McMaster University | Health Forum

Rapid Evidence Profile appendices

Examining the potential causal relationship between post-traumatic stress disorder (PTSD) and Parkinson's disease

30 April 2025

[MHF product code: REP 94]

Appendices

Appendix 1: Methodological details

For this rapid evidence profile (REP), we searched Medline and PsycINFO for:
1) evidence syntheses
2) single studies.

To identify any evidence documents, we conducted our searches on 14 April 2025 using an advanced search strategy ("Post-traumatic stress disorder" OR "Posttraumatic stress disorder" OR PTSD OR "Post traumatic stress") AND (“Parkinson* disease" OR "Parkinson's" OR Parkinsonism OR "Parkinsonian disorder*" OR "Primary Parkinsonism" OR "Idiopathic Parkinson*" OR "Paralysis agitans" OR "Basal ganglia disease*" OR "Movement disorder*").

One team member screened the results to identify potentially relevant documents. A final inclusion assessment was performed both by the person who did the initial screening and the lead author of the rapid evidence profile, with disagreements resolved by consensus or with the input of a third reviewer on the team. The team uses a dedicated virtual channel to discuss and iteratively refine inclusion/exclusion criteria throughout the process, which provides a running list of considerations that all members can consult during the first stages of assessment. Evidence documents were included if they described any aspect of the organizing framework and explored any potential association between PTSD and Parkinson's disease onset. We excluded documents that did not directly address the research questions and the relevant organizing framework (e.g., documents that only focused on a causal relationship between PTSD and other conditions). We also excluded documents where the full text was not accessible.

We did not exclude documents based on the language of a document. However, we were not able to extract key findings from documents that were written in languages other than Chinese, English, French, or Spanish, or were not able to be translated to English via the Google applications. We provided any documents that did not have content available in these languages in an appendix containing documents excluded at the final stages of reviewing.

Assessing relevance and quality of evidence

We assess the relevance of each included evidence document as being of high or low relevance to the question. We did not identify any evidence syntheses for the rapid evidence profile. Therefore, we did not appraise the methodological quality using the first version of the AMSTAR tool. AMSTAR rates overall quality on a scale of 0 to 11, where 11/11 represents a review of the highest quality, medium-quality evidence syntheses are those with scores between four and seven, and low-quality evidence syntheses are those with scores less than four. The AMSTAR tool was developed to assess reviews focused on clinical interventions, so not all criteria apply to evidence syntheses pertaining to delivery, financial, or governance arrangements within health systems or implementation strategies.

Preparing the profile

Each included document is cited in the reference list at the end of the REP. For all included evidence documents, we prepared a small number of bullet points that provide a summary of the key findings, which are used to summarize key messages in the text. We then draft a summary that highlights the key findings from all highly relevant documents as well as key findings from the jurisdictional scan.

Upon completion, the REP is sent to one or more subject-matter experts for their review.

Appendix 2: Details about each identified evidence synthesis

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Living status	Quality (AMSTAR)	Last year literature searched	Availability of GRADE profile	Equity considerations

• Types of PTSD
  ○ General PTSD diagnosis (e.g., diagnostic criteria, code)
• Parkinson's disease assessment
  ○ General Parkinson's diagnosis (e.g., diagnostic criteria, code)
• Priority populations
  ○ Other
• Causality assessment
  ○ Temporal relationship (e.g., PTSD preceding Parkinson's disease onset)
  ○ Strength of association (e.g., association should meet statistical significance to demonstrate that it was not simply a chance occurrence, study reported data as hazard ratios, relative risks, odds ratios)
• Outcomes
  ○ Parkinson's disease incidence/onset
	Meta-analysis of hazard ratios from four retrospective cohort studies provide preliminary evidence of an association between mid- to late-life onset post-traumatic stress disorder (PTSD) and degenerative synucleinopathies including Parkinson's disease (PD) (pooled hazard ratio (HR) 1.88, 95% CI 1.08–3.24; p=0.035) (1)
	• The purpose of this review was to investigate the potential association of PTSD with PD and related synecleinopathies including PD, Dementia with Lewy Bodies (DLB),
	• Six articles comprising seven unique samples (total n=1,747,378) met eligibility criteria, and the risk of PD was reported in three retrospective cohort studies and one case-control study
	  ○ The association of PTSD with PD risk was investigated in three retrospective cohort studies and one case control study
	• The meta package tool was used to pool the results of four retrospective studies reporting time-to-event data, and PTSD was positively correlated with an increased risk of degenerative synucleinopathies (HR 1.88, 95% C.I. 1.08–3.24; p=0.035)
	  ○ The degree of statistical heterogeneity among studies was high (I^2=54%, 95% C.I. 0%–85%; Q=6.51, df=3, p=0.09)
	• Comorbidities such as exposures to traumatic brain injury (TBI) or insomnia may confound the association between PTSD and degenerative synucleinopathies and authors recommend investigating this in future studies
		High	No	8/11	October 2022	No	None Identified

Appendix 3: Details about each identified single study

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Study characteristics	Equity considerations

• Types of PTSD
  ○ General PTSD diagnosis (e.g., diagnostic criteria, code)
  ○ Subtypes of PTSD
  ▪ Comorbid PTSD (including with mood disorders)
• Parkinson's disease assessment
  ○ General Parkinson's diagnosis (e.g., diagnostic criteria, code)
• Risk factors of Parkinson's disease
  ○ Demographic factors (e.g., age, sex, socioeconomic status, income level, urbanization level)
  ○ Medical/psychiatric comorbidities (e.g., depression, diabetes, epilepsy, migraine, traumatic brain injury)
• Priority populations
  ○ Other
• Causality assessment
  ○ Temporal relationship (e.g., PTSD preceding Parkinson's disease onset)
  ○ Strength of association (e.g., association should meet statistical significance to demonstrate that it was not simply a chance occurrence, study reported data as hazard ratios, relative risks, odds ratios)
  ○ Biological plausibility (neuroinflammatory, HPA axis, and other proposed mechanisms)
  ○ Consideration of confounding variables and mediating factors
• Outcomes
  ○ Parkinson's disease incidence/onset
  ▪ Age at Parkinson's disease onset
	The nationwide longitudinal study from Taiwan found that patients with post-traumatic stress disorder (PTSD) had a significantly elevated risk of developing Parkinson's disease (PD) (HR 3.46, 95% confidence interval (CI) 1.72–6.96) compared to matched controls, with earlier onset and higher incidence rates (2)
	• This study used Taiwan's National Health Insurance Research Database to follow 7,280 participants (1,456 patients aged ≥45 years with PTSD and 5,824 age- and sex-matched controls without PTSD) from 2002–2009 until 2011, with PTSD (ICD-9-CM code: 309.81) diagnosed by psychiatrists and Parkinson's disease (ICD-9-CM code: 332.0) diagnosed by neurologists to ensure diagnostic validity
	• Patients with PTSD had a significantly higher risk of developing Parkinson's disease with a hazard ratio of 3.46 (95% CI 1.72–6.96) compared to those without PTSD, even after adjusting for demographic factors and medical and psychiatric comorbidities
	• Patients with PTSD developed PD earlier (3.18 ± 2.07 years after diagnosis) than controls without PTSD (4.51 ± 2.58 years), with a higher incidence rate (2.0% vs. 0.5%) during the follow-up period, and sensitivity analyses excluding early follow-up years (the first year and first three years of observation) confirmed this temporal relationship
	• The epidemiological study proposed multiple human-based biological pathways to explain their observed associations
	  ○ Psychological stress effects: Human studies have shown that individuals exposed to extreme psychological trauma (e.g., war prisoners or those who experienced personal losses) have a higher risk of developing PD later in life, supporting the hypothesis that cumulative psychological stress may contribute to neurodegeneration
	  ○ Hypothalamus-pituitary-adrenal (HPA) Axis Dysregulation: Patients with PTSD often exhibit low cortisol and high corticotropin-releasing hormone levels, reflecting dysregulation of the HPA that may impair immune control and alter brain function, thereby increasing susceptibility to neurodegenerative processes like those in PD
		High	*Publication date:* August 2017
			
			Jurisdiction studied: Taiwan
			
			Methods: Longitudinal study
				• Age
				• Sex
				• Level of urbanization
				• Income level

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Study characteristics	Equity considerations
	○ Inflammatory mechanisms: Studies show elevated levels of pro-inflammatory cytokines (TNF-α, IL-6, IL-1β) in both patients with PTSD and patients with PD, with cytokine levels correlating with PTSD symptom duration and PD disease severity ○ Epilepsy: Epilepsy was significantly associated with PD development (HR: 4.74) even after adjusting for other factors, though the authors caution against strong conclusions due to the low prevalence of epilepsy in their PTSD cohort (2.1%), indicating this potential pathway requires further investigation ○ Traumatic brain injury (TBI): Although patients with PTSD had significantly higher rates of TBI (7.3% vs 1.4%), and TBI showed trend-level association with PD in univariate analysis, this association disappeared in the multivariate model, suggesting PTSD may have an independent relationship with PD development not mediated through TBI			
• Types of PTSD ○ General PTSD diagnosis (e.g., diagnostic criteria, code) • Parkinson's disease assessment ○ General Parkinson's diagnosis (e.g., diagnostic criteria, code) • Risk factors of Parkinson's disease ○ Demographic factors (e.g., age, sex, socioeconomic status, income level, urbanization level) ○ Medical/psychiatric comorbidities (e.g., depression, diabetes, epilepsy, migraine, traumatic brain injury) • Priority populations ○ Military personnel (active and Veterans) • Causality assessment ○ Strength of association (e.g., association should meet statistical significance to demonstrate that it was not simply a chance occurrence, study reported data as hazard ratios, relative risks, odds ratios)	The population-based case-control study identified a significant association between PTSD and an increased risk of developing Parkinson's disease in Veterans (conditional odds ratio: 2.71, 95% CI 2.66–2.77), with an even higher risk observed in those with comorbid PTSD and TBI (3) • This study used nationwide Veterans Affairs (VA) health care databases to evaluate 884,355 Veterans (176,871 PD cases and 707,484 age/sex/enrollment period-matched PD-free controls) between 1999–2013, with participants aged ≥30 years (mean age 75.0 ± 9.4 years, with >58% ≥75 years old), with PTSD identified by ICD-9 code 309.81 (≥1 occurrence) and PD identified using a validated algorithm requiring ≥2 PD codes (ICD-9 code 332.0) from clinical encounters on separate days within a three-year period • Almost all PD cases (~99%) were male, many (>58%) ≥75 years old, with 75% white non-Hispanic • Veterans with PTSD had a significantly increased risk of developing Parkinson's disease with a conditional odds ratio of 2.71 (95% CI 2.66–2.77) in single-risk factor, race-adjusted analyses, reduced to 1.63 (95% CI 1.25-2.11) in dual-risk factor analyses that included TBI	High	*Publication date:* March 2020 *Jurisdiction studied:* United States *Methods:* Case-control study	None identified

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Study characteristics	Equity considerations
○ Consistency across evidence (e.g., similar or the same results generated by studies using different methods in different settings) ○ Biological plausibility (neuroinflammatory, HPA axis, and other proposed mechanisms) • Outcomes ○ Parkinson's disease incidence/onset	• The study found PTSD was more common in PD cases than matched controls (10.3% vs. 4.2%), suggesting a significant association between these conditions • This study aligned with other research and proposed potential biological mechanisms to explain their observed associations ○ Consistency across evidence: This study's findings align with those from the longitudinal nationwide Taiwanese cohort, which reported a 3.5-fold increased PD risk in PTSD patients ○ Biological plausibility (HPA axis dysregulation): Increased activation of the HPA axis and associated increased pro-inflammatory cytokine secretion are hypothesized as potential contributors, supported by clinical studies showing hippocampal atrophy, reduced cortical thickness in adults, and decreased corpus callosum volume in children/adolescents with chronic PTSD ○ Biological plausibility (comorbid structural and functional changes): The study suggests that when TBI and PTSD occur together, they may present with unique structural and functional changes that modify the effect of TBI on PD risk			
• Types of PTSD ○ General PTSD diagnosis (e.g., diagnostic criteria, code) • Parkinson's disease assessment ○ General Parkinson's diagnosis (e.g., diagnostic criteria, code) • Risk factors of Parkinson's disease ○ Demographic factors (e.g., age, sex, socioeconomic status, income level, urbanization level) ○ Lifestyle factors (e.g., smoking status, physical activity, diet) • Priority populations ○ Military personnel (active and Veterans) • Outcomes ○ Parkinson's disease incidence/onset	The retrospective cohort study found statistically significant association between PTSD diagnosis and Parkinson's disease (OR=1.35, P=0.0002), with higher odds when PTSD was diagnosed before PD (OR=1.53, P<0.0001), suggesting PTSD may be a risk factor for PD (4) • This study utilized the data from the Agency for Toxic Substances and Disorders Registry (ATSDR) of 58,122 Veterans who had Veterans Health Administration (VHA) or Medicare health care utilization between 1 October 1999 and 17 February 2021, with participants being primarily male (96.05%) and having a mean age of 62.63 years (±4.4), who had served at either Camp Lejeune, North Carolina, or Camp Pendleton, California, between 1975 and 1985 • PTSD was defined by ≥2 encounters, at least three months apart, with a documented diagnosis using ICD9 (309.81) or ICD10 (F43.10, F43.11, F43.12) codes, while Parkinson's disease was diagnosed based on ICD9 (332.0) or ICD10 (G20) codes • Using a nested case-control design, the study matched 10 controls to each Veteran with PD by age, sex, race, and rank,	High	*Publication date:* September 2024 *Jurisdiction studied:* United States *Methods:* Retrospective cohort study with nested case-control design	None identified

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Study characteristics	Equity considerations

	adjusting for Camp and smoking status in conditional logistic regression models
	• This study used multiple regression models to examine the risk of PD diagnosis associated with a diagnosis of PTSD
	  ○ PTSD was more prevalent among Veterans with PD (15.1%, n=65) compared to matched controls (12.6%, n=544), supporting the potential relationship between these conditions
	  ○ Veterans with PTSD had a significantly higher risk of developing Parkinson's disease with an odds ratio of 1.35 (95% CI 1.15–1.58, P=0.0002) compared to those without PTSD in models adjusted for camp and smoking status, with even higher odds (OR=1.53, 95% CI 1.30–1.81, p<0.0001) when analyses were limited to cases where PTSD was diagnosed before PD
	  ○ When restricting analysis to only cases where PTSD was documented at least one year prior to PD diagnosis, the association became non-significant (OR=0.95, 95% CI 0.84–1.11, p=0.55), which may reflect limitations in determining precise PTSD onset rather than disproving causality, as PTSD in Veterans is often documented years after its actual occurrence
	• While this study does not present direct human-based biological mechanisms linking PTSD and PD (instead primarily referencing animal models for biological plausibility), it relies on epidemiological evidence in humans to establish association, with emphasis on the temporal relationship where PTSD diagnosis preceded PD diagnosis, strengthening the case for potential causality			

• Types of PTSD
  ○ General PTSD diagnosis (e.g., diagnostic criteria, code)
• Parkinson's disease assessment
  ○ General Parkinson's diagnosis (e.g., diagnostic criteria, code)
• Risk factors of Parkinson's disease
  ○ Demographic factors (e.g., age, sex, socioeconomic status, urbanization level)
	The population-based retrospective cohort study from Israel found that people with PTSD had a greater chance of developing Parkinson's (i.e., adjusted hazard ratio of 1.48), especially men diagnosed at 72 or older (i.e., adjusted hazard ratio of 1.95) (5)
	• The study examined whether PTSD might increase the likelihood of Parkinson's over time (i.e., exploring a possible long-term link between the two conditions) using data from Maccabi Health Care Services (second largest health plan in Israel) of 8,336 patients with PTSD matched with 8,336 age- and sex-matched individuals without PTSD from 2000–2019, with PTSD (ICD-9 code 309.81) diagnosed by psychiatrists, psychologists, or neurologists, and Parkinson's disease (ICD-
		High	*Publication date:* August 2022
			
			Jurisdiction studied: Israel
			
			Methods: Retrospective cohort design
				• Gender/sex
				• Socio-economic status
				• Age
				• Exposure to traumatic events

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Study characteristics	Equity considerations
○ Medical/psychiatric comorbidities (e.g., depression, diabetes, epilepsy, migraine, traumatic brain injury) ○ Lifestyle factors (e.g., smoking status, physical activity, diet) • Priority populations ○ Other • Causality assessment ○ Temporal relationship (e.g., PTSD preceding Parkinson's disease onset) ○ Strength of association (e.g., association should meet statistical significance to demonstrate that it was not simply a chance occurrence, study reported data as hazard ratios, relative risks, odds ratios) ○ Biological plausibility (neuroinflammatory, HPA axis, and other proposed mechanisms) ○ Consideration of confounding variables and mediating factors • Outcomes ○ Parkinson's disease incidence/onset ▪ Age at Parkinson's disease onset	9 codes 332 and 332.0) diagnosed by neurologists to ensure diagnostic validity • Patients with PTSD had a significantly higher risk of developing Parkinson's disease with a hazard ratio of 1.48 (95% CI 1.10–1.99) compared to those without PTSD, after adjusting for age, sex, socioeconomic status, smoking status, Holocaust survivor status, survivor of terror attack status, hypertension, depression, migraine, and TBI • The study found a strong age and sex interaction, with males who received a PTSD diagnosis at age 72 years or older having a significantly higher risk of PD (HR 1.95, 95% CI 1.16–3.28), establishing a temporal relationship between PTSD and later PD development • The epidemiological study proposed several human-based biological pathways to explain their observed associations: ○ Sleep disruption mechanisms: Sleep disturbance in humans with PTSD (manifested as nightmares and difficulty falling asleep) may disrupt the balance of oxidants and antioxidants, promoting oxidative stress ○ Psychological stress effects: Studies in humans have shown relationships between psychological stress and PD risk, noting that anxious personality traits increase PD risk in men two-fold ○ Genetic pathway: Human studies show that PARK2, a PD gene involved in dopamine regulation, is associated with PTSD in men, suggesting potential shared genetic vulnerability ○ Prodromal symptoms: Depression and anxiety are well-recognized prodromal symptoms of PD in humans, suggesting that PTSD diagnosed in elderly men might represent early manifestations of the neurodegenerative process ○ Traumatic brain injury: While the study found higher rates of TBI in PTSD patients (10.1% vs. 1.0%), sensitivity analyses excluding those with brain injury history still showed an elevated PD risk (HR 1.54, 95% CI 1.15–2.05), indicating PTSD may have an independent association with PD development in humans			
• Types of PTSD ○ General PTSD diagnosis (e.g., diagnostic criteria, code)	The lifelong nationwide case-control study of military veterans found that PTSD and TBI are both associated with later	High	*Publication date:* 2023	None identified

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Study characteristics	Equity considerations

• Parkinson's disease assessment
  ○ General Parkinson's diagnosis (e.g., diagnostic criteria, code)
• Risk factors of Parkinson's disease
  ○ Medical/psychiatric comorbidities (e.g., depression, diabetes, epilepsy, migraine, traumatic brain injury)
• Priority populations
  ○ Military personnel (active and Veterans)
• Causality assessment
  ○ Temporal relationship (e.g., PTSD preceding Parkinson's disease onset)
  ○ Strength of association (e.g., association should meet statistical significance to demonstrate that it was not simply a chance occurrence, study reported data as hazard ratios, relative risks, odds ratios)
  ○ Specificity (e.g., the exposure is the only cause of the outcome that can be shown)
  ○ Consideration of confounding variables and mediating factors
• Outcomes
  ○ Parkinson's disease incidence/onset
	Parkinson's disease, and have an additive association when they cooccur (6)
	• This study used the U.S. Veterans Health Administration Corporate Data Warehouse to analyze 71,933 PD cases and 287,732 matched controls (4:1 matching by age, sex, ethnicity, race, birth year, and smoking status), with PD identified by ICD-9/10 codes (332.0/G20) and confirmed by PD medication prescriptions, with validation through chart review showing a positive predictive value of 78.6%
	• Veterans with PTSD had odds ratios ranging from OR: 1.5 (95% CI 1.4–1.7) to OR: 1.9 (95% CI 1.9–2.0), after adjusting for demographic factors including race, sex, smoking status, ethnicity, and birth year
	• PTSD prevalence was, on average, 11% (± .9%) in controls and 17% (±4.7) in PD cases, demonstrating a notably higher rate in those who later developed PD
	• This study showed a strong temporal relationship by showing the association between PTSD and PD remained significant at all time epochs extending back 60 years before PD diagnosis, with consistent effect sizes across these time periods, suggesting PTSD preceded PD development by decades
	• TBI and PTSD showed synergistic effects (greater than additive) on PD risk (synergy indices: 1.14 (95% CI 1.09–1.29) to 1.28 (95% CI 1.09–1.51)), with the combination of both conditions substantially increasing the odds of developing PD (OR 2.2 (95% CI 1.6–2.8) to 2.7 (95% CI 2.5–2.8))
	• PTSD showed synergistic effects on PD risk with synergy indices for chronic pain (synergy indices: 1.55 ±0.34), migraine (synergy indices: 1.61±0.33), and sleep apnea (synergy indices: 1.40±0.19)
	• Veterans with PTSD, TBI, and chronic pain had dramatically higher odds of developing PD (OR 2.9 (95% CI 2.6–3.4) to 3.3 (95% CI 2.2–5.0))
	• The study primarily establishes epidemiological evidence for a temporal relationship (PTSD preceding PD by up to 60 years) and synergistic interactions with other conditions, but provides limited direct human evidence for specific biological pathways beyond noting the association patterns
			Jurisdiction studied: United States
			
			Methods: Retrospective case-control	

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Study characteristics	Equity considerations

• Types of PTSD
  ○ General PTSD diagnosis (e.g., diagnostic criteria, code)
• Parkinson's disease assessment
  ○ General Parkinson's diagnosis (e.g., diagnostic criteria, code)
• Risk factors of Parkinson's disease
  ○ Demographic factors (e.g., age, sex, socioeconomic status, urbanization level)
  ○ Genetic factors (e.g., family history, specific gene mutations)
  ○ Medical/psychiatric comorbidities (e.g., depression, diabetes, epilepsy, migraine, traumatic brain injury)
  ○ Lifestyle factors (e.g., smoking status, physical activity, diet)
• Causality assessment
  ○ Temporal relationship (e.g., PTSD preceding Parkinson's disease onset)
  ○ Strength of association (e.g., association should meet statistical significance to demonstrate that it was not simply a chance occurrence, study reported data as hazard ratios, relative risks, odds ratios)
  ○ Consideration of confounding variables and mediating factors
• Outcomes
  ○ Parkinson's disease incidence/onset
	A population-based cohort study found that individuals with PTSD had a non-significantly higher risk of developing Parkinson's disease (HR=1.35, 95% CI 0.61–2.99), suggesting a potential association that may also be underestimated due to diagnostic misclassification and conservative bias controls (7)
	• Using conditional Cox proportional hazards regression model to estimate HR and partial or fully adjusted for potentially confounders including education level, family income, martial status, history of other psychiatric disease, and family history of neurodegenerative diseases, the study examined the association between stress-related disorders and risk of neurodegenerative diseases
	• Hazard ratio for PD among individuals with stress-related disorders versus matched unexposed counterparts or unaffected full siblings was found to be 1.24 (95% CI 0.87–1.78)
	• For PTSD, specifically, HR was 1.35 (95% CI 0.61–2.99) for PD
	• The study accounted for reverse causation and surveillance bias by applying a five-year lag, but misclassifications of early stress-related disorders (before 1987) may have resulted in underestimating the link between stress-related disorders and neurodegenerative diseases such as PD
		Medium	*Publication date:* 2020
			
			Jurisdiction studied: Sweden
			
			Methods: Population-matched sibling cohort study
				None identified

• Types of PTSD
  ○ General PTSD diagnosis (e.g., diagnostic criteria, code)
• Parkinson's disease assessment
  ○ General PTSD diagnosis (e.g., diagnostic criteria, code)
• Risk factors of Parkinson's disease
  ○ Medical/psychiatric comorbidities (e.g., depression, diabetes, epilepsy, migraine, traumatic brain injury)
• Priority populations
	U.S. Veterans with chronic pain, especially combined with PTSD and TBI, showed significantly higher probability of prodromal Parkinson's disease compared to the control group (8)
	• The study used self-reported data from 216 US veterans to assess the risk of prodromal Parkinson's disease (pPD) caused by TBI, PTSD, and chronic pain (CP)
	• 216 veterans with CP and 30 control veterans (i.e., without chronic pain, TBI, or PTSD) were assessed
	• Of the 216 veterans with CP, 44 met the criteria for PTSD (CP+1), 39 met the criteria for TBI (CP+1), and 41 met the criteria for all three conditions (PCT group)
		Medium	*Publication date:* April 2024
			
			Jurisdiction studied: United States
			
			Methods: Cross-sectional observation study
				• Occupation

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Study characteristics	Equity considerations
○ Military personnel (active and Veterans) • Causality assessment ○ Temporal relationship (e.g., PTSD preceding Parkinson's disease onset) • Outcomes ○ Parkinson's disease incidence/onset	• Participants were aged 54.3±14 years • PD diagnosis was assessed using the published prodromal PD calculator guidelines, using risk factors to calculate total likelihood ratios • The highest reported incidence of pPD was found in the PCT group (17%), followed by the CP +1 group (10%), the CP group (6%), compared to the control group (0%) ○ This trend correlation was found to be significant (p=0.03) • Though long term studies are necessary, the study results indicate possible trauma-related risk factors for Parkinson's disease pathogenesis			
• Types of PTSD ○ General PTSD diagnosis (e.g., diagnostic criteria, code) • Parkinson's disease assessment ○ General PTSD diagnosis (e.g., diagnostic criteria, code) • Causality assessment ○ Temporal relationship (e.g., PTSD preceding Parkinson's disease onset) • Outcomes ○ Parkinson's disease incidence/onset	Adults >65 years old with PTSD showed a statistically significant difference in Parkinson's disease rates (2.1% vs. 0.4%, p=0.03, Cramer's V=0.12) compared to adults without PTSD in an American physical and mental health dataset (9) • The study used the National Alzheimer's Coordinating Center Uniform Data Set of adults >65 years of age to assess base rates of co-occurrence of mental health conditions found in adults with PTSD • 472 participants in total were included, with 236 participants having self-reported history of physician diagnosis or treatment for PTSD and 236 age-matched controls without PTSD ○ Between-group differences for sociodemographic and physical health variables including self-reported sex, ethnicity, race, education, marital status, and level of functional independence were assessed • Statistically significant between-group differences were identified in Parkinson's disease between adults with PTSD and adults without PTSD (2.1% vs. 0.4%, p=0.03, effect size Cramer's V=0.12), demonstrating a small-to-medium effect size association even after controlling for age	High	*Publication date:* September 2024 *Jurisdiction studied:* United States *Methods:* Case control study	None identified

Appendix 4: Documents excluded at the final stages of reviewing

Document type	Hyperlinked title
Other types of documents (e.g., editorial, narrative reviews, poster presentation or documents with the wrong patient population)	Genome-wide association study of traumatic brain injury in U.S. military veterans enrolled in the VA million veteran program
	Influence of co-morbid PTSD in Parkinson's disease on motor and non-motor symptoms
	Polysomnographic features of rem sleep behaviour disorder in Vietnam veterans with and without PTSD
	Impact of post traumatic stress disorder (PTSD) on the clinical expression of REM sleep behavior disorder (RBD) in veterans with Parkinson's disease (PD)
	Neuropsychiatric complications of COVID-19
	Impact of COVID-19 pandemic on development of chronic stress syndromes in patients with Parkinson's disease: Preliminary results
	Can we predict the development of rem sleep behavior disorder (RBD) in military veterans with Parkinson's disease
	Post-traumatic stress disorder and risk of Parkinson's disease – 20 years follow-up real world data analysis
	Influence of co-morbid PTSD in Parkinson's disease on motor and non-motor symptoms
	Cognitive deficits in veterans with Parkinson's disease: A national database analysis
	Posttraumatic growth of patients with Parkinson's disease
	The influence of PTSD on Parkinson's disease phenotype
	Co-occurring mental and physical health conditions among older adults with and without post-traumatic stress disorder: A case control study
	Lifelong association of disorders related to military trauma with subsequent Parkinson's disease
	The neurocognitive profile of post-traumatic stress disorder (PTSD), major depressive disorder (MDD), and PTSD with comorbid MDD
	Influence of major earthquakes and their effects on patients with Parkinson's disease: A multi-institutional study
	Mild TBI is associated with increased risk of Parkinson disease: A chronic effects of neurotrauma consortium study
	New onset post-traumatic stress disorder in long-term care home residents with a pre-existing diagnosis of a major neurocognitive disorder
	Cognitive deficits in veterans with Parkinson's disease: A national database analysis

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Wu N, Wang Q, Bain T, DeMaio P, Whitelaw H, Ciurea P, Ali A, Bhuiya AR, Sivanesanathan T, Wilson MG. Rapid evidence profile report #94: Examining the potential causal relationship between post-traumatic stress disorder (PTSD) and Parkinson's disease. Hamilton: McMaster Health Forum, 30 April 2025.

This rapid evidence profile was funded by the Chronic Pain Centre of Excellence for Canadian Veterans and the Atlas Institute for Veterans and Families, which in turn are funded by Veterans Affairs Canada. The McMaster Health Forum received both financial and in-kind support from McMaster University. The views expressed in the rapid evidence profile are the views of the authors and should not be taking to represent the views of the Chronic Pain Centre of Excellence for Canadian Veterans and the Atlas Institute for Veterans and Families or McMaster University.