

**LIMBIC-CENC Clinical Care Monograph Version 2**

**A. TBI and Neurodegeneration**

from LIMBIC-CENC Knowledge Translation Center (LIMBICTM)

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**Key Findings**

1. **TBI and Neurodegenerative Conditions.** LIMBIC-CENC research found that Veterans with mTBI, with or without loss of consciousness, had about a 2.5-fold increase in dementia risk.1 Veterans with moderate-severe TBI approached a 4-fold increase in dementia risk. 1 Veterans with TBI of any severity had a 71% increased risk of a Parkinson’s disease diagnosis but the overall rate of Parkinson’s disease following TBI remained <1%.2 All cause-dementia for Veterans with TBI occurred 1-2 years earlier than for Veterans without TBI. The estimated Veteran U.S. population risk of dementia due to TBI is twice that of the general U.S. population, and three times that of U.S. women.3 Approximately 860,700 U.S. Veteran dementia cases are attributable to TBI exposure.3
2. **Three or More Lifetime mTBIs are Associated with Increased Risk of Neurodegeneration.** Mounting, converging biologic (biomarker) and epidemiological (symptoms, pain related disability) evidence from multiple LIMBIC-CENC PLS studies supports that repetitive (>3) mTBI is associated with elevated neurodegeneration risks.4-9
3. **Early Onset Dementia (EOD).** Veterans with EOD are more likely to have TBI, cardiovascular conditions (stroke, heart disease), mental health conditions (PTSD, depression, anxiety, attention disorders), other significant neurological disorders (epilepsy, Parkinson’s disease, encephalopathy, anoxic brain injury), self-reported memory loss, and renal disease.10
4. **TBI, Dementia, and Health.** There is a high prevalence of alcohol abuse, substance abuse, depression, sleep disorders, PTSD, cardiovascular disease (CVD), and epilepsy among Veterans <65 years of age with comorbid TBI and dementia.10 In a longitudinal study by LIMBIC-CENC researchers, the prevalence of baseline health risk factors, especially depression, cardiovascular disease, PTSD and epilepsy, was higher in Veterans with TBI compared to without TBI; at 6-year follow-up, Veterans with TBI were twice as likely (14%) to develop dementia compared to those with no TBI (6%).11 TBI and cardiovascular disease independently increased the risk for dementia in older Veterans and have an additive effect.11 CVD does not appear to mediate the association between TBI and dementia.11 Preliminary evidence suggests that sleep physiology is a common pathophysiological process that underlies persistent post-concussive, depressive, post-traumatic stress, and sleep-related symptoms in mTBI.9

**Clinical Impact**

* **MTBI Clinical Practice Guideline (CPG).** LIMBIC-CENC findings on the association between TBI and higher risk of Veteran neurodegenerative disorders extend the current literature, especially for mTBI and EOD. These findings improve the specificity and the strength of evidence for number and severity of TBIs as risk factors for neurodegenerative disorders and can be applied in the next VA-DOD mTBI CPG. Findings also highlight the need for CPG recommendations that emphasize making specialty evaluation referrals when early signs of dementia are present, even if Veterans are younger than would normally be expected.
* **Support for VHA and DOD TBI Policies**. The high prevalence and magnitude of preventable behavioral health risk factors (e.g., sleep, mental health, cardiovascular) found in Veterans with TBI and dementia provide clear evidentiary support for VHA and DOD healthcare initiatives such as 1) TBI screening and comprehensive evaluation for lifetime TBI history, 2) General brain health and overall wellness initiatives, and 3) Targeted, proactive treatment and prevention approaches for modifiable, lifestyle health risk factors to prevent or delay the onset of dementia.
* **Brain Health and Wellness Tool**. LIMBIC-CENC findings on preventable behavioral health risk factors after TBI, synthesized with the current research literature, led to the development, testing, and release of the LIMBIC-CENC a brain health and wellness survey that generates personalized recommendations to support Service Members and Veterans efforts to identify and self-manage their health-related risk factors after TBI. The LIMBIC-CENC’s Brain Health and Wellness Video Series complements the survey tool and provides a series of 4-minute primers on how to identify, prevent or self-manage TBI and co-morbid risk factors that can decrease dementia risk.
* **Developing mTBI Phenotypes**. LIMBIC-CENC research using PLS data is underway to identify mTBI phenotypes for neurodegeneration susceptibility that can inform implementation of personalized, high intensity treatments.
* **Contributions to National TBI Research Registries**. LIMBIC-CENC PLS data collection on 3,000+ participants with multiple, longitudinal follow-ups downloaded into FITBIR will spur future collaborative research with lifestyle medicine researchers.
* **More Nuanced Prognostic Models**. Increasing the LIMBIC-CENC PLS cohort and its robust long-term follow-up will allow for analyses of sub-group effects and interactions between risk factors on the long-term risk of dementia. More nuanced prognostic models can then be created to identify individualized, modifiable behavioral and biomarker-based risk factors (phenotypes) and better inform personalized treatments (precision medicine) to enhance long-term outcomes.

**Primary Knowledge Translation Products**

* LIMBIC-CENC assessment tools, including PLS Study Variables and [Concussion Assessment Tools for Identifying and Diagnosing Lifetime mTBI History](https://www.limbic-cenc.org/index.php/knowledge-translation-center/limbic-cenc-concussion-assessment-tools/) are available for clinical and research use.
* LIMBIC-CENC provides a repository of information on [TBI, Aging, and Dementia Risk for SMs, Vs and Families](https://www.limbic-cenc.org/for-service-members-and-veterans-with-tbi/aging-with-tbi-dementia-risk-veterans/) and [TBI, Aging, and Dementia Risk for Clinicians](https://www.limbic-cenc.org/for-tbi-clinicians/aging-with-tbi-dementia-risk-clinicians/).
* LIMBIC-CENC’s [Brain Health and Wellness Survey and Personalized Recommendations Report](https://knowledgetranslation.limbic-cenc.org/BrainHealthWellnessTool/BrainHealthWellnessTool)  provides a yes-no survey for SMs and Vs to identify their behavioral health risk factors for dementia and receive personalized information and recommendations.
* LIMBIC-CENC’s [Brain Health and Wellness Video Series](https://www.limbic-cenc.org/for-service-members-and-veterans-with-tbi/the-brain-health-and-wellness-video-series/) includes 10 easy to understand and apply videos on how to identify, prevent or self-manage behavioral health risk factors for dementia including Depression, PTSD, Hearing Loss, Hypertension, Diabetes, Tobacco Use, Alcohol Use, Obesity-Activity-Nutrition, and Poor Sleep. The series also provides links to self-management tools and/or access to healthcare services.
* The 2024 Ralph G. DePalma Memorial TBI Clinical Strategies Seminar provides [Updates on the Relationship between TBI and Dementia](https://www.hsrd.research.va.gov/for_researchers/cyber_seminars/archives/video_archive.cfm?SessionID=6490).

**LIMBIC-CENC TBI and Neurodegeneration Primary References**

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