2021), which reported that early trauma is associated with worse cardiovascular health only in low-income individuals. Moreover, lower SES was also associated with decreased probability of receiving evidence-based treatment for ischemic heart diseases (Stirbu et al., 2012), stroke (Hyldgård et al., 2019) and mental health conditions (Cummings et al., 2017), and as a result, individuals with lower SES are more exposed to adverse cardiovascular effects of PTSD.

Effect modification sex was also detected in the current study. Sex differences in cardiovascular effects of PTSD were apparent in atherosclerotic CVD (ASCVD), including coronary artery disease and ischemic stroke, particularly in individuals with low SES. Despite the body of epidemiologic evidence suggesting sociodemographic heterogeneity in the adverse cardiovascular effects of PTSD (Gradus et al., 2015; Rosman et al., 2019), the biological mechanism that causes the sex difference is yet to be discovered. Hormonal differences and protective effect of oestrogen might be the mechanisms behind the sex differences (Shearman et al., 2003; Teoh et al., 2020). For deeper understanding, mechanistic research on how PTSD increases the risk of ASCVD should be conducted.

Our study is one of the largest general-population studies in the literature to date, with over 60,000 Korean men and women diagnosed with PTSD and over 190,000 matched controls (Beristianos et al., 2016; Chen et al., 2015). Also, this is one of few studies that tested variances in PTSD-CVD association by sex and SES, providing better understanding on cardiovascular comorbidities in patients with PTSD. However, interpretation of our findings is subject to several limitations. First, ascertainment of the exposures and/or outcomes could be subject to misclassification, given that all diagnoses were based on ICD-10 diagnostic codes. As a result, both PTSD and CVD diagnosis could have been affected by misclassification or misdiagnosis. However, the estimated associations between PTSD and CVD outcomes were largely consistent with each other, and cardiovascular mortality was less likely to be subject to the same misclassification bias. It is reported that diagnostic accuracy for cardiovascular disease in Korean NHIS is acceptable (Park et al., 2000), but diagnostic accuracy for PTSD is yet unknown. Considering that PTSD is commonly underdiagnosed, however (Koenen et al., 2017a; Lewis et al., 2019), this bias is likely to alter the estimand towards null, decreasing the possibility of detecting association by chance. Second, we could not assess the chronicity of PTSD, which is critical in understanding its long-term adverse health effects. Our estimates could have been confounded by ascertainment bias if people with PTSD were more likely to have contact with the healthcare system in such a way that would increase their opportunities to be diagnosed with CVD and related conditions. Lastly, while population-based, our data were derived from an administrative treatment registry, and the study

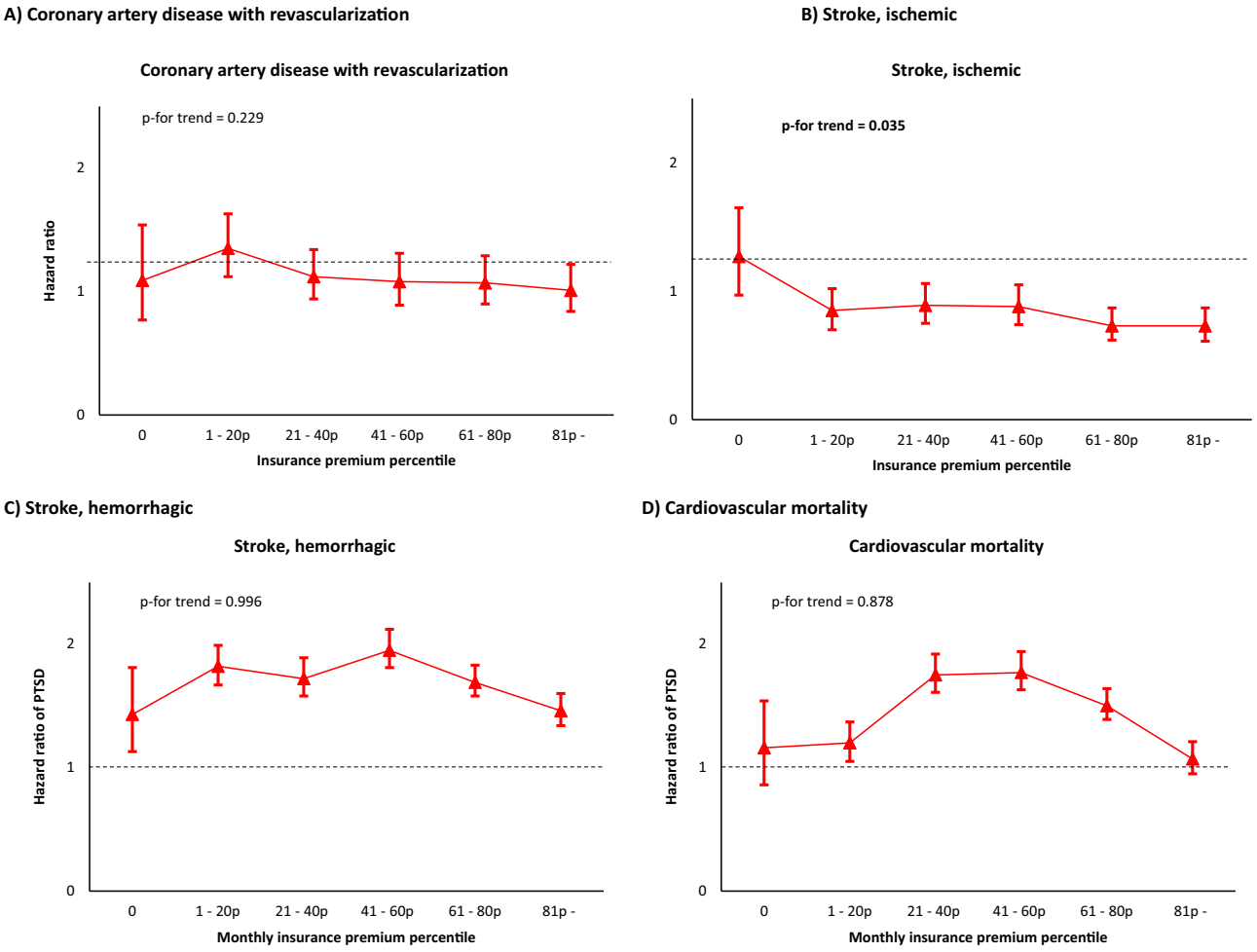

Fig. 2. Hazard ratios of PTSD on major cardiovascular disease in women by insurance premium subgroup. The differential association between PTSD and CVD was detected in ischemic stroke, but was not prominent in other outcome diseases.

participants consisted of people who had some contact with the Korean healthcare system. Therefore, the results of this study may not be generalized for people who do not seek help from medical institutions.

5. Conclusions

We found that PTSD is associated with increased CVD risk, especially among men with low SES. Further mechanistic research is needed to elucidate the pathways linking PTSD to CVD, and to identify the social and structural settings in which these risks are magnified. Such studies would provide important information for potential interventions to attenuate these risks and improve the health of individuals exposed to traumatic stressors.

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CRediT authorship contribution statement

Kwanghyun Kim: Conceptualization, data curation, formal analysis, methodology, project administration, resources, software, validation, visualization, writing – original draft preparation.

Alexander C. Tsai: Supervision, validation, writing – reviewing and editing.

Jennifer A. Sumner: Supervision, validation, writing – reviewing and editing.

Sun Jae Jung: Conceptualization, funding acquisition, resources, software, supervision, validation, writing – reviewing and editing.

Conflict of Interest

Authors have no conflict of interest to report.

Data availability

The data used in this study were from the Korean NHID, a nationwide database on medical utilization by residents of South Korea. The data can only be accessed to registered researchers and cannot be made available to other individuals. In order to access the data, researchers must be registered as a collaborator to the Korean NHIS and visit the designated data laboratories located in South Korea.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.

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