The Role of Trauma and Posttraumatic Stress Disorder in Cognitive Functioning and Dementia: Exploring Trauma-Related, Behavioral, and Psychosocial Factors

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General Abstract

Dementia is a major global health challenge of the 21st century, with increasing longevity and population growth contributing to its rising prevalence. As no disease-modifying cure currently exists, research has increasingly focused on identifying modifiable risk factors to delay or prevent its onset. More recently, posttraumatic stress disorder (PTSD) has emerged as a potential factor increasing dementia risk. However, empirical research on this relationship is still rather in its early stages, and more studies are needed to confirm its role. Specifically, the underlying mechanisms linking PTSD to dementia risk, as well as potential influencing factors, remain unclear. Additionally, alternative explanations for this association have yet to be fully explored. Given that trauma exposure is a widespread global issue, likely to grow in significance, further research is crucial to establish its impact on dementia risk.

The overarching aim of this thesis is to consolidate previous findings on PTSD as a risk factor for all-cause dementia while addressing gaps of previous research to inform targeted intervention strategies. To achieve this, the thesis examines not only PTSD but also childhood adversity as a precursor, dissociative disorders as a severe trauma-related psychopathology, and depression as a common comorbid condition among trauma-related disorders. Cognitive and neurological outcomes are examined through subjective cognitive functioning, objectively measured cognitive performance, and hippocampal volume – each relevant to dementia risk – and dementia.

Study I investigated the association between PTSD severity – assessed through 1) sum score, 2) symptom clusters, and 3) individual symptoms – and subjective cognitive functioning in approximately 1,500 older U.S. veterans (Mdn = 65 years, IQR = 54-73), using network analyses cross-sectionally and longitudinally over three years. PTSD severity correlated with reduced cognitive functioning, particularly through the DSM-5 PTSD symptom clusters "marked alterations in arousal and reactivity associated with the traumatic event(s)" and

"negative alterations in cognitions and mood associated with the traumatic event(s)". The individual symptoms "having difficulty concentrating" and "trouble experiencing positive feelings (for example, being unable to feel happiness or have loving feelings for people close to you)" (American Psychiatric Association, 2013, pp. 271-272; Weathers et al. 2013, items 14 and 19) were robustly linked to reduced subjective cognitive functioning. These findings remained significant after adjusting for sociodemographic factors and depression and were replicated over time, highlighting the need to examine symptom-specific rather than universal PTSD-related associations with cognitive functioning.

Study II extended these findings using data from the United Kingdom (UK) Biobank (N ≈ 500,000) to examine interrelationships between adverse childhood experiences (ACEs), PTSD, dissociative disorders, and depression in predicting dementia risk in middle-aged adults from the general population (mean age 56.58 years, SD = 8.07). Findings revealed that each additional PTSD symptom increased dementia risk by 9%, each additional ACE type by 10%, PTSD and depression diagnoses doubled the risk, and dissociative disorders nearly quadrupled it. Mediation analyses indicated that PTSD symptoms mediated the association between ACEs and dementia, whereas depression mediated smaller parts of the associations between ACEs, PTSD diagnosis, and dissociative disorders with dementia. These results suggest that depression, a well-established modifiable risk factor for dementia, does not fully account for the link between trauma-related psychopathologies and dementia, highlighting distinct and shared pathways among these conditions.

Study III further examined the associations between trauma-related predictors, objective cognitive functioning, dementia risk, and hippocampal volume, again using the UK Biobank database. It also explored interactions with demographic, behavioral, and psychosocial factors, identifying distinct moderators for distinct predictor-outcome combinations. Childhood adversity, trauma-related psychopathology, and depression were associated with poorer cognitive functioning and a higher dementia risk. The moderating factors varied by predictors

and outcomes. For example, hypertension was the strongest moderator of the association between ACEs and dementia, whereas smoking was the strongest moderator between PTSD diagnosis and dementia. These findings emphasize the need for targeted prevention strategies, suggesting that cognitive impairment and dementia risk in trauma-exposed individuals may be modifiable.

In conclusion, this thesis advances the understanding of PTSD as a dementia risk factor by considering the heterogeneity of this disorder, childhood adversity, dissociative disorders, and depression while assessing multiple cognitive outcomes. The findings suggest that, while depression is a known risk factor, it does not solely account for trauma-related dementia risk. Furthermore, these associations may be either exacerbated or mitigated by various factors. While replication in future studies is necessary, the results highlight the potential of considering ACEs, PTSD, and dissociative disorders as additional modifiable risk factors for cognitive decline and dementia. The findings are discussed in the context of methodological limitations and clinical implications, offering directions for future research.

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1. General Introduction

1.1. Dementia – a Complex Construct

1.1.1. Definition, Diagnostic Criteria, and Relevance as a Global Health Issue

Cognitive decline in older age has been recognized since ancient times, with early references found in texts dating back to the 7th century B.C. (Berchtold & Cotman, 1998; Halpert, 1983). Pythagoras identified five distinct life stages, with the final two, referred to as the *senium*, or "old age", characterized by physical decay and cognitive decline (Halpert, 1983). Influential figures in ancient philosophy, science, and medicine, including Hippocrates, Plato, Aristotle, viewed aging as a disease-like process, associating it with inevitable mental deterioration (Berchtold & Cotman, 1998). This view persisted through the medieval period, well until the 19th century. Even in literary works, senile dementia was acknowledged – Shakespeare, for instance, portrayed dementia in several of his plays, most famously in *Hamlet* and *King Lear* (Berchtold & Cotman, 1998; McCrum, 2016).

Interest in dementia intensified between the 15th and 17th centuries, particularly during the height of witch hunting, where many accused individuals may have suffered from neurodegenerative diseases (Berchtold & Cotman, 1998; Halpert, 1983). Until the 19th century, descriptions of dementia remained broad, likely encompassing various conditions. A pivotal shift occurred when Pinel and his student Equirol introduced systematic clinical observation and the development of terminology in psychiatry, laying the groundwork for modern psychiatric classification (Berchtold & Cotman, 1998; Hunter & Macalphine, 1982). The findings paved the way for challenging the notion that senile dementia was an inevitable consequence of aging, but instead, a pathological process.

Alois Alzheimer made a landmark contribution in the early 20th century when he documented an unusual case of early-onset dementia in a woman named Auguste D., who exhibited rapid cognitive decline and behavioral disturbances before her death at age 55. Through clinical observation and postmortem examination, Alzheimer identified a diffuse

atrophy of the entire brain as well as what are now known as amyloid plaques and neurofibrillary tangles – hallmarks of what later became Alzheimer's disease (AD) (Hippius & Neundörfer, 2003; Möller & Graeber, 1998). However, his findings initially received little attention from the scientific community (Hippius & Neundörfer, 2003).

Over the following decades, research in the field increased, and it was confirmed that AD and senile dementia are essentially the same disease, differing mainly in the age of onset (Berchtold & Cotman, 1998). It also became evident that dementia consists of various subtypes, each with distinct pathological features, and that the severity of brain changes correlates with symptom progression. Today, "dementia" is recognized as an umbrella term rather than a single disease (Gale et al., 2018). It is considered a heterogenous syndrome with multiple causes, including neurodegenerative and non-degenerative conditions (Gale et al., 2018; World Health Organization, 1993).

At its core, dementia is characterized by a progressive decline of previous cognitive abilities – such as memory, reasoning, problem-solving, and language – significantly impairing daily functioning, emotional control, social interactions, and motivation (Alzheimer's & Dementia, 2024; World Health Organization, 1993), ultimately, leading to complete dependency on others (World Health Organization, 2017). Some forms of dementia are potentially reversible (e.g., those caused by vitamin deficiencies, chronic alcohol abuse, infections, or severe psychiatric disorders), while others result from irreversible neurodegeneration (Gale et al., 2018). Neurodegenerative diseases represent a large group of neurological disorders with heterogeneous clinical and pathological manifestations, depending on which specific subsets of neurons and parts of functional anatomic systems are affected, arising regularly for unknown reasons and progressing relentlessly (Przedborski et al., 2003). Common neurodegenerative dementias include AD, frontotemporal dementia (FTD), dementia with Lewy bodies (DLB), and Parkinson's disease dementia (Gale et al., 2018). Vascular

dementia (VaD), often co-occurring with AD pathology in mixed dementia (Iadecola, 2010; Jellinger, 2008), is classified separately as a cerebrovascular disorder (Gale et al., 2018).

AD, the most prevalent cause of dementia, accounting for 60-80% of cases, is characterized by the abnormal accumulation of protein fragments throughout the brain (Alzheimer's & Dementia, 2024; Mertaş & Boşgelmez, 2025). These include amyloid-β (Aβ), which forms clumps outside neurons known as Aβ plaques, and tau protein, which undergoes hyperphosphorylation and aggregation, forming tau tangles inside neurons. Amyloid-β plaques disrupt synaptic communication between neurons, while tau tangles impair the transport of nutrients and essential molecules, compromising neuronal function and survival. Additionally, tau pathology contributes to neuron-to-neuron disconnection. As a result, microglia, the brain's immune cells, attempt to clear toxic protein aggregates and dead cells, but when they fail to keep up, this leads to chronic inflammation. Over time, these processes cause progressive brain atrophy (i.e., decreased brain volume) (Alzheimer's & Dementia, 2024), particularly affecting the hippocampus and cortical regions (Arvanitakis et al., 2019). This sequence of pathological events, known as the amyloid cascade hypothesis of AD (Karran & De Strooper, 2022), results in progressive cognitive decline, beginning with memory impairment and executive dysfunction. In later stages, patients experience difficulties with movement, speech, and swallowing (Alzheimer's & Dementia, 2024; American Psychiatric Association, 2013; World Health Organization, 1993). Approximately 5% of all AD cases occur before the age of 65 years, a condition referred to as "early-onset" AD (Zhu et al., 2015).

Vascular dementia, the second most common subtype of dementia (Goodman et al., 2017), affects approximately 25-30% of cases (O'Brien et al., 2003). It results from brain damage due to reduced blood supply, including oxygen and nutrients, often following strokes or chronic vascular disease (Alzheimer's & Dementia, 2024; World Health Organization, 1993). VaD typically presents with a stepwise decline in cognitive abilities, impaired executive

functioning, and motor difficulties, often accompanied by brain infarcts or white matter lesions (Arvanitakis et al., 2019).

Lewy body dementias (LBD) encompass both DLB and Parkinson's disease dementia (Walker et al., 2015) and accounts for approximately 5% of dementia cases (Kane et al., 2018). LBD are the second most common type of neurodegenerative dementia after AD in adults over 65 years, with men being more frequently affected (Walker et al., 2015). LBD are characterized by abnormal deposits of α-synuclein proteins, leading to neuronal loss and neurotransmitter imbalances. Core symptoms include rapid eye movement (REM) sleep disturbances, visual hallucinations, visuospatial impairments, and motor dysfunction resembling Parkinson's disease (Alzheimer's & Dementia, 2024; Walker et al., 2015).

FTD primarily affects middle-aged adults (45 – 65 years), with around 70% of cases occurring in those under 65 years (Bang et al., 2015). It accounts for approximately 3% of dementia cases in older adults (above 65 years) but up to 10% in younger individuals (Hogan et al., 2016). FTD manifests as significant changes in personality, behavior, and language skills, with three subtypes: behavioral-variant FTD, non-fluent variant primary progressive aphasia, and semantic-variant primary progressive aphasia (American Psychiatric Association, 2013; Bang et al., 2015; World Health Organization, 1993). The disease results from neuronal loss in the frontal and temporal lobes, often involving tau or TDP-43 (i.e., transactive response DNA-binding protein) protein aggregates (Alzheimer's & Dementia, 2024; Arvanitakis et al., 2019).

Diagnosing dementia involves a comprehensive assessment, including medical history, cognitive and neuropsychological testing, physical examinations, and brain imaging (Arvanitakis et al., 2019). Mixed dementia, where multiple pathological processes coexist, is common (Brenowitz et al., 2017; Kapasi et al., 2017), particularly involving AD and cerebrovascular disease (Jellinger & Attems, 2007). For a definitive diagnosis of the cause of dementia, an autopsy (i.e., post-mortem brain tissue analysis) is the gold standard (Suemoto &

Leite, 2023), and it remains challenging to determine which symptoms stem from which underlying pathology (Alzheimer's & Dementia, 2024).

There is ongoing debate regarding the relative contributions of genetic and environmental factors in dementia onset (Argentieri et al., 2025; Przedborski et al., 2003). This is particularly intriguing as a significant proportion of older adults remain cognitive normal despite AD pathologies being present (Arenaza-Urquijo & Vemuri, 2018). Although some pathological hallmarks underlying of each dementia subtype have been identified, much remains unclear about their heritability, mechanisms that initiate them, and their causal relationships (Ye et al., 2024). Genetic mutations, such as those in the Aβ precursor protein (APP), presenilin-1 (PSEN1), and presenilin-2 (PSEN2) genes, have been linked to early-onset AD, while the apolipoprotein (APOE) ε4 allele increases the risk of late-onset AD (Mertaş & Boşgelmez, 2025). Biomarker advancements have improved diagnostic accuracy, for instance, by measuring Aβ and tau protein levels in the cerebrospinal fluid (Mertaş & Boşgelmez, 2025).

Despite extensive research efforts, no cure currently exists for neurodegenerative dementia. New pharmacological treatments, such as lecanemab and donanemab, have shown promise in slowing AD progression in its early stages, though significant challenges remain (Belder et al., 2023; Livingston et al., 2017; Parums, 2024; Prince et al., 2015).

Dementia is a growing public health crisis. In 2015, 900 million people worldwide were over the age of 60 (Prince et al., 2015), accounting for approximately one in eight people globally. Among them, it is estimated that 46 million people were living with dementia, a number expected to double every 20 years (Prince et al., 2015). Additionally, a new case of dementia occurs every three seconds worldwide (Patterson, 2018; Prince et al., 2015). Despite this alarming rate, dementia is frequently unrecognized and undiagnosed, especially in primary care settings (Alzheimer's & Dementia, 2024; Boustani et al., 2003; Valcour et al., 2000). By 2050, the number of people with dementia is expected to triple to 131.5 million, largely due to population growth and increased life expectancy. The majority of individuals with dementia

live in low- and middle-income countries (LMICs), and by 2050, this proportion is expected to rise to 68% (Prince et al., 2015). The economic burden of dementia is substantial. In 2015, the global cost of dementia was estimated at US$818 billion. This figure was projected to surpass US$1 trillion by 2018 (Prince et al., 2016) and US$2 trillion dollars by 2030 (Patterson, 2018). Despite these staggering numbers, research on dementia remains significantly underfunded. In 2018, there were 3 million research papers on cancer, compared to only 250,000 on dementia and neurodegeneration, underscoring the urgent need for continued research in this field (Patterson, 2018).

Given these figures, dementia has been recognized as one of the greatest global public health challenges of the 21st century (Livingston et al., 2017). Beyond its impact on individuals, dementia places a significant financial burden on families and society, while also profoundly affecting the physical, mental, and social well-being of both patients and their caregivers (Patterson, 2018; World Health Organization, 2017). It is a key public health goal to prevent or delay the onset of dementia (Livingston et al., 2017, 2020, 2024). Early detection of cognitive impairment, whether as a precursor to dementia or as part of the prodromal phase, is crucial for implementing interventions that could delay, or even prevent, the clinical manifestation of dementia (Assunção et al., 2022; Ismail et al., 2021; Tegethoff et al., 2024).

1.1.2. Early Detection and Prevention of Dementia

Cognitive impairment is often overlooked in clinical practice when treating patients with psychological disorders (Chavez-Baldini et al., 2021), despite its association with lower quality of life (Hill et al., 2017), reduced treatment success (Gonda et al., 2015; Scott et al., 2015), and, importantly, in older age, with an increased risk of developing dementia (Borland et al., 2024; R. O. Roberts et al., 2014).

1.1.2.1. Objective and Subjective Cognitive Functioning and Impairment

Cognitive functioning and impairment can be assessed through two primary methods: objective and subjective evaluations (Hess et al., 2020). While two reviews concluded that subjective cognitive complaints and objective cognitive performance are inconsistently associated with each other (Hutchinson et al., 2012; Reid & MacLullich, 2006), a meta-analysis of 50 studies has found a small but significant association between subjective and objective cognitive function, with poorer performance on objective cognitive assessments being linked to increased subjective cognitive complaints (Burmester et al., 2016). Some evidence suggests that this association is particularly pronounced among highly educated individuals and older adults (Jonker et al., 2000), potentially indicating the very early stages of dementia (Jonker et al., 2000; Reid & MacLullich, 2006).

Objective cognitive assessments rely on standardized neuropsychological tests, widely regarded as the gold standard for evaluating specific cognitive domains (Savard & Ganz, 2016). These tests measure abilities such as visuospatial perception (e.g., Block Design Test) and verbal comprehension (e.g., Token test) (Zucchella et al., 2018). Executive functioning – a collection of higher-order cognitive processes including working memory, cognitive flexibility, impulse control, and fluency (i.e., ability to maximize information production without repetition) – is commonly assessed through tasks like the Stroop Test (measuring inhibitory control and selective attention), the Wisconsin Card Sorting Test (evaluating reasoning and cognitive flexibility), and the digit span subtest of the Wechsler Adult Intelligence Scale-IV (WAIS-IV), which assesses working memory. Other widely used assessments include the Trail Making Test, which measures attention and task-switching ability. In recent years, computerized cognitive assessments have gained popularity due to their efficiency, cost-effectiveness, and ability to minimize examiner bias (Zygouris & Tsolaki, 2015).

In contrast, subjective cognitive assessments involve self-reports, informant reports, or clinical interviews**,** aiming to evaluate an individual's perceived decline in cognitive abilities, a phenomenon known as subjective cognitive decline (SCD) (Molinuevo et al., 2017). SCD is defined as persistent self-experienced decline in cognitive functioning, particularly in memory, concentration, planning, and attention (Broadbent et al., 1982; Rami et al., 2014), compared to their previous abilities (Molinuevo et al., 2017).

While objective assessments reduce self-report bias (Ibnidris et al., 2022; Mulligan et al., 2016) and are said to reflect "real deficits" (Savard & Ganz, 2016, p. E1), subjective cognitive functioning has been assumed to measure more "real world cognitive experiences" (Carrigan & Barkus, 2016, p. 1). That is, subjective assessments may be more sensitive toward subtle, early cognitive changes in cognitive functioning, that individuals recognize before they become detectable through objective testing (Geerlings et al., 1999; Molinuevo et al., 2017). Additionally, subjective cognitive assessments may better reflect everyday cognitive challenges (Carrigan & Barkus, 2016) and their impact on quality of life (Hutchinson et al., 2012). Although most instruments for assessing SCD focus memory, followed by executive functioning and attention, considerable heterogeneity in the measures used should be taken into account when comparing findings across studies (Rabin et al., 2015).

Objective and subjective measures have each been associated with dementia (Brodaty et al., 2017; Mitchell et al., 2014; Pike et al., 2022). Notwithstanding their differences, both approaches contribute valuable insights into cognitive function, and evidence suggests they should be viewed as complementary rather than conflicting (Hess et al., 2020; Hutchinson et al., 2012; Molinuevo et al., 2017; Savard & Ganz, 2016).

An important diagnostic category linked to increased risk of dementia is mild cognitive impairment (MCI). MCI represents an intermediate stage between normal aging and dementia, characterized by both subjective and objective cognitive impairment greater than expected for a person's age and educational level. However, these impairments do not interfere with daily

life (Gauthier et al., 2006). Initially introduced as a clinical concept in the late 1990s (Petersen et al., 1999), MCI remains inconsistently diagnosed (Petersen, 2016). However, when properly identified, individuals with MCI are at an elevated risk of progressing to dementia, although in some cases, the cognitive impairment remains stable or even reverts to normal functioning over time (Gauthier et al., 2006).

1.1.2.2. Risk Factors of Cognitive Impairment and Dementia: An Overview

The global action plan on the public health response to dementia (2017 – 2025), published by the World Health Organization (2017), outlines seven priority areas to address dementia at the global level. In addition to recognizing dementia as a public health priority, raising awareness, and increasing support for affected individuals and caregivers, one action area includes the goal of dementia risk reduction. Growing evidence suggests that several health and lifestyle factors contribute to dementia risk (Livingston et al., 2017, 2020, 2024). Minimizing exposure to these modifiable risk factors, starting as early as possible and continuing across the lifespan, can enhance the ability of individuals to make healthier choices and adopt lifestyles that improve well-being and reduce the likelihood of cognitive decline (World Health Organization, 2017).

The most recent report of the Lancet Commission on dementia prevention, intervention, and care has identified 14 potentially modifiable risk factors that collectively account for approximately 45% of all dementia cases. These findings highlight the significant potential for prevention – nearly half of dementia cases could theoretically be avoided by addressing these risk factors (Livingston et al., 2024). Based on the currently available evidence, those 14 established risk factors are lower levels of education during early life, hearing, loss, high low-density lipoprotein (LDL) cholesterol, depression, traumatic brain injury, physical inactivity, diabetes, smoking, hypertension, obesity, and excessive alcohol consumption during midlife, and social isolation, air pollution, and visual loss during late life (Figure 1).

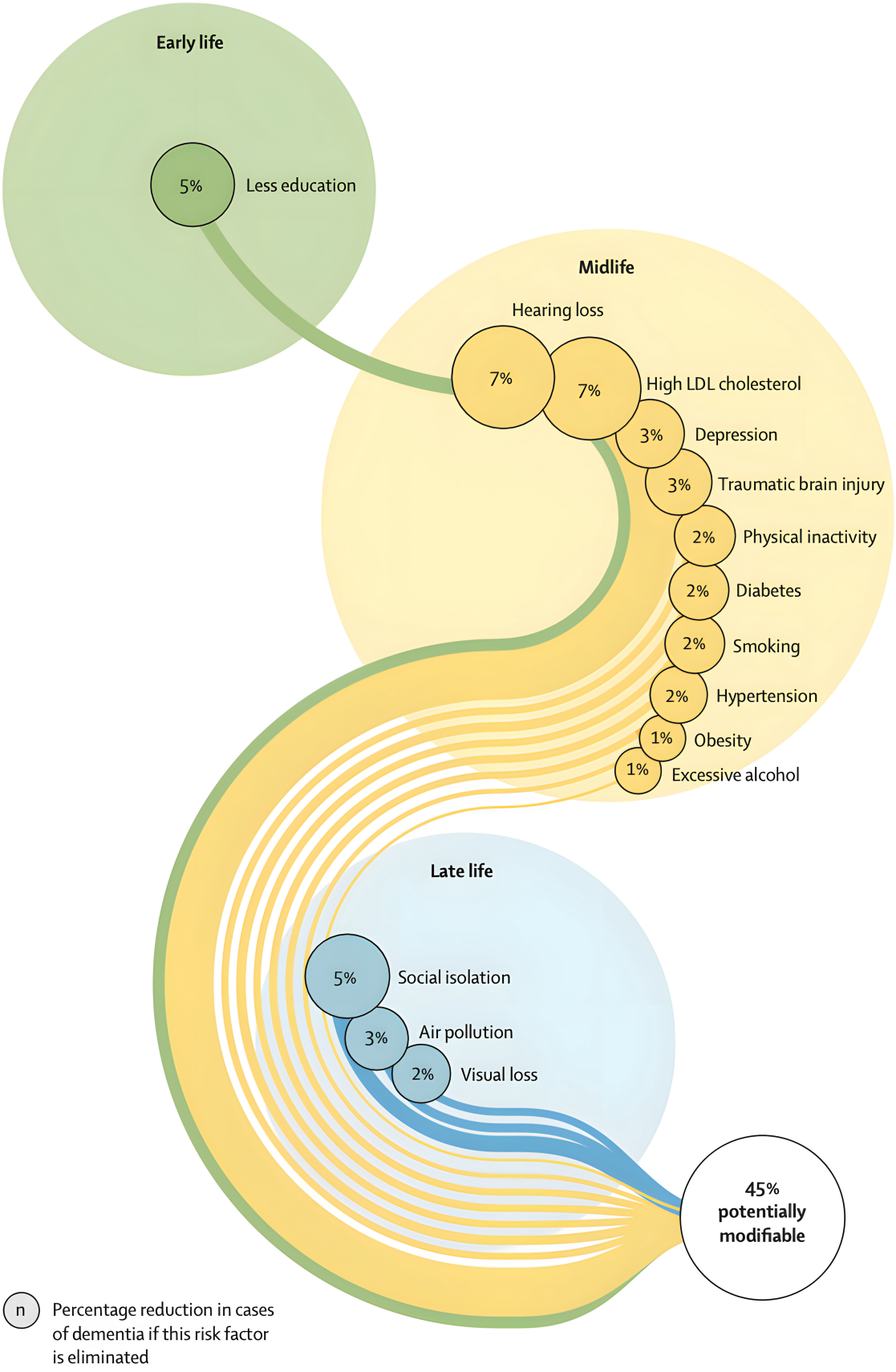

Figure 1. Reproduced from Livingston et al. (2024), showing the population attributable fraction of potentially modifiable risk factors for dementia.

These factors have been consistently linked to an increased risk of dementia in systematic reviews and meta-analyses. The commission's findings underscore the importance of cognitive and physical reserve development across the lifespan and emphasize the benefits of vascular health in reducing age-related dementia risk. While these 14 factors are well-established, other potential contributors to dementia have also been identified. However, due to insufficient high-quality studies or inconsistent findings, they have not yet been included as primary modifiable risk factors. One example is post-traumatic stress disorder (PTSD), which has been associated with an increased risk of dementia in several studies, but further research is needed to confirm its role (Günak et al., 2020; Stafford et al., 2022).

1.2. The Role of PTSD in Cognitive Impairment and Dementia

1.2.1. Definition, Diagnostic Criteria, and Prevalence of PTSD

PTSD is a psychological disorder characterized by four clusters of symptoms: re-experiencing trauma-related memories, avoidance of trauma-related activities, persons, and places, negative alterations in cognitions and mood, and hyperarousal (American Psychiatric Association, 2013). The gold standard for PTSD assessment includes the Clinician-Administered PTSD Scale for Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) (CAPS-5), a structured clinical interview (Weathers et al., 2018). As a self-report measure, the PTSD Checklist for the DSM-5 (PCL-5), a 20-item self-report measure (Weathers et al., 2013) is commonly used. Both instruments were developed by the U.S. Department of Veterans Affairs' National Center for PTSD, originally designed for U.S. veterans.

PTSD is unique among psychological disorders as it is triggered by a specific event – exposure to a traumatic event (American Psychiatric Association, 2013). Trauma is defined as a life-threatening experience, including sexual or physical violence, which can be directly

experienced, witnessed, or learned about if it occurred to a close person. Historical accounts suggest PTSD-like symptoms have been observed for centuries, such as after the Great Fire of London in 1666 and among World War I soldiers, where it was referred to as “shell shock”. However, PTSD was only officially recognized as a distinct psychological disorder in 1980, with its inclusion in the Diagnostic and Statistical Manual of Mental Disorders, Third Edition (DSM-III), largely due to research on Vietnam War veterans, Holocaust survivors, and other trauma-exposed populations (Saigh & Bremner, 1999).

Today, PTSD is a globally recognized disorder that impacts individuals across diverse populations and socioeconomic backgrounds, with women being disproportionately affected (Olff et al., 2007). Among those who experience a traumatic event, approximately 4% develop PTSD (Liu et al., 2017). The highest risk of PTSD is associated with man-made traumas, particularly sexual violence, although other types of trauma, such as natural disasters, can also trigger the disorder (Kessler et al., 2017). Another key factor contributing to PTSD risk is childhood adversity (Messman-Moore & Bhuptani, 2017), often referred to as adverse childhood experiences (ACEs) – a broader conceptual framework (Kalmakis & Chandler, 2014). ACEs include emotional and physical neglect, as well as emotional, physical, and sexual abuse experienced from birth through young adulthood (Kalmakis & Chandler, 2014; O’Neill et al., 2021). The term ACEs is frequently used interchangeably with childhood maltreatment and childhood trauma. However, they are not entirely synonymous as ACEs encompass a wider range of experiences, including less severe events that do not meet the DSM-5 Criterion A for trauma, defined as exposure to (threatened) death, serious injury, or sexual violence (American Psychiatric Association, 2013). ACEs, however, are characterized by five key features: they are harmful, distressing, cumulative, often chronic, and varying in severity, while still disrupting physiological or physical health and development (Kalmakis & Chandler, 2014). Thus, ACEs represent a broader category than childhood trauma alone.

The prevalence of trauma varies across geographical regions, socioeconomic backgrounds, and sex (Kessler et al., 2017; Liu et al., 2017). However, trauma exposure remains highly prevalent worldwide, with an estimated 70.4% of individuals experiencing at least one traumatic event in their lifetime (Kessler et al., 2017). ACEs, in particular, are also common, with 60.1% of adults globally reporting at least one (Madigan et al., 2023). This is likely an underrepresentation due to the high number of unreported cases (Herzog & Schmahl, 2018), making ACEs a pressing global concern on their own (Madigan et al., 2023). Given the rise in global political conflicts, wars, and social and human rights crises, coupled with the tenfold increase in climate-related disasters over the past 60 years (Institute for Economics & Peace, 2020), the already high prevalence of trauma exposure is likely to remain a major societal challenge, for generations to come, or may become an even bigger one.

1.2.2. PTSD as a Memory Disorder: Theoretical Models of the Development of PTSD

When considering PTSD and its relationship to memory, two key aspects should be distinguished. First, PTSD is characterized by directly observable memory-related phenomena, including involuntary intrusive memories that create the sensation of re-experiencing the traumatic event, highly sensory memories, and memory difficulties related to important aspects of the trauma (American Psychiatric Association, 2013). Second, theoretical models have been developed to explain the development, triggering, and persistence of PTSD, with a central focus on memory processing and integration (Brewin et al., 1996; Ehlers & Clark, 2000; Foa & Kozak, 1986). A defining feature of PTSD is the fragmentation and disorganization of trauma memories, which are often stored as sensory fragments rather than structured narratives, leading to intrusive re-experiencing and difficulties distinguishing past from present (American Psychiatric Association, 2013).

Foa and Kozak (1986) suggested that trauma memories form an associative network in which stimuli related to the trauma (e.g., sounds, locations, similarities with a perpetrator)

become linked with strong emotional and behavioral reactions (e.g., fear, hyperarousal, avoidance), and the meanings of these stimuli and responses (e.g., “this is dangerous”). This fear memory structure remains easily activated, even by objectively safe stimuli, resulting in persistent distress and re-experiencing symptoms (Ehlers et al., 2022; Foa & Kozak, 1986).

The dual representation theory (Brewin et al., 1996) proposes that traumatic memories are stored in two parallel systems: the verbally accessible memory system, where memories are contextually bound and consciously retrievable, and the situationally accessible memory system, where trauma-related sensory impressions remain strongly encoded but poorly integrated with contextual information (Brewin et al., 1996; Ehlers et al., 2022). Flashbacks occur when situational cues activate sensation-based memories, while the weaker contextually bound representations fail to inhibit them.

Ehlers and Clark’s cognitive model of PTSD (2000) further explains that persistent PTSD symptoms arise from excessively negative appraisals of the trauma and its aftermath, combined with disturbances in autobiographical memory. Individuals with PTSD often rely on data-driven processing (i.e., focusing on sensory impressions) rather than self-referent processing (i.e., impression that one is no longer the same person), leading to poorly integrated autobiographical memories and a sense of disconnection from their past self. Consequently, cue-driven retrieval of fragmented trauma memories facilitates re-experiencing symptoms while preventing proper contextualization (Ehlers et al., 2022; Ehlers & Clark, 2000).

Taken together, trauma memories are often fragmented and disorganized rather than coherently integrated into autobiographical memory, leading to traumatic experiences being stored as sensory fragments rather than as structured narratives. The disruption in memory processing is linked to impaired contextualization of trauma memories, making it difficult for individuals affected to distinguish past from present. As a result, fear responses become overgeneralized beyond the original trauma context, suggesting impaired memory retrieval and maladaptive consolidation of trauma-related information. This leads to persistent distress and

intrusive memories, which, amongst others, are hallmark symptoms of PTSD (American Psychiatric Association, 2013).

Several key brain regions involved in memory processing are implicated in PTSD. Namely, the hippocampus, critical for learning and memory; the prefrontal cortex, regulating higher-order cognitive processes, including rational thinking, executive functioning, and emotion regulation; and the amygdala, which play a central role in emotional processing and threat detection (Shin et al., 2006). Research suggests that individuals with PTSD often exhibit hippocampal atrophy, hyperactive amygdala responses, and impaired prefrontal cortex regulation. Furthermore, dysfunctional communication between these regions has been observed, affecting both cognitive and emotional regulation (Shin et al., 2006; Wrocklage et al., 2016), although findings on these structural and functional abnormalities have not always been consistent (Greenberg et al., 2014). The hippocampus and prefrontal cortex are essential for cognitive functioning, particularly memory and executive processes. Their dysfunction has been linked to cognitive impairment (Eichenbaum, 2017), and damage to these regions and functional connectivity abnormalities is a hallmark of feature of various neurodegenerative diseases, including AD and FTD (Allen et al., 2007; Jobson et al., 2021). This suggests that PTSD-related neural alterations may contribute to an increased risk of dementia over time.

Treatment guidelines strongly recommend trauma-focused cognitive behavioral therapy (TF-CBT) and eye movement desensitization reprocessing (EMDR) as first-line interventions for PTSD (Martin et al., 2021). These recommended treatment options share two essential components: the exposure to the traumatic memories and cognitive restructuring, which helps individuals process and re-interpret their trauma-related experiences.

Overall, PTSD, has been defined as a disorder of memory, highlighting the strong link between PTSD, cognition, and memory (McNally, 2006).

1.2.3. Current Insights into PTSD, Cognitive Impairment, and Dementia

1.2.3.1. PTSD and Cognitive Impairment

PTSD is associated with various adverse consequences, one of which is impaired cognitive functioning. While difficulty concentrating is an intrinsic symptom of PTSD (Weathers et al., 2013), a meta-analysis of 60 studies, primarily including younger and middle-aged adults, reported that PTSD is linked to deficits in verbal learning, processing speed of information, attention and working memory, and verbal memory (Scott et al., 2015). Similarly, a meta-analysis focused on older adults with PTSD found that these individuals perform worse in processing speed, learning, memory, and executive functioning compared to older adults without PTSD (Schuitevoerder et al., 2013). Both meta-analyses relied on standardized neuropsychological assessments.

To date, however, there is no systematic review or meta-analysis specifically addressing the relationship between PTSD and subjective cognitive functioning or SCD. Individual studies have observed associations between PTSD and self-reported difficulties in memory, attention, concentration, and slowed thinking (Boals & Banks, 2012; Neale et al., 2024; Seal et al., 2016; Singh et al., 2020; Spencer et al., 2010; Vasterling et al., 2012). However, these self-reported ratings of cognitive impairment were not significantly correlated with objective cognitive performance (Spencer et al., 2010). This is unsurprising, as subjective cognitive complaints and objective cognitive performance are often inconsistently associated across different populations (Hutchinson et al., 2012; Reid & MacLullich, 2006), underscoring the distinct value of each measure (Hess et al., 2020; Hutchinson et al., 2012; Molinuevo et al., 2017; Savard & Ganz, 2016).

Interestingly, one study identified PTSD as a mediator between objective cognitive performance assessed with neuropsychological testing, and subjective cognitive complaints (Mattson et al., 2019). The authors argue that this mediation might be explained by the negative

self-appraisals common in PTSD (American Psychiatric Association, 2013; Ehlers & Clark, 2000), such as self-criticism and diminished sense of self-efficacy (Samuelson et al., 2017; Spencer et al., 2010), which may negatively impact individuals' perceptions of their cognitive abilities (Mattson et al., 2019; Samuelson et al., 2017). In another study, Singh and colleagues found that PTSD symptoms, together with depressive symptoms, mediated the relationship between exposure to the World Trade Center disaster and subjective cognitive concerns (Singh et al., 2020).

Both childhood trauma (Petkus et al., 2018) and lifetime trauma exposure (Lynch & Lachman, 2020), including, amongst others, physical or sexual assault, combat experience, and losing a home to a natural disaster, had been associated with cognitive decline across various cognitive domains many years later. However, studies have indicated that the negative association between PTSD and objectively measured cognitive performance is stronger relative to the association between trauma exposure alone, whether in childhood or adulthood, and cognitive performance (Burri et al., 2013; Qureshi et al., 2011; Schuitevoerder et al., 2013). Furthermore, the severity of PTSD symptoms correlates with greater impairments in both subjective (Mattson et al., 2019; Spencer et al., 2010), and objective (A. L. Roberts et al., 2022) measures of cognitive functioning. These findings suggest that PTSD may be the key driver of this relationship, influencing both self-perceived and performance-based cognitive outcomes. This supports a dose-response relationship, in which greater trauma-related symptom severity is linked to greater cognitive impairment, with PTSD having a stronger negative impact on cognitive functioning than trauma exposure alone.

In the past, however, methodological concerns were raised that call into question the repeatedly observed relationship between PTSD and cognitive impairment (Danckwerts & Leathem, 2003). Issues include the difficulty in distinguishing cognitive impairments due to emotional distress versus those with a physical basis, the tendency to generalize findings from specific populations (e.g., veterans) to the broader public, limitations inherent in specific

neuropsychological assessment tools, and strict diagnostic criteria for PTSD that may not fully capture the symptom spectrum. A key challenge is determining whether cognitive difficulties stem from actual brain impairment or are a consequence of PTSD-related symptoms, such as intrusive memories, which may disrupt cognitive functioning in a PTSD-specific manner. This distinction is often unclear in studies examining the PTSD-cognition link, complicating interpretations of the underlying mechanisms.

1.2.3.2. PTSD and Dementia

In addition to its relationship to cognitive impairment, there has been a growing interest in the possibility that PTSD may be a risk factor for dementia. Folnegović-Šmalc et al. (1997) were among the first to observe that war refugees who had experienced three or more traumatic events exhibited more symptoms of AD, as identified with the Diagnostic and Statistical Manual of Mental Disorders, Third Edition, Revised (DSM-III-R) and well-established National Institute of Neurological and Communicative Disorders and Stroke and the AD and Related Disorders Association (NINCDS-ADRDA) criteria (McKhann et al., 1984), compared to individuals from a "normal, peacetime population" (Folnegović-Šmalc et al., 1997, p. 273), meaning those not exposed to war. Interestingly, this increased prevalence of AD was observed across all age groups, except for those 75 years and older. Furthermore, among war refugees who developed AD symptoms, most had experienced at least five war-related traumatic events, suggesting a dose-response relationship, where a greater number of traumatic experiences may contribute to increased dementia risk.

More than a decade later, additional studies reinforced this association. A study of U.S. veterans found that those with PTSD had nearly twice the risk of developing dementia compared to veterans without PTSD (Yaffe et al., 2010). Similarly, another study reported both a higher prevalence and increased incidence of dementia among veterans with PTSD (Qureshi et al., 2010). A meta-analysis of eight longitudinal studies, including over 1.5 million

individuals with follow-up periods ranging from 1 to 17 years, further supported this link. The findings demonstrated that individuals with PTSD have an elevated risk of all-cause dementia, suggesting that PTSD may be a risk factor for dementia (Günak et al., 2020). Several studies published since have continued to support this association (Bergman et al., 2021; H. Kim et al., 2023; H. Song et al., 2020), with one exception (Islamoska et al., 2020). These findings suggest that PTSD may contribute to long-term neurodegenerative processes, underscoring the need for further investigation into the underlying mechanisms linking PTSD to dementia risk.

1.2.3.3. Potential Neurobiological Mechanisms Underlying PTSD, Cognitive Impairment and Dementia

Several studies have explored potential etiological mechanisms that may explain the link between PTSD and dementia. According to the DSM-5, PTSD is classified as a stress-related disorder (American Psychiatric Association, 2013), and both acute and chronic stress have profound physiological effects on multiple organ systems, including the brain (Greenberg et al., 2014; McEwen, 2007). Given that stress plays a critical role in neurodegenerative processes (Esch et al., 2002), it is plausible that PTSD contributes to an increased risk of dementia.

One potential explanation is the concept of allostatic load, which refers to the cumulative wear and tear on the body and brain resulting from chronic stress responses (Danese & McEwen, 2012; McEwen, 1993). PTSD, often persistent (Kessler et al., 2017), may induce a prolonged stress response, heightening allostatic load and increasing susceptibility to disease. This may be particularly relevant when PTSD is untreated or unrecognized, resulting in chronicity of the disorder, which is not uncommon (Kessler et al., 2017).

However, research on hypothalamic-pituitary-adrenal (HPA) axis dysregulation, a major stress-response system that regulates cortisol secretion (Mehta & Binder, 2012; Sapolsky et al., 2000) has produced inconsistent findings regarding its role in PTSD (Schumacher et al.,

2019; Speer et al., 2019). In contrast, hippocampal atrophy has been consistently implicated in PTSD-related cognitive decline (Alves De Araujo Junior et al., 2023). Reduced hippocampal volume has also been observed in trauma-exposed individuals without PTSD, though greater hippocampal deficits have been noted among those who develop PTSD (Greenberg et al., 2014). It remains unclear whether PTSD causes hippocampal atrophy, whether preexisting hippocampal differences predispose individuals to PTSD, or whether the relationship is bidirectional (Greenberg et al., 2014).

Other established structural brain abnormalities in PTSD include changes in the amygdala and medial prefrontal cortex (including the anterior cingulate cortex), which are involved in both cognitive and emotional regulation (Alves De Araujo Junior et al., 2023). While AD neuropathology primarily affects the hippocampus and entorhinal cortex (Igarashi, 2023), alterations in these limbic regions, as well as the prefrontal cortex, have been observed in both PTSD and later stages of AD (Alves De Araujo Junior et al., 2023).

Chronic stress can trigger oxidative stress and neuroinflammation, both of which have been implicated in the relationship between PTSD, cognitive impairment, and dementia (Lohr et al., 2015; Miller et al., 2018). Oxidative stress is a fundamental molecular process in aging and widely associated with various common diseases (Miller et al., 2018). It is a cellular status that occurs when there are more pro-oxidant molecules than available antioxidants, leading to an increased production of antioxidants. However, persistent oxidative stress depletes antioxidants, potentially resulting in cell damage and neuronal death (Aquilano et al., 2014). Neuroinflammation is a physiological response to cell injury, where inflammatory cells release pro-inflammatory cytokines, further contributing to oxidative stress (Miller et al., 2018). Thus, these processes are closely pathophysiologically interlinked, as chronic inflammation can induce oxidative stress, and vice versa (Biswas, 2016). Both mechanisms can be triggered by chronic psychological stress, such as PTSD, leading some researchers to suggest that PTSD may function as a neuroprogressive disorder, exerting cumulative neurotoxic effects on the

brain over time (Miller et al., 2018). Some studies indicate that oxidative stress and neuroinflammation contribute to Aβ plaque accumulation (Greenberg et al., 2014). However, evidence remains inconclusive, with some studies supporting a link between PTSD and Aβ or tau pathology (Clouston, Deri, et al., 2019; Mohamed et al., 2018, 2019), while others do not (Elias, Cummins, et al., 2020; Weiner et al., 2017, 2023).

Recent research has focused on DNA methylation-based measures of cellular aging, known as DNAm age, to investigate PTSD's impact on the aging process (Wolf, Logue, et al., 2018). Epigenetic clock measures compare an individual's biological age (i.e., based on DNA methylation (DNAm) patterns) with their chronological age, providing insight into accelerated aging. The hyperarousal symptom cluster of PTSD was found to be associated with accelerated DNAm age, whereas trauma exposure alone and total PTSD severity were not (Wolf, Logue, et al., 2018). Accelerated cellular aging, in turn, was associated with an increased risk of all-cause mortality over a time period of 6.5 years. A meta-analysis found that both childhood trauma and PTSD severity were associated with accelerated epigenetic age, whereas PTSD diagnosis and life trauma exposure were not (Wolf, Maniates, et al., 2018). An advanced predictor of lifespan, DNAm GrimAge (Lu et al., 2019), was found to be accelerated in individuals with PTSD, suggesting premature biological aging and increased mortality risk (Katrinli et al., 2023). Interestingly, PTSD-related epigenetic aging did not reverse following successful PTSD treatment or remission over a 24-week follow-up (Katrinli et al., 2023), implying long-term biological consequences. These findings suggest that PTSD may contribute to earlier onset of aging-related diseases, including dementia (Katrinli et al., 2023; Wolf, Maniates, et al., 2018).

PTSD is associated with higher rates of premature mortality and medical comorbidities, many of which are common in normal aging, such as cardiovascular disease, type 2 diabetes mellitus, (Lohr et al., 2015; Miller et al., 2018), and hypertension, although evidence for the latter is heterogenous (Lohr et al., 2015; Sumner et al., 2021). Cardiovascular diseases are particularly relevant, as they are associated with dementia (Whitmer et al., 2005), especially

VaD (Javanshiri et al., 2018). One study found that differences in neurocognitive performance between individuals with and without PTSD were largely accounted for by a combination of vascular risk factors, poor health behaviors, and depression (Cohen et al., 2013). Given the well-established relationship between vascular risk factors and dementia, the association between PTSD and these conditions may partially explain its link to cognitive decline and dementia.

Lastly, research has also explored whether certain genetic predispositions contribute to the relationship between PTSD and dementia. For example, the APOE ε4 allele has been found to interact with PTSD severity, with individuals carrying APOE ε4 showing stronger associations between PTSD symptoms and cognitive impairment (Averill et al., 2019; Neale et al., 2024). A meta-analysis also found that APOE ε4 was linked to an increased risk of combat-related PTSD (Roby, 2017), though this finding was not replicated in a more recent cohort study (Wolf et al., 2024). This raises the possibility that APOE ε4 is a shared vulnerability factor for both PTSD and AD.

Altogether, while significant progress has been made in understanding the neurobiological underpinnings of PTSD, cognitive impairment, and dementia, much remains unclear. Multiple mechanisms, including hippocampal atrophy, neuroinflammation, oxidative stress, vascular risk factors, accelerated cellular aging, and genetic predispositions, likely interact in complex ways (Alves De Araujo Junior et al., 2023).

1.3. Toward a Deeper Understanding: PTSD, Cognitive Impairment, and Dementia

Several studies have suggested an association between PTSD, cognitive impairment, and dementia risk, with various neurobiological mechanisms proposed to explain these findings. However, many aspects of this relationship remain unclear, including the potential role of non-neurobiological pathways and whether certain factors may influence the increased risk of

cognitive impairment and dementia observed in individuals with PTSD. This thesis aims to address these gaps by exploring these alternative mechanisms and identifying potential moderators of these associations.

1.3.1. Broadening the Perspectives: PTSD and Risk of Cognitive impairment and Dementia

1.3.1.1. Cognitive Reserve

One framework that may help explain the observed relationship PTSD, cognitive impairment, and dementia is the cognitive reserve hypothesis. Cognitive reserve is a theoretical construct that describes individual differences in resilience to aging-related or disease-related brain pathology, allowing some individuals to better maintain cognitive function despite neuropathology (Stern, 2002; Stern et al., 2020). The idea has evolved through repeated observations that brain pathology does not always directly correspond to the severity of cognitive symptoms (Stern, 2002). For instance, a stroke of a given magnitude can produce significant impairment in one patient, while having a minimal impact on another, suggesting that cognitive reserve serves as a protective factor (Stern, 2002).

The definition of reserve encompasses several levels of complexity and can be divided into passive and active models (Stern, 2002, 2009, 2012; Stern et al., 2020). Passive reserve, also referred to as the brain reserve model, posits that individuals with larger brain volumes or greater synaptic density can tolerate more damage before cognitive symptoms emerge. Active reserve, or cognitive reserve, involves adaptive coping mechanisms that allow the brain to compensate for neuropathology by using pre-existing cognitive strategies or developing alternative neural pathways it (Stern, 2002; Yaffe et al., 2014). This enables individuals to maintain cognitive function despite age-related changes or neurodegenerative diseases. The cognitive reserve hypothesis suggests that life-long cognitive stimulation can delay the onset of age-related decline, MCI, as well as help sustain cognitive performance in the presence of

dementia (Bessi et al., 2018; Mazzeo et al., 2019; M. E. Nelson et al., 2021; Valenzuela & Sachdev, 2006). In this sense, cognitive reserve acts as a buffer, moderating the relationship between brain pathology and cognitive function (M. E. Nelson et al., 2021; Stern, 2009; Stern et al., 2020), thereby delaying symptom onset and enhancing resilience against neurodegenerative conditions (Arenaza-Urquijo & Vemuri, 2018; Bartrés-Faz et al., 2020; Mazzeo et al., 2019).

Cognitive reserve is an abstract concept that cannot be measured directly, leading to the use of various proxies, such as intelligence, educational attainment, occupational complexity, intellectually engaging leisure activities, and social interactions (M. E. Nelson et al., 2021; Stern et al., 2020). Higher levels of these proxies are thought to enhance cognitive resilience by fostering more robust neural networks, enabling individuals to cope with brain pathology more effectively (Stern, 2002). This has led to the hypothesis that lifestyle modifications – even later in life – could enhance cognitive reserve and mitigate cognitive decline (M. E. Nelson et al., 2021; Stern, 2012; Tucker & Stern, 2011).

Individuals with PTSD tend to have lower levels of cognitive reserve, which may increase their vulnerability to cognitive impairment and dementia. Studies have shown that individuals with PTSD have fewer years of education, lower IQ scores, and are less likely to attain higher educational levels compared to those without PTSD compared to those without PTSD (De Bellis et al., 2013; Golier et al., 2006; Green et al., 2016; Vilaplana-Pérez et al., 2020). One population-based cohort study found that individuals with PTSD had up to 87% lower odds of achieving higher education, compared with those without PTSD (Vilaplana-Pérez et al., 2020). Additionally, PTSD symptoms such as social withdrawal, avoidance behaviors, and emotional numbing may limit participation in cognitively and socially enriching activities that are known to support cognitive reserve and protect against dementia (Cohen et al., 2013; Elias, Rowe, et al., 2020; Günak et al., 2020; Pietrzak et al., 2009).

However, cognitive reserve likely is not merely a risk factor but instead, might interact with other vulnerabilities in determining cognitive outcomes. Rather than being a direct cause of cognitive decline in PTSD, low cognitive reserve likely functions as a moderator, reducing an individual's ability to compensate for PTSD-related cognitive deficits and neurobiological alterations (Elias, Rowe, et al., 2020). This aligns with findings from major depressive disorder, for which cognitive reserve was found to moderate the severity of neurocognitive deficits (Venezia et al., 2018). A similar mechanism may apply to PTSD, where individuals with lower cognitive reserve are at greater risk of cognitive decline following trauma exposure.

Although PTSD has been linked to an increased risk of developing dementia, it is important to note that PTSD is neither necessary nor sufficient for dementia development (Greenberg et al., 2014; McEwen, 2007). Instead, it is more likely that PTSD interacts with other risk factors, either mediating (i.e., setting other factors into motion) or moderating (i.e., amplifying existing vulnerabilities) dementia risk. Given this complexity, understanding the role of cognitive reserve in PTSD may help identify pathways for targeted interventions, such as cognitive training, social engagement, and lifestyle modifications, which could enhance cognitive resilience and reduce long-term cognitive decline in PTSD populations. Additionally, TF-CBT and EMDR (Martin et al., 2021) may also help to reduce the risk of developing dementia by alleviating PTSD symptoms, thereby lowering barriers to engagement in cognitively stimulating activities.

1.3.1.2. Characteristics of PTSD

Research on PTSD and its impact on cognitive functioning and dementia risk often relies on a dichotomous approach, distinguishing between those with and without a PTSD diagnosis (Armour et al., 2017). Regarding PTSD specifically, this is not ideal and risks a significant loss of information, as PTSD is a highly heterogeneous disorder. Based on DSM-5 diagnostic criteria, there are 636,120 possible symptom combinations that qualify for a PTSD diagnosis

(Galatzer-Levy & Bryant, 2013). The diversity of PTSD symptomatology has raised ongoing debates regarding the validity and reliability of DSM-5 diagnostic categories, both broadly (Insel, 2013), and specifically for PTSD (Armour, Contractor, et al., 2016; Armour, Műllerová, et al., 2016). As a result, studies investigating the link between PTSD and cognitive impairment or dementia may overlook how the varied symptom presentations manifest in real-world contexts. In addition, most PTSD research has focused on children, young adults, and middle-aged populations, with less attention given to older adults (Böttche et al., 2012; Pless Kaiser et al., 2019). However, PTSD symptom expression may change with age. For example, older adults with PTSD often exhibit more hyperarousal symptoms and fewer re-experiencing symptoms compared to younger individuals (Böttche et al., 2012; Pless Kaiser et al., 2019).

Certain PTSD symptoms may compete for attentional resources, disrupting cognitive processes (Boals, 2008; Boals & Banks, 2012; Kolb, 1987). Intrusive and hyperarousal symptoms may interfere with attentional control, making it difficult to filter irrelevant information (Vasterling et al., 1998) or regulate cognitive content (Bomyea et al., 2012). Avoidance symptoms, while functioning as a (dysfunctional) coping mechanism to suppress trauma-related experiences, may also limit engagement with life, preventing the development of cognitive reserve (M. E. Nelson et al., 2021; Stern, 2012; Tucker & Stern, 2011). The findings of the few studies that have looked at PTSD clusters and cognitive functioning or impairment suggest that intrusive symptoms play a particularly significant role in cognitive dysfunction (Boals, 2008; Bomyea et al., 2012; Clouston, Diminich, et al., 2019; Clouston et al., 2016; Johnsen et al., 2008; Kivling-Bodén & Sundbom, 2003; Parslow & Jorm, 2007; Saltzman et al., 2006; Vasterling et al., 1998). Findings on avoidance (Boals, 2008; Bomyea et al., 2012; Clouston et al., 2016; Wrocklage et al., 2016) or hyperarousal (Bomyea et al., 2012; Clouston et al., 2016; Judah et al., 2018; Kivling-Bodén & Sundbom, 2003; Parslow & Jorm, 2007; Vasterling et al., 1998; Wrocklage et al., 2016) symptoms are more mixed, with some studies reporting an associations and others not. Currently, no studies have examined how

individual PTSD symptoms related to cognitive functioning or impairment, or dementia risk. Moreover, while intrusive symptoms appear to be most strongly associated with reduced cognitive functioning, this relationship may differ in older adults, who are said to experience fewer intrusive symptoms than younger PTSD patients (Pless Kaiser et al., 2019).

1.3.2. Understanding and Trauma and Trauma-Related Psychopathology Beyond PTSD

In addition, the association between trauma and cognitive impairment or dementia may be heterogeneous, encompassing ACEs, dissociative disorders, and depression.

1.3.2.1. Adverse Childhood Experiences

ACEs have been associated with both reduced cognitive functioning (Fabio et al., 2024; Hawkins et al., 2021; Petkus et al., 2018) and an increased risk of dementia (Abouelmagd et al., 2024; Severs et al., 2023). A meta-analysis found that childhood trauma is linked to accelerated epigenetic aging, suggesting that neurobiological changes begin early in life (Wolf, Maniates, et al., 2018). Pediatric PTSD has also been associated with epigenetic modifications, leading to structural brain abnormalities, including altered synaptic plasticity, hippocampal volume reduction, and HPA axis dysregulation (Ensink et al., 2021). Additionally, children exposed to adversity are more likely to be from minoritized ethnic backgrounds, born to non-married mothers with low education and low-income backgrounds (Marini et al., 2020). This, in turn, may lead to lower educational attainment (Blodgett & Lanigan, 2018) and weaker social networks (McCrory et al., 2022) – factors that can reduce cognitive simulation the following years or even decades.

Among the negative mental health consequences frequently linked to ACEs is not only PTSD (Messman-Moore & Bhuptani, 2017), but also depression (Gardner et al., 2019) and dissociative disorders (Şar, 2014).

1.3.2.2. Dissociative Disorders

Dissociative disorders refer to various clinical syndromes that share the disruption in typically integrated mental processes such as perception, consciousness, memory, sense of self, agency, and sensory-motor functioning (American Psychiatric Association, 2013; Şar, 2011). Specific subtypes include dissociative identity disorder, depersonalization/derealization disorder, and dissociative amnesia (American Psychiatric Association, 2013; Dorahy et al., 2014; Şar, 2020; World Health Organization, 1993). Frequently overlooked in research in the past decades, dissociative disorders have been observed across countries and cultures (Dorahy et al., 2014; Şar, 2011). Dissociative disorders are strongly linked to PTSD and depression (American Psychiatric Association, 2013; Şar, 2011; Schalinski et al., 2016).

To date, no study has investigated whether dissociative disorders are associated with an increased dementia risk. However, research has demonstrated a connection between dissociative symptoms and cognitive dysfunction, with impairments observed in domains such as attention, executive functioning, memory, and social cognition (i.e., the ability to remember and process social information) (McKinnon et al., 2016). The authors argue that this may be explained by the so-called defense cascade model, which describes dissociative states along a continuum of automatic responses to threat to ensure survival (Kozlowska et al., 2015). If escape is not possible, the body enters a freezing state to facilitate information gathering. This is where depersonalization and derealization may begin to occur, leading to a mental disconnection from oneself (i.e., depersonalization) and from the external environment (i.e., derealization). When the threat becomes inescapable, the body shifts into tonic or collapsed immobility (sometimes with loss of consciousness) as a last resort. After the threat passes, a state of quiescent immobility may follow, allowing for recovery and healing. This model helps explain why dissociative states can emerge in response to overwhelming danger, as they are deeply rooted in the body's evolutionary survival mechanisms (Kozlowska et al., 2015; McKinnon et al., 2016). McKinnon and colleagues (2016) argue that dissociation-related

cognitive dysfunction is linked to altered states of arousal, as described in the defense cascade model, where functional sensory disconnection at the cortico-sensory level disrupts sensory integration and impairs cognitive processing. When dissociative processes and cognitive operations functions rely on shared processing resources, interference between them may lead to impairments across multiple cognitive domains. Additionally, they highlight the role of opioid-mediated analgesia, suggesting that its effects on memory, combined with opioid dysregulation, may further impact neurogenesis and neuroplasticity, exacerbating cognitive dysfunction in highly dissociative individuals. However, while there is evidence of cognitive dysfunction in dissociative individuals, a more recent review found that only subjective cognitive complaints are well-established, whereas both the relationship between dissociative symptoms and objective cognitive impairment, as well as the underlying mechanisms, remain unclear (Alexis et al., 2023). One study found that middle-aged veterans with PTSD and comorbid dissociative disorders showed greater impairments in attention, autobiographical memory, and verbal memory compared to those with PTSD alone (Roca et al., 2006). Similar results were observed for individuals with depression, trauma history and dissociative symptoms (Parlar et al., 2016).

Recognizing the significance of dissociative symptoms, the DSM-5 introduced a dissociative PTSD subtype (PTSD-DS), characterized by depersonalization and derealization (American Psychiatric Association, 2013). Recent research additionally suggests that in individuals with severe PTSD, dissociative symptoms beyond depersonalization and derealization are highly prevalent, including auditory-verbal hallucinations, identity confusion, and dissociative amnesia (Kratzer et al., 2024). Dissociative disorders – predominantly dissociative identity disorder (DID) – are often regarded as a particularly severe consequence of trauma, closely linked to early and severe trauma exposure as well as greater psychopathology severity (Dalenberg et al., 2012; Vissia et al., 2016). Despite these findings,

the relationship between dissociation and long-term cognitive decline or dementia risk remains poorly understood and warrants further investigation (McKinnon et al., 2016).

1.3.2.3. Depression

Depression is well-documented as a risk factor for cognitive impairment and dementia, affecting executive function, memory, and attention (Marazziti et al., 2010; Rock et al., 2014). It also is one of the 14 modifiable risk factors for all-cause dementia identified by the Lancet Commission for dementia prevention, intervention, and care (Livingston et al., 2024). More research on depression and cognitive impairment or dementia is available than for ACEs, PTSD, and dissociative disorders. For instance, one study found that greater cognitive reserve, based on education, occupational complexity, and cognitive and leisure activities, attenuates depression-associated risk of developing dementia (Jia et al., 2022).

Importantly, however, depression is frequently comorbid with PTSD (Flory & Yehuda, 2015) and dissociative disorders (Şar, 2014). Studies on PTSD and dementia have typically adjusted for depression (Bhattarai et al., 2019; Flatt et al., 2018; H. Kim et al., 2023; Mawanda et al., 2017; Meziab et al., 2014; Wang et al., 2016; Yaffe et al., 2010) with risk of dementia associated with PTSD remaining significantly increased. Two studies found that the risk of dementia is further increased in people with PTSD and comorbid depression (Flatt et al., 2018; Wang et al., 2016), one study specifically examined older female veterans with PTSD-only and depression-only diagnoses and found that both disorders independently increased the risk of dementia (Yaffe et al., 2019).

ACEs, PTSD, dissociative disorders, and depression may all contribute to cognitive decline and dementia risk by reducing cognitive reserve formation (Stern, 1994, 2002; Tucker & Stern, 2011). They may promote social withdrawal, lower educational attainment, and fewer cognitively stimulating activities, diminishing the brain's ability to compensate for neurodegenerative changes (Almeida-Meza et al., 2021). However, the interplay between

PTSD, depression, dissociation, and dementia risk remains an open question, requiring further research.

1.4. Aims of the Thesis

Previous research suggests a relationship between traumatic stress and trauma-related psychopathology on the one hand, and an increased risk of cognitive impairment and dementia on the other hand. However, the nature of this relationship remains unclear. Specifically, it is unknown whether certain direct associations exist (e.g., whether dissociative disorders are linked to an increased risk of incident dementia), and which factors contribute to, mitigate, or exacerbate these associations. There is limited knowledge on the contribution of various trauma-related, behavioral, and psychosocial factors that are implicated in deterioration of cognitive outcomes and increased dementia risk.

This thesis aims to provide a deeper understanding of the relationship between PTSD, cognitive impairment and dementia by adopting a broader framework of risk factors and methodological approaches using longitudinal data. While PTSD remains the central focus, the thesis takes a more comprehensive view on traumatic stress and trauma-related psychopathology by incorporating:

- Adverse Childhood Experiences (ACEs) as a precursor of trauma-related pathology.
- PTSD, examined comprehensively as the primary research focus.
- Dissociative disorders, conceptualized as a particularly severe trauma-related pathology.
- Depression, given its frequent comorbidity with PTSD and dissociative disorders.

Furthermore, PTSD is examined beyond categorical diagnosis by considering:

- Symptom clusters and individual symptoms as defined by the DSM-5 (American Psychiatric Association, 2013).

- Symptom severity rather than relying solely on the diagnostic status.

Additionally, the thesis also examines how these trauma-related disorders interplay in their association with dementia, while accounting for behavioral, psychosocial, and health-related factors that may influence these relationships.

With trauma experiences continuing to be ubiquitous, the global population and life expectancy steadily increasing, and cognitive impairment being linked to numerous adverse consequences – including an increased risk of dementia in later life – yet no cure for dementia currently available, gaining a better understanding of trauma-related cognitive decline is essential.

Specifically, the thesis comprises three empirical studies, each addressing different aspects of the relationship between trauma-related psychopathology and cognitive decline.

Study I

Study I examined the relationships between PTSD symptom clusters, individual symptoms, and overall symptom severity, as defined by the DSM-5, and subjective cognitive functioning. Based on data of nearly 1,500 older U.S. veterans who were followed over a three-year period, cross-sectional and longitudinal network models were estimated to analyze these associations (Fried et al., 2017).

Study II

Study II used data from the United Kingdom (UK) Biobank, a large-scale cohort of approximately 500,000 participants from the general UK population. This study investigated whether ACEs, PTSD, dissociative disorders, and depression are independently associated with an increased risk of all-cause incident dementia. This is the first study, to date, to examine dissociative disorders as a potentially modifiable risk factor for dementia. Additionally, mediation analyses explored whether PTSD and dissociative disorders mediate the association between ACEs and dementia; as well as whether depression is a mediator of the associations between ACEs and dementia, PTSD and dementia, and dissociative disorders and dementia.

Study III

Study III also used UK Biobank data to investigate potential moderators in the associations between trauma-related psychopathology and cognitive outcomes. Specifically, this study examines the role of various demographic, behavioral, and psychosocial factors in moderating the relationships between ACEs, PTSD, dissociative disorders, and depression as predictors and three key outcomes: objective cognitive functioning (reaction time, visual memory, and reasoning ability), all-cause incident dementia, and left and right hippocampal volume.

By integrating diverse predictors, mediators, and moderators, the findings from these three studies contribute to the existing literature on traumatic stress, trauma-related psychopathology, and cognitive aging. Ultimately, this research aims to inform targeted prevention and intervention strategies that may improve cognitive health and mitigate dementia risk in individuals affected by trauma.

2. Cumulative Publications of the Thesis

Study I:

Using network models to explore the associations between posttraumatic stress disorder symptoms and subjective cognitive functioning

This chapter is a post-peer-review, pre-copyedit version of an article published in *Journal of Anxiety Disorders*.

Data, code, and materials are available online (https://osf.io/5w6k4/), and the study was pre-registered (https://aspredicted.org/n5sw7.pdf).

Günak, M. M., Ebrahimi, O. V., Pietrzak, R. H., & Fried, E. I. (2023). Using network models to explore the associations between posttraumatic stress disorder symptoms and subjective cognitive functioning. *Journal of Anxiety Disorders*, *99*, 102768. https://doi.org/10.1016/j.janxdis.2023.102768

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Abstract

Several studies have identified relationships between posttraumatic stress disorder (PTSD) and cognitive functioning. Here, we aimed to elucidate the nature of this relationship by investigating cross-sectional associations between subjective cognitive functioning (SCF) and 1) the PTSD sum score, 2) symptom domains, and 3) individual symptoms. We also investigated temporal stability by testing whether results replicated over a 3-year period. We estimated partial correlation networks of DSM-5 PTSD symptoms (at baseline) and SCF (at baseline and follow-up, respectively), using data from the National Health and Resilience in Veterans Study (NHRVS; N = 1,484; Mdn = 65 years). The PTSD sum score was negatively associated with SCF. SCF was consistently negatively associated with the PTSD symptom domains 'marked alterations in arousal and reactivity' and 'negative alterations in cognitions and mood', and showed robust relations with the specific symptoms 'having difficulty concentrating' and 'trouble experiencing positive feelings'. Results largely replicated at the 3-year follow-up, suggesting that some PTSD symptoms both temporally precede and are statistically associated with the development or maintenance of reduced SCF. We discuss the importance of examining links between specific PTSD domains and symptoms with SCF—relations obfuscated by focusing on PTSD diagnoses or sum scores—as well as investigating mechanisms underlying these relations.

1. Introduction

Posttraumatic stress disorder (PTSD) may arise in response to a traumatic event such as life-threatening violence, combat, abuse, or injury (American Psychiatric Association, 2013). According to the DSM-5, symptoms are clustered into four domains: intrusions, avoidance of reminders and distressing memories of the trauma, negative alterations in cognitions and mood, and alterations in arousal and reactivity (American Psychiatric Association, 2013). Varying greatly across trauma types, the conditional risk for developing PTSD after any trauma exposure is estimated to be 4.0%, and 3.5% after any lifetime war-related trauma exposure (Kessler et al., 2017). Delay in treatment for PTSD is common (Wang et al., 2005), often resulting in a chronic condition accompanied by impairments across a range of areas, including cognitive functioning, daily living, and mental health-related quality of life (Hunnicutt-Ferguson et al., 2018; Pittman et al., 2012; Qureshi et al., 2011; Ross et al., 2018).

Cognitive impairment in PTSD has attracted attention in recent years. Several studies have found impairment across cognitive domains in both veteran and non-military populations with PTSD compared to those without, including impairments in (working) memory, attention, learning, executive function, and processing speed, assessed using neuropsychological tests (Clouston et al., 2016; Cohen et al., 2013; Koso & Hansen, 2006; Samuelson et al., 2006; Schuitevoerder et al., 2013; Vasterling et al., 1998, 2012, 2018; Yehuda et al., 2005), traditionally assessed using behavioral and computerized tasks (Schuitevoerder et al., 2013; Scott et al., 2015), which have been considered the gold standard to assess specific cognitive functions (Savard & Ganz, 2016). PTSD has also been associated with *subjective* cognitive difficulties (Boals & Banks, 2012; Singh et al., 2020; Vasterling et al., 2012), which, in turn, have been shown to predict future objective cognitive decline and dementia (Jessen et al., 2010; Koppara et al., 2015; Mitchell et al., 2014). While less often investigated, everyday subjective cognitive concerns likely represent different—though also valid and relevant—facets of cognition relative to those assessed in the lab (Carrigan & Barkus, 2016). In fact, some of the

subjective difficulties may be too subtle to be detected by objective neuropsychological assessment (Geerlings et al., 1999) and only noted by the individual (Molinuevo et al., 2017); such difficulties can indicate early-stage cognitive impairment (Singh et al., 2020). Another advantage of subjective cognitive assessment is that this is much more feasible in clinical practice (Silverberg et al., 2017). Studies increasingly indicate that both objective and subjective cognitive measures have their benefits and limitations, and are not interchangeable (Hess et al., 2020; Lau et al., 2021; Savard & Ganz, 2016).

Most prior studies have examined the association between a diagnosis of PTSD and cognitive functioning. The few studies that have decomposed PTSD into symptom domains[1] have found that intrusive symptoms in particular are strongly linked to cognitive difficulties (Boals, 2008; Bomyea et al., 2012; Clouston et al., 2016, 2019; Johnsen et al., 2008; Kivling-Bodén & Sundbom, 2003; Parslow & Jorm, 2007; Saltzman et al., 2006; Vasterling et al., 1998). Both intrusive and hyperarousal symptoms have been suggested to compete for attentional resources with ongoing cognitive processes (Boals, 2008; Boals & Banks, 2012; Kolb, 1987). This may be associated with a reduced ability to inhibit reactions to irrelevant information (Vasterling et al., 1998) and regulate the content of cognition (Bomyea et al., 2012). Yet, evidence is inconsistent whether hyperarousal symptoms are related to impaired cognitive functioning (Bomyea et al., 2012; Clouston et al., 2016; Judah et al., 2018; Kivling-Bodén & Sundbom, 2003; Parslow & Jorm, 2007; Vasterling et al., 1998; Wrocklage et al., 2016). Vasterling and colleagues (1998) found that in Persian Gulf War veterans, such disinhibition was negatively associated with avoidance-numbing symptoms, which may reflect the tendency to avoid (i.e., inhibit), at least superficially, intense trauma-related experiences and thereby,

[1] In this paper, symptom domains correspond to symptom clusters as defined in the DSM-5.

preserve cognitive functioning. Other studies found no link between avoidance and cognitive functioning (Boals, 2008; Bomyea et al., 2012; Clouston et al., 2016; Wrocklage et al., 2016).

In addition to these mixed findings, research has generally focused on the dichotomy between individuals with a diagnosis of a mental disorder and those without (Armour et al., 2017). Most mental health studies are based on case-control or randomized controlled trial study designs. This is suboptimal, however, as not all treatment-seeking individuals meet diagnostic criteria for mental disorders. Additionally, there are 636,120 possible symptom combinations that qualify for a DSM-5 PTSD diagnosis alone (Galatzer-Levy & Bryant, 2013), calling into question the usefulness of categorical diagnoses for research purposes. The heterogeneity of symptom presentations has led to ongoing debates about the validity and reliability of DSM diagnostic criteria, both in general (Insel, 2013) and specific to PTSD (Armour, Contractor, et al., 2016; Armour, Műllerová, et al., 2016). Taken together, this work suggests that there may be value in trying to understand the relation between PTSD symptoms with cognitive functioning by examining the symptoms people experience, both within their domains and individually, rather than as a more diffuse, homogeneous syndrome.

Statistical network models lend themselves well as a tool to examine the link between individual PTSD symptoms and cognitive functioning. First, they are well suited to model a larger number of variables simultaneously. Second, commonly used network models are conditional dependence models, i.e., they estimate the link between two variables A and B after controlling for all other variables in the network, helping to identify potential mechanisms. Finally, network models can visualize statistical relations, which can guide interpretation of highly multivariate dependency structures (Borsboom, 2017; Fried et al., 2017). Non-technical introductions to network analyses can be found in Isvoranu et al. (2022) (Isvoranu et al., 2022).

To date, no known published network analysis study has investigated the link between PTSD symptoms and (subjective) cognitive functioning. Moreover, the majority of previous (non-network) studies have used cross-sectional designs to examine this association

(Schuitevoerder et al., 2013). Although existing cohort studies indicate longitudinal associations between the two constructs (Gould et al., 2019; Vasterling et al., 2018), little is known whether PTSD-related (subjective) cognitive impairment is stable over time. Clarifying the associations of PTSD symptom domains and specific symptoms with subjective cognitive functioning (SCF), and their temporal relations, may facilitate future work to identify individuals with PTSD who may be at risk of cognitive decline, and guide individualized treatment planning (Fried et al., 2017; Kivling-Bodén & Sundbom, 2003).

The aim of the present study is to identify specific PTSD symptoms and symptom domains that are associated with SCF, and to investigate temporal stability of the relations by analyzing a second wave of data three years later. We investigated four specific research questions (RQs): (1) Is overall severity of PTSD symptoms associated with SCF in U.S. veterans; (2) which PTSD symptom domains are most strongly related to SCF; (3) which individual PTSD symptoms are most robustly associated with SCF; and (4) do the findings of questions 1-3 hold over a three-year follow-up? We predicted that the overall severity of PTSD symptoms would be negatively associated with SCF; that the symptom domain of intrusion shows the strongest overall link to reduced SCF compared to other symptom domains; and that the associations of the estimated network models at baseline (i.e., Wave 1) will hold at a three-year follow-up (i.e., Wave 2). The main analyses of the present study were pre-registered (https://aspredicted.org/n5sw7.pdf). All data, code, measures, and supplementary materials (Appendix A) are freely accessible online (https://osf.io/5w6k4/).

2. Methods

2.1. Participants and Procedure

We analyzed data drawn from the second cohort of the National Health and Resilience in Veterans Study (NHRVS), a survey of a nationally representative sample of U.S. military

veterans (Wisco et al., 2016). This prospective cohort was recruited in September and October 2013 (i.e., baseline; Wave 1) from a research panel of U.S. households that has been developed and maintained by Growth for Knowledge (GfK) Incorporated (now Ipsos), a survey research company based in Menlo Park, California (*GfK Knowledge Networks*, 2020). Panel members were employed through a sampling procedure that includes listed and unlisted phone numbers; telephone, non-telephone, and cell-phone only households; and households with or without Internet access, allowing coverage of approximately 98% of U.S. households. Of 1,602 veterans who were in the survey panel when the NHRVS cohort was recruited, 1,484 (92.6%) took part in the NHRVS and completed a confidential, 60-min Web-based survey that assessed a range of sociodemographic, psychiatric and health variables. The cohort was re-assessed in September and October 2016 (i.e., follow-up; Wave 2). A total of 713 (48.0%) veterans completed both assessments at baseline and follow-up. All participants provided informed consent. The Human Subjects Subcommittee of the Veterans Affairs (VA) Connecticut Healthcare System and VA Office of Research & Development approved the study.

2.2. Measures

2.2.1. Lifetime Exposure to Trauma

The 14-item self-report measure Trauma History Screen (THS) (Carlson et al., 2011) assesses lifetime exposure to 14 DSM-5 Criterion A-qualifying trauma events for PTSD (*Yes/No*) (American Psychiatric Association, 2013). It includes traumatic experiences across the lifespan such as physical or sexual assault, accidents, traumatic incidences during military service, and unexpected loss of a close person. “Life-threatening illness or injury” was added as a potentially traumatic event before data collection, given a sample of older military veterans. Participants who endorsed multiple traumatic experiences were asked, “Which of these experiences was the worst for you?”.

2.2.2. PTSD symptoms

The PTSD Checklist-5 (PCL-5) is a self-report measure that assesses the presence and severity of PTSD symptoms (Weathers et al., 2013). It comprises 20 items, which are rated on a 5-point Likert scale ranging from 0 (*Not at all*) to 4 (*Extremely*). The items on the PCL-5 assess individual DSM-5 symptoms of PTSD and represent clusters B-E (i.e., 'intrusion', 'persistent avoidance', 'negative alterations in cognitions and mood', 'marked alterations in arousal and reactivity') (American Psychiatric Association, 2013; Weathers et al., 2013). In the NHRVS cohort, the PCL-5 was modified to include both lifetime (at baseline) and past-month (at baseline and follow-up) ratings of PTSD symptoms with regards to respondents' self-selected "worst" stressful experience identified on the THS. Higher sum scores indicate greater severity of PTSD symptoms. Internal consistency was excellent for baseline past-month and lifetime PCL-5 (Cronbach's $\alpha = .95$, respectively). Probable PTSD was determined as a past-month PCL-5 sum score of ≥31, as recommended by previous evidence (Bovin et al., 2016). While this cut-off score served to identify participants with probable PTSD to describe the sample, no cut-off score was applied for the analyses to examine the relationship between PTSD on a dimensional continuum rather than categorically. Thus, all participants in the sample who were exposed to trauma and consequently filled out the PCL-5 were included in the study. This also mitigates the impact of Berkson's bias, which threatens inferences when including participants based on a specific threshold of symptoms (De Ron et al., 2021).

2.2.3. Cognitive Functioning

One subscale of the Medical Outcomes Study scale assesses past-month cognitive functioning (MOS-CF) and is a self-report measure encompassing six Likert-type items on difficulties in the following cognitive domains: reasoning, memory, attention, concentration and thinking, confusion, psychomotor speed (Averill et al., 2019; Stewart & Ware, 2017). Sample item: "During the past month, how much of the time did you forget (e.g., things that

happened recently, where you put things, appointments)?" The responses to the individual items were standardized to a scale ranging from 0 (*All of the time*) – 100 (*None of the time*), and then averaged (Hays et al., 1995). The MOS-CF has been shown to be a reliable and valid measure (Revicki et al., 1998; Yarlas et al., 2013). Internal consistency in our data was excellent at baseline and follow-up (Cronbach's $\alpha = .93$, respectively).

2.2.4. Covariates

Age, sex, level of education, depression and alcohol misuse were included as pre-registered covariates. A demographic questionnaire assessed, amongst others, the first three covariates. Lifetime history of major depressive disorder and alcohol abuse/dependence were measured with the Mini International Neuropsychiatric Interview for DSM-IV (Sheehan et al., 1998).

2.3. Statistical Analysis

We compared baseline and follow-up sample characteristics using the Wilcoxon Signed-Rank Test, the McNemar, and the McNemar's-Bowker test. Additionally, to test for systematic dropout, we compared baseline characteristics (i.e., age, sex, race/ethnicity, level of education, employment, number of lifetime traumatic events, combat exposure, lifetime major depressive episode and alcohol abuse/dependence, past-month and lifetime PCL-5 sum scores, probable PTSD, and MOS-CF average scores) of veterans who completed the follow-up assessment relative to those who did not, using the Mann-Whitney U test and Chi-squared test.

To test whether severity of overall PTSD symptoms was associated with SCF cross-sectionally and longitudinally, three years later (RQ1 and RQ4), we computed Spearman correlations between PTSD (past-month and lifetime PCL-5 sum scores) at baseline and SCF (MOS-CF mean scores) at baseline and follow-up, respectively; we used Spearman correlations because distributions of PCL-5 and MOS-CF items were skewed and were measured on an ordinal scale.

2.3.1. Network Estimation

For RQ2, RQ3, and RQ4—which symptom domains/individual PTSD symptoms are most strongly associated with SCF and whether these associations persist at follow-up—we estimated two types of networks (see Table 1.1 for an overview). Network 1 included baseline past-month PCL-5 items and SCF scores. Network 2 included baseline past-month PCL-5 items and follow-up SCF scores. We use the term "cross-sectional network models" if all included variables were measured at Wave 1 (i.e., baseline) and "longitudinal network models" if associations between the variables of interest were assessed across two waves (i.e., baseline and three-year follow-up). We estimated network models based on Spearman correlations (Epskamp & Fried, 2018) and controlled for all preregistered covariates in each network. In network models, 'nodes' represent variables and 'edges' between these nodes conditional dependence relations (akin to partial correlations), which are associations between nodes after controlling for the influence of all other nodes (i.e., variables) (Epskamp et al., 2018; Epskamp & Fried, 2018). As the data involves mostly ordinal variables, we estimated the networks by means of the Gaussian Graphical Model (GGMs) with the R-package *bootnet* (Epskamp et al., 2018). Sex, level of education, lifetime depression, and lifetime alcohol abuse/dependence were treated as ordinal. To avoid false positive findings and reduce the risk of overfitting, we estimated GGMs by using the 'least absolute shrinkage and selection operator' (LASSO) (Tibshirani, 1996). LASSO shrinks all coefficients towards zero and sets small weights exactly to zero. The strength of the shrinkage is controlled via the tuning parameter λ, which is selected by minimizing the Extended Bayesian Information Criterion (EBIC) (Chen & Chen, 2008; Epskamp et al., 2018; Epskamp & Fried, 2018; Foygel & Drton, 2010). The EBIC itself involves γ, a hyperparameter that controls to what extent the EBIC favors simpler models with fewer edges, which was set to 0.5 (the default setting) for all network analyses.

2.3.2. Network Inference

To test which PTSD symptom domain was most strongly associated with SCF scores (RQ2), we computed average connectivity of each symptom domain with SCF scores. That is, signed values of edge weights between all PTSD symptoms of a domain and SCF scores were summed and then divided by the total number of potential edges within that domain (that is, domains with more variables are penalized, otherwise they are more likely to relate to SCF simply because they have more nodes). Differences in average connectivity between PTSD symptom domains and SCF scores were bootstrapped with 1000 iterations using the R-package *bootnet* (Epskamp et al., 2018). As a minor deviation from the pre-registration, we used signed rather than absolute edge weight values in these calculations, given that negative and positive edges are meaningfully different here.

We estimated node predictability using the *mgm* R-package which can be interpreted akin to R^2, quantifying how well a node can be predicted by other nodes (Haslbeck & Fried, 2017; Haslbeck & Waldorp, 2018).

We quantified the accuracy of estimated edge weights using bootstrapping routines from the *bootnet* R-package (Epskamp et al., 2018), see Supplementary Materials (Appendix A) for details (https://osf.io/5w6k4/).

2.3.3. Network visualization

We visualized all resulting associations as network graphs using the R-package *qgraph*. The layout was constrained across all figures, and we set the same maximum value as the strongest edge in all networks, to allow for comparisons between the network structures.

2.3.4. Network Comparison Test

To investigate temporal stability (RQ4), we statistically compared Network 1 with Network 2. First, to obtain a coefficient of similarity for the networks, we computed Spearman correlations of the adjacency matrices. Second, we tested whether network models 1 and 2 differed from one another, using the R-package *NetworkComparisonTest* (NCT) (van Borkulo

et al., 2017); NCT is a permutation test, and we used 1000 iterations. By the time of the preregistration, samples for Networks 1 and 2 needed to have equal size. We deviate from the preregistration and include a larger sample for Network 1, because the NCT-package no longer requires this restriction. We tested whether the two network models had equal global strength (i.e., sum of signed edge weight values) and edge weight distributions (i.e., network structure). If the network structures differed statistically significantly, we specifically investigated individual edges.

2.3.5. Missing Data

Our pre-registration protocol did not specify how missing data would be handled. We used multiple imputation by chained equations to impute missing past-month and lifetime PCL-5 item values prior to analysis for participants who were missing less than 5% of data. For further details and an overview of sample sizes for each analysis, see Supplementary Materials (Appendix A; https://osf.io/5w6k4/).

2.3.6. Robustness Analyses

We performed several analyses to assess the robustness of the results. Our main models were estimated regularized network models without thresholding, which are the default in the literature. However, since recent research identified potential problems with regularization under specific scenarios (Williams et al., 2019), we also used alternative approaches to estimate network models with 1) thresholding (Epskamp, 2018; Epskamp & Fried, 2018; Muthén, 1984) and 2) using *ggmModSelect* (Epskamp, 2018), see Supplementary Materials (Appendix A) for more information (https://osf.io/5w6k4/). Second, we computed Spearman correlations between the adjacency matrices of PTSD symptoms at baseline and three-year follow-up to estimate similarity between the two, followed by repeating all the above analyses with PTSD symptoms assessed during lifetime rather than last month (i.e., Network 3: lifetime PCL-5 with SCF scores at baseline; Network 4: lifetime PCL-5 at baseline with SCF at follow-up, see Table

1.1). Third, we correlated SCF at baseline and at follow-up; this was followed by repeating the analyses of the two longitudinal networks of past-month and lifetime PCL-5 at baseline with SCF at follow-up (i.e., Networks 2 and 4)—but this time additionally adjusting for SCF at baseline. In total, we estimated six network models, see Table 1.1 for an overview. Fourth, we compared cross-sectional (i.e., Network 1 with Network 3), and longitudinal networks (i.e., Network 2 with Network 4, both with and without adjusting for SCF at baseline) using NCT. The R-package NCT currently cannot compare network models that do not contain an equal number of variables. Hence, the re-estimated longitudinal networks taking SCF at baseline into account cannot be compared to the cross-sectional models (which had one variable less), and therefore, were included as robustness analyses. Finally, we repeated the above analyses on the subsample of 91% (or more depending on the subsample) individuals with complete (i.e., non-imputed) data.

Table 1.1

Overview of the Six Network Models

Network	PTSD Symptoms	Cognitive Functioning
1	PCL-5[a] past-month	MOS-CF[a]
2	PCL-5[a] past-month	MOS-CF[b]
2_{adj}	PCL-5[a] past-month	MOS-CF[b,c]
3	PCL-5[a] lifetime	MOS-CF[a]
4	PCL-5[a] lifetime	MOS-CF[b]
4_{adj}	PCL-5[a] lifetime	MOS-CF[b,c]

Note. PTSD = Posttraumatic stress disorder; PCL-5 = DSM-5 PTSD Checklist; MOS-CF = Medical Outcomes Study – Cognitive Functioning scale. Each estimated network model is adjusted for age, sex, level of education, lifetime depression, and lifetime alcohol abuse/dependence. We use the term "cross-sectional network model" for models 1 and 3, and "longitudinal network model" for models 2, 2_{adj}, 4 and 4_{adj}.

[a]Wave 1, baseline; [b]Wave 2**,** three-year follow-up; [c]additionally adjusted for SCF at baseline.

The analyses were conducted in June 2022, using R (version 4.2.0) for all statistical analyses except for the Wilcoxon Signed-Rank Test, the McNemar, and the McNemar-Bowker test, which were performed using SPSS (version 28.0.1.1). All R-packages and versions can be found online (https://osf.io/5w6k4/).

3. Results

3.1. Sample Characteristics

Respondents were predominantly non-combat veterans (61.7%), male (89.4%), non-Hispanic White (81.1%), and older adults, with a median age of 65 years (*IQR* = 54–73 years); see Table 1.2 for baseline characteristics. Of the 1,484 veterans, 1,268 (85.4%) had been exposed to at least one traumatic event at baseline and on average, experienced approximately three such events. Types of trauma experienced are listed online (https://osf.io/5w6k4/). Participants of the 3-year follow-up significantly differed from those at baseline on three variables: race/ethnicity (p = .046), with fewer non-Hispanic veterans at follow-up; reduced SCF (p = .002), likely explained by aging; and employment (p < .001) with more veterans being retired and fewer currently looking for work.

Table 1.2

Baseline Characteristics

	Entire Sample (N = 1,484)	Participants Exposed to Trauma (n = 1,268)
Age		
Median (*IQR*)	65 (54-73)	65 (54-73)
Mean (*SD*)	62.8 (14.7)	62.8 (14.6)
Female, *n* (%)	158 (10.6)	132 (10.4)
Race/Ethnicity, *n* (%)		
Non-Hispanic White	1,204 (81.1)	1028 (81.1)
Non-Hispanic Black	112 (7.5)	95 (7.5)

	Entire Sample (N = 1,484)	Participants Exposed to Trauma (n = 1,268)
Hispanic	99 (6.7)	85 (6.7)
Other, Non-Hispanic	23 (1.5)	20 (1.6)
2+ Races, Non-Hispanic	46 (3.1)	40 (3.2)
Education, *n* (%)		
Less than high school	26 (1.8)	23 (1.8)
High school	211 (14.2)	174 (13.7)
Some college	629 (42.4)	548 (43.2)
Bachelor's degree or higher	618 (41.6)	523 (41.2)
Employment, *n* (%)		
Working	476 (32.1)	403 (31.8)
Retired	718 (48.4)	604 (47.6)
Not working	290 (19.5)	261 (20.6)
Number of lifetime traumatic events		
Median (*IQR*)	3.0 (1.0-5.0)	3.0 (2.0-5.0)
Mean (*SD*)	3.3 (2.8)	3.9 (2.7)
Combat exposure, *n* (%)	564 (38.0)	508 (40.1)
Major depressive episode (lifetime), *n* (%)	137 (9.2)	131 (10.3)
Alcohol abuse/dependence (lifetime), *n* (%)	542 (36.5)	490 (38.6)
PCL-5 (past month)		
Median (*IQR*)	4.5 (1.0-13.0)	4.5 (1.0-13.0)
Mean (*SD*)	9.7 (13.0)	9.7 (13.0)
Probable PTSD, *n* (%)	93 (6.3)	93 (7.3)
PCL-5 (lifetime)		
Median (*IQR*)	9.0 (4.0-19.0)	9.0 (4.0-19.0)
Mean (*SD*)	14.1 (14.6)	14.1 (14.6)
MOS-CF		
Median (IQR)	96.7 (86.7-100.0)	96.7 (83.3-100.0)
Mean (SD)	90.0 (15.0)	89.1 (15.5)
MOS-CF – Wave 2		
Median (*IQR*)	96.7 (86.7-100.0)	95 (85.8-100.0)
Mean (*SD*)	89.5 (15.3)	89.2 (15.5)

Note. N = sample size; IQR = Interquartile range; SD = standard deviation; PCL-5 = PTSD Checklist-5; MOS-CF = Medical Outcomes Study – Cognitive Functioning scale.

Veterans who did not complete the follow-up assessment did not differ significantly from those who did with respect to most sociodemographic or clinical variables, except for employment (p = .017), past-month PCL-5 sum scores (p = .024), and MOS-CF average scores (p = .043). Details can be found in Supplementary Materials (Appendix A; https://osf.io/5w6k4/).

The main results will be presented in the following order: the overall association between SCF and the sum score of PTSD symptoms (RQ1); results of the network analyses, including the associations between SCF and both individual PTSD symptoms and PTSD symptom domains (RQ3, RQ2); followed by testing the temporal stability of the associations over three years (RQ4).

3.2. Overall Association between PTSD and SCF

Associations between PTSD and SCF were of similar magnitude for past-month and lifetime PTSD scores. At baseline, past-month and lifetime PCL-5 sum score were negatively associated with MOS-CF scores (r = −0.58 and −0.54, respectively, both p < .001). Similarly, baseline past-month and lifetime PTSD symptoms were each negatively associated with MOS-CF scores at three-year follow-up (r = −0.32 and −0.33, respectively, both p < .001). Our hypothesis of a negative relationship between the total PTSD symptom score and SCF was supported (RQ1), and they remained negatively associated at follow-up (RQ4).

3.3. Individual PTSD Symptoms and SCF

We report edge weights and predictability values that were most relevant to our research questions. Unless stated otherwise, edge weights represent negative relationships. Figure 1.1 shows Networks 1 and 2. Edges between SCF and PTSD mostly emerged for symptoms of 'alterations in arousal and reactivity', and 'negative cognitions and mood' (RQ2, RQ3), with similar findings at follow-up (RQ4). At baseline, 182 (56.0%) of 325 possible edges were estimated to be non-zero, with an overall mean edge weight of the respective network model of 0.025. At follow-up, these values were 178 (54.8%) and 0.027, implying a similar level of sparsity. With the aim to identify consistent, robust edges across network models, we defined robustly estimated (thereafter: "robust") edges as above the overall average edge weight of the respective network model; we consider these edges robust in the sense that they are reliably estimated above zero. Table 1.3 provides an overview of such robust edges between individual PTSD symptoms and SCF for each network model, and all edge weights of each network model can be found in Supplementary Materials (Appendix A; https://osf.io/5w6k4/).

In both network models 1 and 2, robust edges emerged between SCF and the two PTSD symptoms 'having difficulty concentrating' (E5) and 'trouble experiencing positive feelings' (D7). In Network 1, robust edges were found between SCF and 'irritable behavior, angry outbursts, or acting aggressively' (E1), 'avoiding memories, thoughts, or feelings related to the stressful experience' (C1), 'trouble falling or staying asleep' (E6), 'feeling jumpy or easily startled' (E4), 'trouble remembering important parts of the stressful experience' (D1), and 'loss of interest in activities that you used to enjoy' (D5). In Network 2, robust edges were found between SCF at follow-up and 'having strong negative beliefs about yourself, other people, or the world' (D2) and 'blaming yourself or someone else for the stressful experience or what happened after it' (D3).

Similarity between the adjacency matrices of PCL-5 in the past month and during lifetime (i.e., network models estimated based on PCL-5 past month and lifetime, respectively,

excluding SCF and covariates) was high (r = 0.79). Figure 1.2 shows the estimated networks of lifetime PTSD symptoms and SCF at baseline (Network 3; panel A) vs. SCF at follow-up (Network 4; panel B). In both networks, robust edges appeared between SCF and the three PTSD symptoms E5, D1, and D7. Thus, across network models 1 to 4, consistent, robust edges have been found between SCF and the two PTSD symptoms E5 and D7 (RQ3). Further information is provided in the Supplementary Materials (Appendix A; https://osf.io/5w6k4/).

There was a positive association between SCF at baseline and SCF three years later (r = 0.53, $p < .001$). We re-estimated the longitudinal networks of past-month (Network 2_{adj}) and lifetime (Network 4_{adj}) PTSD symptoms at baseline and SCF at follow-up, with additional adjustment for SCF at baseline. The magnitude of edge weights generally was attenuated in the adjusted network models 2 and 4. Robust edges emerged between SCF at follow-up and E5, D3, and D2 in Network 2_{adj} and 4_{adj}, and a robust edge between D7 and SCF at follow-up was found in Network 4_{adj}.

Table 1.3

Overview of Robust Edges between Individual PTSD Symptoms and SCF

PTSD Symptoms	Robust Edges with SCF in Network Models
B1–Intrusive memories	
B2–Nightmares	
B3–Flashbacks	N3
B4–Emotional cue reactivity	$N2_{adj}$ (positive), N3
B5–Physiological cue reactivity	N3
C1–Avoidance of thoughts	N1, N3
C2–Avoidance of reminders	
D1–Trauma-related amnesia	N1, N3, N4
D2–Negative beliefs	N2, $N2_{adj}$, N4, $N4_{adj}$
D3–Blame of self or others	N2, $N2_{adj}$, N4, $N4_{adj}$
D4–Negative trauma-related emotions	
D5–Loss of interest	N1, N3
D6–Detachment	
D7–Restricted affect	N1, N2, N3, N4, $N4_{adj}$
E1–Irritability/anger	N1, N3

E2–Self-destructive/reckless behavior	$N2_{adj}$ (positive)
E3–Hypervigilance	
E4–Exaggerated startle response	N1, N3
E5–Difficulty concentrating	N1, N2, $N2_{adj}$, N3, N4, $N4_{adj}$
E6–Sleep disturbance	N1

Note. PTSD = Posttraumatic stress disorder; SCF = Subjective cognitive functioning; N1 = Network 1 (past-month PTSD symptoms and SCF at baseline); N2 = Network 2 (past-month PTSD symptoms at baseline and SCF at follow-up; N3 = Network 3 (lifetime PTSD symptoms and SCF at baseline); N4 = Network 4 (lifetime PTSD symptoms at baseline and SCF at follow-up); adj = additionally adjusted for SCF at baseline.

List of symptoms based on the PTSD Checklist for DSM-5 (PCL-5). Edges are identified as "robust" if their weight is above the overall mean edge weight of the respective network model. Unless stated otherwise, edge weights are negative.

Node predictability of SCF for Networks 1 and 2 dropped from 60.1% (baseline) to 21.6% (follow-up). That is, at baseline, a large proportion of the variability in SCF was predominantly explained by PTSD symptoms and covariates, whereas over time this was reduced. Similar results were found for network models 3 and 4, with predictability of SCF changing from 52.6% (baseline) to 17.7% (follow-up). When added, SCF at baseline explained an additional eight to nine percent of the variance of SCF at follow-up (i.e., predictability was increased to 29.7% and 26.5% in Network 2_{adj} and 4_{adj}, respectively). We found similar results in the complete case analyses.

Across all network models, accuracy analyses revealed that the edge between E5 and SCF was stronger than all other edges between PTSD symptoms and SCF [see Figures in the Supplementary Materials (Appendix A) for Network 1, https://osf.io/5w6k4/].

Figure 1.1

Network Models: Past-Month PTSD Symptoms and Subjective Cognitive Functioning

Networks displaying the relationship between baseline past-month PTSD symptoms and subjective cognitive functioning (SCF) at baseline (Network 1; panel A) and SCF at follow-up (Network 2; panel B), after controlling for covariates. Blue lines indicate positive associations, dashed red lines negative associations, and thickness and brightness of an edge represent the association strength. Rings around nodes convey predictability, with shadowed parts depicting variance explained by connected nodes. For comparison, the maximum edge weight was set to the strongest edge across all estimated networks (0.36). For color, see online version.

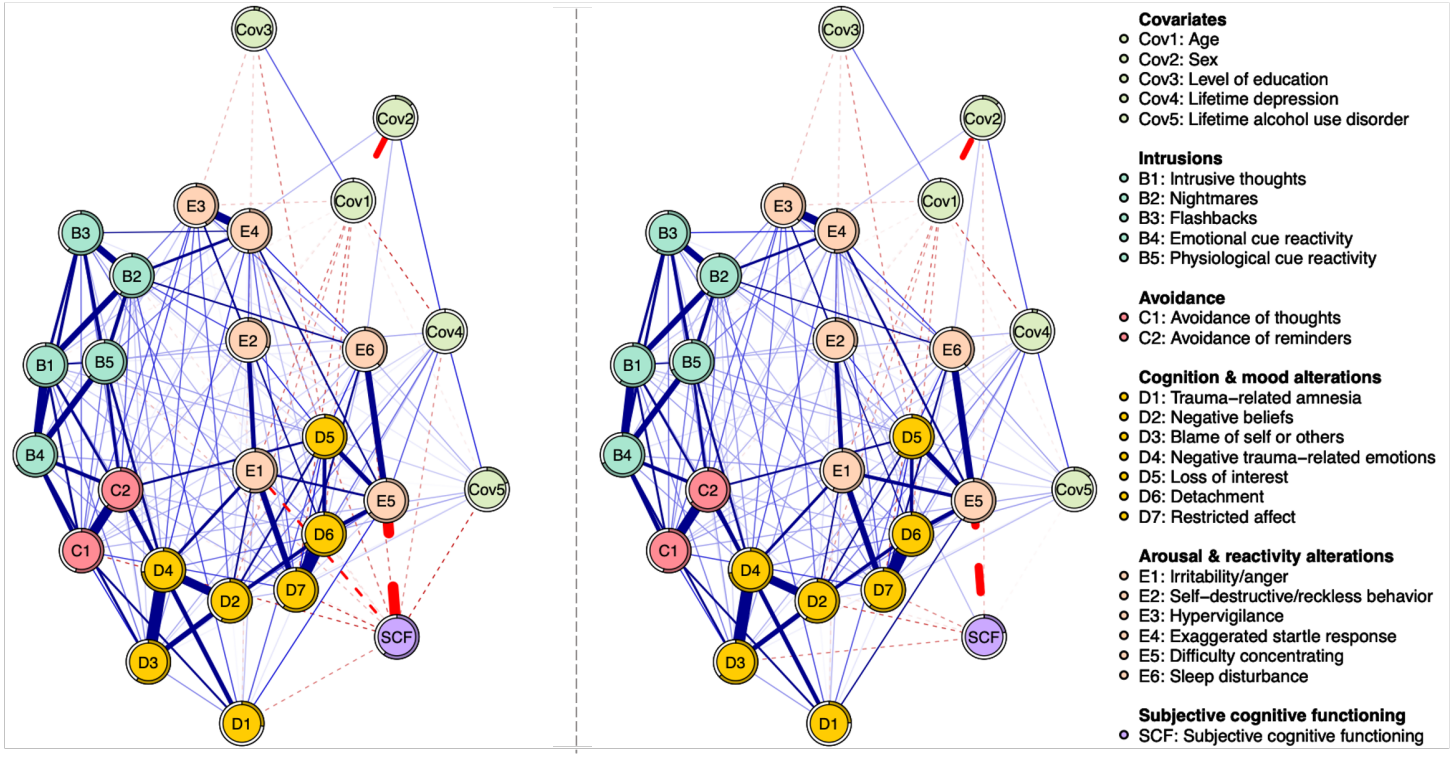
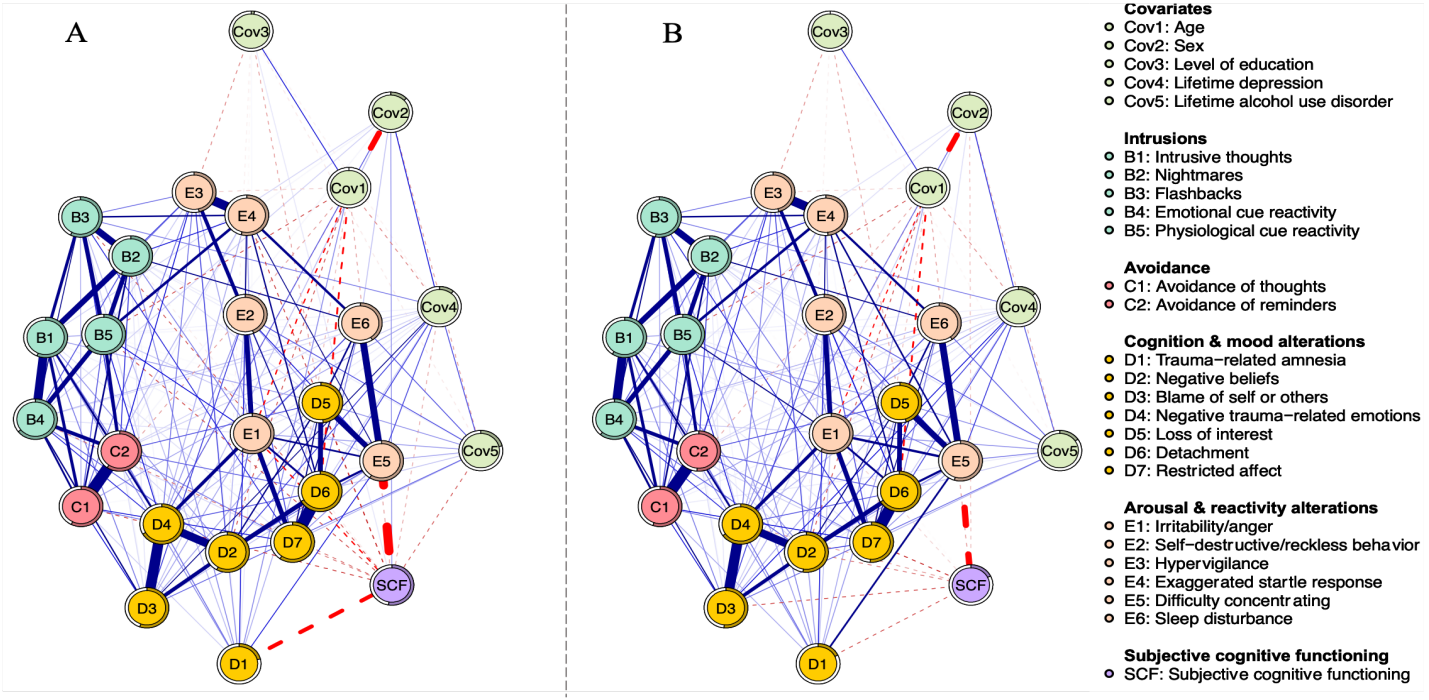


Figure 1.2

Network Models: Lifetime PTSD Symptoms and Subjective Cognitive Functioning

Networks displaying the relationship between baseline lifetime PTSD symptoms and subjective cognitive functioning (SCF) at baseline (Network 3; panel A) and SCF at follow-up (Network 4; panel B), after controlling for covariates. Blue lines indicate positive associations, dashed red lines negative associations, and thickness and brightness of an edge represent the association strength. Rings around nodes convey predictability, with shadowed parts depicting variance explained by connected nodes. For comparison, the maximum edge weight was set to the strongest edge across all estimated networks (0.36). For color, see online version.



3.4. PTSD Symptom Domains and SCF

Although mean differences in average connectivity (i.e., average edge weight) between PTSD symptom domains with SCF were small, we observed robust and consistent patterns based on bootstrapped confidence intervals. Cross-sectionally (Networks 1 and 3), the domain of 'alterations in arousal and reactivity' was most strongly associated with SCF (RQ2). Over the three-year follow-up (Networks 2, 2_{adj}, 4, and 4_{adj}), both symptom domains of 'alterations in arousal and reactivity', as well as 'negative cognitions and mood', were most strongly associated with SCF (RQ2, RQ4). Our hypothesis that 'intrusion' symptoms would be most strongly linked to SCF is therefore not supported (more detailed results are available in the Supplementary Materials; Appendix A; https://osf.io/5w6k4/). Results remained the same following complete case analyses.

3.5. Network Comparison Test

How stable were the relations between PTSD symptoms and SCF at baseline compared to 3 years later (RQ4)? Overall, results indicate considerable temporal stability. First, the two corresponding Networks 1 and 2 were nearly identical ($r = 0.97$), indicating temporal stability of the association between PTSD symptoms and SCF. However, according to the NCT, the two networks did significantly differ from each other regarding global strength ($p < .001$) and network structure ($p = .03$). Individual edges between SCF and PTSD symptoms that significantly differed between Networks 1 and 2 included B4, E1 and E2, of which E1 is a robust edge in Network 1. Comparing Networks 3 and 4 revealed differences regarding global strength ($p < .001$) but no differences in network structure ($p = .077$), with a strong correlation between the two ($r = 0.97$). Additionally, we formally compared the cross-sectional (Networks 1 and 3) and longitudinal network models (Networks 2 and 4; both with and without adjustment for SCF at baseline). Similarity was high within each pair of networks, with r~0.8 between the

respective adjacency matrices. The permutation tests of NCT revealed that global strength and network structure did not differ across networks within each pair ($p > .05$). The above results did not meaningfully change following the complete case analyses.

4. Discussion

Four core findings are worth noting. First, as hypothesized, having had PTSD symptoms both in the past month or during lifetime was significantly and negatively associated with SCF, with a correlation of ~0.6 at baseline and ~0.3 at follow-up. Second, we did not find support for the hypothesis that intrusive symptoms of PTSD are most strongly associated with SCF relative to other domains. Instead, the two symptom domains of 'alterations in arousal and reactivity' (in cross-sectional and longitudinal network models), as well as 'negative cognitions and mood' (in longitudinal network models), were most strongly related to reduced SCF. Third, various individual PTSD symptoms were negatively associated with SCF. Across estimated networks, the PTSD symptoms of 'difficulty concentrating' and 'trouble experiencing positive feelings' were consistently and robustly linked to reduced SCF. Cross-sectionally, additional PTSD symptoms associated with reduced SCF included 'irritable behavior, angry outbursts or acting aggressively', 'trouble remembering important parts of the stressful experience', 'avoiding memories, thoughts, or feelings related to the stressful experience', 'feeling jumpy or easily started', and 'loss of interest in activities'. At the three-year follow-up, the additional PTSD symptoms 'blaming yourself or someone else' and 'negative beliefs about yourself, other people, or the world' were linked to reduced SCF, with and without adjusting for baseline SCF. Fourth, the association between PTSD symptoms and reduced SCF held over a three-year follow-up. Across all models, node predictability of SCF remained substantial and findings largely replicated at follow-up, despite some differences in global strength and network structures.

Some of our results are consistent with prior literature. PTSD symptoms are associated with impaired cognitive functioning (Brewin et al., 2007; Schuitevoerder et al., 2013; Scott et al., 2015) and the association is stable over time (Gould et al., 2019; Vasterling et al., 2018), with the former predicting the latter in the present study. Our results are also in line with prior findings that the symptom domain of 'avoidance' is not (strongly) associated with reduced cognitive functioning (Boals, 2008; Bomyea et al., 2012; Clouston et al., 2016; Kivling-Bodén & Sundbom, 2003). Some of our findings are inconsistent, however, with previous evidence. Namely, that symptoms of 'intrusion' are most strongly linked to reduced cognitive functioning (Boals, 2008; Bomyea et al., 2012; Clouston et al., 2016, 2019; Johnsen et al., 2008; Kivling-Bodén & Sundbom, 2003; Parslow & Jorm, 2007; Saltzman et al., 2006; Vasterling et al., 1998).

A potential mechanism for the relationship between SCF and 'alterations in arousal and reactivity' as well as 'negative cognitions and mood' symptoms is that the latter two may preoccupy cognitive capacities, which are then less available for other actions (Kolb, 1987; Schweizer & Dalgleish, 2016). With regard to the PTSD symptom 'trouble experiencing positive feelings', evidence suggests that positive feelings are associated with less memory decline over time (Hittner et al., 2020), and enhance cognitive performance including working memory, decision making (Carpenter et al., 2013), and the ability to think flexibly (Isen, 2004). The broaden-and-build theory is one example of how positive emotions may improve cognitive function: by broadening a person's mindset and momentary thought-action repertoire, the scopes of attention, cognition and action are expanded and various long-term personal resources (e.g., intellectual complexity) built (Fredrickson, 2001, 2004). Conversely, restricted positive affect may result in impaired cognitive performance.

Lower cognitive abilities may also serve as a pre-existing risk factor for PTSD (Gilbertson et al., 2001; Marx et al., 2009; McNally & Shin, 1995; Moore, 2009; Parslow & Jorm, 2007; Vasterling et al., 1997, 2002, 2018). Indeed, pathways between PTSD symptoms and cognitive functioning likely are bidirectional and complex. PTSD previously also has been

identified as a risk factor for dementia (Günak et al., 2020), indicating longitudinal processes. Collectively, current evidence on mechanisms underlying the relationship of PTSD and cognitive functioning is preliminary. Future research is needed to provide a better understanding of the observed associations.

4.1. Implications

The findings of the present study, if replicated in other samples and populations, may have several implications for the clinical management of individuals with PTSD symptoms. The results highlight the importance for clinicians' awareness of potentially impaired cognitive functioning among patients, specifically, in older-aged individuals, and to monitor cognitive functioning when treating them (Clouston et al., 2016). Based on our findings, this may be even more relevant when there are elevations in symptoms of 'alterations in arousal and reactivity' and 'negative cognitions and mood'. The findings that these association persisted over a three-year follow-up suggest that they may reflect stable processes.

Previous findings of a meta-analysis indicate that samples of individuals seeking or undergoing treatment for PTSD (compared to samples who do not) are more likely to show objectively measured cognitive difficulties (Scott et al., 2015). This may suggest that treatment-seeking individuals have more severe PTSD symptoms, greater comorbidity, and/or a chronic duration of the symptoms (Scott et al., 2015); that treatment does not prevent or protect from a decline in cognitive functioning; and/or that patients with impaired cognitive functioning are particularly likely to seek professional help. Cognitive impairment may also impede effective treatment as it might entail reduced ability to comply with therapeutic regimes and self-management during the treatment (Clouston et al., 2016). Indeed, poorer performance on certain objective cognitive measures such as verbal memory and neural activity underlying inhibitory control have been linked to a poorer treatment outcome in cognitive-behavioral therapy in people with PTSD (Falconer et al., 2013; Wild & Gur, 2008). Additionally, objective memory

performance has been shown to predict occupational and social functioning (Geuze et al., 2009), and perceived cognitive problems to mediate the association between PTSD diagnosis, and perceived physical, emotional and social functioning and reintegration in veterans (Samuelson et al., 2017). The extent to which implementation of and response to PTSD treatment is affected by subjective cognitive impairment, and how this may relate to the previously found impact of objective cognitive impairment on treatment, should be further examined in future.

4.2. Strengths and Limitations

The present study extends current knowledge by providing evidence regarding the potential link between PTSD and the regularly overlooked, yet relevant, subjectively experienced cognitive functioning (Hess et al., 2020; Lau et al., 2021; Savard & Ganz, 2016; Schuitevoerder et al., 2013; Scott et al., 2015) by exploring unique mutual associations between PTSD symptoms and SCF. The prospective cohort study design allowed us to examine temporal stability and to determine precedence of PTSD symptoms to cognitive functioning. We controlled for important covariates to minimize potential confounding, including SCF at baseline in the longitudinal network models.

Our study has several limitations. First, given the observational design and correlational results, we consider our findings to be hypothesis-generating for future studies on the link between PTSD and cognitive impairment. Second, although veterans represent an important subpopulation of individuals at heightened risk of developing PTSD symptoms (Wisco et al., 2016, 2022), the homogeneity of the sample (i.e., predominantly older-aged White males) may reduce the generalizability of the results to the general population and more sociodemographically diverse veteran populations. As post-stratification weights based on demographic distributions, to date, cannot be incorporated into network analyses, generalization might be further compromised. Replication studies are needed, in non-veteran and other ethnic populations. Third, we used self-report measures to assess PTSD symptoms

and cognitive functioning instead of structured interviews and objective cognitive testing, respectively. While PTSD has repeatedly been related to neurocognitive deficits, presence, extent, and nature of change in cognitive functioning are not invariant (Scott et al., 2015). Moreover, despite the previously mentioned relevance of measuring SCF and one study suggesting that the MOS-CF correlates moderately with objective measures of corresponding cognitive domains (i.e., memory, attention, psychomotor speed) (Klein et al., 2002), results of the present study necessitate validation using comprehensive neuropsychological assessment. Fourth, we could have disaggregated SCF to investigate the relations between PTSD symptoms and individual SCF items. Likewise, we could have included covariates as moderators to control for their impact on existing associations between nodes of interest (Haslbeck, 2022; Haslbeck et al., 2021). However, both were not feasible in the current sample due to power constraints. Fifth, we defined "robust" edges as edges with weights above the mean edge weight of the respective network, and no, or other operationalizations could plausibly be chosen. Finally, we analyzed data from the entire sample in order to prevent Berkson's bias leading to spurious correlations when analyzing a subset of the sample only (De Ron et al., 2021). The minority of the sample screened positive for PTSD and results may not generalize to clinical populations of individuals with PTSD but rather exhibit the average network structure of the broader population of trauma-exposed veterans (von Stockert et al., 2018). Thus, our results may describe more normative developmental patterns.

4.3. Conclusion

Notwithstanding the aforementioned limitations, our results indicate that not all PTSD symptoms are equally important in the relationship between PTSD and self-perceived cognitive functioning, both cross-sectionally and longitudinally. Certain individual PTSD symptoms as well as the symptom domains of 'alterations in arousal and reactivity', and 'negative cognitions and mood' are more strongly related to reduced self-reported cognitive functioning than

symptoms of ‘intrusion’ or ‘avoidance’. The results of the present study aim at stimulating new research as much remains unknown regarding this striking relationship, which may have important implications for effective clinical care of people with PTSD symptoms.

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Study II:

Impact of adverse childhood experiences, post-traumatic stress disorder, dissociative disorders, and depression on dementia risk: A prospective analysis of associations and mediational pathways in the UK Biobank cohort

This chapter is a pre-print version of an article currently in submission, before formal peer-review and publication.

The analytic code is available online (https://osf.io/b28y3/).

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Abstract

Background: Little is known about the interrelationships among adverse childhood experiences (ACEs), post-traumatic stress disorder (PTSD), dissociative disorders, depression, and dementia risk. We sought to investigate associations of ACEs, PTSD, dissociative disorders, and depression with incident dementia and explore mediational pathways among them.

Methods: This prospective cohort study used population-based UK Biobank data, including 502 355 participants recruited at 22 assessment centres who completed questionnaires, an interview, and physical assessments at baseline (2006-2010). Data are linked to participants' electronic health records from primary care, hospital admissions, and death registers through November 30, 2022, and to the results of the UK Biobank online mental health survey (2016-2017). Cox regression and g-formula-based mediation analyses were used to examine associations between self-reported ACEs, PTSD symptoms, diagnosed PTSD, dissociative disorders, depression, and dementia.

Results: In the final sample (n = 434 215, mean (SD) age 56.58 (8.07) years), ACEs (hazard ratio $(HR)_{1point}$: 1.10; 95% CI 1.02-1.20), diagnosed PTSD (HR: 2.09; 95% CI 1.38-3.18), dissociative disorders (HR: 3.96; 95% CI 2.55-6.15), depression (HR: 2.17; 95% CI 2.05-2.30), and PTSD symptoms (HR_{1point}: 1.09; 95% CI 1.06-1.11) were associated with increased dementia risk, after adjusting for sociodemographic characteristics. PTSD symptoms (75.26%; P<.001) mediated the association between ACEs and dementia, whereas depression mediated associations between ACEs and dementia (4.51%; P=.02), diagnosed PTSD and dementia (8.42%; P<.001), and dissociative disorders and dementia (10.29%; P<.001).

Conclusions: Individuals with ACEs, PTSD, dissociative disorders, or depression are at increased risk of dementia, with shared and distinct pathways contributing to this increased risk.

Introduction

Dementia is expected to become more prevalent as the global population ages (Prince et al., 2015). Identifying modifiable risk factors to prevent or delay its onset and progression has been a major focus of dementia research (Livingston et al., 2024). Studies indicate that adverse childhood experiences (ACEs), including neglect and abuse (Anda et al., 2010; Gilbert et al., 2009), are associated with an increased risk of all-cause dementia (Abouelmagd et al., 2024; Severs et al., 2023). Among the negative mental health consequences frequently linked to ACEs are depression (Gardner et al., 2019), post-traumatic stress disorder (PTSD) (Messman-Moore & Bhuptani, 2017), and dissociative disorders (Şar, 2014). Although depression (Livingston et al., 2024) and PTSD (Günak et al., 2020) have both been suggested as risk factors for dementia, no study to date has examined the role of dissociative disorders, which are frequently overlooked in research (Şar, 2011), nor the interrelationships among ACEs, PTSD, dissociative disorders, and depression in increasing dementia risk. Prior studies investigating the relationship between PTSD and incident dementia (Bhattarai et al., 2019; Flatt et al., 2018; Kim et al., 2023; Mawanda et al., 2017; Meziab et al., 2014; Wang et al., 2016; Yaffe et al., 2010, 2019) have typically adjusted for depression, which is often comorbid with PTSD (Flory & Yehuda, 2015) and dissociative disorders (Şar, 2014). The associations adjusted for depression, while attenuated, have remained significant. However, mediational pathways have not been examined despite evidence of the comorbidity and sequential occurrence of ACEs, PTSD, dissociative disorders, and depression.

The aim of our study was to use prospective data from a large cohort of the general population in the United Kingdom (UK) to investigate the associations between ACEs, PTSD, dissociative disorders, depression, and subsequent dementia. Additionally, we sought to explore the interrelationships among these exposures and their link to dementia via mediational pathways. Three research questions were investigated: 1) Are ACEs, PTSD, dissociative disorders, and depression each associated with incident all-cause dementia?; 2) Do PTSD and

dissociative disorders each mediate the association between ACEs and dementia?; and 3) Is depression a mediator of the associations between ACEs and dementia, PTSD and dementia, and dissociative disorders and dementia?

Methods

Data and Participants

We analysed data from the UK Biobank, which is a population-based prospective cohort study that included more than half a million participants. Between 2006 and 2010 (baseline), individuals aged 37-73 years attended one of 22 assessment centres across England, Scotland, and Wales to complete a self-administered touchscreen questionnaire and a face-to-face interview inquiring about various aspects of life, such as sociodemographics and lifestyle. Trained staff conducted physical assessments and collected biological samples. These baseline data are linked to electronic health records from primary care, hospital admissions, and death registers, with retrospective data coverage extending to at least 10 years before the UK Biobank baseline. At the time of our analysis in July 2024, data were available until November 30, 2022. In 2016 and 2017, approximately one-third (n = 157 329, 31.32%) (Davis et al., 2020) of the overall sample completed an online mental health questionnaire capturing symptoms of possible mental disorders, as well as items on ACEs, including neglect and abuse. The UK Biobank received ethics approval from the North-West Multi-centre Research Ethics Committee (21/NW/0157), and all participants provided written informed consent at baseline and were free to withdraw at any time. Further information about the UK Biobank protocol can be found online (http://www.ukbiobank.ac.uk).

We calculated age at baseline using the date of birth and date of assessment. Sex, ethnicity, highest attained level of education, sleep duration, weekly alcohol consumption, smoking status, cardiovascular diseases, and traumatic brain injury (TBI) were self-reported at

baseline. The Townsend deprivation index was derived from area-based aggregated data on unemployment, car and home ownership, and household overcrowding (Townsend et al., 2023). Weekly physical activity was assessed using the validated International Physical Activity Questionnaire (IPAQ; Craig et al., 2003). We defined hypertension as a measured systolic blood pressure of at least 140 mmHg or self-reported prescription of antihypertensive medication at baseline. We specified the increasing risk of harm from alcohol consumption as 15-34 units per week for women and 15-49 units per week for men in accordance with the National Institute for Health and Care Excellence guidance (NICE, 2010). Consumption below and above these ranges was considered lower and higher risk.

Measures

Adverse Childhood Experiences

Information on ACEs was collected by the UK Biobank in its online mental health questionnaire using the validated Childhood Trauma Screener (CTS; Glaesmer et al., 2013), a shortened version of the Childhood Trauma Questionnaire (CTQ; Bernstein et al., 1994). Respondents rate five types of child maltreatment (i.e., sexual, emotional, and physical abuse; emotional and physical neglect) on a five-point Likert scale. Cut-off scores were used to determine the presence or absence of each type of ACE, resulting in a total number of ACE types experienced (0-5; Glaesmer et al., 2013). In our analyses, we took into account the time points at which ACEs were measured.

PTSD, Dissociative Disorders, and Depression

We identified diagnoses of PTSD, dissociative disorders, and depression through linked electronic health records. The date of diagnosis was based on the first recorded occurrence in primary care, hospital admissions, or death registers. We included only those participants who received any of the mentioned diagnoses before a dementia diagnosis or censoring (i.e., last date of observation). The comparison group comprised participants without any exposure

diagnoses before any dementia diagnosis or censoring. We used *International Classification of Diseases, Tenth Revision* (ICD-10) (World Health Organization, 1993) codes to identify a diagnosis of PTSD (F43.1), dissociative disorders (F44.x, F48.1), or depression (F32.0 to F32.3, F32.8, F32.9, F33.0 to F33.3, F33.8, F33.9).

An adapted five-item version of the PTSD Checklist – Civilian Version (PCL-C; Wilkins et al., 2011) included in the online mental health survey measured past-month PTSD symptoms. Items assessed intrusive thoughts, distress when reminded of a trauma, avoidance, feeling distant from others, and irritability (Davis et al., 2020). These were rated on a five-point Likert scale and summed to a total severity score. Participants who completed the adapted PCL-C were included if any dementia diagnosis was recorded only after the online mental health survey or not at all until censoring.

Dementia

We also ascertained all-cause dementia incidence and date of first diagnosis through the linked electronic health records using the following ICD-10 (World Health Organization, 1993) codes: A81.0, F00.x, F01.x, F02.x, F03, F05.1, F10.6, G30.x, G31.0, G31.1, G31.8.

Statistical Analyses

We used Cox proportional hazard models to estimate the associations of ACEs, PTSD, dissociative disorders, and depression with incident all-cause dementia, reporting hazard ratios (HR) and 95% confidence intervals (CI). The outcome variable consisted of the event status and time-to-event. We adjusted our main model for age, sex, ethnicity (White vs. Asian, Black, Mixed, or Other), education level (with vs. without college or university degree), and Townsend deprivation index (≥ vs. < median) as potential confounders. These factors have been shown to influence the risk of dementia, trauma-related conditions, and depression (Livingston et al.,

2024; Sareen, 2014; Stansfeld & Rasul, 2006). We tested proportional hazard assumptions using statistical tests based on Schoenfeld residuals.

We conducted two sensitivity analyses. First, we repeated the main analyses but with an additional adjustment for lifestyle factors and medical comorbidities (i.e., sleep duration, weekly alcohol consumption, smoking status, weekly physical activity, cardiovascular conditions, TBI, and hypertension). These variables could be mediators between exposures and dementia and were therefore only adjusted for in sensitivity analyses. Second, we repeated the first sensitivity analysis but with an additional adjustment for depression in the models in which ACEs, PTSD, or dissociative disorders were the exposures. In the model in which depression was the exposure, we repeated the first sensitivity analysis but with an additional adjustment for ACEs, PTSD, and dissociative disorders combined (due to small numbers in the PTSD and dissociative disorder groups). Given the relatively low prevalence of diagnosed PTSD, we performed a post-hoc analysis of the association between self-reported PTSD symptoms and subsequent dementia incidence. Hereinafter, "PTSD" refers to diagnoses from electronic health records, while "PTSD symptoms" refer to self-reported PTSD symptoms from the online mental health survey. Additionally, we conducted two post-hoc subgroup analyses: one comprising participants with depression but no PTSD or dissociative disorders, and another comprising participants with depression but no ACEs, PTSD, or dissociative disorders.

We implemented two mediation models (Shi et al., 2021). First, we examined whether PTSD (diagnosis [binary] and symptoms [continuous]) and dissociative disorders (binary) mediated the relationship between ACEs (ordinal) as the exposure and incident all-cause dementia (binary) as the outcome. Second, we examined whether depression (binary) mediated the relationship between trauma-related conditions (ACEs, PTSD, PTSD symptoms, or dissociative disorders) as the exposure and incident all-cause dementia as the outcome. We regressed dementia (outcome) on the potential mediator, primary exposure variable, and covariates (i.e., age, sex, ethnicity, education level, area-based deprivation) using logistic

models for binary mediators and multiple linear models for continuous mediators. We also regressed the potential mediators on the primary exposure and covariates. We then combined the results of the outcome and mediator regression models using the g-formula with bootstrapping to estimate the proportion of the total effect mediated. We considered the time sequence, coding the primary exposure and mediators as 'present' only if they occurred before the mediator and dementia diagnosis, respectively.

We included participants in the analyses only if they had complete data on all variables, except for the online survey measures (due to power issues). All analyses were conducted between January 2023 and May 2024 using R (version 4.2.0; details in Supplementary Material; Appendix B).

Results

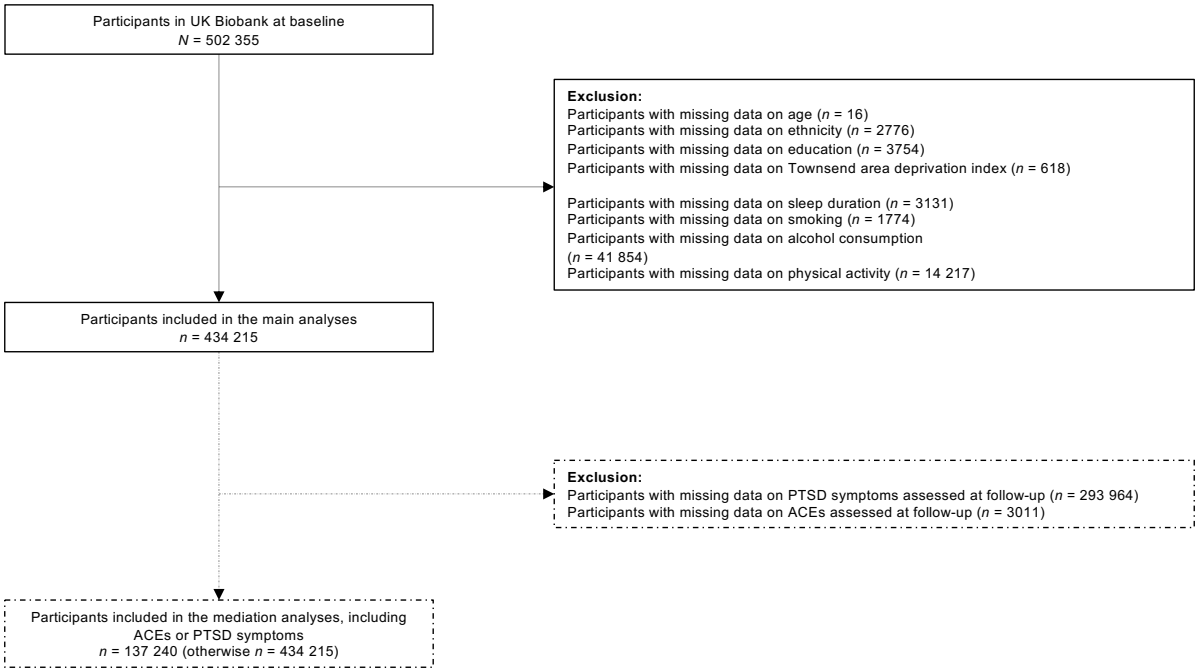
Sample Characteristics

After excluding participants with missing values for any of the covariates included in the analyses (n = 68 140; Figure 2.1), the final cohort comprised 434 215 participants (mean (SD) age 56.58 (8.07) years, 53.52% female; Table 2.1). Median follow-up was 13.66 years (IQR = 12.87 - 14.39). In total, 941 (0.22%) participants were diagnosed with PTSD, 325 (0.07%) with any dissociative disorder, and 44 140 (10.17%) with depression before any dementia diagnosis or censoring. People with any of these diagnoses were generally less educated, more deprived, current smokers, and less physically active, and reported more sleep duration deviations and cardiovascular diseases. Approximately one-third (n = 45 536) of the participants who took part in the online mental health survey (n = 140 251) experienced at least one type of ACE. Of these ACEs, emotional neglect was the most common (66.26%), followed by emotional abuse (27.82%), sexual abuse (26.37%), physical abuse (23.97%), and physical neglect (16.66%; Supplementary Material, Appendix B Table B2). Dementia developed in 266

individuals with ACEs (0.58%), 22 of those with PTSD (2.34%), 20 of those with any dissociative disorder (6.15%), and 1397 of those with depression (3.16%). In comparison, dementia occurred in 6703 individuals without PTSD, dissociative disorders, or depression (1.72%), and in 454 individuals without these diagnoses or ACEs (0.52%; Supplementary Material Appendix B Table B2 and B3).

Figure 2.1

Diagram of Participants Included in the Analyses



N = sample size; ACEs = adverse childhood experiences; PTSD = post-traumatic stress disorder.

Table 2.1

Baseline Characteristics by Group

	Overall (*n* = 434 215)	**Comparison Group[a] (*n* = 389 516)**	**Comparison Group 2[b] (*n* = 86 496)**	**ACEs[c] (*n* = 45 536)**	**PTSD (*n* = 941)**	**Dissociative Disorders (*n* = 325)**	**Depression (*n* = 44 140)**	**Depression Only[d] (*n* = 43 452)**	**Depression Only 2[e] (*n* = 5489)**
Age, mean (SD)	56.58 (8.07)	56.65 (8.07)	56.25 (7.69)	55.52 (7.75)	52.81 (8.00)	55.26 (8.01)	55.98 (8.04)	56.03 (8.04)	55.78 (7.60)
Age groups, *n* (%)									
37-50	112 822 (25.98)	100 206 (25.73)	21 980 (25.41)	12 983 (28.51)	407 (43.25)	92 (28.31)	12 419 (28.14)	12 126 (27.91)	1449 (26.40)
51-60	153 432 (35.34)	137 068 (35.19)	34 009 (39.32)	18 336 (40.27)	332 (35.28)	133 (40.92)	16 163 (36.62)	15 908 (36.61)	2274 (41.43)
61-73	167 961 (38.68)	152 242 (39.08)	30 507 (35.27)	14 217 (31.22)	202 (21.47)	100 (30.77)	15 558 (35.25)	15 418 (35.48)	1766 (32.17)
Sex, *n* (%)									
Female	232 395 (53.52)	203 870 (52.34)	46 154 (53.36)	26 431 (58.04)	439 (46.65)	230 (70.77)	28 257 (64.02)	27 866 (64.13)	3626 (66.06)
Male	201 820 (46.48)	185 646 (47.66)	40 342 (46.64)	19 105 (41.96)	502 (53.35)	95 (29.23)	15 883 (35.98)	15 586 (35.87)	1863 (33.94)
Asian, Black, Mixed, or Other ethnic background, *n* (%)[f]	23 078 (5.31)	21 104 (5.42)	1768 (2.04)	2028 (4.45)	97 (10.31)	15 (4.62)	1934 (4.38)	1863 (4.29)	78 (1.42)
Education, *n* (%) College or university degree	146 714 (33.79)	134 553 (34.54)	41 683 (48.19)	20 206 (44.37)	261 (27.74)	78 (24.00)	12 014 (27.22)	11 823 (27.21)	2254 (41.06)
Townsend deprivation index >=Mdn[g]	213 920 (49.27)	188 502 (48.39)	36 751 (42.49)	22 736 (49.93)	599 (63.66)	203 (62.46)	25 083 (56.83)	24 628 (56.68)	2537 (46.22)
Sleep duration, *n* (%)									
< 6 hours	23 186 (5.34)	18 912 (4.86)	2444 (2.83)	2289 (5.03)	165 (17.53)	51 (15.69)	4203 (9.52)	4063 (9.35)	299 (5.45)
6 – 9 hours	403 188 (92.85)	364 723 (93.63)	83 376 (96.39)	42 619 (93.59)	729 (77.47)	246 (75.69)	38 001 (86.09)	37 503 (86.31)	5058 (92.15)
> 9 hours	7841 (1.81)	5881 (1.51)	676 (0.78)	628 (1.38)	47 (4.99)	28 (8.62)	1936 (4.39)	1886 (4.34)	132 (2.40)
Smoking, *n* (%)									
Current	44 596 (10.27)	37 035 (9.51)	5108 (5.91)	4176 (9.17)	206 (21.89)	48 (14.77)	7473 (16.93)	7311 (16.83)	536 (9.76)
Never	236 450 (54.45)	215 457 (55.31)	52 036 (60.16)	23 502 (51.61)	430 (45.70)	179 (55.08)	20 717 (46.93)	20 392 (46.93)	2967 (54.05)
Former	153 169 (35.27)	137 024 (35.18)	29 352 (33.93)	17 858 (39.22)	305 (32.41)	98 (30.15)	15 950 (36.14)	15 749 (36.24)	1986 (36.18)

	Overall (*n* = 434 215)	**Comparison Group[a] (*n* = 389 516)**	**Comparison Group 2[b] (*n* = 86 496)**	**ACEs[c] (*n* = 45 536)**	**PTSD (*n* = 941)**	**Dissociative Disorders (*n* = 325)**	**Depression (*n* = 44 140)**	**Depression Only[d] (*n* = 43 452)**	**Depression Only 2[e] (*n* = 5489)**
Alcohol consumption per week, Mdn (IQR)	10.50 (2.76 – 22.50)	11.25 (3.00 – 22.65)	12.00 (4.50 – 22.50)	10.65 (3.00 – 22.20)	7.20 (1.50 – 21.00)	1.50 (1.38 – 11.40)	8.70 (1.50 – 20.40)	8.70 (1.50 – 20.40)	9.15 (2.35 – 20.40)
Risk of harm from alcohol, *n* (%)									
Higher risk	30 881 (7.11)	27 345 (7.02)	4872 (5.63)	3089 (6.78)	93 (9.88)	12 (3.69)	3490 (7.91)	3433 (7.90)	328 (5.98)
Increasing risk	143 439 (33.03)	131 500 (33.76)	31 507 (36.34)	15 100 (33.16)	242 (25.72)	53 (16.31)	11 782 (26.69)	11 646 (26.80)	1692 (30.83)
Lower risk	259 895 (59.85)	230 671 (59.22)	50 117 (57.94)	27 347 (60.06)	606 (64.40)	260 (80.00)	28 868 (65.40)	28 373 (65.30)	3469 (63.20)
Physical activity, minutes per week, Mdn (IQR)	1582.00 (678.00 – 3332.00)	1605.00 (693.00 – 3342.00)	1572.00 (720.00 – 3066.00)	1590.00 (699.00 – 3172.00)	1413.00 (438.00 – 3333.00)	1050 (311.00 – 3066.00)	1386.00 (495.00 – 3150.00)	1386.00 (495.00 – 3150.00)	1386.00 (594.00 – 2892.00)
Cardiovascular diseases, *n* (%)	28 609 (6.59)	24 304 (6.24)	3547 (4.10)	2229 (4.90)	104 (11.05)	57 (17.54)	4235 (9.59)	4146 (9.54)	284 (5.17)
Traumatic brain injury, *n* (%)	1399 (0.31)	1138 (0.29)	208 (0.24)	130 (0.29)	8 (0.85)	4 (1.23)	198 (0.45)	189 (0.43)	15 (0.27)
Hypertension, *n* (%)	217 304 (50.05)	195 526 (50.20)	39 585 (45.77)	19 649 (43.15)	453 (48.14)	165 (50.77)	21 503 (48.72)	21 166 (48.71)	2406 (43.83)
Depression, *n* (%)	44 140 (10.17)	NA	NA	5381 (11.82)	526 (59.90)	177 (54.46)	44 140 (100.00)	43 452 (100.00)	5489 (100.00)
PTSD, *n* (%)	941 (0.22)	NA	NA	111 (0.24)	941 (100)	19 (5.85)	526 (1.19)	NA	NA

N = sample size; ACEs = adverse childhood experiences; PTSD = post-traumatic stress disorder; SD = standard deviation; Mdn = median; IQR = interquartile range; TBI = traumatic brain injury; NA = not applicable.

[a]"Comparison group" refers to participants without PTSD, dissociative disorders, or depression (PTSD–/Dissociative disorders–/Depression–).

[b]"Comparison group 2" refers to participants without PTSD, dissociative disorders, or depression, who self-reported as part of the online mental health survey that they had no ACEs (ACEs–/PTSD–/Dissociative disorders–/Depression–).

[c]"ACEs" group refers to participants who self-reported that they had at least one type of ACEs, as part of the online mental health survey (ACEs+).

[d]"Depression only" group refers to participants with depression but without PTSD or dissociative disorders (Depression+/ PTSD–/Dissociative disorders–).

[e]"Depression only 2" group refers to participants without PTSD, dissociative disorders, or depression, who self-reported as part of the online mental health survey that they had no ACEs (Depression+/ACEs–/PTSD–/Dissociative disorders–).

[f]Including Asian or Asian British, Black or Black British, Chinese, Mixed, or Other ethnic group

[g]Median = -2.135

ACEs, PTSD, Dissociative Disorders, Depression, and Dementia

After adjusting for sociodemographic characteristics, we found that each additional type of ACE was associated with a 10% increase in the risk of developing dementia (HR_{1point}: 1.10; 95% CI 1.02-1.20; $P = .018$). The risk of all-cause dementia was 2.09 to 3.96 times higher in people with diagnosed PTSD (HR: 2.09; 95% CI 1.38-3.18; $P < .001$), any dissociative disorders (HR: 3.96; 95% CI 2.55-6.15; $P < .001$), or depression (HR: 2.17; 95% CI 2.05-2.30; $P < .001$) compared with people without the respective diagnosis (Table 2.2).

Regarding self-reported PTSD symptoms, each one-point increase in the total PTSD severity score was associated with a 9% increase in the risk of dementia (HR_{1point}: 1.09; 95% CI 1.06-1.11; $P < .001$). Compared with people without depression, those with depression but without diagnosed PTSD or dissociative disorder had a 2.15-fold increased risk of developing dementia (HR: 2.15; 95% CI 2.02-2.27; $P < .001$), whereas those with depression but without any ACEs, diagnosed PTSD, or dissociative disorder showed a decreased dementia risk (HR: 0.66; 95% CI 0.50-0.88; $P = .005$).

Lastly, our sensitivity analyses revealed that although the associations with dementia were generally attenuated, they remained significant for ACEs, PTSD symptoms, and depression (Table 2.2). When adjusting for depression in the models in which ACEs, PTSD, or dissociative disorders were the exposure variables, and when adjusting for ACEs, PTSD, and dissociative orders in the model in which depression was the exposure variable, PTSD symptoms, and depression remained significantly associated with incident all-cause dementia.

Table 2.2

Unadjusted and Adjusted Risk of Dementia by Group

	HR (95% CI)			
Model	**Unadjusted**	**Main Model[a]**	**Sensitivity Analysis 1[b]**	**Sensitivity Analysis 2[c]**
ACEs (n = 45 536)	1.03 (0.95, 1.11), P = .50	1.10 (1.02, 1.20), P = .018*	1.09 (1.00, 1.19), P = .039*	1.07 (0.99, 1.17), P = .10
PTSD (n = 941)	1.27 (0.84, 1.93), P = .30	2.09 (1.38, 3.18), P < .001**	0.94 (0.45, 1.97), P = .90	0.68 (0.32, 1.44), P = .30
Self-reported PTSD Symptoms (n = 140 251)	1.03 (1.01, 1.05), P = .005*	1.09 (1.06, 1.11), P < .001**	1.08 (1.06, 1.11), P < .001**	1.07 (1.05, 1.10), P < .001**
Dissociative Disorders (n = 325)	3.46 (2.23, 5.36), P < .001**	3.96 (2.55, 6.15), P < .001**	1.73 (0.84, 3.58), P = .14	1.37 (0.65, 2.86), P = .40
Depression (n = 44 140)	1.91 (1.80, 2.02), P < .001**	2.17 (2.05, 2.30), P < .001**	2.00 (1.83, 2.17), P < .001**	1.75 (1.40, 2.20), P < .001**
Depression Only[d] (n = 43 452)	1.90 (1.79, 2.01), P < .001**	2.15 (2.02, 2.27), P < .001**	2.01 (1.84, 2.19), P < .001**	1.75 (1.39, 2.19), P < .001**[e]
Depression Only 2[f] (n = 5489)	0.51 (0.38, 0.67), P < .001**	0.66 (0.50, 0.88), P = .005*	0.61 (0.41, 0.91), P = .016*	NA

HR = hazard ratio; CI = confidence Interval; ACEs = adverse childhood experiences; n = sample size; P = p-value; PTSD = post-traumatic stress disorder; NA = not applicable.

[a]Main Model: adjusted for demographics (i.e., age, sex, ethnicity, Townsend deprivation index, highest level of education attained).

[b]Sensitivity analysis 1: adjusted for demographics + lifestyle factors/medical comorbidities (i.e., sleep duration, smoking status, risk group of harm from alcohol consumption, physical activity per week, cardiovascular diseases, traumatic brain injury, hypertension).

[c]Sensitivity analysis 2: adjusted for demographics + lifestyle factors/medical comorbidities + depression (or ACEs, PTSD, and dissociative disorders when depression is the exposure).

[d-f]"Depression only" group refers to participants with depression but without PTSD or dissociative disorders (Depression+/ PTSD–/Dissociative disorders–).

[e]adjusted for demographics + lifestyle factors/medical comorbidities + ACEs.

[f]"Depression only 2" group refers to participants without PTSD, dissociative disorders, or depression, who self-reported as part of the online mental health survey that they had no ACEs (Depression+/ACEs–/PTSD–/Dissociative disorders–).

** P < .001, * P < .05.

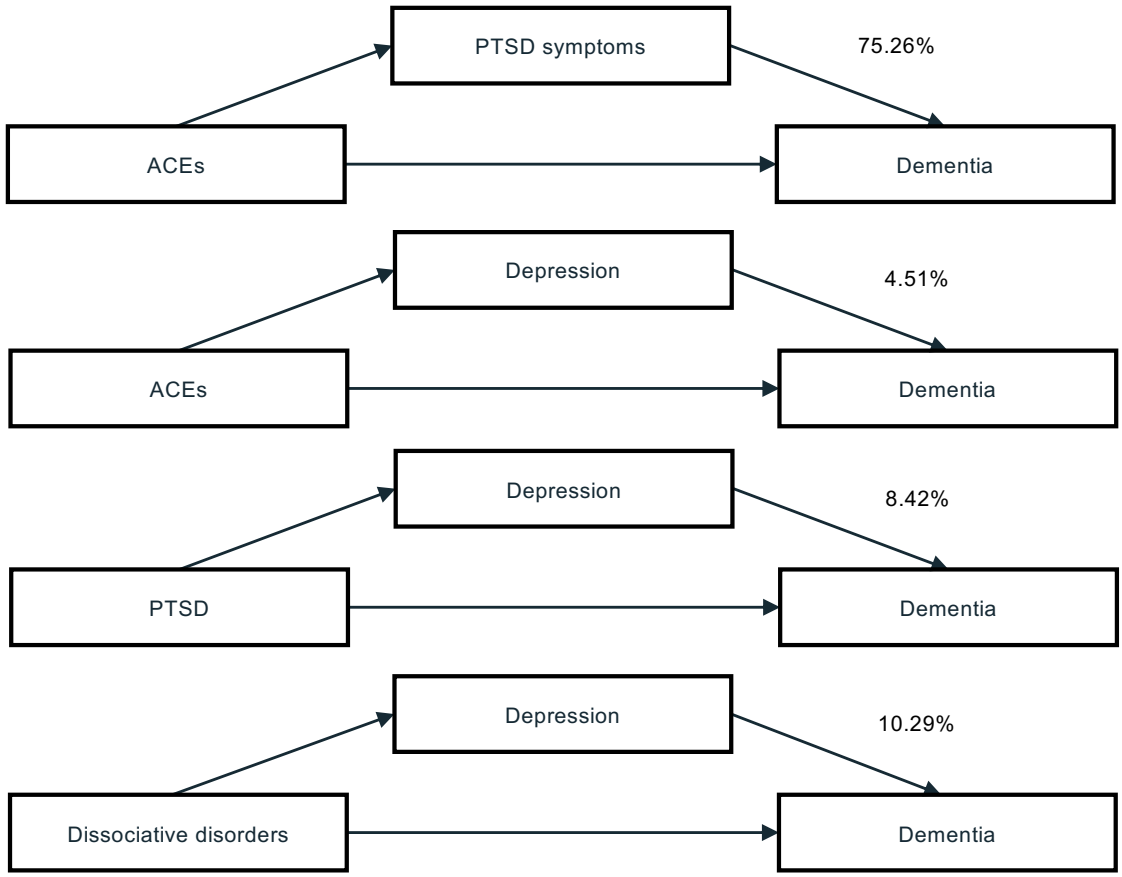
Mediation Analyses

Our mediation analyses (Table 2.3) found little evidence to support PTSD diagnosis as a mediator between ACEs and dementia (P = .07), whereas PTSD symptoms significantly mediated the association (P < .001), accounting for 75.26% of the excess dementia risk associated with ACEs. Dissociative disorders were not a significant mediator between ACEs and dementia (P = .72).

Depression was a significant mediator between ACEs and dementia (P = .02; 4.51%) as well as between diagnosed PTSD (P < .001; 8.42%) or dissociative disorders (P < .001; 10.29%) and dementia, but not between PTSD symptoms (P = .15) and dementia (Figure 2.2).

Figure 2.2

Significant Mediators



ACEs = adverse childhood experiences; PTSD = post-traumatic stress disorder. Hypothesised Casual Pathways based on Mediation Analyses. Direct Associations were Omitted for Clarity

Table 2.3

Mediation Analyses

	Total Effect		Total Natural Indirect Effect		Overall Proportion Mediated
	HR (95% CI)	*P*	HR (95% CI)	*P*	
Association between Number of Types of ACEs (Exposure) and Dementia (Outcome)					
PTSD as a Mediator	1.13 (1.03, 1.21)	.01*	1.00 (0.99, 1.00)	.07	NA
PTSD Symptoms as a Mediator[a]	1.11 (1.01, 1.18)	.03*	1.08 (1.06, 1.10)	< .001**	75.26
Dissociative Disorders as a Mediator	1.12 (1.03, 1.21)	.01*	1.00 (0.999, 1.002)	.72	NA
Depression as a Mediator in the Association between					
ACEs (Exposure) and Dementia (Outcome)	1.12 (1.03, 1.21)	.01*	1.005 (1.001, 1.01)	.02*	4.51
PTSD (Exposure) and Dementia (Outcome)	2.04 (1.19, 2.90)	< .001**	1.04 (1.02, 1.07)	< .001**	8.42
PTSD Symptoms (Exposure) and Dementia (Outcome)	1.10 (1.07, 1.12)	< .001**	1.00 (0.999, 1.002)	.15	NA
Dissociative Disorders (Exposure) and Dementia (Outcome)	3.93 (2.47, 6.42)	< .001**	1.08 (1.05, 1.13)	< .001**	10.29

HR = hazard ratio; CI = confidence interval; P = p-value; ACEs = adverse childhood experiences; PTSD = post-traumatic stress disorder; NA = not applicable.
Mediation analyses including ACEs or PTSD symptoms included 137 240 participants in the analyses.
Adjusted for demographics (i.e., age, sex, ethnicity, Townsend deprivation index, highest level of education attained).
[a]ACEs and PTSD symptoms were assessed concurrently during the online mental health survey.
**$P < .001$, *$P < .05$.

Discussion

In this large UK Biobank cohort, ACEs, PTSD, dissociative disorders, and depression were significantly associated with an increased risk of all-cause dementia. After adjustment for sociodemographic characteristics, we found a dose-response relationship between the number of ACE types and dementia, and between PTSD symptom severity and dementia. The risk of dementia was 2.09, 3.96, and 2.17 times higher for those diagnosed with PTSD, any dissociative disorder, and depression compared to those without these diagnoses. For individuals with depression but without ACEs, PTSD, or dissociative disorders, the associated risk of dementia was reduced by 34%. PTSD symptoms accounted for most of the excess dementia risk associated with ACEs. Depression mediated associations between ACEs, diagnosed PTSD, or dissociative disorders and dementia. Thus, PTSD symptoms were an important mediator of the relationship between ACEs and dementia risk, while depression played a smaller role in the observed associations of ACEs and trauma-related conditions with dementia risk.

Our finding that ACEs are associated with dementia is in line with a recent meta-analysis showing that childhood trauma increases dementia risk by 76% (Severs et al., 2023). Another recent study using data from the UK Biobank found that the risk of all-cause dementia in later life was higher in people who experienced childhood trauma compared to adulthood trauma (Xie et al., 2023), although it included only ACEs related to abuse, not neglect. Moreover, our findings confirm those of a meta-analysis linking PTSD to increased dementia risk (Günak et al., 2020). Studies conducted since then have found further evidence that PTSD is a risk factor for dementia (Bergman et al., 2021; Kim et al., 2023; Song et al., 2020), with one exception (Islamoska et al., 2020). To our knowledge, no studies to date have looked at PTSD symptom severity, rather than diagnosis, and dementia risk.

Our study is the first to investigate the relationship between dissociative disorders and dementia. We propose that dissociative disorders should be considered a potentially modifiable

risk factor for dementia. Our findings build on prior studies showing that higher levels of dissociative symptoms are correlated with reduced performance across various cognitive domains (Alexis et al., 2023; McKinnon et al., 2016).

Consistent with prior research (Kuring et al., 2020; Livingston et al., 2020; Ownby et al., 2006; Stafford et al., 2022), we found depression to be a significant risk factor for dementia. While earlier studies indicate that later-life depression is associated with, and in fact might be a prodrome of, dementia (Livingston et al., 2017, 2020), the recent update from the Lancet Commission on dementia found that depression increases the risk of dementia at all stages of adulthood and therefore classified mid-life depression as a risk factor for dementia (Livingston et al., 2024), which our results further support. However, our findings indicate that the observed link between depression and dementia may be crucially influenced by ACEs because the risk of dementia associated with depression was reduced in individuals who reported not having had any ACEs.

To our knowledge, our study is the first to explore the interrelationships between ACEs, trauma-related conditions, and depression in their associations with dementia through mediational pathways. Previous studies have used different exposures or have focused on cognitive impairment as the outcome (Cohn-Schwartz et al., 2024; Singh et al., 2020). Their and our findings suggest that ACEs, PTSD, dissociative disorders, and depression likely have both shared and distinct pathways leading to cognitive impairment and dementia.

Several mechanisms may explain our results. Early and chronic stress from ACEs, PTSD, dissociative disorders, and depression may cause structural and functional brain changes, increasing vulnerability to neuropathology (McEwen, 2007), including dementia. This might occur through prolonged activation of stress- and threat-related pathways (McEwen, 2007) and impaired development of brain areas like the hippocampus, amygdala, and frontal cortex (Lupien et al., 2009; Nilaweera et al., 2019). ACEs, PTSD, dissociative disorders, and depression may also hinder cognitive reserve formation (Stern, 1994, 2002; Tucker & Stern,

2011) by reducing engagement in cognitively stimulating activities due to withdrawal from daily life, thereby diminishing the protective buffer against neurodegenerative pathology (Almeida-Meza et al., 2021). This may begin soon after ACEs through impoverished social networks (McCrory et al., 2022) and lower levels of educational attainment (Blodgett & Lanigan, 2018). Engagement in repetitive negative thinking (RNT), a transdiagnostic process (Ehring & Watkins, 2008), may contribute to cognitive debt, heightening susceptibility to brain pathology (Marchant & Howard, 2015). Higher RNT levels in cognitively intact older adults have been linked to faster declines in global cognition and memory, as well as higher levels of neuropathological markers of Alzheimer's disease (Marchant et al., 2020). Our mediation findings suggest that underlying mechanisms may be exacerbated when PTSD symptoms and/or depression follow ACEs, or when depression follows diagnosed PTSD or dissociative disorders.

Implications

It is important to consider ACEs, PTSD, dissociative disorders, and depression when assessing dementia risk. Early intervention for these conditions may help reduce the likelihood of developing dementia (Livingston et al., 2024). Evidence is sparse on population-level primary prevention strategies for addressing depression as a risk factor for dementia (Walsh et al., 2024); an even greater gap exists for ACEs, PTSD, and dissociative disorders. Future research should attempt to disentangle specific dissociative disorder diagnoses and investigate whether the observed increased risk of dementia is causal, or if a third variable, such as genetic disposition, is at play. Our findings suggest that ACEs, PTSD, dissociative disorders, and depression independently contribute to a higher risk of dementia.

Strengths and Limitations

Strengths of our study include the use of a large, population-based cohort with clinical diagnoses of PTSD, dissociative disorders, and depression, enabling us to adjust for important confounders. Our mediation analyses accounted for the sequence of diagnoses, ensuring that the predictor, mediator, and outcome occurred consecutively. Several limitations should be considered when interpreting our findings. Relatively few cases of PTSD and dissociative disorders were identified, possibly due to underdiagnosis or underreporting in the linked data, thus reducing statistical power. Our sensitivity analyses showed non-significant associations between diagnosed PTSD or dissociative disorders and the risk of dementia. The added exposures likely further reduced the power of these analyses, especially with high collinearity between trauma-related disorders and impaired sleep duration, smoking, cardiovascular diseases, and depression. The finding that PTSD symptoms remained significantly associated with dementia in both sensitivity analyses supports this. Due to power issues, we were not able to adjust the mediation analyses for the remaining exposures. Because ACEs were self-reported, recall bias may have influenced our results. People of ethnic minority and people living with lower socioeconomic circumstances are underrepresented in the UK Biobank, limiting the generalizability of our findings.

Conclusions

Our study identifies dissociative disorders as a potentially modifiable risk factor for all-cause dementia and provides further evidence that ACEs, PTSD, and depression are risk factors as well. These conditions have both common and unique pathways in their associations with increased dementia risk and thus cannot be fully explained by the other investigated exposures. Future studies should attempt to disentangle the underlying mechanisms, both transdiagnostic and disorder-specific, to aid in the development of timely interventions that mitigate the increased risk of dementia associated with ACEs, PTSD, dissociative disorders, and depression

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Study III:

Moderators of childhood adversity and psychopathology on cognitive outcomes in the UK Biobank

This chapter is a pre-print version of an article currently in submission, before formal peer-review and publication.

The analytic code is available online (https://osf.io/k4b5w/).

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Abstract

Introduction: Adverse childhood experiences (ACEs), PTSD, depression, and dissociative disorders were associated with cognitive health, including dementia. These associations may vary depending on other factors.

Methods: Using UK Biobank data, we applied LASSO and stepwise selection to identify the most relevant predictors (childhood trauma and psychopathology) and their interactions with moderators (age, sex, ethnic background, education, deprivation, smoking, alcohol, physical activity, hypertension, social activities) for cognitive outcomes.

Results: In 417,486 participants (mean age 56.55 years, mean follow-up 13.66 years), poorer cognitive functioning and higher dementia risk were found in people with all included trauma and psychopathology predictors. The moderators varied by the predictors and the outcomes. For example, hypertension was the strongest moderator between ACEs and dementia, but smoking was the strongest between PTSD diagnosis and dementia.

Discussion: Trauma and psychopathology were robustly associated with cognitive outcomes, but the associations could be affected by different factors. Targeted interventions should be explored.

1. Background

Adverse childhood experiences (ACEs) negatively impact health and well-being throughout life (Kalmakis & Chandler, 2014). ACEs, including abuse, neglect, and household dysfunction during childhood and adolescence (Brown et al., 2009), have been linked to various forms of psychopathology later in life, including posttraumatic stress disorder (PTSD), dissociative disorders, and depression (American Psychiatric Association, 2013; Schalinski et al., 2016). In turn, ACEs, and ACE-related psychopathology are associated with impaired cognitive ability in younger, middle-aged (Fabio et al., 2024; Hawkins et al., 2021; McKinnon et al., 2016; Rock et al., 2014; Scott et al., 2015), and older adults (Haczkewicz et al., 2024; Rock et al., 2014; Schuitevoerder et al., 2013), and have been proposed as risk factors for all-cause dementia (Günak et al., 2020; Severs et al., 2023; Stafford et al., 2022).

ACEs, PTSD, dissociative disorders, and depression have also been associated – albeit not always consistently – with dysregulations and reductions in hippocampal volume (Blihar et al., 2021; Herzog & Schmahl, 2018; Logue et al., 2018; Nolan et al., 2020). Notably, the hippocampus plays a central in learning and memory and is one of the first brain regions affected in dementia (Laakso et al., 1996). Hippocampal atrophy is considered an early marker of neuropathology in Alzheimer's disease (Lyall et al., 2013), and is regularly used as an indicator of Alzheimer's disease risk (Potkin et al., 2009). Additionally, cognitive impairment in older age have been associated with dementia and may signal its early stages (Brodaty et al., 2017).

Given the absence of a disease-modifying cure, preventing or delaying the onset of dementia remains a primary goal in dementia research (Livingston et al., 2024). The Lancet Commission has identified fourteen modifiable risk factors linked to dementia, including lower education, physical inactivity, smoking, hypertension, excessive alcohol consumption, and social isolation (Livingston et al., 2024). One mechanism by which these factors may influence cognitive decline is through their impact on cognitive reserve – a concept that suggests

individuals can buffer against neuropathology through lifelong cognitive, social, and physical engagement (Stern, 2002, 2009). Cognitive reserve is thought to moderate the relationship between aging-related or pathology-related brain changes and clinical or cognitive outcome (Stern, 2002, 2009). Engaging in activities that build cognitive reserve may help to mitigate the impact of neuropathology and preserve cognitive function (Nelson et al., 2021). However, despite cognitive reserve being a widely accepted concept, there is no universally agreed-upon operationalization and studies use different proxies to measure it (Stern et al., 2020). Furthermore, it remains unclear whether cognitive reserve functions as a unified construct across different dementia risk factors.

Age is the most significant risk factor for dementia, with the incidence doubling every 6.3 years from age of 60 years onward (Prince et al., 2015). Many of the observed risk factors for dementia are also related to socioeconomic deprivation (Livingston et al., 2024), which itself has been associated with an increased risk of dementia (Klee et al., 2023). Disparities in dementia incidence have also been observed across ethnic backgrounds (Mayeda et al., 2016), while evidence regarding sex differences remains inconsistent (Geraets & Leist, 2023). One meta-analysis suggested that the previously reported higher dementia incidence and prevalence in women may be attributed to greater longevity and historical disparities in education access (Huque et al., 2023).

Although ACEs, trauma-related psychopathology, depression, demographic and lifestyle factors have been independently studied as risk factors for cognitive decline and dementia, their interactions remain unclear. Certain demographic, behavioral, and psychosocial factors may either exacerbate or buffer the effects of ACEs, trauma-related psychopathology, and depression on cognitive outcomes. Specifically, lifestyle variables could impair cognitive reserve – worsening the impact of ACEs, trauma-related psychopathology, and depression – or enhance it, mitigating adverse effects. One study found that greater cognitive reserve, measured using a combined score of education, occupational complexity, social and cognitive activities,

attenuated the dementia risk associated with depression (Jia et al., 2022). Yet, to our knowledge, no study to date has systematically examined how demographic, behavioral, and psychosocial factors moderate these associations. Understanding these interactions would help identify individuals who are most vulnerable to cognitive decline and dementia, allowing for more targeted prevention efforts in the future.

Thus, the purpose of this study was to examine whether demographic, behavioral, and psychosocial factors moderate the relationships between ACEs, PTSD, dissociative disorders, and depression with cognitive functioning, hippocampal volume, and dementia using large-scale data from the United Kingdom (UK) Biobank.

2. Methods

2.1. Data and Participants

We analyzed data from the UK Biobank, a large biomedical database, containing de-identified individual-level health information from over half a million participants (Sudlow et al., 2015). Individuals from the UK general population aged 37 – 73 years participated in baseline assessments (conducted between 2006 and 2010) across 22 assessment centers across England, Scotland, and Wales. Participants completed a self-administered touchscreen questionnaire, including sociodemographic characteristics, psychosocial and lifestyle factors, and a battery of brief cognitive tests. Trained staff conducted verbal interviews and physical assessments and collected biological samples. These baseline data are linked to electronic health records from primary care, hospital admissions, and death registers, with retrospective data coverage extending to at least 10 years before the UK Biobank baseline assessments. At the time of our analysis, linked follow-up data were available until November 30, 2022. Additionally, on average, four years after initial recruitment, a subset of UK Biobank participants underwent head magnetic resonance imaging (MRI; Miller et al., 2016). The present study utilized brain MRI data up to March 2019. Finally, in 2016 and 2017, participants

(n = 156,576, 31.18%) who had provided an email address were invited to complete an online mental health questionnaire, assessing adverse childhood experiences (ACEs) and PTSD symptoms (Davis et al., 2020). The UK Biobank cohort study was conducted with approval from the North-West Multi-centre Research Ethics Committee (21/NW/0157). Written informed consent was obtained from all participants at baseline, and they were free to withdraw at any time. Additional details about the UK Biobank protocol are available online (http://www.ukbiobank.ac.uk).

2.2. Measures

2.2.1. Predictors

2.2.1.1. Adverse Childhood Experiences. Information on ACEs was gathered through the follow-up online mental health questionnaire, using Childhood Trauma Screener (CTS; Glaesmer et al., 2013), a validated, condensed version of the Childhood Trauma Questionnaire (CTQ; Bernstein et al., 1994). On a five-point Likert scale, participants rated five types of child maltreatment (i.e., sexual, emotional, and physical abuse; emotional and physical neglect). Cut-off scores were applied to determine the presence or absence of each type of ACE, yielding a cumulative score (0-5), representing the total number of ACE types experienced (Glaesmer et al., 2013).

2.2.1.2. PTSD, Dissociative Disorders, and Depression. PTSD, dissociative disorders and depression were identified through linked health records using codes from the *International Classification of Diseases, Tenth Revision* (ICD-10; World Health Organization, 1993; PTSD, F43.1; any dissociative disorder, F44.x, F48.1; any depression, F32.x; or recurrent depressive disorder F33.x). The date of diagnosis was ascertained by the first recorded occurrence in primary care records, hospital admission data, or death registers. For analyses with cognitive functioning as the outcome, we included only those participants who received any of the

specified diagnoses prior to the baseline assessment (when cognitive functioning was assessed) or before the censoring date (i.e., last recorded observation). For analyses with incident all-cause dementia as the outcome, we included only participants who received the specified diagnoses before either a dementia diagnosis or censoring. For analyses with hippocampal volume as the outcome, we included only those participants who received any of the specified diagnoses prior to the date of hippocampal imaging or before the censoring date.

The online mental health questionnaire included an adapted, shortened version of the PTSD Checklist – Civilian Version (PCL-C; Wilkins et al., 2011), assessing PTSD symptoms over the past month. Five items, rated on a five-point Likert scale, evaluated intrusive thoughts, trauma-related distress, avoidance, feelings of detachment from others, and irritability, with a total sum score reflecting symptom severity (Davis et al., 2020). As the online mental health survey was administered several years after the baseline assessment, analyses using the PCL-C were limited to hippocampal volume and incident all-cause dementia as outcomes. Participants were included in these analyses if they had an MRI scan when hippocampal volume was the outcome, or when dementia diagnosis occurred only after completing the survey or not recorded until censoring.

From this point onward, ACEs, PTSD diagnosis and symptoms, dissociative disorders, and depression, are referred to as the main predictors.

2.2.2. Moderators

The following variables were used as moderators in the analyses: age, sex, ethnicity, deprivation, educational level, tobacco smoking status, alcohol consumption, hypertension, social and physical activity. Age at baseline was calculated using the date of birth and date of assessment. Sex (male, female), ethnicity, highest attained level of education (i.e., College/university degree or one five other qualification levels), smoking status (i.e., “Never”, “Previous”, “Current”), and social activities was self-reported at baseline. Social activities encompassed the frequency of friend or family visits (i.e., “How often do you visit friends or

family or have them visit you?"), ability to confide in someone (i.e., "How often are you able to confide in someone close to you?"), and leisure activities (i.e., "Which of the following do you attend once a week or often?", including sports club or gym, pub or social club, religious group, adult education class, or other group activities). The first two questions were rated on a 6-point Likert scale, while the latter was transformed into a numerical variable representing number of memberships. The Townsend deprivation index was calculated based on area-level aggregated data, including unemployment rates, car and home ownership, and household overcrowding (Townsend et al., 2023). Weekly physical activity, measured as total Metabolic Equivalent Task (MET) minutes per week for walking, moderate, and vigorous activities, was assessed using the validated International Physical Activity Questionnaire (IPAQ; Craig et al., 2003) Activity durations were weighted by energy expenditure associated with each activity category, and data were processed according to the guidelines published by IPAQ (2005). Hypertension was defined as either a systolic blood pressure of at least 140 mmHg or self-reported use of antihypertensive medication at baseline. The thresholds for "increased" risk of harm from alcohol consumption were set at 15–34 units per week for women and 15–49 units per week for men in line with National Institute for Health and Care Excellence guidance (NICE, 2010). Alcohol consumption below or above these ranges was categorized as "lower" and "higher" risk, respectively.

2.2.3. Outcomes

2.2.3.1. Cognitive Functioning. Cognitive ability was assessed at baseline by means of five computerized touch-screen tests (Lyall et al., 2016). Three of these cognitive tests were used in the present study, covering three important domains, namely reaction time (n = 417,586), memory (n = 420,901), and fluid intelligence (n = 151,415).

2.2.3.1.1. Reaction Time. Reaction time, also known as processing speed, was measured by a timed test of symbol matching, based on the card game "Snap", in which participants must press a button as quickly as possible if a pair of cards on the screen match. The score on this

test is the mean response time in milliseconds across eight rounds to correctly identify matches. Higher scores represent worse reaction time. Due to positive skewness, the scores were log-transformed. The test's Cronbach's alpha has previously been reported elsewhere as 0.85 (Hagenaars et al., 2016).

2.2.3.1.2. Visual Memory Errors. The pairs-matching task was used to assess visual memory. In this task participants are asked to memorize the position of matching cards displayed on a computer screen. The cards are then turned face down, and participants must recall the positions of matching pairs with the fewest possible attempts. The first round includes three pairs of cards, while the second round includes six pairs of cards. The task score reflects the number of incorrect matches per round, with higher scores indicating poorer visual memory. Notably, in the UK Biobank the pairs-matching task is zero-inflated, indicating floor effects. Despite this limitation, we chose to include the task to cover an additional cognitive domain, acknowledging this constraint.

2.2.3.1.3. Reasoning Ability. To evaluate verbal-numerical reasoning, participants were given two minutes to complete as many of the 13 tasks assessing verbal and arithmetic deduction as possible. Cronbach's alpha for this task has previously been reported as 0.62 (Hagenaars et al., 2016). In the UK Biobank, this task is formally referred as "fluid intelligence", representing the capacity to solve problems independently of acquired knowledge, using logic and reasoning abilities. Hereafter, it will be referred to as reasoning ability. The maximum score is 13, with higher scores representing better reasoning ability. Notably, the reasoning task was added to the cognitive ability battery later during the baseline assessment phase, which explains the smaller number of participants who completed it compared to the other cognitive tests.

2.2.3.2. Dementia. Incident all-cause dementia and date of first diagnosis was determined through the linked electronic health records using the ICD-10 (Creutzfeldt-Jakob disease, A81.0, F02.1; Alzheimer's disease, F00.x, G30.x; vascular dementia, F01.x; dementia

in other diseases classified elsewhere, including frontotemporal dementia, F02.x, G31.0; unspecified dementia, F03, delirium superimposed on dementia, F05.1; amnesic syndrome, F10.6; senile degeneration of brain, not elsewhere classified, G31.1; other specified degenerative diseases of nervous system including Lewy body dementia, G31.8x; World Health Organization, 1993). Dementia is analyzed as a time-to-event variable where the end of follow-up was the linked data censor date (for people who were alive and did not have the outcome), date of death (for people who died), or date of first dementia diagnosis (for people who had the outcome).

2.2.3.3. Hippocampal Volume. Imaging protocols were designed by the UK Biobank Imaging Working Group (http://www.ukbiobank.ac.uk/expert-working-groups). The UK Biobank pre-processed and conducted quality checks on all brain imaging data (Alfaro-Almagro et al., 2018; Miller et al., 2016). Brain images were acquired using a Siemens Skyra 3.0T scanner (Siemens Medical Solutions, Germany) equipped with a 32-channel head coil. T1-weighted images, a structural technique providing high-resolution visualization of brain anatomy through strong contrast between grey and white matter – reflecting differences in the interaction of water with surrounding tissues – were acquired at 1 mm^3 isotropic resolution and previously analyzed using the FMRIB Software Library (FSL; http://fsl.fmrib.ox.ac.uk/fsl). Image-derived phenotypes (IDPs), including summary statistics such as hippocampal volume, were subsequently made available for available researchers (Alfaro-Almagro et al., 2018; Miller et al., 2016). Further details on MRI acquisition and analysis are freely available elsewhere: the UK Biobank brain scan protocol (https://biobank.ctsu.ox.ac.uk/crystal/refer.cgi?id=2367), the UK Biobank Brain Imaging Documentation (https://biobank.ndph.ox.ac.uk/showcase/refer.cgi?id=1977) and elsewhere (Alfaro-Almagro et al., 2018; Miller et al., 2016). For the present study, volume of whole-hippocampal head in both the left and right hemisphere was used.

2.3. Statistical Analyses

We conducted a series of regression analyses for each of the predictor-outcome combinations. First, visual memory errors, reaction time, and physical activity scores were log-transformed (log(x + 1)) to address positive skewness. Second, to enhance interpretability, predictor variables were recoded as a 'risk factor', where necessary, so that higher scores consistently represented more adverse conditions. Categorical variables were dichotomized: ethnicity (White vs. Asian, Black, Mixed, and Other) as they were very small number of Asian, Black, Mixed, and Other ethnic backgrounds after exclusion, education level (with vs. without college or university degree), smoking status (never vs. previous/current), and alcohol consumption (lower vs. increasing/higher risk). Additionally, continuous predictor variables (age, physical activity, deprivation, and social activity measures, PTSD symptoms) were standardized. Third, we generated interaction terms between main predictors and each moderator, to examine potential moderation effects on the outcomes. These interaction terms were included in the set of predictors alongside the main predictors.

We used a two-step approach to identify the most relevant interactions modifying the associations between the primary predictors (trauma and psychopathology) and outcomes (Qian et al., 2020). This was done by applying the least absolute shrinkage and selection operator (LASSO), a widely used method for simultaneous parameter estimation and variable selection (Tibshirani, 1996), followed by a stepwise selection of the LASSO selected models.

The LASSO-models had ACEs, PTSD diagnosis, PTSD symptoms, dissociative disorders, and depression as primary predictors, and the interaction of these with moderators as independent variables. For continuous outcomes (i.e., cognitive functioning, hippocampal volume), we used a Gaussian family model (Hastie et al., 2009; McCullagh & Nelder, 2019). For dementia diagnosis, we estimated a Cox proportional hazards model, with time to dementia diagnosis as the event time, allowing us to model the hazard of developing dementia as a function of the predictor variables (Tibshirani, 1997).

LASSO applies an ℓ_1 penalty, which encourages sparsity by shrinking some coefficients toward zero while setting others to exactly zero, thereby improving interpretability and preventing overfitting. This was done via a penalty parameter (λ) to suppress predictors' coefficients to zero. This parameter was selected based on a 10-fold cross-validation. Briefly, the dataset was randomly split into 10 folds, with each fold serving as a validation set once, while the model was trained on the remaining nine folds. This process was repeated 10 times until each fold had served as the validation set once. The model performance in the validation set for all λ values was computed across all iterations to select the best λ (Ebrahimi et al., 2022; Hastie et al., 2009). Model performance was assessed using mean squared error (MSE) for continuous outcomes (cognitive functioning, hippocampal volume) and Harrell's concordance index (C-index) for dementia diagnosis, to measure model discrimination in the Cox model. Because LASSO is for prediction and does not produce inferential statistics, this was followed by a stepwise approach to further explore the relative importance of the moderators (Freijeiro-González et al., 2022; Su et al., 2017; Zhou et al., 2024).

We tested linear regression assumptions (e.g., normality of residuals, homoscedasticity), and checked the global proportional hazard assumptions for the Cox models using Schoenfeld residuals. When a violation was suspected, we addressed it by stratifying the affected variables.

For each analysis, the temporal sequence of events was considered: For cognitive functioning outcomes, participants diagnosed with PTSD, dissociative disorders, or depression prior to baseline were categorized accordingly. For hippocampal volume and dementia diagnosis outcomes, we ensured that predictor diagnoses preceded the outcome assessment to maintain temporal validity. Dementia cases diagnosed before baseline were additionally excluded to prevent reverse causation regarding the moderators, which were assessed at baseline. Since PTSD symptoms were assessed at follow-up, they were only analyzed as predictors of hippocampal volume and dementia diagnosis. Cognitive functioning was

measured at baseline, inherently preceding the assessment of PTSD symptoms, making it unsuitable as an outcome in this context.

To handle missing data, we used pairwise deletion, maximizing the use of available data for each analysis while maintaining statistical power. Specifically, participants with missing data on any of the diagnoses, their timing, or any moderators were excluded. However, missing data were not removed for reasoning assessment and MRI scans of hippocampal volume at baseline, nor for the online follow-up measures (i.e., ACEs, PTSD symptoms), as only a subset of participants completed these assessments.

All analyses were conducted between October 2024 and January 2025 using R (version 4.4.1). Details on specific packages and versions are provided in the Supplementary Material (Appendix C).

3. Results

3.1. Sample Characteristics

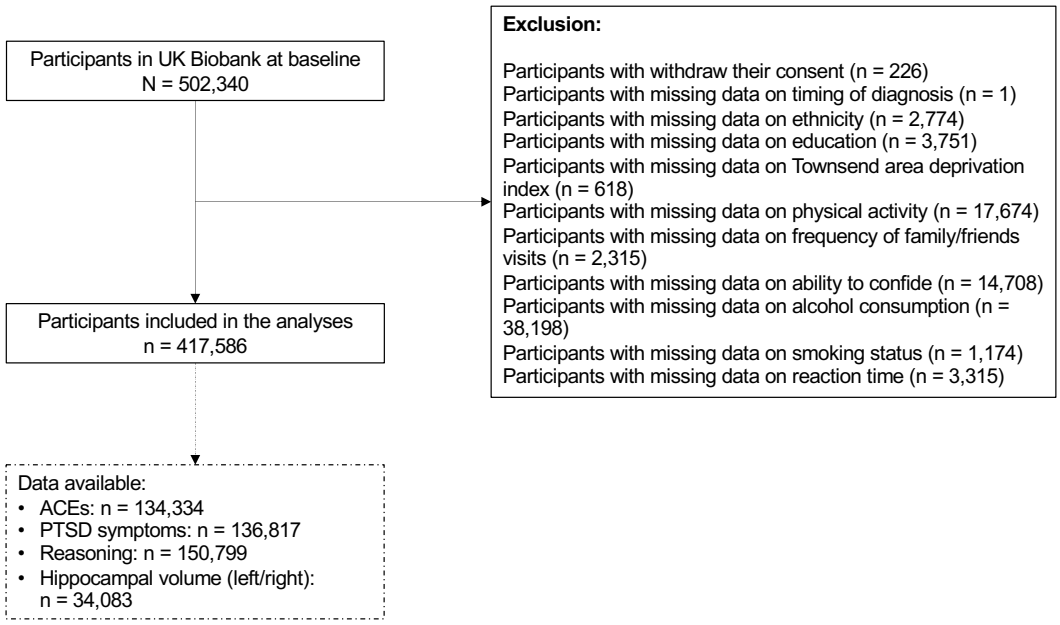
The primary sample included 417,586 participants (Figure 3.1), with a mean age of 56.55 years (SD = 8.06). Women made up 53.77% of the sample and 4.63% of participants identified as Asian, Black, Mixed, and Other. Additionally, 275,268 (65.92%) had an educational level below a college or university degree. The mean follow-up was 13.66 years (SD = 2.05). In total, 903 (0.22%) participants were diagnosed with PTSD, 322 (0.08%) with any dissociative disorder, and 43,346 (10.38%) with depression. People with any of these diagnoses generally had lower education levels, a higher proportion of being current smokers, greater lower-risk alcohol consumption, were less physically active, engaged less in leisure activities, and had a lower ability to confide in others (Table 3.1). Among those who completed the online mental health survey (n = 134,334), approximately one-third (n = 44,515, 33.14%) reported experiencing at least one type of adverse childhood experience (ACE). Among those, the most reported ACE was emotional neglect (66.27%), followed by emotional abuse

(27.93%), sexual abuse (26.48%), physical abuse (24.00%), and physical neglect (16.52%; Supplementary Material, Appendix C eTable C1). After excluding participants with dementia diagnosed before the baseline assessment (n = 34), dementia developed in 249 individuals with ACEs (0.56%), in 20 individuals with PTSD (2.24%), 17 of those with any dissociative disorder (5.48%), and 1,291 of those with depression (3.02%). In comparison, dementia occurred in 5,538 individuals without PTSD, dissociative disorders, or depression (1.48%), and in 390 individuals without these diagnoses or ACEs (0.46%; Table 3.1; Supplementary Material, Appendix C eTable C2 for dementia diagnoses by number of ACEs).

In reporting the main results, we focus on the associations between trauma- and trauma-related psychopathology, and depression (i.e., main predictors), as well as their interactions with moderators, on the outcomes. The coefficients of each final model and additional results are available in the Supplementary Material (Appendix C). Unless otherwise stated, assumptions for the analyses were met. Larger model parameter values indicate a greater effect magnitude. Table 3.2 presents all relevant interactions between the main predictors and each cognitive outcome.

Figure 3.1

Diagram of Participants Included in the Analyses



N = sample size; ACEs = adverse childhood experiences; PTSD = posttraumatic stress disorder.

Table 3.1

Baseline and Outcome Characteristics by Group

	Overall (n = 417,586)	Comparison Group* (n = 373,699)	Comparison Group 2† (n = 84,296)	ACEs‡ (n = 44,515)	PTSD§ (n = 903)	Dissociative Disorders§ (n = 322)	Depression§ (n = 43,346)
Moderators at baseline							
Age, mean (SD)	56.55 (8.06)	56.61 (8.06)	56.21 (7.70)	55.49 (7.74)	53.02 (7.93)	55.25 (8.03)	56.05 (8.04)
Age groups, *n* (%)							
37-50	108,869 (26.07)	96,590 (25.85)	21,583 (25.60)	12,731 (28.60)	379 (41.97)	93 (28.88)	12,093 (27.90)
51-60	148,145 (35.48)	132,129 (35.36)	33,191 (39.37)	17,952 (40.33)	326 (36.10)	129 (40.06)	15,819 (36.49)
61-73	160,572 (38.45)	144,980 (38.80)	29,522 (35.02)	13,832 (31.07)	198 (21.93)	100 (31.06)	15,434 (35.61)
Sex, *n* (%)							
Female	224,523 (53.77)	196,457 (52.57)	45,106 (53.51)	25,901 (58.18)	431 (47.73)	225 (69.88)	27,803 (64.14)
Male	193,063 (46.23)	177,242 (47.43)	39,190 (46.49)	18,614 (41.82)	472 (52.27)	97 (30.12)	15,543 (35.86)
Asian, Black, Mixed, or Other ethnic background, *n* (%)¶	19,350 (4.63)	17,627 (4.72)	1,644 (1.95)	1,895 (4.26)	73 (8.08)	15 (4.66)	1,690 (3.90)
College or university degree, *n* (%)	142,318 (34.08)	130,282 (11.47)	40,773 (48.37)	19,805 (44.49)	257 (28.46)	76 (23.60)	11,892 (27.44)
Townsend deprivation index, mean (SD)	-1.40 (3.03)	-1.47 (2.99)	-1.92 (2.70)	-1.39 (2.96)	0.00 (3.58)	-0.28 (3.42)	-0.77 (3.28)
Smoking status, *n* (%)							
Current	42,774 (10.24)	35,361 (9.46)	4,962 (5.89)	4,088 (9.18)	196 (21.71)	53 (16.46)	7,326 (16.90)
Former	147,976 (35.44)	132,062 (35.34)	28,577 (33.90)	17,482 (39.27)	299 (33.11)	100 (31.06)	15,725 (36.28)
Never	226,836 (54.32)	206,276 (55.20)	50,757 (60.21)	22,945 (51.54)	408 (45.18)	169 (52.48)	20,295 (46.82)
Risk of harm from alcohol, *n* (%)							
Higher risk	29,974 (7.18)	26,497 (7.09)	4,752 (5.64)	3,029 (6.80)	90 (9.97)	12 (3.73)	3,432 (7.92)
Increasing risk	138,930 (33.27)	127,128 (34.02)	30,733 (36.46)	14,774 (33.19)	233 (25.80)	56 (17.39)	11,651 (26.88)
Lower risk	248,682 (59.55)	220,074 (58.89)	48,811 (57.90)	26,712 (60.01)	580 (64.23)	254 (78.88)	28.263 (65.20)
Log-transformed physical activity, minutes per week	7.01 (1.87)	7.04 (1.83)	7.09 (1.62)	7.05 (1.73)	6.65 (2.38)	6.21 (2.71)	6.72 (2.20)
Physical activity, minutes per week, Mdn (IQR)	1,593.00 (693.00 – 3,339.00)	1622.00 (693.00 – 3360.00)	1,575.00 (727.50 – 3,066.00)	1,590.00 (700.00 – 3,172.00)	1,470.00 (459.00 – 3,364.00)	1,050.00 (330.00 – 3,010.00)	1,386.00 (495.00 – 3,176.00)
Hypertension, *n* (%)	208,017 (49.81)	186,595 (49.93)	38,410 (45.57)	19,154 (43.03)	434 (48.06)	169 (52.48)	21,157 (48.81)
Frequency of family or friends' visits, *n* (%)							

	Overall (*n* = 417,586)	Comparison Group* (*n* = 373,699)	Comparison Group 2† (*n* = 84,296)	ACEs‡ (*n* = 44,515)	PTSD§ (*n* = 903)	Dissociative Disorders§ (*n* = 322)	Depression§ (*n* = 43,346)
No friends/family outside household	951 (0.23)	753 (0.20)	58 (0.07)	82 (0.18)	10 (1.11)	2 (0.62)	194 (0.45)
Never or almost never	5,986 (1.43)	4.965 (1.33)	661 (0.78)	744 (1.67)	29 (3.21)	10 (3.11)	1,005 (2.32)
Once every few months	27,402 (6.56)	24,482 (6.55)	5,456 (6.47)	3,646 (8.19)	75 (8.31)	21 (6.52)	2,882 (6.65)
About once a month	56,348 (13.49)	51,131 (13.68)	12,775 (15.15)	7,263 (16.32)	107 (11.85)	35 (10.87)	5,151 (11.88)
About once a week	149,593 (35.82)	135,110 (36.15)	31,538 (37.41)	16,548 (37.17)	274 (30.34)	98 (30.43)	14,317 (33.03)
2-4 times a week	128,954 (30.88)	115,141 (30.81)	25,754 (30.55)	12,359 (27.76)	278 (30.79)	106 (32.92)	13,640 (31.47)
Almost daily	48.352 (11.58)	42,117 (11.27)	8,054 (9.55)	3,873 (8.70)	130 (14.40)	50 (15.53)	6,157 (14.20)
Ability to confide in others							
Never or almost never	60,208 (14.42)	52,352 (14.01)	8,831 (10.48)	7,014 (15.76)	191 (21.15)	59 (18.32)	7,759 (17.90)
Once every few months	23,500 (5.63)	20,709 (5.54)	4,177 (4.96)	2,594 (5.83)	41 (4.54)	23 (7.14)	2,760 (6.37)
About once a month	22,234 (5.32)	19,408 (5.19)	4,043 (4.80)	2,808 (6.31)	57 (6.31)	15 (4.66)	2,794 (6.45)
About once a week	46,212 (11.07)	40,373 (10.80)	8,632 (10.24)	5,461 (12.27)	125 (13.84)	43 (13.35)	5,768 (13.31)
2-4 times a week	40,811 (9.77)	36,071 (9.65)	8,538 (10.13)	4,813 (10.81)	104 (11.52)	24 (7.45)	4,691 (10.82)
Almost daily	224,621 (53.79)	204,786 (54.80)	50,075 (59.40)	21,825 (49.03)	385 (42.64)	158 (49.07)	19,574 (45.16)
Attendance at leisure activities per week, mean (SD)¥	1.03 (0.86)	1.04 (0.86)	1.12 (0.89)	1.05 (0.88)	0.91 (0.85)	0.90 (0.88)	0.95 (0.87)
Outcomes							
At baseline	***n* = 417,586**	***n* = 373,699**	***n* = 84,296**	***n* = 44,515**	***n* = 360****	***n* = 138****	***n* = 19,465****
Log-transformed reaction time score, mean (SD)	6.31 (0.19)	6.30 (0.19)	6.28 (0.17)	6.29 (0.18)	6.34 (0.22)	6.37 (0.21)	6.32 (0.20)
Untransformed reaction time score, Mdn (IQR)	536.00 (480.00 – 610.00)	535.00 (480.00 – 609.00)	524.00 (473.00 – 590.00)	527.00 (473.00 – 594.00)	551.00 (481.00 – 640.50)	578.00 (500.00 – 668.00)	543.00 (485.00 – 621.00)
Log-transformed visual memory error score, mean (SD)	1.54 (0.65)	1.53 (0.65)	1.46 (0.63)	1.49 (0.63)	1.53 (0.69)	1.58 (0.72)	1.56 (0.66)
Untransformed visual memory error score, Mdn (IQR)	4.00 (2.00 – 6.00)	4.00 (2.00 – 6.00)	4.00 (2.00 – 6.00)	4.00 (2.00 – 6.00)	4.00 (2.00 – 6.00)	4.00 (2.00 – 7.00)	4.00 (2.00 – 6.00)
Reasoning ability score, mean (SD)	6.06 (2.13)	6.10 (2.13)	6.83 (2.03)	6.50 (2.06)	5.27 (2.23)	5.88 (2.29)	5.88 (2.13)

	Overall (*n* = 417,586)	**Comparison Group* (*n* = 373,699)**	**Comparison Group 2† (*n* = 84,296)**	**ACEs‡ (*n* = 44,515)**	**PTSD§ (*n* = 903)**	**Dissociative Disorders§ (*n* = 322)**	**Depression§ (*n* = 43,346)**
During the study period††							
Dementia	***n* = 417,452**	***n* = 373,613**	***n* = 84,289**	***n* = 44,508**	***n* = 893**	***n* = 310**	***n* = 42,687**
n (%)	7,438 (1.78)	5,538 (1.48)	390 (0.46)	249 (0.56)	20 (2.24)	17 (5.48)	1,291 (3.02)
Hippocampal volume, mm^3, mean (SD)	***n* = 34,083**	***n* = 31,326**	***n* = 14,691**	***n* = 44,515**	***n* = 27**	***n* = 8**	***n* = 2,034**
Left	3,674.89 (394.36)	3,677.48 (394.54)	3,680.84 (391.96)	3,673.36 (390.49)	3,674.65 (445.84)	3,495.48 (407.84)	3657.64 (391.03)
Right	3,793.33 (402.00)	3,795.81 (402.13)	3,797.17 (400.34)	3,794.52 (395.09)	3,761.21 (394.63)	3,639.36 (241.04)	3,775.09 (396.05)

N = sample size; ACEs = adverse childhood experiences; PTSD = posttraumatic stress disorder; SD = standard deviation; Mdn = median; IQR = interquartile range.

*"Comparison group" refers to participants without PTSD, dissociative disorders, or depression (PTSD–/Dissociative disorders–/Depression–).

†"Comparison group 2" refers to participants without PTSD, dissociative disorders, or depression, who self-reported as part of the online mental health survey that they had no ACEs (ACEs–/PTSD–/Dissociative disorders–/Depression–).

‡"ACEs" group refers to participants who self-reported that they had at least one type of ACEs, as part of the online mental health survey (ACEs+).

§Including participants with the corresponding diagnoses in the final sample.

¶Including Asian or Asian British, Black or Black British, Chinese, Mixed, Other ethnic background.

#Including sports club or gym, pub or social club, religious group, adult education class, other group activity, or none of those.

**Including participants with the predictor diagnosis prior to baseline (i.e., before the cognitive functioning assessment).

††Including participants for whom the predictor diagnosis preceded either a dementia diagnosis or the hippocampal volume assessment.

Table 3.2

Relevant Interactions between Trauma- and Depression-Related Main Predictors and Cognitive Outcomes in the Final Models

Main Predictors	ACEs	PTSD[a]	PTSD symptoms[b]	Dissociative disorders[c]	Depression[c]
Outcomes					
Log reaction time	• ACEs (main association) • Males • Higher education • Lower ability to confide in others • Lower physical activity • Lower-risk alcohol consumption	• PTSD (main association) • Asian, Black, Mixed, or Other ethnic background[f] • Lower physical activity	NA	• Dissociative disorders (main association) • Lower-risk alcohol consumption	• Depression (main association) • Males • Greater deprivation • Lower-risk alcohol consumption • Lower physical activity
Log visual memory errors	• ACEs (main association) • White ethnic background • Higher education	• Greater deprivation • Greater ability to confide in others	NA	• Less engagement in leisure activities	• Depression (main association) • Males • Current or former smoker
Reasoning ability	• ACEs (main association) • Younger age • Males • White ethnic background • Higher education	• PTSD (main association) • Greater deprivation • Lower physical activity	NA	• Less engagement in leisure activities	• Depression (main association) • Lower physical activity
Dementia	• Hypertension	• Current or former smoker	• Asian, Black, Mixed, or Other ethnic background[f] • Hypertension • Lower education • Lower frequency of family or friends' visits	• Dissociative disorders (main association) • Younger age	• Depression (main association) • Younger age • Males • Higher-risk alcohol consumption

Left hippocampal volume	• None	• None	• None	• Current or former smoker	• Asian, Black, Mixed, or Other ethnic background‡
Right hippocampal volume	• None	• None	• None	• None	• Asian, Black, Mixed, or Other ethnic background‡ • Lower physical activity

ACEs = adverse childhood experiences; PTSD = posttraumatic stress disorder; NA = Not applicable (i.e., no analyses conducted).
The listed moderators indicate that the association between the corresponding main predictor and on the corresponding outcome is more pronounced in this subgroup.
*Based on diagnoses from electronic health records, including primary care, hospital admissions, and death registers.
†Based on a self-report measures at follow-up.
‡Including Asian or Asian British, Black or Black British, Chinese, Mixed, Other ethnic group.

3.2. ACEs as a Main Predictor

3.2.1. Cognitive Functioning

3.2.1.1. Reaction Time. In a LASSO regularized regression model (n = 134,334), all, main predictors and interactions, except the interaction between ACEs and age, were retained. Predictors selected by LASSO were then entered into the non-regularized regression model, with stepwise method used to derive a parsimonious model containing only predictors most relevant to reaction time. ACEs were associated with slower reaction times (β = 0.0063, 95% CI 0.0041, 0.0084). Relevant interactions were found with alcohol consumption (β = -0.0028, 95% CI -0.0047, -0.0008), education (β = -0.0027, 95% CI -0.0045, -0.0009), sex (β = -0.0026, 95% CI -0.0046, -0.0007), ability to confide (β = 0.0009, 95% CI 0.0001, 0.0018), and physical activity (β = 0.0009, 95% CI 0.0001, 0.0017). These results indicate that the association between ACEs and slower reaction time is stronger in individuals with higher education (versus not), males (versus females), those with lower ability to confide in others (versus high), or lower physical activity (versus high). In contrast, high-risk alcohol consumption appears to buffer or mitigate the negative association between ACEs and reaction time.

3.2.1.2. Visual Memory Errors. The LASSO-model (n = 134,334) retained 18 predictors of visual memory errors. Cross-validation determined the optimal penalty term, and the model retained ACEs along with interactions involving ethnicity, education, deprivation, engagement in leisure activities, ability to confide in others, and frequency of family or friends' visits. The final model based on the stepwise method of LASSO-selected predictors showed that ACEs were associated with worse visual memory (β = 0.0224, 95% CI 0.0172, 0.0276), with interactions observed for ethnicity (β = -0.0220, 95% CI -0.0371, -0.0069) and education (β = -0.0112, 95% CI -0.0179, -0.0045). Thus, the association between ACEs and visual memory errors is stronger in White individuals and those with higher education, compared to

in individuals from Asian, Black, Mixed, or Other ethnic backgrounds and those with lower attained levels of education.

3.2.1.3. Reasoning Ability. All 25 predictors were retained in the LASSO-model (n = 53,203), including ACEs and all interactions with ACEs. The final model included ACEs (β = -0.1677, 95% CI -0.2025, -0.1329) and relevant interactions between ACEs and ethnicity (β = 0.1010, 95% CI 0.0361, 0.1660), sex (β = 0.0357, 95% CI 0.0009, 0.0705), education (β = 0.0353, 95% CI 0.0018, 0.0687), and age (β = 0.0170, 95% CI 0.0003, 0.0338). Therefore, the negative association between ACEs and reasoning ability is weaker in individuals from Asian, Black, Mixed, or Other ethnic backgrounds, in females, those with lower education, and in older adults, compared to in White and younger individuals, in males, and those with higher education.

3.2.2. Dementia

The analyses included 134,316 individuals, retaining nine predictors in the LASSO regularized regression model, including ACEs and its interaction with hypertension. The final model rendered the interaction as relevant (HR = 1.13, 95% CI, 1.03, 1.23). Thus, among individuals with hypertension, higher levels of ACEs were associated with a higher risk of developing dementia compared to individuals with the same number of ACEs but no hypertension (Figure 3.2). The assumption of proportional hazards was violated for age, but stratification had no impact on the results (Supplementary Material; Appendix C).

3.2.3. Hippocampal Volume

3.2.3.1. Left. The LASSO-model (n = 18,435) retained 20 predictors. ACEs alone were not retained, but interactions with hypertension, age, education, alcohol consumption, frequency of family or friends' visits, engagement in leisure activities, ability to confide in others, sex, and deprivation, were included. After stepwise method, reduced left hippocampal volume was associated with being female, older, from Asian, Black, Mixed, or Other ethnic

background, lower education, higher deprivation, alcohol consumption, and fewer family or friends' visits.

3.2.3.2. Right. A similar pattern was observed in the LASSO-model (n = 18,435, 10 retained predictors) predicting right hippocampal volume, where ACEs interacted with age, family or friends' visits and ability to confide in others, though these did not remain relevant post-stepwise method. Final model results were consistent with the left hippocampus findings.

3.3. PTSD as a Main Predictor

3.3.1. Cognitive Functioning

3.3.1.1. Reaction Time. In a LASSO-model (n = 417,586), 18 predictors were retained, including PTSD diagnosis and interactions with ethnicity, physical activity, age, smoking status, and engagement in leisure activities. In the final model, PTSD diagnosis was associated with longer reaction time (β = 0.0352, 95% CI 0.0158, 0.0546), with relevant interactions found for ethnicity (β = 0.0939, 95% CI 0.0311, 0.1566) and physical activity (β = 0.0198, 95% CI 0.0046, 0.0351). These results indicate that the association between PTSD and slower reaction time is stronger in individuals from Asian, Black, Mixed, or Other ethnic backgrounds and in those with lower physical activity, compared to White individuals and those with higher physical activity.

3.3.1.2. Visual Memory Errors. Fifteen predictors were retained in the LASSO-model (n = 417,586), including interactions between PTSD diagnosis and ability to confide in others, deprivation, and physical activity. Stepwise method revealed that PTSD diagnosis interacted with the ability to confide in others (β = -0.0692, 95% CI -0.1328, -0.0055) and deprivation (β = 0.0646, 95% CI 0.0075, 0.1218). PTSD-related visual memory errors were amplified in those with higher deprivation compared to lower deprivation but were weaker in those who confided less, compared to those who confided more.

3.3.1.3 Reasoning Ability. In the LASSO-model (n = 150,799), 22 predictors were retained, including PTSD diagnosis and interactions with ethnicity, physical activity, age, ability to confide in others, alcohol consumption, deprivation, hypertension, frequency of family or friends' visits, and engagement in leisure activities. The final model identified PTSD diagnosis (β = -0.5596, 95% CI -0.8986, -0.2206) as a predictor of reasoning ability. Interactions were found with physical activity (β = -0.4328, 95% CI -0.6883, -0.1773) and deprivation (β = -0.3069, 95% CI -0.5948, -0.0190). The negative association between PTSD and reasoning ability was stronger in individuals with higher deprivation compared to those with lower deprivation and in those who engaged in less physical activity compared to those who were more physically active.

3.3.2. Dementia

Analyses identified 18 retained predictors (n = 417,452), including interactions between PTSD diagnosis and deprivation, physical activity, frequency of family and friends' visits, ability to confide in others, alcohol consumption, smoking status, and hypertension. After stepwise method of those retained predictors, PTSD interacted with ever-smoking (vs. not) (Figure 3.2). Among current or former smokers, PTSD diagnosis was linked to an almost threefold increase in dementia risk (HR = 2.93, 95% CI 1.75, 4.91), compared to individuals who have never smoked. The assumption of proportional hazards was violated for age, engagement in leisure activities, and alcohol consumption. Stratified analyses addressed assumption violations without affecting results (Supplementary Material; Appendix C).

To examine potential power issues due to the low number of PTSD diagnoses, PTSD symptoms at follow-up were analyzed as well (n = 136,705). LASSO retained 17 predictors. The final model, after stepwise selection of the LASSO-selected predictors, found that among individuals from Asian, Black, Mixed, or Other ethnic backgrounds, more PTSD symptoms were associated with a higher risk of developing dementia (HR = 1.39, 95% CI 1.01, 1.90). PTSD symptoms were especially linked to an increased dementia risk in individuals with

hypertension (HR = 1.19, 95% CI 1.06, 1.35) and in those with lower education (HR = 1.19, 95% CI 1.05, 1.34), compared to those with the same severity of PTSD symptoms but without hypertension or with higher education. Similarly, individuals with more PTSD symptoms who had less frequent visits from family or friends had a higher risk of developing dementia (HR = 1.09, 95% CI 1.02, 1.15), compared to individuals with more frequent family or friends' visits. In contrast, individuals with more PTSD symptoms who engaged less in leisure activities had a lower dementia risk (HR = 0.88, 95% CI 0.83, 0.94) (Figure 3.2), compared to those with greater engagement. Stratifying for age removed the interaction between PTSD symptoms and ethnicity but did not affect other results (Supplementary Material; Appendix C).

3.3.3. Hippocampal Volume

3.3.3.1. Left. In the LASSO-model (n = 26,653, 17 retained predictors), PTSD diagnosis interacted with ethnicity, age, alcohol, smoking status, frequency of family or friends' visits, and ability to confide in others, though none remained relevant post-stepwise method. The LASSO-model with PTSD symptoms (n = 12,405, 19 retained predictors) found interactions with ethnicity, hypertension, frequency of family and friends' visits, education, deprivation, age, and alcohol consumption, but similar to PTSD diagnosis, none remained in the final model.

3.3.3.2. Right. Similar results were observed for the right hippocampal volume. In the LASSO-regularized model (n = 26,653, 15 retained predictors), PTSD diagnosis interacted with ethnicity, frequency of family or friends' visits, smoking status, and deprivation but no interaction remained included in the final model. Similar results were found for PTSD symptoms (n = 12,405, 14 retained predictors).

3.4. Dissociative Disorders as a Main Predictor

3.4.1. Cognitive Functioning

3.4.1.1, Reaction Time. A LASSO regression (n = 417,586) identified 22 out of 25 predictors at an optimal penalty term, including dissociative disorders alone and their interactions with alcohol consumption, smoking status, physical activity, hypertension, frequency of family or friends' visits, ability to confide in others, engagement in leisure activities, and deprivation. After stepwise selection, dissociative disorders were associated with reaction times (β = 0.0789, 95% CI 0.0371, 0.1207). The interaction between dissociative disorders and alcohol consumption (β = -0.0845, 95% CI -0.1640, -0.0049) was also relevant. These findings suggest that dissociative disorders are linked to slower reaction times, particularly in individuals with lower-risk alcohol consumption compared to those with higher-risk consumption, aligning with patterns observed in ACEs.

3.4.1.2. Visual Memory Errors. The LASSO-model (n = 417,586) retained 15 predictors, including interactions between dissociative disorders and ethnicity, engagement in leisure activities, and physical activity. After stepwise selection, the interaction between dissociative disorders and engagement in leisure activities was associated with poorer visual memory (β = 0.1764, 95% CI 0.0198, 0.3330). This suggests that individuals with dissociative disorders who engage in fewer leisure activities, compared to those who engage in more, experience greater impairment in visual memory performance.

3.4.1.3. Reasoning Ability. In 150,799 participants, 14 predictors were retained in the LASSO-model, including interactions between dissociative disorders, ethnicity, and engagement in leisure activities. After stepwise selection, the interaction between dissociative disorders and engagement in leisure activities remained included (β = -0.7678, 95% CI -1.4114, -0.1243). Individuals with dissociative disorders who engage in fewer leisure activities, compared to those who engage in more, are particularly prone to impaired reasoning ability.

3.4.2. Dementia

The LASSO-model (n = 417,452) retained 19 predictors, including dissociative disorders and their interactions with ethnicity, education, engagement in leisure activities, deprivation, frequency of family's or friends' visits, and hypertension. Stepwise selection identified dissociative disorders (HR = 5.67, 95% CI 1.35, 23.77) and their interaction with age (HR = 0.31, 95% CI 0.18, 0.52) as relevant (Figure 3.2). Individuals with dissociative disorders had over a fivefold increased risk of developing dementia compared to those without a dissociative disorder. The interaction suggests that this elevated dementia risk associated with dissociative disorders is particularly strong in younger individuals but diminishes with older age. Stratification did not significantly alter results, except for slightly reducing the HR associated with dissociative disorders alone to HR = 4.59 (Supplementary Material; Appendix C).

3.4.3. Hippocampal Volume

3.4.3.1. Left. The LASSO-model (n = 26,653) retained 16 predictors, including interactions between dissociative disorders and smoking status, hypertension, engagement in leisure activities, deprivation, and physical activity. After stepwise selection, only the interaction with smoking remained relevant (β = -463.71, 95% CI -872.78, -54.64). Among smokers, individuals with a dissociative disorder were associated with a reduced hippocampal volume compared to those without a dissociative disorder.

3.4.3.2. Right. The LASSO-model (n = 26,653) retained 20 predictors, including interactions between dissociative disorders and frequency of family or friends' visits, smoking status, alcohol consumption, age, sex, engagement in leisure activities, hypertension, and physical activity. However, none remained included after stepwise selection. Right hippocampal volume was instead associated with sex, age, ethnicity, education, deprivation, smoking status, and hypertension.

3.5. Depression as a Main Predictor

3.5.1. Cognitive Functioning

3.5.1.1. Reaction Time. The LASSO-model (n = 417,586) retained 23 out of 25 predictors, including depression and its interactions with ethnicity, alcohol consumption, education, smoking status, sex, physical activity, deprivation, hypertension, frequency of family and friends' visits, and ability to confide in others. After stepwise selection, depression was associated with slower reaction time (β = 0.0164, 0.0093, 0.0235), with interactions involving alcohol consumption (β = -0.0091, 95% CI -0.0148, -0.0034), sex (β = -0.0086, 95% CI -0.0143, -0.0030), physical activity (β = 0.0034, 95% CI 0.0017, 0.0056), and deprivation (β = 0.0025, 95% CI 0.00003, 0.005). The link between depression and slower reaction time was weaker in females and in individuals with higher-risk alcohol consumption compared to males and those with lower-risk alcohol consumption, but stronger in those with lower physical activity and higher deprivation, relative to those with greater physical activity and lower deprivation. The observed mitigating effect of higher-risk alcohol consumption is consistent with the findings in ACEs and dissociative disorders.

3.5.1.2. Visual Memory Errors. The LASSO-model (n = 417,586) retained 22 predictors. Among them were depression and its interactions with ethnicity, sex, smoking status, deprivation, engagement in leisure activities, age, education, physical activity, ability to confide in others. Depression was associated with poorer visual memory (β = 0.0541, 95% CI 0.0347, 0.0734), with interactions involving sex (β = -0.0230, 95% CI -0.0426, -0.0035) and smoking (β = -0.0203, 95% CI -0.0389, -0.0017). These findings indicate that the association between depression and visual memory errors is weaker in females and former or current smokers, compared to males and those who have never smoked.

3.5.1.3. Reasoning Ability. The LASSO-model (n = 150,799) retained 24 predictors, including depression, and its interactions with ethnicity, physical activity, smoking status, hypertension, education, engagement in leisure activities, deprivation, alcohol consumption,

ability to confide in others, age, and frequency of family or friends' visits. After stepwise selection, depression remained associated with lower reasoning ability (β = -0.1366, 95% CI -0.1820, -0.0913), particularly in individuals with lower, compared to higher, levels of physical activity (β = -0.0710, -0.1093, -0.0327).

3.5.2. Dementia

The LASSO-model (n = 417,452) retained 20 predictors, including depression and its interactions with age, alcohol consumption, sex, frequency of family or friends' visits, ability to confide in others, physical activity, deprivation, and engagement in leisure activities. After stepwise selection, depression was associated with a 173% increased risk of developing dementia (HR = 2.73, 95% CI 2.36, 3.16). Relevant interactions were observed with sex (HR = 0.87, 95% CI 0.77, 0.99) and age (HR = 0.78, 95% CI 0.71, 0.86) (Figure 3.2). These findings indicate that males and younger adults with depression are particularly vulnerable to developing dementia, compared to females and older adults. Assumptions were violated for age, engagement in leisure activities, and alcohol consumption. However, stratification on these variables did not alter the key findings, except for the interaction between depression and alcohol consumption, which emerged as relevant (HR = 1.14, 95% CI 1.001, 1.31). This suggests that among individuals with depression, higher, relative to lower, alcohol consumption is associated with an increased risk of dementia (Supplementary Material; Appendix C).

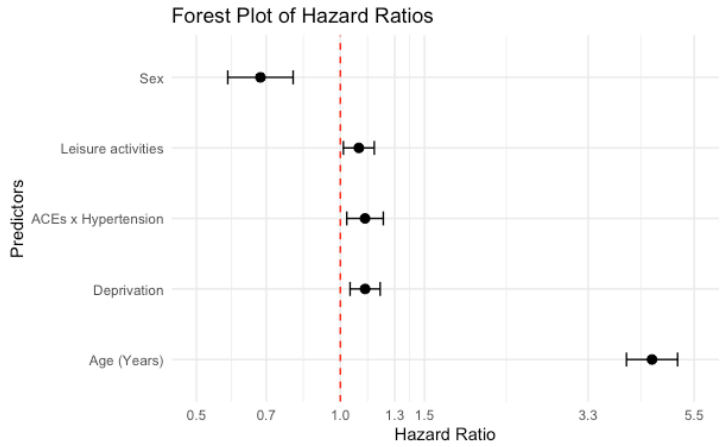
3.5.3. Hippocampal Volume

3.5.3.1. Left. The LASSO-model (n = 26,653), retained 14 predictors, including interactions between depression and ethnicity, smoking status, engagement in leisure activities, and physical activity. Stepwise selection identified a relevant interaction between depression and ethnicity (β = -121.26, 95% CI: -230.08, -12.43). This suggests that the association between depression and reduced left hippocampal volume is more pronounced in individuals from Asian, Black, Mixed, or Other ethnic backgrounds compared to White individuals.

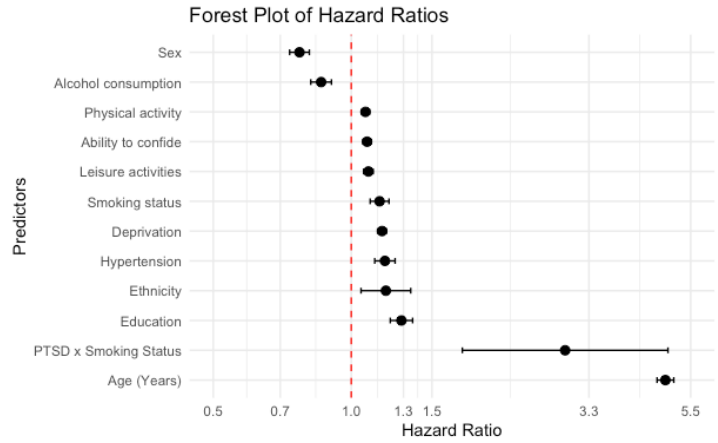
3.5.3.2. Right. The LASSO-model predicting right hippocampal volume (n = 26,653), retained 18 predictors, including interactions between depression and ethnicity, physical activity, engagement in leisure activities, smoking status, frequency of family or friends' visits, and ability to confide in others (Supplementary Material; Appendix C). After stepwise method, relevant interactions were found between depression and ethnicity (β = -112.72, 95% CI, -224.86, -0.58) and depression and physical activity (β = -15.58, 95% CI: -29.16, -2.01). The association between depression and reduced right hippocampal volume is stronger in individuals from Asian, Black, Mixed, or Other ethnic backgrounds compared to White individuals and is further exacerbated in those who are less physically active compared to those who are more physically active.

Figure 3.2

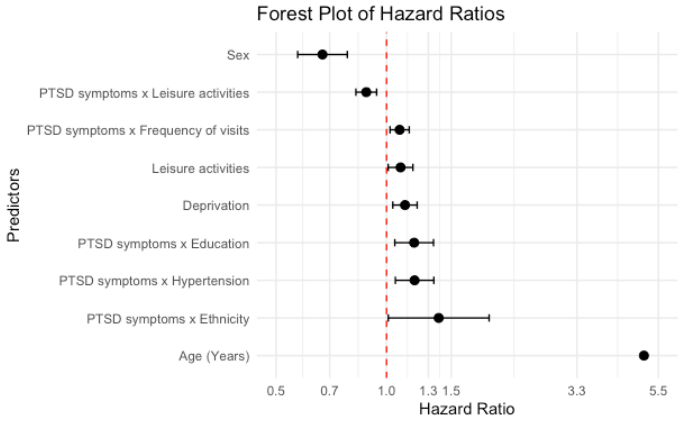
Forest Plots of Selected Variables and Dementia in the Final Models



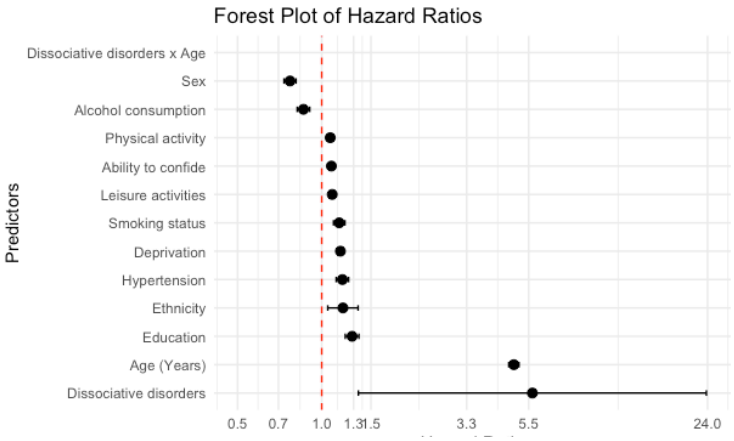
ACEs – Dementia



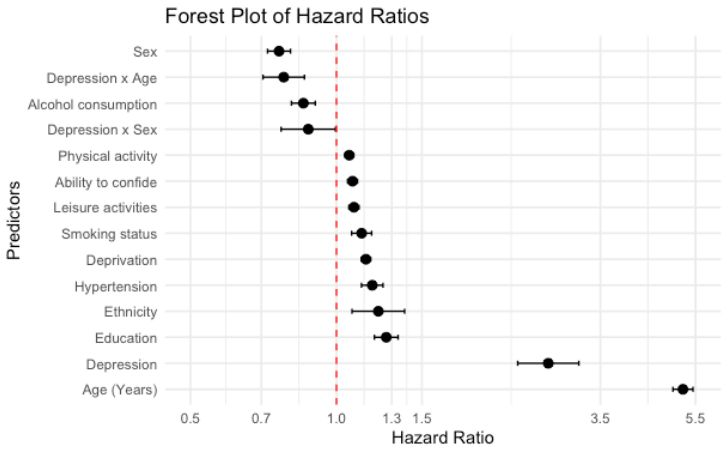
PTSD Diagnosis – Dementia



PTSD Symptoms – Dementia



Dissociative Disorders – Dementia



Depression – Dementia

ACEs = adverse childhood experiences; PTSD = posttraumatic stress disorder.

4. Discussion

In this large population-based cohort study, we examined how demographic, lifestyle, and health-related moderators may interact with ACEs, PTSD, dissociative disorders, and depression in predicting multiple aspects of brain health in the general population. The findings suggest a diverse set of moderators relevant to different predictor-outcome combinations.

4.1. Summary of Findings

4.1.1. Cognitive Functioning

ACEs were associated with slower reaction time, poorer visual memory, and reduced reasoning ability, with stronger associations (i.e. greater risk conferred) observed in individuals with higher education (all three domains), White ethnicity and male sex (two domains), and lower ability to confide in others, younger age, and lower physical activity (one domain). Higher-risk alcohol consumption appeared to mitigate the negative impact on reaction time.

PTSD diagnosis was linked to poorer cognitive functioning (slower reaction time and reduced reasoning ability). However, these associations were moderated by greater deprivation (two domains), lower physical activity (two domains), and Asian, Black, Mixed, or Other ethnic

background (one domain). The negative association between PTSD diagnosis and visual memory was unexpectedly stronger in those who confide in others more regularly.

Dissociative disorders were associated with slower reaction time, with this association being more pronounced in individuals with lower-risk alcohol consumption. Dissociative disorders were not directly associated with visual memory errors or reasoning ability. However, interactions suggest that these associations were present only in individuals who engaged less in leisure activities.

Depression was negatively associated with all three cognitive domains, with a stronger association in males (two domains), individuals with lower physical activity (two domains), and current or former smokers (one domain). Greater deprivation and lower-risk alcohol consumption further amplified its link with slower reaction time.

4.1.2. Dementia Risk

ACEs were linked to a higher all-cause dementia risk in individuals with hypertension. PTSD diagnosis was associated with an almost three-fold increased risk of dementia among former or current smokers. PTSD symptoms interacted with hypertension, lower education, and fewer visits from family/friends when predicting dementia risk. Interestingly, dementia risk was lower among those with reduced engagement in leisure activities. Dissociative disorders were associated with a nearly fivefold increased risk of dementia, with stronger associations in younger individuals. Depression was also linked with an almost threefold increased risk of dementia, with males, younger adults, and higher-risk alcohol consumers appearing particularly vulnerable.

4.1.3. Hippocampal Volume

ACEs, PTSD diagnosis, and PTSD symptoms were not associated with changes in hippocampal volume in the final models. Dissociative disorders were associated with lower left hippocampal volume in current or former smokers, while depression was associated with

reductions in both hippocampal hemispheres, particularly in individuals from Asian, Black, Mixed, or Other ethnic backgrounds (left, right) and those with lower physical activity (left).

Our results align with previous research indicating that ACEs, PTSD, dissociative disorders, and depression are associated with cognitive impairment across multiple domains (Haczkewicz et al., 2024; McKinnon et al., 2016; Scott et al., 2015; Varghese et al., 2022). However, our study extends this literature by systematically exploring and identifying key moderators of these relationships.

Higher education, White ethnicity, and younger age – typically considered protective against cognitive decline in older adults (Rexroth et al., 2013) – exacerbated the negative association between ACEs and cognitive functioning. Individuals with lower education, older age, or Asian, Black, Mixed, or Other ethnic background may already experience cognitive challenges due to socioeconomic disadvantage, cumulative stress, or health conditions (LaPlume et al., 2022), thereby muting the negative impact of ACEs. Alternatively, protective factors, such as religious involvement or social support, may offset some of the negative effects of early adversity (Zahodne, 2021). The stronger negative association between ACEs and reasoning ability in younger adults may be related to the natural decline of fluid intelligence with age (Horn & Cattell, 1967).

Regarding modifiable behavioral and psychosocial factors, lower physical activity exacerbated cognitive impairment across ACEs, PTSD, and depression, emphasizing its role in cognitive reserve (Song et al., 2022). Other moderators included greater deprivation (PTSD diagnosis, depression) and the ability to confide in others, which showed opposing effects depending on the predictor. Lower engagement in leisure activities heightened cognitive vulnerability in individuals with dissociative disorders.

These findings support the role of both socioeconomic factors (Gireesh et al., 2024) and social connections (Samtani et al., 2022) in cognitive resilience. Confiding in others might reflect relationship quality rather than quantity (Benca-Bachman et al., 2020). While social

engagement is generally protective, different aspects of social interactions may have distinct effects on cognitive resilience. Quantity may provide cognitive and mental stimulation, whereas quality might buffer neurotoxic stress effects (Zahodne, 2021).

Notably, a greater ability to confide in others exacerbated the negative association between PTSD diagnosis and visual memory, possibly due to PTSD-related symptoms, such as intrusive memories and impaired autobiographical memory (American Psychiatric Association, 2013; Ehlers & Clark, 2000). While confiding can be beneficial, certain contexts may heighten trauma-related distress (Bonnan-White et al., 2018), as reflected in the emphasis on structured and purposeful disclosure in the well-established trauma-focused therapy (Martin et al., 2021).

Current or former smoking aggravated the link between depression and visual memory errors, consistent with prior evidence (Anstey et al., 2007). Interestingly, higher-risk alcohol consumption appeared to buffer cognitive impairment in individuals with ACEs, dissociative disorders, or depression. Previous research on alcohol consumption and cognitive functioning has been mixed, with some studies indicating adverse effects, and others suggesting neutral or protective effects (Ilomaki et al., 2015), including cardiovascular and neuroprotective benefits of low to moderate alcohol consumption through anti-inflammatory processes (Collins et al., 2009).

Previous studies identified ACEs, PTSD, and depression as risk factors for dementia (Günak et al., 2020; Severs et al., 2023; Stafford et al., 2022), but our study shows that this risk is influenced by additional factors, particularly hypertension (ACEs, PTSD symptoms) and smoking (PTSD diagnosis), being male, younger age, higher-risk alcohol consumption (depression), from Asian, Black, Mixed, or Other ethnic background, lower education, lower frequency of family or friends' visits, greater engagement in leisure activities (PTSD symptoms). Prior research suggests that while less frequent engagement with social and leisure activities is linked to increased dementia risk, this is stronger for social contact with others than activity participation (Sommerlad et al., 2023).

Dissociative disorders were associated with an increased dementia risk, particularly in younger adults, which may indicate a link with early-onset dementia (<65 years; Alzheimer's & Dementia, 2024). Previous studies have identified PTSD as being associated with fronto-temporal dementia (Bonanni et al., 2018; Yaffe et al., 2010), regularly diagnosed before the age of 65 years (Alzheimer's & Dementia, 2024). While PTSD and dissociative disorders are distinct diagnoses, dissociative disorders may represent a particularly severe posttraumatic condition (American Psychiatric Association, 2013; Şar, 2020).

Prior studies yielded mixed evidence regarding trauma-related predictors and hippocampal volume (Blihar et al., 2021; Herzog & Schmahl, 2018; Logue et al., 2018). It was suggested that specific time periods and ACE types influence neurobiological alterations (Herzog & Schmahl, 2018). In contrast, evidence linking depression to lower hippocampal volume appears more consistent (Nolan et al., 2020). Our findings suggest this association is particularly pronounced in individuals from Asian, Black, Mixed, or Other ethnic backgrounds and those with lower physical activity.

Overall, our findings support the cognitive reserve hypothesis, which posits that individuals with greater cognitive reserve can better withstand neuropathology and age-related cognitive decline (Nelson et al., 2021). Several modifiable factors, including physical, cognitive, and social activities, have been identified as contributors to such cognitive reserve throughout the lifespan and into older age (Nelson et al., 2021; Stern et al., 2020). Our findings suggest that certain demographic, behavioral, and psychosocial factors may mitigate cognitive decline in individuals with ACEs, trauma-related psychopathology and depression.

4.2. Implications

Promoting positive psychosocial factors and fostering healthy lifestyles is critical for preventing cognitive decline in individuals with trauma-related psychopathology or depression.

Our findings emphasize the importance of clinicians recognizing the associations between childhood adversity, trauma-related disorders, and cognitive impairment. Targeted interventions, such as promoting exercise and social engagement, could be beneficial (Livingston et al., 2024). Future research should explore the effectiveness of integrating psychosocial and cognitive interventions into treatment plans for high-risk individuals. Based on our findings, these include individuals with ACEs, PTSD, dissociative disorders, and/or depression, as well as specific moderating factors. Importantly, our findings of the study also indicate that moderators vary across different trauma- and psychopathology-related predictors, suggesting that tailored interventions may be warranted.

4.3. Strengths and Limitations

Our study used a large, population-based cohort with clinical and various baseline assessments, allowing for robust moderator analyses. We accounted for the temporal sequence of diagnoses and outcomes, and applied LASSO regularization and stepwise selection to refine our models and retrieve the most relevant predictors.

Limitations include the observational design, which does not establish causation. PTSD and dissociative disorders may be underdiagnosed or underreported in health records. The cross-sectional assessment of moderators and cognitive functioning limits conclusions regarding directionality. Additionally, behavioral, psychosocial, and health-related factors may change across the life course. We did not adjust for intracranial or total brain volume when including hippocampal volume as the outcome. However, prior research suggests that this adjustment does not significantly impact findings (Lyall et al., 2013). The 95% confidence intervals (CI) and p-values obtained after the LASSO and stepwise approach do not accurately reflect the true statistical significance due to the variable selection process and should be

interpreted with caution. Finally, the UK Biobank sample underrepresents ethnic minority groups and individuals from lower socioeconomic backgrounds, limiting generalizability.

4.4. Conclusion

ACEs, PTSD, dissociative disorders, and depression were associated with cognitive outcomes and increased dementia risk, with some evidence suggesting links with reduced hippocampal volume. Importantly, these relationships are influenced by demographic, psychosocial, behavioral, and health-related factors. Identifying individuals who are particularly vulnerable to cognitive decline following trauma, trauma-related psychopathology, and depression is essential for developing targeted interventions aimed at modifiable risk factors to promote healthier cognitive aging.

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3. General Discussion

The overarching goal of this thesis was to investigate the relationship between traumatic stress, trauma-related psychopathology, cognitive functioning, and dementia. Specifically, it aimed to replicate and expand previous research showing a link between PTSD, cognitive impairment, and dementia by accounting for the heterogeneity of PTSD, and incorporating a broader spectrum of traumatic stress and trauma-related psychopathology, while considering multiple cognitive outcomes. This included examining both direct associations between trauma-related psychopathology and cognitive or neurological outcomes, as well as identifying potential mediators and moderators to further elucidate the mechanisms underlying the impact of traumatic stress on cognitive aging.

To address these objectives, three studies employing different methodological approaches were conducted.

Study I investigated the relationship between PTSD and subjective cognitive functioning (SCF) at a single time point and over a three-year period. Moving beyond a categorical PTSD diagnosis, PTSD symptom levels were decomposed into three dimensions: overall PTSD symptom severity, PTSD symptom clusters, and individual PTSD symptoms. *Study II* extended earlier research by considering multiple levels of traumatic stress and trauma-related psychopathology – namely ACEs, PTSD, dissociative disorders, and depression – as potential risk factors for incident (i.e., newly diagnosed) all-cause dementia. Additionally, this study explored whether and how these trauma-related predictors and depression may mediate one other in their association with increased dementia risk. *Study III* examined various psychosocial and behavioral moderators that may influence the relationship between trauma-related psychopathology and different levels of cognitive outcomes.

3.1. Summary of Findings

Study I investigated cross-sectional and longitudinal (three-year) associations between SCF and 1) PTSD total symptom score, 2) PTSD symptom clusters, and 3) individual PTSD

symptoms. Network analyses, a method well-suited for estimating unique mutual relationships among a large number of variables simultaneously (Borsboom, 2017; Fried et al., 2017), were conducted using data from nearly 1,500 older U.S. veterans. The goal was to identify specific PTSD symptoms and symptom clusters that are associated with SCF. Results revealed that 1) the overall PTSD symptom score was negatively associated with SCF; 2) SCF showed consistent and negative associations with the PTSD symptom clusters "marked alterations in arousal and reactivity associated with the traumatic event(s)" and "negative alterations in cognitions and mood associated with the traumatic event(s)"; and 3) SCF was robustly associated with the specific symptoms "having difficulty concentrating" and "trouble experiencing positive feelings (for example, being unable to feel happiness or have loving feelings for people close to you)" (American Psychiatric Association, 2013, pp. 271-272; Weathers et al., 2013, items 14 and 19). These findings remained stable over time, replicating at the three-year follow-up. Thus, the results highlight that PTSD symptoms are associated with reduced SCF in older adults, both at a single time point and longitudinally, suggesting their involvement in the development or maintenance of cognitive difficulties. Importantly, not all PTSD symptoms and symptom clusters contributed equally to this association.

Study II and *Study III* adopted a broader perspective of trauma and trauma-related psychopathology by including ACEs and dissociative disorders, alongside PTSD and depression, recognizing the close link between depression, ACEs and trauma-related disorders (Flory & Yehuda, 2015; Şar, 2011; Schalinski et al., 2016). Both studies used data from the UK Biobank, a cohort of approximately half a million individuals from the general UK population, spanning from younger to older adulthood. The dataset includes extensive baseline and follow-up assessments, as well as linkage to electronic health records containing psychological diagnoses.

Study II was the first study to identify dissociative disorders as a potentially modifiable yet strong risk factor for incident all-cause dementia. Additionally, the study provided further

evidence that ACEs, PTSD, and depression are associated with an increased dementia risk. Moreover, PTSD symptoms and diagnosed depression were found to mediate the relationship between ACEs and risk of dementia. PTSD symptoms accounted for a substantial part of this association, whereas depression played a smaller but still significant role. Similarly, depression also mediated the associations between diagnosed PTSD or dissociative disorders and dementia, though it did not mediate the relationship between PTSD symptoms and dementia. However, a significant portion of these associations remained unexplained by depression alone. These findings suggest that ACEs, trauma-related psychopathology, and depression have both common and unique pathways in their associations with dementia risk, which cannot be fully explained by the other investigated exposures.

Finally, *Study III* further examined the relationships between ACEs, PTSD (both diagnosed and self-reported) diagnosis and self-reported symptoms, dissociative disorders and various cognitive outcomes. Cognitive outcomes in this study extended beyond all-cause dementia, to include cognitive functioning, assessed through computerized neuropsychological assessment tools (i.e., reaction time, visual memory, and reasoning ability), as well as hippocampal volume – a key brain structure that is involved in cognitive impairment and dementia pathology (Eichenbaum, 2017; Igarashi, 2023). This study also incorporated behavioral and psychosocial factors as potential moderators of these associations. The results demonstrated that ACEs, PTSD, dissociative disorders, and depression were all associated with poorer cognitive functioning and an increased dementia risk. Dissociative disorders and depression were linked to reduced hippocampal volume, whereas ACEs and PTSD were not. Furthermore, these associations were moderated by various factors, either amplifying or mitigating them. While no single moderator showed a consistently dominant pattern across all analyses, several moderators significantly strengthened the observed associations across multiple models. These included lower physical or social activity, lower-risk alcohol consumption, and smoking, hypertension, higher deprivation, and younger age. At the same

time, the findings suggest that the relationship between trauma-related psychopathology and cognitive outcomes is not uniform.

3.2. Unraveling the Link Between Trauma and Cognitive Aging: Findings, Implications, and Future Directions

Understanding the complex relationship between traumatic stress and cognitive outcomes is crucial, given the high prevalence of trauma exposure – both in childhood and adulthood – and dementia worldwide (Kessler et al., 2017; Madigan et al., 2023; Prince et al., 2015). The integration of findings from this thesis represents an important first step toward a better understanding of the increased risk of cognitive impairment and dementia in older adults.

While the previous three chapters discussed the implications of each individual study, this chapter provides a comprehensive synthesis of the results, offering a clearer perspective on how trauma-related psychopathology contributes to cognitive decline and dementia risk. Additionally, it outlines key implications for future research and clinical practice, identifying potential intervention targets to mitigate these risks.

3.2.2. Trauma, Trauma-Related Psychopathology, Cognitive Impairment, and Dementia

Across *Studies I*, *II*, and *III*, it was found that various levels of traumatic stress and trauma-related disorders, namely ACEs, PTSD, and dissociative disorders, showed consistent relationships with reduced cognitive functioning and an increased risk of dementia, both cross-sectionally and longitudinally. This key finding of the thesis underlines the importance of further investigating the complex relationship between psychological trauma, cognitive impairment, and dementia.

3.2.2.1. Characteristics of PTSD, Cognitive Impairment, and Dementia

3.2.2.1.1. PTSD Diagnosis vs. Symptoms: Associations with Cognitive Functioning and Dementia

The thesis found that both PTSD diagnoses and self-reported PTSD symptoms were associated with cognitive impairment and dementia risk, largely independent of depression. The findings suggest that these associations are not limited to individuals who meet the full DSM-5 (American Psychiatric Association, 2013) or ICD-10 (World Health Organization, 1993) diagnostic criteria. Instead, subclinical levels of PTSD symptoms may also contribute to cognitive decline.

While PTSD severity played a role – evidenced by the negative association between PTSD symptom sum scores and various cognitive measures in *Study I* and *Study III*, and with dementia in *Study II* and *Study III* – the findings generally support a link between PTSD and cognitive outcomes in both clinical and non-clinical populations. This has two important implications: First, the cut-off scores used for the PCL-5 vary substantially across studies (Forkus et al., 2023). Diagnostic cut-off thresholds are debated in the literature (Kendell & Jablensky, 2003), including for PTSD (Armour et al., 2017; Armour, Műllerová, et al., 2016; Galatzer-Levy & Bryant, 2013). The categorical approach to PTSD diagnosis (i.e., meeting vs. not meeting diagnostic criteria) may oversimplify the disorder's heterogeneity, leading to a loss of valuable information (Galatzer-Levy & Bryant, 2013).

Second, *Study II* found a dose-response relationship, where a higher number of types of ACEs and greater PTSD symptom severity were associated with an increased risk of dementia. This aligns with prior research showing that higher PTSD severity, measured by psychiatric clinic visit frequency, predicts increased dementia risk (Wang et al., 2016).

3.2.2.1.2. PTSD Symptom Clusters, Individual Symptoms, and Cognitive Functioning

Study I identified two PTSD symptom clusters and specific symptoms that were particularly associated with reduced SCF. Namely, symptoms of the PTSD clusters "marked alterations in arousal and reactivity associated with the traumatic event(s)" and "negative alterations in cognitions and mood associated with the traumatic event(s)" (American Psychiatric Association, 2013, pp. 271-272). These findings underscore the importance of looking beyond PTSD diagnosis and considering which specific symptoms contribute most strongly to cognitive impairment.

Symptoms of hyperarousal and hypervigilance, in particular, may reflect stress-related physiological dysregulation, including dysregulated HPA-axis activity, increased sympathetic nervous system activation, amygdala hyperactivity, and neuroinflammatory responses (Alves De Araujo Junior et al., 2023; Cohen et al., 2013; Danese & McEwen, 2012; Greenberg et al., 2014; Herzog & Schmahl, 2018; Katrinli et al., 2023; Lohr et al., 2015; Miller et al., 2018; Shin et al., 2006; Wolf, Logue, et al., 2018). These symptoms may also consume cognitive resources, as individuals remain constantly alert to potential threats, impairing attentional control and working memory (Danese & McEwen, 2012; Kolb, 1987; Schweizer & Dalgleish, 2016). Belonging to this cluster, "having difficulty concentrating", a core PTSD symptom (American Psychiatric Association, 2013; Weathers et al., 2013, item 19), was consistently associated with reduced SCF cross-sectionally and at the three-year follow-up of *Study I*. This finding highlights the importance of monitoring cognitive functioning and impairment in daily life in individuals with PTSD symptoms in clinical practice.

Regarding symptoms of "negative alterations in cognitions and mood associated with the traumatic event(s)" (American Psychiatric Association, 2013, p. 271), "trouble experiencing positive feelings (for example, being unable to feel happiness or have loving feelings for people close to you)" (American Psychiatric Association, 2013; Weathers et al., 2013, item 14) was consistently linked to reduced SCF, highlighting the potential role of positive affect in cognitive

health. In addition to TF-CBT and EMDR, the recommended first-line treatments for trauma-related symptoms (Martin et al., 2021), these findings suggest the need to evaluate interventions aimed at enhancing positive emotions as one potential approach to improving SCF. Potential strategies could include engaging in pleasurable activities aligned with personal interests, such as social, leisure, and physical activities, as well as practicing gratitude and performing acts of kindness. These approaches have been linked to increased positive affect and psychological well-being (Lyubomirsky & Layous, 2013), even in individuals with anxiety and depression (Taylor et al., 2017). Positive affect has also been associated with favorable physiological outcomes, including lower systolic blood pressure, reduced cortisol levels, and lower heart rate in adding adults, further highlighting its potential as one intervention target in older populations (Steptoe & Wardle, 2005).

Consistently, a loss of interest in previously enjoyed activities was also repeatedly associated with reduced SCF in the cross-sectional network models. This may be linked to cognitive reserve, as re-engaging in past interests and activities could help rebuild cognitive reserve, which, in turn, may serve as a protective factor against subjective cognitive decline (SCD) over time (Scarmeas & Stern, 2003; S. Song et al., 2022; Stern, 2012).

Study I also found that self-blame, blame of others, and strong negative beliefs about oneself, other people, or the world – symptoms belonging to the PTSD cluster of negative alterations in cognitions and mood (Weathers et al., 2013) – were consistently associated with reduced SCF over time. Negative thoughts might claim cognitive capacities (Takano et al., 2014). While blame and strong negative beliefs do not inherently involve worrying and rumination, cognitive models suggest that these processes can interfere with cognitive tasks by the occupying working memory capacity (Eysenck & Calvo, 1992) and interfering with attentional control (Hirsch & Mathews, 2012), ultimately depleting cognitive resources over time. Worry has been identified as a mediator in anxiety-related difficulties with concentration (Blendermann et al., 2025), and internalized negative beliefs have been found to mediate the

relationship between ACEs and the development of PTSD and depression (Aafjes-van Doorn et al., 2020). In clinical practice, it is important not only to consider such beliefs and worry processes as part of symptomatology but also to recognize their impact on cognitive functioning in daily life.

A concept relevant to these findings is Cognitive Debt (CD), which refers to thoughts and behaviors that increase the vulnerability to neurodegeneration and may underlie the heightened risk of dementia associated with depression, anxiety, PTSD, and sleep disturbances (Marchant & Howard, 2015). Repetitive negative thinking (RNT), a transdiagnostic process characterized by perseverative, intrusive negative thought patterns that are difficult to disengage from – including worry and rumination (Ehring & Watkins, 2008; McEvoy et al., 2013) – has been proposed as a key driver of cognitive debt (Marchant & Howard, 2015). In PTSD, rumination is considered a dysfunctional emotional regulation strategy commonly used by trauma survivors (Ehring & Ehlers, 2014) in an attempt to avoid emotionally arousing and painful material, such as trauma memories (Borkovec, 1994; Fresco et al., 2002; Michael et al., 2007). As a result, it serves as a maintaining factor in PTSD, reinforcing symptoms over time (Ehlers et al., 2022; Ehring & Watkins, 2008). Marchant and Howard (2015) suggested that engagement in such cognitive processes actively depletes cognitive reserves, accruing to CD, and increasing vulnerability to dementia pathology. Higher levels of RNT have been associated with faster cognitive decline in older adults and an greater accumulation of Aβ and tau proteins over a four-year period (Marchant et al., 2020). Additionally, RNT has been found to moderate the association between SCD and progression to mild cognitive impairment (MCI) and dementia (Jessen et al., 2010, 2014; Miebach et al., 2019; Pike et al., 2022).

This thesis provides compelling evidence that PTSD contributes to cognitive impairment and dementia risk beyond a formal diagnosis, with symptom severity, hyperarousal, decreased positive affect, negative cognitions, and RNT emerging as particularly relevant mechanisms. Future research should explore how cognitive-emotional dysregulation in PTSD

contributes to CD and long-term neurodegenerative processes. Additionally, studies should examine whether targeting these components through therapy can help mitigate cognitive decline.

3.2.2.2. ACEs, Cognitive Impairment, and Dementia

ACEs include neglect, abuse, and other significant stressors during early life (Kalmakis & Chandler, 2014; O'Neill et al., 2021). These experiences can disrupt normal brain, social, and intellectual development throughout the lifespan (Herzog & Schmahl, 2018). ACEs disrupt the expectable environment, and when such violations occur during a critical periods of brain development, their negative effects are likely to persist long-term (C. A. Nelson & Gabard-Durnam, 2020), leading to lower educational attainment (Houtepen et al., 2020), impaired social-emotional development (Babad et al., 2022; Ray et al., 2020), alterations in the brain, endocrine, and immune systems (Danese & McEwen, 2012; McEwen, 2007), and increased risk of psychopathology (Daníelsdóttir et al., 2024).

ACEs are established risk factors for PTSD and depression (Schalinski et al., 2016). In *Study II*, PTSD symptoms and depression were found to partially mediate the relationship between ACEs and dementia risk, suggesting that these conditions contribute to this association. While it is not possible to establish a causal pathway, the study's longitudinal design ensured that ACEs preceded PTSD symptoms and depression, both of which were subsequently linked to an increased incidence of dementia. However, depression did not fully explain the relationship between childhood adversity and dementia risk, suggesting that additional pathways, such as neurobiological changes, chronic stress responses, or behavioral factors, may also play a role.

Study II and *Study III* examined ACEs as a cumulative count of different types of adverse experiences (i.e., physical and emotional neglect; sexual, physical, and emotional abuse). While this provides valuable insight, there is an ongoing debate regarding whether the

number or nature of ACEs exerts a greater impact on later-life outcomes (C. A. Nelson & Gabard-Durnam, 2020). Examining only the number of ACEs overlooks key factors such as timing, severity, and type, whereas focusing solely on the nature of ACEs without considering cumulative exposure may also miss relevant information (C. A. Nelson & Gabard-Durnam, 2020). Regarding timing of ACEs, future studies should investigate sensitive vs. critical periods for cognitive risk. The distinction between sensitive periods (where negative effects may be reversible) and critical periods (which lead to irreversible brain changes) is particularly important (C. A. Nelson & Gabard-Durnam, 2020). Regarding the nature of ACEs, prior research differentiates between deprivation-related ACEs (i.e., absence of expected environmental stimulation) and threat-related ACEs (i.e., direct exposure to danger) (McLaughlin et al., 2014). Future work should examine how these subtypes impact neurodevelopmental trajectories and dementia risk.

Two recent meta-analyses found that both ACEs and adulthood trauma are associated with an increased risk of dementia (Abouelmagd et al., 2024; Severs et al., 2023). Notably, the association between ACEs and risk of dementia appeared stronger than that of traumatic life events in general and war/Holocaust trauma, specifically (Severs et al., 2023). However, these findings are based on a limited number of studies, and replication is necessary.

Future research should also examine adulthood trauma and its role in cognitive aging. A meta-analysis found that natural disasters (e.g., hurricanes, earthquakes, and heat waves) are linked to cognitive decline and dementia (Thompson & Vasefi, 2025). Similarly, cognitive impairment has been observed in trauma-affected refugees (Nordin et al., 2024), yet only one study (Folnegović-Šmalc et al., 1997), to date, has examined dementia risk specifically in refugee populations. Given the increasing number of political conflicts, forced migrations, human rights crises, and climate change disasters worldwide (Institute for Economics & Peace, 2020), further research is needed to determine whether refugees, who face unique traumatic stressors, are at heightened risk for dementia.

In sum, ACEs are linked to both cognitive impairment and an increased risk of dementia. PTSD symptoms, to a larger extent, and depression, to a smaller part, explain the association between ACEs and dementia risk. However, ACEs seems associated with cognitive impairment and dementia, also independent of following psychopathology. Future research should explore how the timing, severity, and chronicity of ACEs, as well as adulthood trauma, influence long-term cognitive health.

3.2.2.3. Dissociative Disorders, Cognitive Impairment, and Dementia

The thesis identified dissociative disorders as being strongly associated with an increased risk of dementia. In *Study II*, individuals with dissociative disorders had a fourfold increased risk of developing dementia, and in *Study III*, the risk was more than fivefold higher compared to those without dissociative disorders. The findings position dissociative disorders as a newly recognized, potentially modifiable risk factor for all-cause dementia.

Since adjusting for medical comorbidities, lifestyle factors, and depression in sensitivity analyses rendered the association non-significant in *Study II*, the robustness of this finding requires replication in future research. Notably, although depression mediated part of the relationship between dissociative disorders and dementia – similar to its mediating role in the associations with ACEs and PTSD – it did not account for the majority of the association.

Dissociative symptoms have been associated with cognitive impairment across domains (McKinnon et al., 2016), particularly in relation to subjective cognitive complaints (Alexis et al., 2023). However, the underlying mechanisms remain largely unknown, but several potential explanations have been proposed. As mentioned in the introduction, the defense cascade model suggests that dissociation serves as a neurobiological response to extreme stress, altering cognitive processing (Kozlowska et al., 2015; McKinnon et al., 2016). Additionally, it was observed that cognitive dysfunction is especially evident when there is an emotional context to the cognitive tasks (Alexis et al., 2023), suggesting cognitive dysfunction especially in

emotional contexts. Dissociative disorders, as one of the most severe trauma-related disorders (American Psychiatric Association, 2013; Kratzer et al., 2024) may share overlapping neural mechanisms with PTSD, potentially leading to even greater cognitive dysfunction and risk of dementia.

Given the strong association between dissociative disorders and dementia, further research is needed to identify underlying neurobiological pathways, examine the link between specific dissociative disorders, such as the dissociative identity disorder, and cognitive impairment and dementia, and explore potential intervention strategies to mitigate cognitive decline in in affected individuals.

These findings also have clinical implications, as dissociative disorders should be considered a potential risk factor for dementia. Future research should continue investigating this association, and clinicians should be aware of the cognitive vulnerabilities associated with dissociative disorders, particularly in aging populations.

3.2.2.4. Depression, Cognitive Impairment, and Dementia

Depression, a well-established risk factor for dementia (Livingston et al., 2024), has been linked to ACEs and frequently co-occurs with PTSD and dissociative disorders (Flory & Yehuda, 2015; Şar, 2011; Schalinski et al., 2016). Therefore, it was accounted for in all three studies.

Depression was consistently associated with impaired cognitive functioning and an increased risk of dementia (*Study II* and *Study III*). However, the findings of this thesis suggest that the observed relationship between childhood adversity, PTSD (both diagnosis and symptoms), dissociative disorders, and cognitive and neurological outcomes cannot be fully explained by comorbid depression. *Study I* found that associations between PTSD symptom clusters, individual symptoms, and SCF remained significant even after controlling for depression. In *Study II*, mediation analyses showed that depression accounted for only a small

portion of the relationships between ACEs and dementia, PTSD diagnosis and dementia, and dissociative disorders and dementia. In the main models of *Study II*, individuals with depression (but without PTSD or dissociative disorders) had more than twice the risk of dementia compared to those without depression. However, when depression was isolated from PTSD, dissociative disorders, and ACEs, it was unexpectedly associated with a reduced risk of dementia. This finding suggests that ACEs may be a crucial factor in the depression-dementia relationship, potentially influencing long-term cognitive decline.

Due to the relatively low number of PTSD and dissociative disorder diagnoses in the UK Biobank (*Study II* and *Study III*), it was not possible to exclude individuals with ACEs or depression within those groups. Future studies therefore should further investigate the role of ACEs in shaping the relationship between depression and dementia, examine whether depression alone, when not preceded by early-life adversity, presents the same long-term dementia risk, and explore the cumulative impact of trauma-related psychopathology and depression on cognitive decline over time.

The findings of this thesis challenge the hypothesis that the repeatedly observed association between PTSD and increased dementia risk may be solely attributable to co-occurring depression (Cohen et al., 2013; Yaffe et al., 2010). Instead, ACEs, PTSD, and dissociative disorders appear to contribute to dementia risk through independent pathways, with depression playing a secondary role in mediating their impact.

3.2.3. Behavioral and Psychosocial Factors Contributing to Cognitive Decline

Although *Study III* did not identify a single moderator that consistently influenced all associations, the findings indicate that behavioral and psychosocial risk factors significantly moderated the relationships between trauma-related predictors, depression, and cognitive impairment or dementia risk. As different moderators were relevant for different associations, with no single factor emerging as a universal moderator, some moderators appeared repeatedly,

underscoring the general importance of behavioral and psychosocial factors in the link between trauma-related psychopathology and cognitive outcomes. Regarding cognitive functioning, some of the most frequently observed moderators included lower physical activity was associated with cognitive impairment across multiple groups (ACEs, PTSD, and depression). Similarly, lower-risk alcohol consumption moderated the association between ACEs, depression, and dissociative disorders, particularly affecting reaction time. Greater socioeconomic deprivation (PTSD and depression) and reduced engagement in leisure activities (dissociative disorders) also emerged as significant moderators of the associations with cognitive performance.

When dementia was the outcome, the moderating influences were even more varied. For example, ACEs interacted with hypertension in predicting dementia, while the association between PTSD diagnosis and dementia was moderated by current or former smoking. In the case of PTSD symptoms, moderators including hypertension, lower education, infrequent family or friends' visits increased risk of dementia, although interestingly, greater engagement in leisure activities also emerged as a moderator. For depression, higher-risk alcohol consumption played a moderating role in dementia risk. These diverse findings underscore that there is no universal moderator. Instead, the impact of trauma-related psychopathology on cognitive outcomes is multifaceted, calling for targeted, personalized interventions.

In individuals with Asian, Black, or Other ethnic background and those with lower physical activity levels, depression was associated with reduced hippocampal volume. Similarly, dissociative disorders were linked to lower left hippocampal volume among current or former smokers. While no main association was found, and ACEs and PTSD showed no relationship with hippocampal volume, *Study III* still identified the influence of behavioral factors – specifically, physical activity and smoking – on this outcome.

3.2.3.1. Cognitive Reserve

An important conceptual framework that may help integrate these findings is the notion of cognitive reserve (Stern, 2002), as outlined in the General Introduction. Cognitive reserve refers to the brain's ability to cope with pathology including neurodegeneration, which is built over a lifetime through engagement in intellectually stimulating activities, education, complex occupations, as well as social, physical, and leisure activities (M. E. Nelson et al., 2021; Stern, 2002; Tucker & Stern, 2011). A higher cognitive reserve can delay the onset of cognitive decline and dementia symptoms (M. E. Nelson et al., 2021; Stern, 2002; Tucker & Stern, 2011). This generally has been supported by previous studies (Clare et al., 2017; S. Song et al., 2022; Zijlmans et al., 2022), especially regarding cognitive leisure and physical activity (S. Song et al., 2022). Some evidence also suggests that depression interacts with cognitive reserve, affecting cognitive performance (Lara et al., 2022; Ponsoni et al., 2020; Venezia et al., 2018).

The various moderators identified in *Study III* may be understood as determinants of cognitive reserve. However, it remains an open question whether cognitive reserve functions as an independent protective factor against cognitive decline or is itself negatively impacted by trauma-related psychopathology, or both. Future research should examine whether cognitive reserve acts as a buffer against PTSD, dissociative disorders, and depression in cognitive aging; how trauma-related psychopathology affects cognitive reserve over time, and whether enhancing cognitive reserve through interventions could mitigate cognitive decline in trauma-affected populations. The findings of this thesis align with prior research on modifiable risk factors for dementia. Several identified moderators correspond to the 14 established modifiable risk factors outlined in the Lancet Commission on dementia prevention, intervention, and care (Livingston et al., 2024), including education, physical inactivity, smoking, hypertension, and social isolation.

This suggests that public health interventions targeting these factors may not only reduce general dementia risk but also mitigate the specific cognitive vulnerabilities associated with trauma and mental health disorders. Potential strategies include tailored health policies and lifestyle interventions, such as increasing access to education, promoting physical, social, and leisure activities, and encouraging smoking cessation, ensuring adequate mental health care and treatment for trauma survivors, could play a crucial role in mitigating cognitive decline or delaying the onset of dementia (Livingston et al., 2024) in individuals affected by traumatic stress, trauma-related psychopathology, and depression.

One of the most important conclusions from this thesis is that increased dementia risk associated with trauma and trauma-related psychopathology is not necessarily a fixed outcome. These findings provide evidence that risk can be influenced by behavioral, psychosocial, and lifestyle factors. While further research is needed to replicate and refine these findings across diverse populations, this thesis contributes to an emerging body of work that highlights the potential for intervention. After replicating the findings of the thesis, the next critical step is to explore whether interventions – whether through targeted therapy, lifestyle modifications, or cognitive training – can actively reduce cognitive decline in trauma-affected individuals.

3.2.4. Cognitive Outcomes Across Different Levels

One of the key findings of this thesis, observed across *Study I*, *Study II*, and *Study III* is that trauma-related predictors and depression are associated with various cognitive and neurological outcomes: subjective and objective cognitive functioning, incident dementia, and hippocampal volume. With the exception of hippocampal volume, significant associations were observed for all predictors and the mentioned outcomes, highlighting that trauma-related psychopathology affects cognition in a multi-faceted manner.

This is particularly noteworthy as both subjective and objective cognitive impairment have been linked to increased dementia risk (Brodaty et al., 2017; Mitchell et al., 2014; Pike et

al., 2022). While subjective cognitive impairment may represent an early stage of cognitive decline, objective cognitive impairment is considered an intermediate (albeit reversible) step toward dementia (Gauthier et al., 2006; Jonker et al., 2000; Reid & MacLullich, 2006; Zucchella et al., 2018). Given these associations, adjunctive therapies focusing on cognitive improvement may be beneficial alongside existing treatments for trauma-related psychopathology and depression.

One promising approach is **Cognitive Remediation Therapy (CRT)**, which targets cognitive deficits such as attention, memory, executive function, and social cognition (E. J. Kim et al., 2018; Legemaat et al., 2022; Thérond et al., 2021). CRT includes both drill-and-practice exercises and cognitive strategy training and can be adapted to different formats and durations (E. J. Kim et al., 2018; Legemaat et al., 2022; Thérond et al., 2021). CRT has been extensively studied in individuals with schizophrenia (Wykes & Spaulding, 2011), but previous research suggests benefits on global cognition and specific domains also for individuals with depression (Thérond et al., 2021), with short term effectiveness (Legemaat et al., 2022). A small feasibility study on Goal Management Training (GMT), a cognitive remediation approach, in individuals with PTSD symptoms found significant improvements across cognitive domains (Boyd et al., 2019). While these findings suggest that cognitive enhancement interventions may be valuable, further research is needed to evaluate their effectiveness in trauma-affected populations.

Study III found that the associations between ACEs and reaction time and reasoning ability, as well as between depression and reaction time, visual memory errors, and dementia, were more pronounced in males than females. Future research should replicate these findings to determine whether **sex differences** represent a fixed contributor to cognitive risk or if clinicians' awareness and targeted cognitive interventions could help address these disparities.

Study III also found that the associations between ACEs and reasoning ability, as well as dissociative disorders and depression with risk of dementia was moderated by age, namely that the associations were stronger in younger individuals. This aligns with the hypothesis that

trauma-related pathology and depression contribute to **accelerated aging** and may increase susceptibility to early-onset neurodegenerative diseases, such as dementia (Katrinli et al., 2023; Wolf, Maniates, et al., 2018).

A limited number of studies have examined the associations between PTSD and specific dementia subtypes. While PTSD is generally linked to all-cause dementia (Günak et al., 2020), some evidence suggests a particularly strong association with frontotemporal dementia (FTD) (Yaffe et al., 2010). Individuals with PTSD history appear overrepresented in FTD cases, compared to the general population (Bonanni et al., 2018). FTD is a common **early-onset** (< 65 years) **dementia** subtype (Bang et al., 2015), which further supports the hypothesis that PTSD may contribute to early neurodegenerative processes. Since *Study II* and *Study III* did not investigate dementia subtypes separately, future research should disentangle the relationships between ACEs, trauma-related pathology, depression, across dementia subtypes.

A key question in dementia research is whether depression and trauma-related psychopathology serve as risk factors for dementia or whether they are part of the **prodromal stage** of neurodegeneration (Brommelhoff et al., 2009; Qureshi et al., 2010). Alzheimer's disease (AD) has been observed to have a five to six-year prodromal stage characterized by accelerated cognitive decline (Wilson et al., 2011). Late-life depression has been consistently linked to an increased risk of dementia (Livingston et al., 2017, 2020), while mid-life depression has now been added as an established modifiable risk factor (Livingston et al., 2024). Similarly, PTSD symptoms may reflect early neurodegenerative changes rather than serving as a direct risk factor, given its overlap with dementia-related cognitive and neural abnormalities, such as hippocampal atrophy and executive dysfunction. It is possible that both pathways are relevant, with some individuals experiencing prodromal dementia-related depression or PTSD, while others develop dementia as a consequence of chronic psychiatric illness (Brommelhoff et al., 2009). Future research should aim to distinguish between these mechanisms by examining the timing of psychiatric symptoms in relation to cognitive decline.

The **bidirectional nature** of the observed associations across the studies in this thesis cannot be ruled out. Cognitive decline may not only result from PTSD but could also reactivate or exacerbate PTSD symptoms. Case reports suggest that PTSD symptoms can emerge or worsen following the onset of dementia (Johnston, 2000; Van Achterberg et al., 2001), further supporting the possibility that PTSD may be part of a prodromal stage of dementia. This could be due to neurodegeneration in (sub-) cortical brain regions, leading to disinhibition of previously dormant PTSD symptoms (Mittal et al., 2001). Additionally, delayed-onset PTSD has also been misdiagnosed as behavioral and psychological symptoms associated with dementia (Lachmann & Hu, 2018; Martinez-Clavera et al., 2017). PTSD and dementia have been observed to co-occur, though symptom presentations can vary, necessitating specialized treatment approaches (Ritchie et al., 2022; Van Dongen et al., 2022). These findings underscore the importance of careful differential diagnosis and tailored intervention strategies for individuals experiencing PTSD and cognitive decline.

3.3. Future Research and Clinical Implications

While this thesis provides important insights into the relationship between trauma, trauma-related psychopathology, cognitive impairment, and dementia, many questions remain open for future research.

3.3.1. Future Research Directions

The findings reinforce that PTSD is associated with an increased risk of cognitive decline and dementia. While replication in future studies is necessary, the results provide substantial support for including PTSD as a potentially modifiable risk factor in upcoming updates of the Lancet Commission report on dementia prevention, intervention, and care (Livingston et al., 2024). However, for PTSD to be formally recognized as an established risk factor at present, further research is required. The Lancet Commission primarily relies on

systematic reviews and meta-analyses, and although one meta-analysis has identified PTSD as a potential risk factor for dementia, the high heterogeneity across studies limits definitive conclusions (Günak et al., 2020). To strengthen the evidence base, future research should use consistent diagnostic criteria, control for key confounding variables, and employ prospective study designs.

Beyond PTSD, this thesis highlights the need to expand research beyond depression when examining psychological disorders in relation to dementia. Most studies to date have focused on depression, but this thesis demonstrates that trauma and trauma-related psychopathology – including ACEs and dissociative disorders – should also be investigated as potential contributors to cognitive aging. Ideally, future studies should employ large, prospective cohort designs that follow individuals from early life into old age to better capture long-term impact and counteract potential recall bias in retrospective assessments, such as for ACEs and other relevant variables.

Further, the methodological challenge of distinguishing between cognitive impairments with a physical basis (e.g., structural brain changes) versus those influenced by emotional distress (Danckwerts & Leathem, 2003) should be addressed. Future studies should assess cognitive functioning at multiple time points, including before, during, and after trauma-focused therapy, across different times of the day (to capture mood-dependent fluctuations), and through long-term follow-up after treatment. Combining subjective and objective cognitive assessments with neuroimaging could help clarify whether cognitive deficits in PTSD reflect underlying neuropathology or trauma-related cognitive interference.

Additional factors warrant further investigation, including trauma exposure in adulthood, MCI as an intermediate outcome, and the role of specific dissociative disorder diagnoses. Dissociative disorders – particularly dissociative identity disorder – should be examined as potential risk factors for dementia, as their association with cognitive impairment and neurodegeneration remains largely unexplored. Moreover, disentangling the relationships

between ACEs, trauma-related disorders, and depression across different dementia subtypes (e.g., AD, VaD, FTD) would further clarify the pathways linking trauma to neurodegeneration.

Another critical avenue for future research is the extent to which interventions can prevent or mitigate trauma-related cognitive impairment. Trauma-focused therapy, such as TF-CBT and EMDR (Martin et al., 2021), may already contribute to cognitive health by alleviating PTSD symptoms, potentially reducing barriers to engaging in cognitively stimulating activities. However, adjunct interventions such as cognitive training or structured programs aimed at enhancing cognitive reserve should be explored. Encouraging engagement in intellectually and socially stimulating activities could be an effective strategy to build resilience against cognitive decline.

3.3.2. Clinical Implications

The extent to which cognitive dysfunction and decline are reversible is a key question for both research and clinical practice. SCD and MCI are both linked to an increased risk of dementia, with MCI carrying a particularly high conversion rate (Brodaty et al., 2017; Mitchell et al., 2014; Pike et al., 2022). However, both conditions are modifiable, highlighting opportunities for early intervention. Identifying and addressing trauma-related risk factors could contribute to cognitive resilience and potentially delay or prevent the progression to dementia.

Impaired cognition may also be relevant for trauma-focused treatment. A meta-analysis found that individuals with PTSD seeking treatment exhibited greater objective cognitive impairments compared to those not seeking treatment (Scott et al., 2015). This could suggest that treatment-seeking individuals have more severe PTSD symptoms, higher comorbidity, and/or a longer symptom duration. Alternatively, it raises the possibility that cognitive impairment itself may influence help-seeking behavior. Importantly, cognitive deficits may also interfere with treatment efficacy by reducing the ability to comply with therapeutic

interventions and self-manage symptoms (Clouston et al., 2016). Future studies should examine whether addressing cognitive impairment as part of PTSD treatment could enhance therapeutic outcomes.

From a clinical standpoint, healthcare providers should remain vigilant to the cognitive vulnerabilities associated with trauma-related psychopathology, particularly in aging populations. Routine screening for cognitive impairment in individuals with a history of trauma, PTSD, or dissociative disorders could facilitate early interventions, such as promoting engagement in cognitively stimulating activities or re-activating prior interests. Given the well-documented prevalence of lifetime trauma among older adults and its association with physical and psychosocial health (Duchowny et al., 2025), systematic trauma screening should be integrated into geriatric healthcare settings. Even if older adults present with different PTSD symptoms than younger individuals (Pless Kaiser et al., 2019) or primarily report somatic complaints, underlying trauma should be considered.

Overall, this thesis underscores the importance of considering ACEs, PTSD, and dissociative disorders as potential risk factors for cognitive impairment and dementia. However, further research is needed to replicate these findings, elucidate underlying mechanisms, and identify protective factors that may mitigate cognitive decline in trauma-exposed individuals.

3.4. General Strengths and Limitations

The following sections outlines overarching strengths and limitations of all three studies. For a more detailed discussion of the strengths and limitations of each individual study, the reader is referred to the respective sections within the single chapters.

3.4.1. Strengths

One major strength of this thesis is its consideration of the heterogeneity of trauma and trauma-related psychopathology in two ways: First, it examined both PTSD diagnosis and

symptoms, with PTSD being the primary focus of this thesis. Second, it included one specific type of trauma – ACEs – which is both a highly prevalent (Madigan et al., 2023), and an important precursor of trauma-related psychopathology. Additionally, the study incorporated dissociative disorders, a particularly severe trauma-related disorder (American Psychiatric Association, 2013; Dalenberg et al., 2012; Vissia et al., 2016). This approach enabled a comprehensive examination of traumatic stress in relation to cognitive outcomes. Furthermore, the inclusion of depression as an additional predictor, a disorder commonly comorbid with PTSD and dissociative disorders (Flory & Yehuda, 2015; Şar, 2011; Schalinski et al., 2016), enhanced the thesis' depth. In *Study I*, depression was adjusted for in the analyses, in *Study II*, depression was tested as a mediator between all trauma-related predictors and dementia, and in *Study III*, depression was taken as a predictor in addition to all trauma-related predictors. This helped to disentangle the impact of trauma of that of depression.

Another major strength of this thesis is the comprehensive assessment of cognitive outcomes across studies. It examined subjective cognitive functioning (*Study I*), objectively measured cognitive functioning (*Study III*), and dementia (*Study II, Study III*). By incorporating multiple levels of cognitive assessment, this research captured both early cognitive difficulties and more severe neurodegenerative outcomes. Since both subjective and objective cognitive impairments have been linked to dementia (Brodaty et al., 2017; Mitchell et al., 2014; Pike et al., 2022) and may serve as early warning signs (though, importantly, not necessarily) (Gauthier et al., 2006; Jonker et al., 2000; Reid & MacLullich, 2006; Zucchella et al., 2018), this multi-faceted approach enabled a holistic examination of the associations in question.

A further strength lies in the different statistical approaches employed: a network analysis (*Study I*), mediation (*Study II*), and moderation analyses (*Study III*). These different methodologies provided complementary perspectives, offering a deeper and more comprehensive understanding of the relationships examined.

Additionally, all three studies were conducted using large sample sizes, including a substantial number of individuals diagnosed with PTSD, dissociative disorders, depression, and dementia. The availability of both self-reported, that is, subjectively and objectively measured cognitive functioning as well as MRI scans of hippocampal volumes further strengthened the study's design. Another key advantage was the access to recorded diagnoses based on the ICD-10 (World Health Organization, 1993) and access to the well-established self-report measure of PTSD symptoms (Weathers et al., 2013).

The longitudinal design of the studies allowed for an examination of temporal relationships, ensuring that trauma-related psychopathology preceded cognitive outcomes. This helped assess whether trauma serves as a predictor of cognitive decline rather than merely co-occurring with it, or the other way round.

In terms of sample characteristics, Study I included older U.S. veterans, while *Study II* and *Study III* focused on the general population from the UK Biobank. This is particularly relevant because PTSD research in older adults has predominantly focused on U.S. veterans, limiting generalizability. By incorporating UK Biobank data, this research extended its findings beyond veterans and provided insights into the general population. Moreover, while UK Biobank participants were predominantly middle-aged, *Study I* specifically included older adults, addressing the underrepresentation of older individuals in PTSD research (Böttche et al., 2012; Pless Kaiser et al., 2019), who are regularly excluded in participating in from PTSD studies (Dinnen et al., 2015).

Finally, this thesis adhered to open science principles whenever possible. *Study I* was pre-registered prior to data analysis, and both the data and analysis code were made publicly available. Similarly, for *Study II* and *Study III*, analysis codes were shared openly.

3.4.2. Limitations

Despite its strengths, this thesis has several limitations that should be considered when interpreting its findings.

First, although the longitudinal design ensured the temporal ordering of predictors, mediators, moderators, and outcomes, all three studies were observational in nature. As a result, causal inferences cannot be drawn.

Second, while the thesis draws on large-scale datasets, these samples were limited to individuals from the U.S. and the UK – both of which are classified as Western, Educated, Industrialized, Rich, and Democratic (WEIRD) societies. Research has shown that WEIRD populations are among the least representative globally (Henrich et al., 2010), raising concerns about the generalizability of these findings to non-WEIRD populations. This is particularly important given that the majority of individuals with dementia live in in low- and middle-income countries (LMICs) (Prince et al., 2015).

Third, two of three studies have used the same data, namely UK Biobank data. In that regard, it would have been interesting to have a third different population to see how the observed relationships would have unfolded there. Simultaneously, the UK Biobank is a large cohort study including many individuals from the general population, making *Study III* a valuable addition to the field regardless.

Fourth, PTSD, dissociative disorders, and depression may be underreported or underdiagnosed in *Study II* and *Study III*, as the linked health records were limited to primary care, hospital admissions, and death registers, but did not include psychiatric inpatient or outpatient care. While diagnoses were based on ICD-10 criteria (World Health Organization, 1993), it remains unclear how practitioners in these settings identified and assigned them, potentially limiting their accuracy and reliability. This limitation should be considered when interpreting the findings.

Fifth, ACEs were included as number of types of adverse events experienced (*Study II* and *Study III*). However, considering the timing of childhood adversity would have strengthened the findings of this thesis by identifying potential sensitive (reversible) or critical (irreversible) periods during childhood when ACEs may be particularly relevant for an increased long-term dementia risk. Additionally, ACEs generally include less severe events (Kalmakis & Chandler, 2014) than specified in the DSM-5 Criterion for trauma (i.e., exposure to (threatened) death, serious injury, or sexual violence) (American Psychiatric Association, 2013). It is possible that childhood trauma, as defined by the DSM-5 Criterion A, would result in different, potentially stronger, associations.

Sixth, while all-cause dementia was investigated, dementia subtypes (e.g., AD, VaD, FTD) were not distinguished. This decision was made due to low numbers of participants with PTSD and certain dementia subtypes.

Seventh, this thesis did not account for trauma exposure during adulthood, despite the fact that such experiences are common and significant contributors to PTSD, dissociative disorders, and depression (Hong et al., 2024; Kessler et al., 2017; Liu et al., 2017; Şar, 2011). However, it is important to note that childhood adversity is widely considered a particularly relevant form of trauma in shaping long-term mental health and cognitive outcomes (Kalmakis & Chandler, 2014; O'Neill et al., 2021). Future research should also consider the impact of prolonged or repeated trauma in adulthood, such as intimate partner violence or war-related trauma, which may have distinct effects on cognitive health.

Lastly, while different statistical approaches were used across the three studies to provide complementary perspectives, it is important to note that network analyses (*Study I*) and the application of the least absolute shrinkage and selection operator (LASSO; *Study I* and *Study III*) are data-driven methods (Epskamp et al., 2018; Tibshirani, 1996, 1997). This should be kept in mind when interpreting the results and further highlights the need for replication.

3.5. Conclusion

This thesis provides a comprehensive investigation of the complex relationship between traumatic, trauma-related psychopathology, depression, and cognitive and neurological outcomes, including cognitive functioning, dementia risk, and hippocampal volume. By integrating findings from three studies, this work enhances our understanding of the underlying mechanisms linking trauma-related disorders to cognitive decline and dementia.

The key findings of the thesis can be summarized as follows: 1) PTSD is associated with multiple levels of cognitive outcomes, including subjective and objective cognitive functioning and dementia risk; 2) ACEs, as a precursor of trauma-related pathology, and dissociative disorders, as a particularly severe trauma-related disorder, are also linked to cognitive impairment and dementia risk. Their associations with PTSD symptom severity might suggest a dose-response relationship, where greater trauma exposure correlates with increased cognitive decline; 3) specific PTSD symptom clusters and individual symptoms play a distinct role in their association with SCF. Not all PTSD symptoms contribute equally to cognitive impairment, highlighting the heterogeneity of PTSD's cognitive impact; 4) depression, frequently comorbid with trauma-related psychopathology, is also associated with cognitive impairment, dementia risk, and hippocampal volume. 5) However, its role as a mediator in the trauma-dementia link is only partial, meaning that it does not fully explain the repeated associations between ACEs, PTSD, dissociative disorders, and dementia risk. 6) The observed associations are influenced by multiple behavioral and psychosocial factors, such as physical activity, smoking, hypertension, and social interactions, which either mitigate or exacerbate cognitive decline. These findings emphasize the need for tailored interventions to address individual risk profiles.

A central takeaway from this thesis is that dementia risk is not a fixed, and certainly no inevitable, outcome of trauma-related psychopathology. Rather than a uniform link between trauma, cognitive impairment, and dementia, the results suggest a complex interplay of trauma-

specific, behavioral, psychosocial, and biological factors that interact dynamically over the lifespan. This challenges the notion of a single causal mechanism and instead highlights the importance of personalized prevention strategies. One promising avenue for intervention might be the CRT, which has shown some effectiveness in improving cognitive functioning in individuals with depression and PTSD. Future research should explore whether CRT or other cognitive training approaches could help mitigate the cognitive consequences of trauma-related disorders and potentially delay the onset of dementia.

Another key insight is that while depression partially mediates the relationship between ACEs, PTSD symptoms, dissociative disorders, and dementia risk, it does not fully account for these associations. This contradicts an earlier hypothesis that depression might be the primary underlying mechanism. Instead, these findings suggest that childhood adversity, PTSD, dissociative disorders, and depression each contribute to dementia risk through both shared and distinct pathways.

A final key finding is that not all PTSD symptoms contribute equally to cognitive impairment. The severity of symptoms plays an essential role, with subclinical PTSD symptoms already associated with subjective cognitive difficulties, while more severe cases experience significant cognitive impairments. This underscores the need to consider symptom-specific interventions when addressing PTSD-related cognitive decline.

Overall, these findings corroborate prior research that PTSD is associated with cognitive impairment and increased dementia risk but also introduce new insights. ACEs – one of the earliest markers of trauma – are linked to cognitive aging, while dissociative disorders emerge as a particularly strong and potentially modifiable risk factor for dementia. The findings also suggest a dose-response relationship, meaning that more severe symptoms appear to contribute to an increased risk of cognitive decline.

While this thesis provides valuable insights, it represents only the beginning of a long path toward understanding the intricate relationship between trauma, trauma-related

psychopathology, and cognitive aging. With global trauma exposure on the rise, an aging population, and increasing life expectancy, unraveling these connections is more important than ever.

Future research should replicate findings across diverse populations, particularly in LMICs, which are often underrepresented in dementia research despite higher rates of trauma exposure and dementia burden. Further investigations should examine the role of different trauma types, including adulthood trauma, in cognitive decline; explore dementia subtypes separately, given PTSD's particularly strong association with FTD; and further assess the impact of trauma-related psychopathology on accelerated aging. Additionally, studies should investigate the relationship between specific dissociative disorders and dementia risk, replicate findings related to various lifestyle, behavioral, and psychosocial moderators, and evaluate the effectiveness of diverse intervention strategies, including TF-CBT and EMDR, in improving cognitive functioning. Finally, future research should distinguish between prodromal and risk factor associations, clarifying whether PTSD, dissociative disorders, and depression are precursors to dementia or early manifestations of neurodegenerative disease, and explore bidirectional relationships, as cognitive decline may reactivate or worsen PTSD symptoms, complicating dementia diagnosis and management in trauma-affected individuals.

Rather than a linear relationship between trauma and dementia, this thesis highlights a dynamic, multifaceted process, where (childhood) trauma, related mental health disorders, and cognitive decline interact in complex ways. However, the good news is that this also presents multiple intervention opportunities. The findings suggest that prevention efforts and tailored interventions – including lifestyle modifications, cognitive training, and trauma-focused therapies – may help reduce or delay cognitive decline in individuals with trauma-related psychopathology.

While much remains to be investigated and found out in future research, the findings of this thesis advance our understanding of these relationships and lay the groundwork for more

targeted prevention and intervention strategies in the future, ensuring that individuals affected by trauma are not inevitably at increased risk for cognitive decline or dementia.

4. Deutsche Zusammenfassung

Die Rolle von Trauma und Posttraumatischer Belastungsstörung in kognitiven Fähigkeiten und Demenz: Untersuchung traumaassoziierter, verhaltensbezogener und psychosozialer Faktoren

Demenz stellt eine der größten globalen gesundheitlichen Herausforderungen des 21. Jahrhunderts dar (Livingston et al., 2017). Die steigende Lebenserwartung und das anhaltende Bevölkerungswachstum tragen maßgeblich zu ihrer zunehmenden Prävalenz bei (Prince et al., 2015). Da bislang keine krankheitsmodifizierende Therapie existiert, konzentriert sich die Forschung auf die Identifikation modifizierbarer Risikofaktoren, um den Krankheitsbeginn hinauszuzögern oder gar zu verhindern (Livingston et al., 2017, 2020, 2024). Der jüngste Bericht der Lancet-Kommission zur Demenzprävention, -intervention und -versorgung identifizierte 14 potenziell modifizierbare Risikofaktoren, die zusammen etwa 45% aller Demenzfälle ausmachen (Livingston et al., 2024). Zu diesen zählen unter anderem eine geringe Bildung, Depression, körperliche Inaktivität, Rauchen, erhöhter Blutdruck, exzessiver Alkoholkonsum und soziale Isolation. Diese Ergebnisse unterstreichen das erhebliche Präventionspotenzial: Nahezu die Hälfte aller Demenzfälle könnte theoretisch durch gezielte Interventionen verhindert werden. Diese Risikofaktoren wurden in systematischen Übersichtsarbeiten und Metaanalysen konsistent mit einem erhöhten Demenzrisiko in Verbindung gebracht. Die Ergebnisse der Kommission betonen zudem die Bedeutung der kognitiven und physischen Reservebildung über die gesamte Lebensspanne sowie den positiven Einfluss vaskulärer Gesundheit auf die Reduktion des altersbedingten Demenzrisikos.

Neben diesen 14 etablierten Faktoren wurden weitere potenzielle Risikofaktoren für Demenz identifiziert. Durch die noch begrenzte Anzahl hochwertiger Studien und inkonsistenter Befunde wird die Anerkennung dieser primären modifizierbaren Faktoren bislang erschwert. Ein potenzieller Risikofaktor ist die Posttraumatische Belastungsstörung (PTBS), eine psychische Störung, die durch vier zentrale Symptomcluster gekennzeichnet ist: das Wiedererleben traumabezogener Erinnerungen, das Vermeiden von traumaassoziierten Aktivitäten, Personen und Orten, negative Veränderungen in Kognitionen und Stimmung sowie ein erhöhtes Erregungsniveau (American Psychiatric Association, 2013). Da PTBS durch eine

gestörte autobiografische Erinnerung charakterisiert ist (Brewin et al., 1996; Ehlers & Clark, 2000; Foa & Kozak, 1986) und mit kognitiven Beeinträchtigungen assoziiert wurde (Schuitevoerder et al., 2013; Scott et al., 2015), haben mehrere Studien untersucht, ob PTBS mit einem erhöhten Demenzrisiko verbunden ist – mit positiven Ergebnissen (Günak et al., 2020; Stafford et al., 2022).

Als potenzielle zugrunde liegende Mechanismen dieser Assoziation wurden verschiedene neurobiologische Prozesse vorgeschlagen, darunter das Konzept der allostatischen Last (englisch: „allostatic load“), das die kumulative physiologische Abnutzung des Organismus durch chronische Stressreaktionen beschreibt (Danese & McEwen, 2012; McEwen, 1993), eine Dysregulation der Hypothalamus-Hypophysen-Nebennierenrinden-Achse (HPA-Achse), Neuroinflammation sowie strukturelle Hirnveränderungen, insbesondere eine Atrophie des Hippocampus (Alves De Araujo Junior et al., 2023; Greenberg et al., 2014). Weitere Erklärungsansätze umfassen beschleunigte Alterungsprozesse (Wolf, Maniates, et al., 2018) sowie genetische Prädispositionen (Averill et al., 2019). Darüber hinaus wurde das Konzept der kognitiven Reserve (englisch: „cognitive reserve“) (Stern, 2002, 2009, 2012) diskutiert, das sich auf die Fähigkeit des Gehirns bezieht, altersbedingten Abbau oder pathologische Veränderungen durch die Nutzung alternativer neuronaler Netzwerke oder kompensatorischer Mechanismen auszugleichen.

Insgesamt befindet sich die Forschung in diesem Bereich jedoch noch in einem eher frühen Stadium, sodass weitere Untersuchungen erforderlich sind, um den Zusammenhang zwischen PTBS und Demenzrisiko besser zu verstehen. Zudem ist unklar, welche Mechanismen dieser Beziehung tatsächlich zugrunde liegen, ob alternative Erklärungen existieren und welche Faktoren das erhöhte Demenzrisiko bei Personen mit PTBS beeinflussen könnten.

Das übergeordnete Ziel dieser Dissertation, bestehend aus drei Studien, ist es, frühere Forschungsergebnisse zu PTBS als potenziellem Risikofaktor für Demenz zu festigen und

darüber hinaus, bestehende Forschungslücken zu adressieren, um langfristig gezielte Interventionsstrategien zu ermöglichen. Neben PTBS werden dabei auch frühkindliche Traumata als prädisponierender oder auslösender Faktor (Messman-Moore & Bhuptani, 2017), dissoziative Störungen als schwerwiegende traumaassoziierte Psychopathologie (Şar, 2011) sowie Depression als häufige Komorbidität berücksichtigt (Flory & Yehuda, 2015; Şar, 2011; Schalinski et al., 2016). Kognitive Ergebnisse (englisch „outcomes“) werden anhand subjektiver kognitiver Leistungsfähigkeit, objektiv gemessener kognitiver Leistung, Hippocampusvolumen – jeweils als relevante Marker für das Demenzrisiko – sowie Demenz untersucht.

Studie I hat den Zusammenhang zwischen PTBS und subjektiver kognitiver Leistungsfähigkeit bei etwa 1.500 älteren US-Veteranen (Mdn = 65 Jahre) unter Verwendung von Netzwerkanalysen sowohl querschnittlich als auch längsschnittlich über einen Zeitraum von drei Jahren untersucht. Die Schwere der PTBS korrelierte dabei mit einer verringerten subjektiven kognitiven Leistungsfähigkeit, insbesondere über die Symptomcluster „Deutliche Veränderungen des Erregungsniveaus und der Reaktivität im Zusammenhang mit dem oder den traumatischen Ereignissen“ sowie „Negative Veränderungen von Kognitionen und der Stimmung im Zusammenhang mit dem oder den traumatischen Ereignissen“ (American Psychiatric Association, 2013, S. 271-272; Falkai et al., 2015, S. 370-371). Die Symptome „Konzentrationsschwierigkeiten“ und „Anhaltende Unfähigkeit, positive Gefühle zu empfinden (z.B. Glück, Zufriedenheit, Gefühle der Zuneigung)“ waren wiederholt und robust mit kognitiven Beeinträchtigungen assoziiert. Diese Befunde sind auch nach Kontrolle soziodemografischer Faktoren und Depression bestehen geblieben und wurden über den dreijährigen Untersuchungszeitraum hinweg repliziert. Dies deutet darauf hin, dass bestimmte PTBS-Symptome sowohl zeitlich dem Auftreten als auch der Aufrechterhaltung einer verringerten subjektiven kognitiven Leistungsfähigkeit vorausgehen und statistisch damit

assoziiert sind. Die Ergebnisse unterstreichen zudem die Relevanz der Untersuchung spezifischer PTBS-Symptomschweregrade sowie einzelner PTBS-Symptomcluster und -Symptome in Bezug auf die subjektive kognitive Leistungsfähigkeit – Zusammenhänge, die durch die ausschließliche Betrachtung von PTBS-Diagnosen oder Gesamtwerte auf Selbstberichtfragebögen möglicherweise verdeckt werden. Darüber hinaus wird die Notwendigkeit hervorgehoben, die zugrunde liegenden Mechanismen dieser Beziehungen weiter zu erforschen.

Studie II erweiterte diese Erkenntnisse unter Verwendung von Daten aus der United Kingdom (UK) Biobank ($N \approx 500.000$), um die Wechselwirkungen zwischen belastenden Kindheitserfahrungen (englisch: „adverse childhood experiences“, ACEs), PTBS, dissoziativen Störungen und Depression im Hinblick auf das Demenzrisiko bei Erwachsenen mittleren Alters zu untersuchen. Zu den ACEs zählen emotionale und physische Vernachlässigung sowie emotionale, physische und sexuelle Misshandlung (Kalmakis & Chandler, 2014; O'Neill et al., 2021). Die Ergebnisse haben gezeigt, dass jeder zusätzlicher Punkt auf einer PTBS-Symptom-Skala das allgemeine Demenzrisiko um 9% erhöhte, jede zusätzliche ACE-Art um 10%, während PTBS- und Depressionsdiagnosen das Risiko verdoppelten und dissoziative Störungen es nahezu vervierfachten. Mediationsanalysen ergaben, dass PTBS-Symptome den größten Teil der Assoziation zwischen ACEs und Demenz erklärten, während Depression einen geringeren Teil der Zusammenhänge zwischen ACEs, PTBS und dissoziativen Störungen mit Demenz vermittelte. Die Befunde legen nahe, dass Depression – obwohl ein etablierter Risikofaktor für Demenz – nicht allein für das erhöhte Demenzrisiko im Zusammenhang mit traumaassoziierten Psychopathologien verantwortlich ist. Dies unterstreicht die Bedeutung sowohl gemeinsamer als auch spezifischer Prozesse zwischen traumaassoziierten Psychopathologien und Depression in ihrem Zusammenhang mit Demenz.

Studie III untersuchte diese traumaassoziierten Prädiktoren weiter in Bezug auf objektive kognitive Leistungsfähigkeit, Demenzrisiko und Hippocampusvolumen, erneut unter

Verwendung der UK Biobank-Daten. Zudem wurden Interaktionen mit demografischen, verhaltensbezogenen und psychosozialen Faktoren (Alter, Geschlecht, ethnische Zugehörigkeit, Bildung, Deprivation, Rauchen, Alkoholkonsum, körperliche Aktivität, erhöhter Blutdruck, soziale Aktivitäten) analysiert. Die moderierenden Faktoren variierten je nach Prädiktor und Ergebnis. So war beispielsweise Bluthochdruck der stärkste Moderator der Assoziation zwischen ACEs und Demenz, während Rauchen die stärkste Moderation zwischen PTBS-Diagnose und Demenz zeigte. Diese Ergebnisse unterstreichen die Notwendigkeit gezielter Präventionsstrategien und legen nahe, dass kognitive Beeinträchtigungen und das Demenzrisiko bei Menschen mit Traumaerfahrungen und traumabezogenen Störungen potenziell veränderbar sind.

Die vorliegende Dissertation weist zwei zentrale Stärken auf. Erstens wurde die Heterogenität von Trauma und damit verbundener Psychopathologie auf zwei Ebenen berücksichtigt: Zum einen wurden sowohl die PTBS-Diagnose als auch einzelne PTBS-Symptome untersucht, wobei PTBS den primären Fokus dieser Arbeit bildet. Zum anderen wurden verschiedene Formen von Trauma und traumaassoziierter Psychopathologie einbezogen. Dazu zählen belastende Kindheitserfahrungen, eine spezifische Form von Trauma, die nicht nur hochprävalent sind (Madigan et al., 2023), sondern auch einen bedeutsamen Prädiktor für die Entwicklung traumaassoziierter Psychopathologien darstellen (Schalinski et al., 2016). Zusätzlich wurden dissoziative Störungen als eine besonders schwere Form traumaassoziierter Psychopathologie berücksichtigt (American Psychiatric Association, 2013; Dalenberg et al., 2012; Vissia et al., 2016). Dieser Ansatz ermöglichte eine differenzierte Untersuchung von traumatischem Stress in Bezug auf kognitive Outcomes. Darüber hinaus wurde Depression als zusätzlicher Prädiktor einbezogen – eine Störung, die häufig komorbid mit PTBS und dissoziativen Störungen auftritt (Flory & Yehuda, 2015; Şar, 2011; Schalinski

et al., 2016) und deren Rolle im Zusammenhang mit kognitiven Beeinträchtigungen und Demenz in der bisherigen Forschung vorrangig untersucht wurde.

Zweitens wurde eine umfassende Erfassung kognitiver Outcomes über die verschiedenen Studien hinweg vorgenommen. Diese Arbeit untersuchte sowohl die subjektive kognitive Leistungsfähigkeit (*Studie I*), als auch die objektiv gemessene kognitive Leistungsfähigkeit (*Studie III*) sowie die Diagnose einer Demenz (*Studie II* und *Studie III*). Durch die Berücksichtigung mehrerer Ebenen kognitiver Messung konnten sowohl frühe kognitive Beeinträchtigungen als auch schwerwiegendere neurodegenerative Verläufe erfasst werden. Da sowohl subjektive als auch objektive kognitive Beeinträchtigungen mit einem erhöhten Demenzrisiko assoziiert wurden (Brodaty et al., 2017; Mitchell et al., 2014; Pike et al., 2022) und als potenzielle Frühwarnzeichen gelten (wenn auch nicht zwingend) (Gauthier et al., 2006; Jonker et al., 2000; Reid & MacLullich, 2006; Zucchella et al., 2018), ermöglichte dieser facettenreiche Ansatz eine differenzierte Untersuchung der relevanten Zusammenhänge.

Weitere Stärken dieser Arbeit sind die verschiedenen angewandten statistischen Methoden: eine Netzwerkanalyse (*Studie I*), Mediationsanalysen (*Studie II*) und Moderationsanalysen (*Studie III*). Diese unterschiedlichen methodischen Ansätze ergänzten sich gegenseitig und lieferten eine tiefere sowie umfassendere Perspektive auf die untersuchten Zusammenhänge.

Zu den methodischen Einschränkungen dieser Dissertation gehört das Beobachtungsdesign der Studie, das keine kausalen Schlussfolgerungen zulässt. Zudem liegt der Fokus auf westlichen Ländern (USA, Großbritannien), wodurch die Generalisierbarkeit der Ergebnisse auf andere Bevölkerungen eingeschränkt ist. Eine weitere Limitation ist die fehlende Differenzierung zwischen verschiedenen Demenzsubtypen wie Alzheimer-Demenz, vaskulärer Demenz oder frontotemporaler Demenz. Darüber hinaus wurden traumatische Erfahrungen im Erwachsenenalter nicht berücksichtigt, ebenso wenig wie der genaue Zeitpunkt belastender Kindheitserfahrungen.

Um diese Einschränkungen zu adressieren, sollten zukünftige Studien auf vielfältigere Bevölkerungen ausgeweitet werden, Demenzsubtypen differenzierter analysiert und sowohl traumatische Erfahrungen im Erwachsenenalter als auch das zeitliche Auftreten von Kindheitstraumata berücksichtigt werden. Zudem sollte erforscht werden, ob kognitive Trainingsansätze die kognitiven Folgen traumaassoziierter Störungen abmildern und möglicherweise das Demenzrisiko verzögern können. Darüber hinaus ist es essenziell, den Einfluss traumafokussierter Psychotherapie – welche als erste Wahl bei der PTBS-Behandlung empfohlen wird (Martin et al., 2021) – auf das erhöhte Risiko für kognitive Beeinträchtigungen und Demenz bei PTBS-Betroffenen zu untersuchen. Ebenso sollte erforscht werden, ob die gezielte Förderung kognitiv stimulierender Aktivitäten zur Prävention oder Verlangsamung kognitiven Abbaus beitragen kann, indem sie die kognitive Reserve stärkt.

Für die klinische Praxis scheint es wichtig, dass behandelnde Psychotherapeut:innen die kognitiven Vulnerabilitäten im Zusammenhang mit traumaassoziierter Psychopathologie und das damit einhergehende erhöhte Demenzrisiko über die Lebensspanne hinweg erkennen. Zukünftige Forschung sollte zudem untersuchen, ob Personen mit traumaassoziierten Störungen systematisch auf kognitive Beeinträchtigungen gescreent werden sollten und ob eine frühzeitige Erkennung die Wirksamkeit gezielter Interventionen erhöhen könnte.

Insgesamt trägt die Dissertation insofern zum Verständnis von PTBS als Risikofaktor für Demenzerkrankungen bei, indem sie die Heterogenität der Störung, belastende Kindheitserfahrungen, dissoziative Störungen und die häufige Komorbidität mit Depression berücksichtigt, während sie gleichzeitig verschiedene kognitive Outcomes analysiert. Die Ergebnisse deuten darauf hin, dass die Schwere der PTBS-Symptome eine entscheidende Rolle spielt, dass bestimmte Symptome besonders relevant sein könnten und dass Depression allein das traumaassoziierte Demenzrisiko nicht vollständig erklärt. Diese Zusammenhänge können durch traumaassoziierte, verhaltensbezogene und psychosoziale Faktoren entweder verstärkt

oder abgemildert werden. Während eine Replikation dieser Befunde in zukünftigen Studien erforderlich ist, stützen die Ergebnisse der Dissertation die Evidenz für die Aufnahme von PTBS als potenziellen modifizierbaren Risikofaktor in zukünftige Aktualisierungen des Lancet-Kommissionsberichts. Darüber hinaus unterstreichen die Befunde die Bedeutung belastender Kindheitserfahrungen und dissoziativer Störungen als weitere potenzielle Einflussfaktoren auf kognitive Beeinträchtigungen und Demenzrisiko, was wiederum weitere Untersuchungen erfordert.

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Appendix

Appendix A: Supplementary Materials Study I

1 Open materials: measurement

Demographic characteristics

Age: What is your age and date of birth?

☐☐☐ years ☐☐ Month ☐☐ Day ☐☐☐☐ Years of birth

Sex: What is your sex?

☐ Male ☐ Female

Race/Ethnicity: Please answer both questions about Hispanic origin and about race. For this census, Hispanic origins are not races.

Ethnicity: Are you Hispanic, Latino, or Spanish origin?

☐ No, not of Hispanic, Latino or Spanish origin

☐ Yes, Mexican, Mexican Am., Chicano

☐ Yes, Puerto Rican

☐ Yes, Cuban

☐ Yes, another Hispanic, Latino or Spanish Origin – Print for example Salvadoran; Dominican, Colombian, Guatemalan, Spaniard, Ecuadorian, etc.

Race: What is your race? Mark one or mor boxes and print origins.

☐ White – Print, for example, German, Irish, English, Italian, Lebanese, Egyptian, etc.

☐ Black or African Am. – Print, for example, African American, Jamaican, Haitian, Nigerian, Ethiopian, Somali, etc.

☐ American Indian or Alaska Native – Print name of enrolled or principal tribe(s), for example, Navajo Nation, Blackfeet Tribe, Mayan, Aztec, Native Village of Barrow Inupiat Traditional Government, Nome Eskimo Community, etc.

☐ Chinese ☐ Vietnamese ☐ Native Hawaiian

☐ Filipino ☐ Korean ☐ Samoan

☐ Asian Indian ☐ Japanese ☐ Chamorro

☐ Other Asian – Print, for example, Pakistani, Cambodian, Hmong, etc.

☐ Other Pacific Islander - Print, for example, Tongan, Fijian, Marshallese, etc.

☐ Some other race – Print race or origin.

Highest level of school completed or degree received:

☐ Less than 1st grade
☐ 1st, 2nd, 3rd or 4th grade
☐ 5th or 6th grade
☐ 7th or 8th grade
☐ 9th grade
☐ 10th grade
☐ 11th grade
☐ 12th grade or no diploma
☐ High school grad-diploma or equiv (GED)
☐ Some college but no degree
☐ Associate degree-occupational/vocational
☐ Associated degree-academic program
☐ Bachelor's degree (Ex: BA, AB, BS)
☐ Masters's degree (Ex: MA, MS, Meng, Med, MSW)
☐ Professional school deg (Ex: MD, DDS, DVM)
☐ Doctorate degree (Ex: PhD, EdD)

More information can be found here: https://www2.census.gov/programs-surveys/cps/techdocs/cpsaug21.pdf, last accessed on 26.08.2022:

Current employment status

Based on several questions (e.g., "Last week, did you do any work for (either) pay (or profit)?" that can be found here: https://www2.census.gov/programs-surveys/cps/techdocs/cpsaug21.pdf, last accessed on 26.08.2022, the following categories were listed:

1. Employed – at work
2. Employed – absent
3. Unemployed – on layoff
4. Unemployed – looking
5. Not in labor force – retired
6. Not in labor force – disabled
7. Not in labor force – other

PTSD Checklist for DSM-5 (PCL-5)

PCL-5

Instructions: Below is a list of problems that people sometimes have in response to a very stressful experience. Please read each problem carefully and then circle one of the numbers to the right to indicate how much you have been bothered by that problem in the past month.

	In the past month, how much were you bothered by:	Not at all	A little bit	Moderately	Quite a bit	Extremely
B1	1. Repeated, disturbing, and unwanted memories of the stressful experience?	0	1	2	3	4
B2	2. Repeated, disturbing dreams of the stressful experience?	0	1	2	3	4
B3	3. Suddenly feeling or acting as if the stressful experience were actually happening again (as if you were actually back there reliving it)?	0	1	2	3	4
B4	4. Feeling very upset when something reminded you of the stressful experience?	0	1	2	3	4
B5	5. Having strong physical reactions when something reminded you of the stressful experience (for example, heart pounding, trouble breathing, sweating)?	0	1	2	3	4
C1	6. Avoiding memories, thoughts, or feelings related to the stressful experience?	0	1	2	3	4
C2	7. Avoiding external reminders of the stressful experience (for example, people, places, conversations, activities, objects, or situations)?	0	1	2	3	4
D1	8. Trouble remembering important parts of the stressful experience?	0	1	2	3	4
D2	9. Having strong negative beliefs about yourself, other people, or the world (for example, having thoughts such as: I am bad, there is something seriously wrong with me, no one can be trusted, the world is completely dangerous)?	0	1	2	3	4
D3	10. Blaming yourself or someone else for the stressful experience or what happened after it?	0	1	2	3	4
D4	11. Having strong negative feelings such as fear, horror, anger, guilt, or shame?	0	1	2	3	4
D5	12. Loss of interest in activities that you used to enjoy?	0	1	2	3	4
D6	13. Feeling distant or cut off from other people?	0	1	2	3	4
D7	14. Trouble experiencing positive feelings (for example, being unable to feel happiness or have loving feelings for people close to you)?	0	1	2	3	4
E1	15. Irritable behavior, angry outbursts, or acting aggressively?	0	1	2	3	4
E2	16. Taking too many risks or doing things that could cause you harm?	0	1	2	3	4
E3	17. Being "superalert" or watchful or on guard?	0	1	2	3	4
E4	18. Feeling jumpy or easily startled?	0	1	2	3	4
E5	19. Having difficulty concentrating?	0	1	2	3	4
E6	20. Trouble falling or staying asleep?	0	1	2	3	4

PCL-5 (11 April 2018) National Center for PTSD Page 1 of 1

Note. PCL-5 = PTSD Checklist for DSM-5. The letters on the left side of the PCL-5 represent the symptoms of the corresponding domain. D: Intrusion. C: Persistent avoidance. D: Negative alterations in cognitions and mood. E: Marked alterations in arousal and reactivity.

Weathers, F.W., Litz, B.T., Keane, T.M., Palmieri, P.A., Marx, B.P., & Schnurr, P.P. (2013). The PTSD Checklist for *DSM-5* (PCL-5). Scale available from the National Center for PTSD at www.ptsd.va.gov.

Medical Outcomes Study – Cognitive Functioning scale

Rating of each item: 1 = None of the time; 2 = A little of the time; 3 = Some of the time; 4 = A good bit of the time; 5 = Most of the time; 6 = All of the time

1. How much of the time during the past month did you have difficulty reasoning and solving problems (e.g., making plans, making decisions, learning new things)?

1 ——— 2 ——— 3 ——— 4 ——— 5 ——— 6

2. During the past month, how much of the time did you forget (e.g., things that happened recently, where you put things, appointments)?

1 ——— 2 ——— 3 ——— 4 ——— 5 ——— 6

3. How much of the time during the past month did you have trouble keeping your attention on any activity for long?

1 ——— 2 ——— 3 ——— 4 ——— 5 ——— 6

4. During the past month how much of the time did you have difficulty doing activities involving concentration and thinking?

1 ——— 2 ——— 3 ——— 4 ——— 5 ——— 6

5. How much of the time did you become confused and start several actions at a time?

1 ——— 2 ——— 3 ——— 4 ——— 5 ——— 6

6. Did you react slowly to things that were said or done?

1 ——— 2 ——— 3 ——— 4 ——— 5 ——— 6

Note. The Medical Outcome Study – Cognitive Functioning (MOS-CF) scale is reproduced here with permission from the RAND Corporation. Copyright © the RAND Corporation. RAND's permission to reproduce the survey is not an endorsement of the products, services, or other uses in which the survey appears or is applied.

For the original and most current version, please visit RAND Corporation (https://www.rand.org/health-care/surveys_tools/mos/20-item-short-form.html)

Hays, R. D., Sherborne, C. D., & Mazel, R. M. (1995). User's Manual for the Medical Outcomes Study (MOS) Core Measures of Health-Related Quality of life. In *Santa Monica: Rand Corporation.* Rand Corporation.

Trauma History Screen – Lifetime exposure to traumatic events

Traumatic Events listed in the THS	Entire Sample (*N* = 1,484), *n* (%)	Participants Exposed to Trauma (*n* = 1,268), *n* (%)
1. Life-threatening illness or injury	419 (28.2)	419 (33.0)
2. A really bad car, boat, train, or airplane accident	329 (22.2)	329 (25.9)
3. A really bad accident at work or home	162 (10.9)	162 (12.8)
4. A hurricane, flood, earthquake, tornado, or fire	504 (34.0)	504 (39.7)
5. Hit or kicked hard enough to injure – as a child	218 (14.7)	218 (17.2)
6. Hit or kicked hard enough to injure – as an adult	224 (15.1)	224 (17.7)
7. Forced or made to have sexual contact – as a child	103 (6.9)	103 (8.1)
8. Forced or made to have sexual contact – as an adult	62 (4.2)	62 (4.9)
9. Attacked with a gun, knife, or weapon	317 (21.4)	317 (25.0)
10. During military service – saw something horrible or was badly scared	434 (29.2)	434 (34.2)
11. Sudden death of close family member or friend	885 (59.6)	885 (69.8)
12. Seeing someone die suddenly or get badly hurt or killed	548 (36.9)	548 (43.2)
13. Sudden move or loss of home and possessions	253 (17.0)	253 (20.0)
14. Suddenly abandoned by spouse, partner, parent, or family	269 (18.1)	269 (21.2)
15. Some other sudden event that made you feel very scared, helpless, or horrified	163 (11.0)	163 (12.9)

Note. THS = Trauma History Screen; *N* = sample size. Number of missing values ranges from 6 to 40 per THS item in the entire sample.

Carlson, E.B., Smith, S.R., Palmieri, P.A., Dalenberg, C.J., Ruzek, J.I., Kimerling, R., Burling, T.A. & Spain, D.A. (2011). Development and validation of a brief self-report measure of trauma exposure: The Trauma History Screen (PDF). *Psychological Assessment, 23*, 463-477. doi: 10.1037/a0022294. Scale available from the National Center for PTSD at www.ptsd.va.gov.

2 Missing data

Missing data and multiple imputation by chained equations

We used multiple imputation by chained equations to impute missing past-month and lifetime PCL-5 item values prior to analysis for participants who were missing less than 5% of data. Missing values were not imputed for PCL-5 items of participants who were missing more than 5% of data, and for MOS-CF item values or single-item questions (i.e., sociodemographic questions). When possible (i.e., for network estimation, network accuracy, average connectivity, network comparison), we used pairwise complete observations (i.e., using all available data) to deal with remaining missing data. If this was not possible (i.e., for overall association between PTSD and SCF, node predictability), we used listwise deletion. For an overview of sample sizes for each analysis, please see S1.

Out of all participants (N = 1,484), 210 veterans had not previously experienced a traumatic event according to the THS, additional six participants had not filled out the THS; for 271 and 259 veterans, respectively, ~2-3 individual past-month and lifetime PCL-5 values, on average, were imputed; overall, past-month and lifetime PCL-5 missing values (i.e., non-imputed) remained for 134 (9.0%) and 22 (1.5%) participants, respectively. Scores of MOS-CF were missing for 45 participants (3.0%) at baseline and for eight participants (1.1%) at follow-up, with an overall sample size of 713 at follow-up.

S1: Sample sizes for each analysis

Analysis	*n* in Main Analyses
Association between PTSD and SCF	
Past-month PTSD and SCF at baseline	1,104
Past-month PTSD at baseline and SCF at follow-up	543
Lifetime PTSD and SCF at baseline	1,213
Lifetime PTSD at baseline and SCF at follow-up	602
Individual PTSD Symptoms and SCF (N1 – $N4_{adj}$)	1,484†
Association between SCF at baseline and at follow-up	684
Accuracy analyses	1,484†
Node predictability	
N1	1,104
N2	543
$N2_{adj}$	530
N3	1,213
N4	602
$N4_{adj}$	586
PTSD symptom domains and SCF	1,484†
Network Comparison Test	1,484†

Note. N = 1,484 out of which n = 1,268 have experienced at least one traumatic event.

PTSD = Posttraumatic stress disorder; SCF = Subjective cognitive functioning; N1 = Network 1 (past-month PTSD symptoms and SCF at baseline); N2 = Network 2 (past-month PTSD symptoms at baseline and SCF at follow-up; N3 = Network 3 (lifetime PTSD symptoms and SCF at baseline); N4 = Network 4 (lifetime PTSD symptoms at baseline and SCF at follow-up); adj = additionally adjusted for SCF at baseline.

†Analyses are based on pairwise complete observations.

3 Drop-out

Relative to veterans who did not complete the follow-up assessment, veterans who did complete this assessment did not differ with respect to most sociodemographic or clinical variables, including age (p = .279), sex (p = .280), race/ethnicity (p = .239), level of education (p = .146), number of lifetime traumatic events (p = .405), combat exposure (p = .929), lifetime major depressive episode (p = 0.631), lifetime alcohol abuse/dependence (p = .327), probable PTSD (p = .065), lifetime PCL-5 sum scores (p = .119). Statistically significant differences were found for employment (p = .017), past-month PCL-5 sum scores (p = .024), and MOS-CF average scores (p = .043). More details are provided in the table below. Similar results were found following the complete case analyses, only that past-month PCL-5 scores were not statistically significantly different (p = .134).

S2: Baseline characteristics between respondents and drop-outs

	Respondents (n = 713)	Drop-out (n = 771)
Age		
Median (*IQR*)	65 (56-72)	65 (52-73.5)
Female, *n* (%)	69 (9.7)	89 (11.5)
Race/Ethnicity, *n* (%)		
Non-Hispanic White	590 (82.7)	614 (79.6)
Non-Hispanic Black	49 (6.9)	63 (8.2)
Hispanic	42 (5.9)	57 (7.4)
Other, Non-Hispanic	14 (2.0)	9 (1.2)
2+ Races, Non-Hispanic	18 (2.5)	28 (3.6)
Education, *n* (%)		
Less than high school	7 (1.0)	19 (2.5)
High school	107 (15.0)	104 (13.5)
Some college	299 (41.9)	330 (42.8)
Bachelor's degree or higher	300 (42.1)	318 (41.2)
Employment, *n* (%)		
Working	242 (33.9)	234 (30.4)
Retired	353 (49.5)	365 (47.3)
Not working	118 (16.5)	172 (22.3)
Number of lifetime traumatic events		
Median (*IQR*)	3.0 (1.0-5.0)	3.0 (1.0-5.0)
Combat exposure, *n* (%)	270 (37.9)	294 (38.1)
Major depressive episode (lifetime), *n* (%)	69 (9.7)	68 (8.8)
Alcohol abuse/dependence (lifetime), *n* (%)	270 (37.9)	272 (35.3)
PCL-5 (past month)		
Median (*IQR*)	4 (1.0-11.0)	5 (1.0-15.0)

	Respondents (*n* = 713)	Drop-out (*n* = 771)
Probable PTSD, *n* (%)	36 (5.05)	57 (7.4)
PCL-5 (lifetime)		
Median (*IQR*)	9 (4.0-19.0)	10 (4.0-20.0)
MOS-CF		
Median (IQR)	96.7 (86.7-100.0)	96.7 (86.7-100.0)

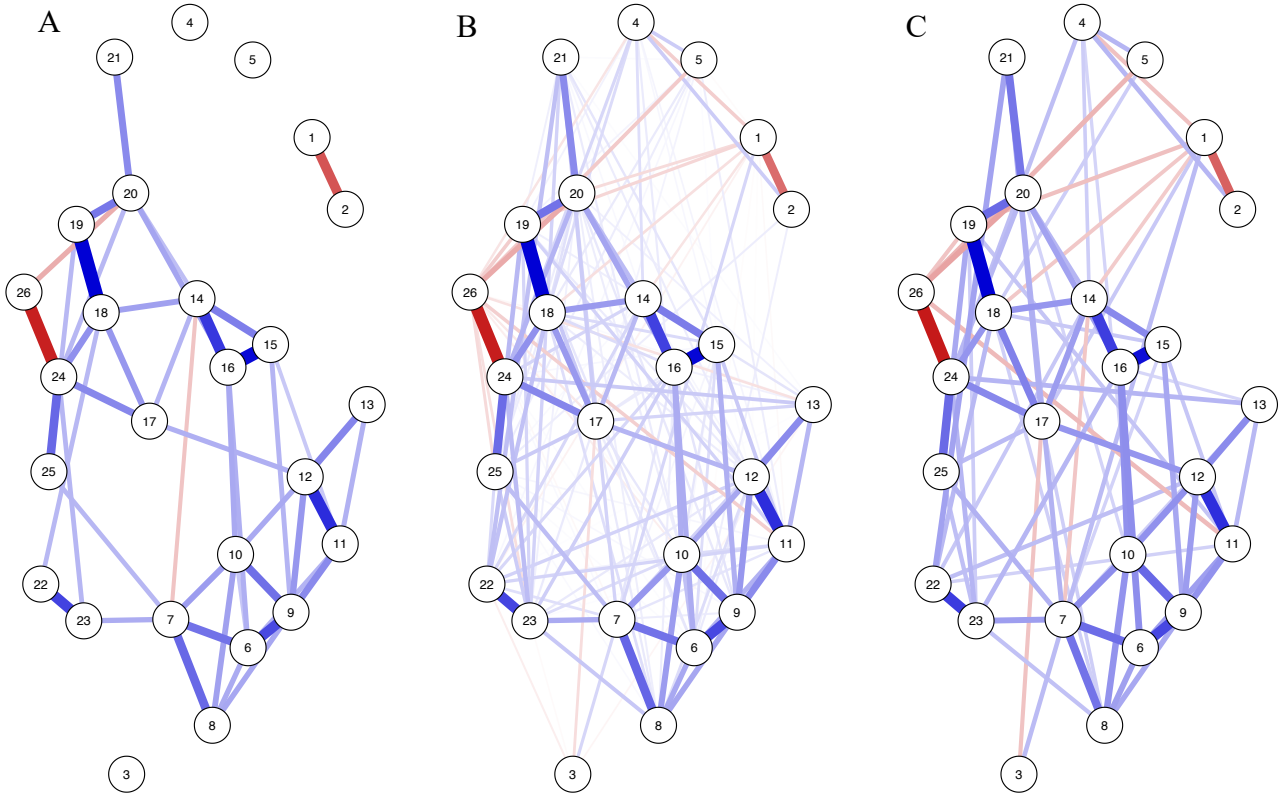
Note. N = sample size; IQR = Interquartile range; SD = standard deviation; PCL-5 = PTSD Checklist for DSM-5; MOS-CF = Medical Outcomes Study – Cognitive Functioning scale.

4 Network estimation

Alternative approaches to estimate network models

Since recent research identified potential problems with regularisation (Williams et al., 2019), we used two alternative approaches to estimate network models for each a priori specified network as robustness analyses: 1) with thresholding, which additionally sets coefficients that are lower than the threshold to zero in both the EBIC computation of all considered models and the returned final model (Epskamp, 2018; Epskamp & Fried, 2018; Muthén, 1984); and 2) using *ggmModSelect* (Epskamp, 2018). The latter entails a model search of unregularized GGM models, where 100 models are re-fitted without regularization to choose the optimal unregularized GGM according to EBIC. During this selection process, all possible models are tested by adding and removing one edge at a time until the EBIC can no longer be improved. For each network, the three models corresponding to each approach of network estimation were nearly the same, with the highest correlation occurring between the regularized model without thresholding and the two other models (i.e., regularized model with thresholding, and the novel network estimation method *ggmModSelect*). Thus, regularized network models estimated without thresholding (which are the default in the literature) were used for further analyses.

S3: Three approaches to Network 1 estimation: regularized network model with thresholding (panel A), regularized network model without thresholding (panel B), and network model estimated with *ggmModSelect* (panel C).

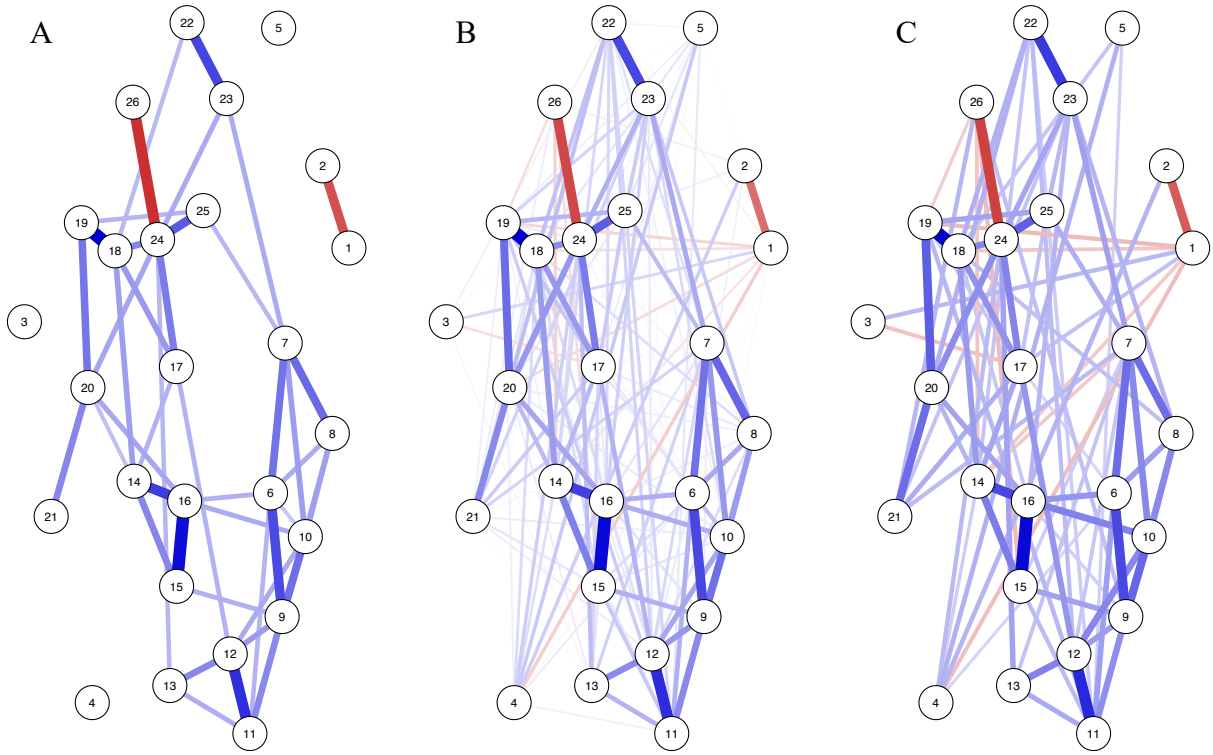


S4: Correlations between three estimations of Network 1

	1.	2.	3.
1. A	-		
2. B	0.93	-	
3. C	0.91	0.95	-

Note. $N = 1{,}484$.

S5: Three approaches to Network 2 estimation: regularized network model with thresholding (panel A), regularized network model without thresholding (panel B), and network model estimated with *ggmModSelect* (panel C).



S6: Correlations between three estimations of Network 2

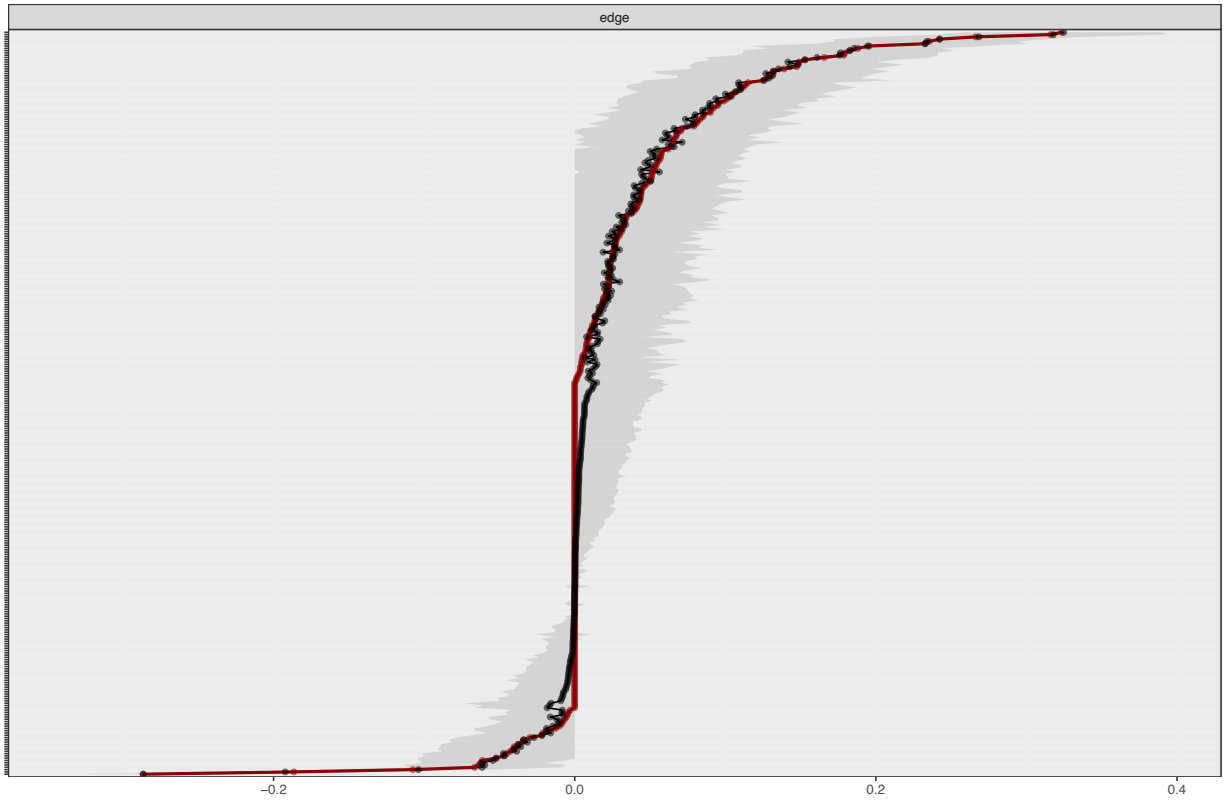
	1.	2.	3.
1. A	-		
2. B	0.93	-	
3. C	0.90	0.95	-

Note. N = 1,484.

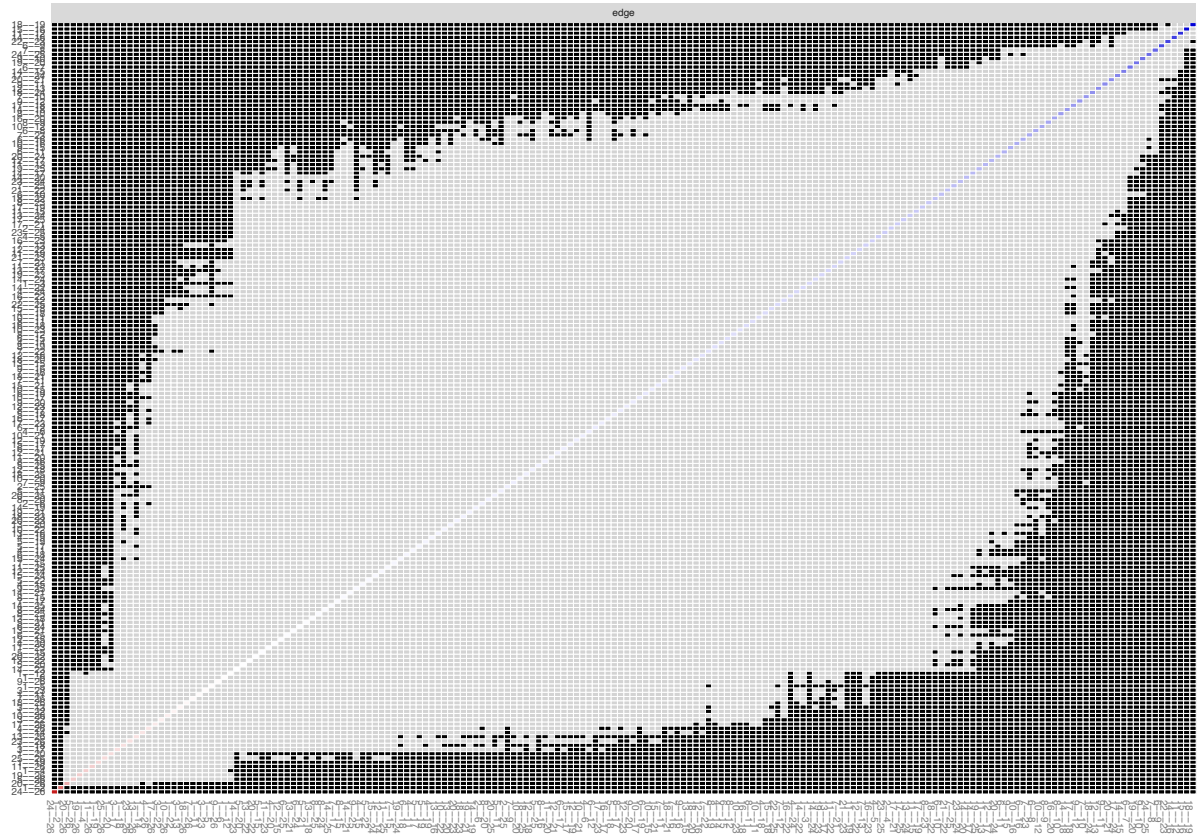
Network accuracy

Bootstrapping routines were implemented to estimate edge weight accuracy for each network model (i.e., how precisely parameters were estimated). Therefore, for each network, we calculated 95% confidence intervals around the edge weights based on 2500 bootstrap samples to quantify precision of all edge-estimates using the R-package *bootnet* (Epskamp et al., 2018). Based on these bootstrapped samples, we conducted edge-weight difference tests as indicators of edge weight accuracy, testing for significant differences between any two edges of the network.

S7: Bootstrapped confidence intervals (CIs) of estimated edge weights for Network 1: The red line represents sample edge weight values, the black dots the bootstrapped means and the gray area the bootstrapped 95% CIs. Each horizontal line indicates one edge of the network, ordered from the edge with the highest edge weight to the edge with the lowest edge weight, based on the mean of the bootstrap samples. The *y*-axis labels have been removed to avoid confusion.



S8: Bootstrapped difference tests (α = .05) between edge weights that were non-zero in the estimated Network 1: Black boxes indicate edges that significantly differ from one another. Gray boxes represent edges that do not significantly differ from one another.



Network models with lifetime PTSD symptoms (Networks 3 and 4)

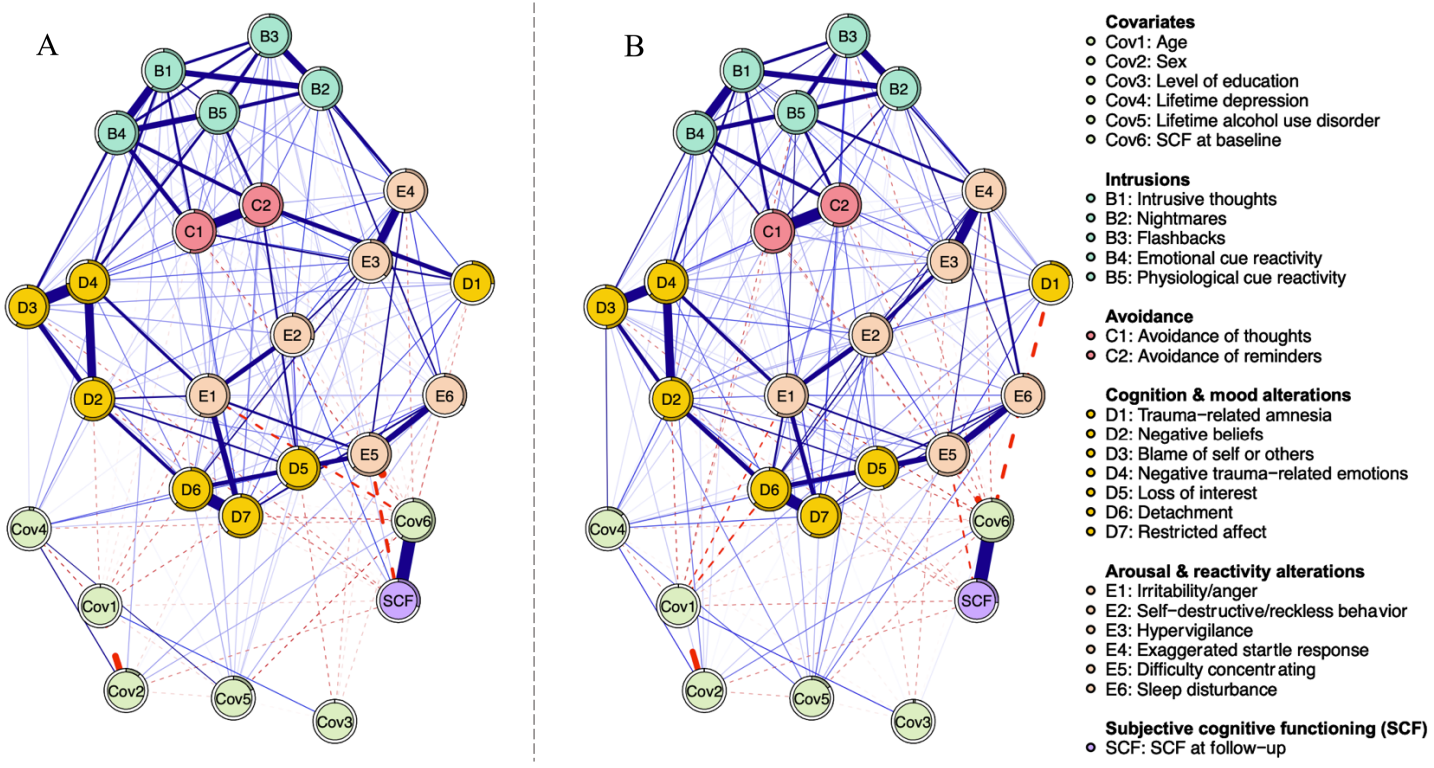
Figure 2 within the paper shows the estimated networks of lifetime PTSD symptoms and SCF at baseline (Network 3; panel A) and SCF at follow-up (Network 4; panel B). Results were essentially the same as for Network 1 and 2. In both networks, strong edges appeared between SCF and the three PTSD symptoms 'difficulty concentrating' (E5), 'trouble remembering important parts of the trauma (D1), and 'trouble experiencing positive feelings' (D7). Strong edges in both cross-sectional Network models 1 and 3 consistently emerged between SCF and PTSD symptoms 'difficulty concentrating' (E5), 'irritable behavior, angry outbursts, or acting aggressively' (E1), 'trouble remembering important parts of the trauma' (D1), 'avoiding memories, thoughts, or feelings related to the trauma' (C1), 'trouble experiencing positive feelings' (D7), 'feeling jumpy or easily startled' (E4), and 'loss of interest in activities' (D5). Additional strong edges in Network 3 not present in any other network model emerged between SCF and symptoms of intrusion, namely 'having strong physical reactions when something reminded you of the trauma' (B5), 'suddenly feeling or acting as if the stressful experience were actually happening again' (B3), 'feeling very upset when something reminded you of the trauma' (B4), as well as between sex and SCF. Strong edges present in both longitudinal Network models 2 and 4 were between SCF and 'difficulty concentrating' (E5), 'trouble experiencing positive feelings' (D7), 'negative beliefs about yourself, other people or the world' (D2), and 'blaming yourself or someone else' (D3). Additionally, a strong edge in Network 4 not present in Network 2 emerged between 'trouble remembering important parts of the trauma' (D1) and SCF.

Re-estimated longitudinal network models (Networks 2_{adj} and 4_{adj})

There was a positive association between SCF at baseline and SCF three years later ($r = 0.53$, $p < .001$). We re-estimated the longitudinal networks with past-month (Network 2_{adj}) and lifetime (Network 4_{adj}) PTSD symptoms at baseline with SCF at follow-up, with additional adjustment for SCF at baseline. Although the magnitude of edge weights generally was attenuated in the re-estimated network models, networks remained largely unaffected by the additional adjustment. In both re-estimated networks, strong edges between the three PTSD symptoms 'difficulty concentrating' (E5), 'blaming yourself or someone else' (D3), and 'negative beliefs about yourself, other people, or the world' (D2) and SCF at follow-up emerged. In the re-estimated Network 2_{adj}, two positive strong edges occurred between SCF at follow-up and 'taking too many risks or doing things that could cause you harm' (E2) and 'feeling very upset when something reminded you of the trauma' (B4). In the re-estimated Network 4_{adj}, a strong edge emerged between SCF and 'trouble experiencing positive feelings' (D7).

In both network models, the symptom domain of cognitions and mood alterations was more strongly related to SCF at follow-up compared to the other domains, except for the domain of arousal alterations.

S9: Figure of $N2_{adj}$ and $N4_{adj}$: Networks displaying the relationship between baseline past-month posttraumatic stress disorder (PTSD) symptoms and subjective cognitive functioning (SCF) at baseline (Network 2_{adj}; panel A) and SCF at follow-up (Network 4_{adj}; panel B), after controlling for covariates including baseline SCF. Blue lines indicate positive associations, dashed red lines negative associations, and thickness and brightness of an edge represent the association strength. Rings around nodes convey predictability, with shadowed parts depicting variance explained by connected nodes. For comparison, the maximum edge weight was set to the strongest edge across all estimated networks (0.36). For color, see online version.



Average connectivity

S10: Bootstrapped differences of average connectivity with SCF across PTSD symptom domains: Because the associations between PTSD symptoms and SCF are negative, positive values denote that average connectivity of SCF with the former symptom domain is smaller than with the latter. Negative values signify that average connectivity of SCF with the latter symptom domain is smaller than with the former. For example, average edge weight between the PTSD symptom domain of 'negative cognitions and mood' and SCF is bigger than between the symptom domain of 'intrusion' and SCF, albeit non-significantly in Network 1. Symptom domains written in bold were found to have significantly greater average connectivity with SCF in some network models, compared to the other symptom domain in the respective row.

	Network 1	Network 2	Network 2_{adj}	Network 3	Network 4	Network 4_{adj}
			Mean [95% CI]			
Intrusion vs. **Cognitions/Mood**	0.012 [−0.004, 0.028]	0.030 [0.007, 0.060]*	0.026 [0.005, 0.056]*	0.005 [−0.014, 0.024]	0.025 [0.003, 0.048]*	0.019 [0.002, 0.043]*
Intrusion vs. **Arousal/Reactivity**	0.072 0.052, 0.091]*	0.039 [0.011, 0.068]*	0.020 [−0.009, 0.049]	0.035 [0.013, 0.057]*	0.027 [0.004, 0.049]*	0.013 [−0.008, 0.034]
Intrusion vs. Avoidance	0.019 [−0.008, 0.048]	0.004 [−0.024, 0.027]	0.005 [−0.026, 0.027]	−0.002 [−0.033, 0.029]	−0.007 [−0.034, 0.010]	−0.006 [−0.037, 0.012]
Cognitions/Mood vs. **Arousal/Reactivity**	0.060 [0.038, 0.082]*	0.009 [−0.018, 0.039]	−0.006 [−0.036, 0.021]	0.030 [0.010, 0.051]*	0.002 [−0.026, 0.030]	−0.007 [−0.032, 0.018]
Cognitions/Mood vs. Avoidance	0.007 [−0.023, 0.036]	−0.027 [−0.059, −0.002]*	−0.022 [−0.057, −0.003]*	−0.008 [−0.035, 0.021]	−0.033 [−0.062, −0.013]*	−0.025 [−0.063, −0.005]*
Arousal/Reactivity vs. Avoidance	−0.053 [−0.083, −0.021]*	−0.036 [−0.068, −0.011]*	−0.015 [−0.049, 0.012]	−0.038 [−0.065, −0.008]*	−0.035 [−0.060, −0.014]*	−0.019 [−0.051, 0.003]

Note. PTSD = Posttraumatic stress disorder; SCF = Subjective cognitive functioning; vs. = versus; CI = Confidence interval.

*Statistically significant differences in average connectivity between PTSD symptom domain and SCF

Complete case analyses

Results replicated following the complete case analyses. The same strong edges emerged. Predictability was similarly high to the main analyses, varying from 50.2% (Network 3) to 62.5% (Network 1) in the cross-sectional network models, and from 18.7% (Network 4) to 32.0% (Network 2_{adj}) in the longitudinal network models. The two symptom domains of 'alterations in arousal and reactivity' as well as 'negative cognitions and mood' were found to have the greatest average connectivity with SCF. When adjusting for SCF at baseline, average connectivity was greatest within the domain of 'negative cognitions and mood'. Results did not meaningfully change with regards to similarity between corresponding network models and temporal stability between the relations of PTSD symptoms with SCF at baseline and three years later

5 Adjacency matrices of network models

Based on imputed data analyses

Network model	**N1**	**N2**	**$N2_{adj}$**	**N3**	**N4**	**$N4_{adj}$**
	SCF at baseline	SCF at follow-up	SCF at follow-up	SCF at baseline	SCF at follow-up	SCF at follow-up
1 – Age	0.000000000	0.000000000	-0.01524031	-0.024581544	-0.0261547900	-0.037704197
2 – Sex	0.000000000	-0.021781867	-0.03880903	0.026936763	-0.0171576917	-0.037135512
3 – Education	0.000000000	0.000000000	0.00000000	0.006148603	0.0000000000	0.000000000
4 – Lifetime depression	-0.034073249	0.000000000	0.00000000	-0.021366199	0.0000000000	0.000000000
5 – Alcohol use	-0.066587390	-0.002169374	0.00000000	-0.042837412	0.0000000000	0.000000000
6 – B1	0.000000000	0.000000000	0.00000000	0.000000000	0.0000000000	0.000000000
7 – B2	-0.008633081	0.000000000	0.00000000	-0.004925691	-0.0008996873	0.000000000
8 – B3	0.000000000	0.000000000	0.01899580	-0.044816163	0.0000000000	0.000000000
9 – B4	-0.004956245	0.000000000	0.02648870	-0.037317908	0.0000000000	0.000000000
10 – B5	-0.021150412	0.000000000	0.00000000	-0.048502584	0.0000000000	0.000000000
11 – C1	-0.061386451	0.000000000	0.00000000	-0.053405320	0.0000000000	0.000000000
12 – C2	0.000000000	0.000000000	0.00000000	0.000000000	0.0000000000	0.000000000
13 – D1	-0.037666223	0.000000000	0.00000000	-0.140395669	-0.0481405197	0.000000000
14 – D2	0.000000000	-0.057125059	-0.05026080	0.000000000	-0.0374036782	-0.025765633
15 – D3	0.000000000	-0.043303871	-0.04231443	0.000000000	-0.0509237094	-0.037821203
16 – D4	0.000000000	-0.008194805	-0.00207062	0.000000000	-0.0261130143	-0.007526939
17 – D5	-0.029755156	0.000000000	0.00000000	-0.054252383	0.0000000000	0.000000000
18 – D6	-0.010163592	0.000000000	0.00000000	0.000000000	0.0000000000	0.000000000
19 – D7	-0.063787192	-0.040138177	-0.00804591	-0.035415668	-0.0640856344	-0.036000947
20 – E1	-0.107507885	0.000000000	0.00000000	-0.073730275	-0.0112315746	0.000000000
21 – E2	0.000000000	0.022411566	0.05806260	0.000000000	0.0000000000	0.000000000
22 – E3	0.000000000	0.000000000	0.00000000	0.000000000	0.0000000000	0.000000000
23 – E4	-0.040250436	0.000000000	0.00000000	-0.052049638	0.0000000000	0.000000000
24 – E5	-0.286555399	-0.234284710	-0.12830229	-0.245031277	-0.1869278181	-0.084898460
25 – E6	-0.047314945	0.000000000	0.00000000	0.000000000	0.0000000000	0.000000000
26 – SCF at baseline	0.000000000	-	0.33760876	0.000000000	-	0.355984903
27 – SCF at follow-up	-	0.000000000	0.00000000	-	0.0000000000	0.000000000

Network 1 – Edges between past-month PTSD symptoms SCF at baseline

	SCF at baseline
1 – Age	0.000000000
2 – Sex	0.000000000
3 – Education	0.000000000
4 – Lifetime depression	-0.034073249
5 – Alcohol use	-0.066587390
6 – B1	0.000000000
7 – B2	-0.008633081
8 – B3	0.000000000
9 – B4	-0.004956245
10 – B5	-0.021150412
11 – C1	-0.061386451
12 – C2	0.000000000
13 – D1	-0.037666223
14 – D2	0.000000000
15 – D3	0.000000000
16 – D4	0.000000000
17 – D5	-0.029755156
18 – D6	-0.010163592
19 – D7	-0.063787192
20 – E1	-0.107507885
21 – E2	0.000000000
22 – E3	0.000000000
23 – E4	-0.040250436
24 – E5	-0.286555399
25 – E6	-0.047314945
26 – SCF at baseline	0.000000000

```
=== Estimated network ===
Number of nodes: 26
Number of non-zero edges: 182 / 325
Mean weight: 0.02455826
Network stored in x$graph
```

```
> N1b$graph
             1           2           3           4           5           6           7
1   0.000000000 -0.18645228  0.051499215 -0.062434991 -0.005424667 -0.004178144  0.000000000
2  -0.186452281  0.00000000  0.000000000  0.065195379  0.000000000  0.021084765  0.000000000
3   0.051499215  0.00000000  0.000000000  0.000000000  0.000000000  0.000000000  0.000000000
4  -0.062434991  0.06519538  0.000000000  0.000000000  0.064413421  0.025614472  0.000000000
5  -0.005424667  0.00000000  0.000000000  0.064413421  0.000000000  0.000000000  0.000000000
6  -0.004178144  0.02108476  0.000000000  0.025614472  0.000000000  0.000000000  0.178716226
7   0.000000000  0.00000000  0.000000000  0.000000000  0.000000000  0.178716226  0.000000000
8   0.000000000  0.00000000  0.000000000  0.000000000  0.000000000  0.110180705  0.195547575
9   0.000000000  0.00000000  0.000000000  0.000000000  0.000000000  0.232467782  0.022519239
10  0.000000000  0.00000000  0.000000000  0.000000000  0.000000000  0.080547289  0.131902906
11 -0.008005529  0.00000000  0.000000000  0.013763106  0.022478303  0.099144527  0.032351795
12 -0.002982455  0.00000000  0.000000000  0.000000000  0.000000000  0.026035890  0.050476949
13  0.000000000  0.00000000 -0.012570084  0.000000000  0.000000000  0.000000000  0.057728811
14 -0.034632981  0.00000000  0.000000000  0.042218822  0.000000000  0.000000000  0.000000000
15  0.000000000  0.00000000  0.000000000  0.009717959  0.003597687  0.043114154  0.013257570
16  0.000000000  0.00000000  0.000000000  0.000000000  0.000000000  0.104703647  0.033599403
17  0.000000000  0.00000000 -0.042807589  0.000000000  0.015732700  0.023984744  0.007888430
18 -0.040258185  0.00000000  0.000000000  0.045191033  0.027113220  0.013593620  0.000000000
19 -0.052151558  0.00000000  0.000000000  0.016927217  0.015753348  0.031245654  0.000000000
20 -0.045171213  0.00000000  0.000000000  0.003928675  0.001178495  0.000000000  0.000000000
21  0.000000000  0.00000000  0.000000000  0.000000000  0.005501288  0.000000000  0.056060914
22 -0.016905033  0.00000000 -0.022046583  0.000000000  0.010446659  0.000000000  0.040938954
23  0.000000000  0.00000000 -0.006677775  0.000000000  0.000000000  0.000000000  0.107246825
24  0.000000000  0.00000000  0.000000000  0.051040368  0.000000000  0.005249629  0.000000000
25  0.000000000  0.02248943  0.000000000  0.000000000  0.023173140  0.004678066  0.083145709
26  0.000000000  0.00000000  0.000000000 -0.034073249 -0.066587390  0.000000000 -0.008633081
```

```
             8           9          10          11          12          13          14          15
1  0.000000000  0.000000000  0.00000000 -0.008005529 -0.002982455  0.000000000 -0.034632981 0.000000000
2  0.000000000  0.000000000  0.00000000  0.000000000  0.000000000  0.000000000  0.000000000 0.000000000
3  0.000000000  0.000000000  0.00000000  0.000000000  0.000000000 -0.012570084  0.000000000 0.000000000
4  0.000000000  0.000000000  0.00000000  0.013763106  0.000000000  0.000000000  0.042218822 0.009717959
5  0.000000000  0.000000000  0.00000000  0.022478303  0.000000000  0.000000000  0.000000000 0.003597687
6  0.110180705  0.232467782  0.08054729  0.099144527  0.026035890  0.000000000  0.000000000 0.043114154
7  0.195547575  0.022519239  0.13190291  0.032351795  0.050476949  0.057728811  0.000000000 0.013257570
8  0.000000000  0.113362919  0.12502391  0.044133924  0.043499064  0.000000000  0.000000000 0.008306737
9  0.113362919  0.000000000  0.18263848  0.148600791  0.131871144  0.000000000  0.000000000 0.101356654
10 0.125023906  0.182638478  0.00000000  0.044214001  0.111869491  0.000000000  0.000000000 0.031537393
11 0.044133924  0.148600791  0.04421400  0.000000000  0.266345618  0.092345734  0.000000000 0.068417884
12 0.043499064  0.131871144  0.11186949  0.266345618  0.000000000  0.147426916  0.011676692 0.004677495
13 0.000000000  0.000000000  0.00000000  0.092345734  0.147426916  0.000000000  0.000000000 0.034835900
14 0.000000000  0.000000000  0.00000000  0.000000000  0.011676692  0.000000000  0.000000000 0.165703135
15 0.008306737  0.101356654  0.03153739  0.068417884  0.004677495  0.034835900  0.165703135 0.000000000
16 0.023323473  0.033948318  0.10420364  0.000000000  0.039668421  0.017476142  0.242259611 0.316069734
17 0.027650171  0.000000000  0.02985506  0.000000000  0.094908832  0.054249611  0.090145480 0.025043944
18 0.000000000  0.000000000  0.00000000  0.000000000  0.023117972  0.006950542  0.127474229 0.046643900
19 0.041506271  0.000000000  0.00000000  0.057182425  0.025205211  0.000000000  0.021002928 0.000000000
20 0.021399018  0.029526861  0.02283357  0.023340907  0.000000000  0.018815517  0.085624257 0.000000000
21 0.000000000  0.000000000  0.02532562  0.000000000  0.023856021  0.004867513  0.009017791 0.032345933
22 0.000000000  0.000000000  0.01821442  0.054423202  0.057471351  0.002122332  0.051333508 0.000000000
23 0.071191980  0.000000000  0.04379739  0.003777410  0.027716357  0.000000000  0.001074647 0.000000000
24 0.007615121  0.000000000  0.00000000  0.000000000  0.000000000  0.067439513  0.053024384 0.010705015
25 0.007443129  0.009683267  0.00000000  0.011700276  0.000000000  0.000000000  0.007871274 0.000000000
26 0.000000000 -0.004956245 -0.02115041 -0.061386451  0.000000000 -0.037666223  0.000000000 0.000000000
```

	16	17	18	19	20	21	22	23
1	0.00000000	0.00000000	-0.040258185	-0.05215156	-0.045171213	0.000000000	-0.016905033	0.000000000
2	0.00000000	0.00000000	0.000000000	0.00000000	0.000000000	0.000000000	0.000000000	0.000000000
3	0.00000000	-0.04280759	0.000000000	0.00000000	0.000000000	0.000000000	-0.022046583	-0.006677775
4	0.00000000	0.00000000	0.045191033	0.01692722	0.003928675	0.000000000	0.000000000	0.000000000
5	0.00000000	0.01573270	0.027113220	0.01575335	0.001178495	0.005501288	0.010446659	0.000000000
6	0.10470365	0.02398474	0.013593620	0.03124565	0.000000000	0.000000000	0.000000000	0.000000000
7	0.03359940	0.00788843	0.000000000	0.00000000	0.000000000	0.056060914	0.040938954	0.107246825
8	0.02332347	0.02765017	0.000000000	0.04150627	0.021399018	0.000000000	0.000000000	0.071191980
9	0.03394832	0.00000000	0.000000000	0.00000000	0.029526861	0.000000000	0.000000000	0.000000000
10	0.10420364	0.02985506	0.000000000	0.00000000	0.022833569	0.025325622	0.018214424	0.043797394
11	0.00000000	0.00000000	0.000000000	0.05718243	0.023340907	0.000000000	0.054423202	0.003777410
12	0.03966842	0.09490883	0.023117972	0.02520521	0.000000000	0.023856021	0.057471351	0.027716357
13	0.01747614	0.05424961	0.006950542	0.00000000	0.018815517	0.004867513	0.002122332	0.000000000
14	0.24225961	0.09014548	0.127474229	0.02100293	0.085624257	0.009017791	0.051333508	0.001074647
15	0.31606973	0.02504394	0.046643900	0.00000000	0.000000000	0.032345933	0.000000000	0.000000000
16	0.00000000	0.02698294	0.043878727	0.00000000	0.115075377	0.000000000	0.050813085	0.062061488
17	0.02698294	0.00000000	0.129846323	0.07057425	0.000000000	0.065259090	0.000000000	0.026358909
18	0.04387873	0.12984632	0.000000000	0.32341503	0.037514893	0.033202276	0.079086789	0.019135682
19	0.00000000	0.07057425	0.323415026	0.00000000	0.179366398	0.020111739	0.000000000	0.053144187
20	0.11507538	0.00000000	0.037514893	0.17936640	0.000000000	0.148930509	0.002832804	0.018883774
21	0.00000000	0.06525909	0.033202276	0.02011174	0.148930509	0.000000000	0.081511007	0.056841496
22	0.05081309	0.00000000	0.079086789	0.00000000	0.002832804	0.081511007	0.000000000	0.235334486
23	0.06206149	0.02635891	0.019135682	0.05314419	0.018883774	0.056841496	0.235334486	0.000000000
24	0.00000000	0.15311109	0.139097212	0.01333852	0.095774072	0.000000000	0.000000000	0.085081444
25	0.00000000	0.06706277	0.023064499	0.09020029	0.022406866	0.000000000	0.047873568	0.065010844
26	0.00000000	-0.02975516	-0.010163592	-0.06378719	-0.107507885	0.000000000	0.000000000	-0.040250436

	24	25	26
1	0.000000000	0.000000000	0.000000000
2	0.000000000	0.022489433	0.000000000
3	0.000000000	0.000000000	0.000000000
4	0.051040368	0.000000000	-0.034073249
5	0.000000000	0.023173140	-0.066587390
6	0.005249629	0.004678066	0.000000000
7	0.000000000	0.083145709	-0.008633081
8	0.007615121	0.007443129	0.000000000
9	0.000000000	0.009683267	-0.004956245
10	0.000000000	0.000000000	-0.021150412
11	0.000000000	0.011700276	-0.061386451
12	0.000000000	0.000000000	0.000000000
13	0.067439513	0.000000000	-0.037666223
14	0.053024384	0.007871274	0.000000000
15	0.010705015	0.000000000	0.000000000
16	0.000000000	0.000000000	0.000000000
17	0.153111091	0.067062767	-0.029755156
18	0.139097212	0.023064499	-0.010163592
19	0.013338515	0.090200291	-0.063787192
20	0.095774072	0.022406866	-0.107507885
21	0.000000000	0.000000000	0.000000000
22	0.000000000	0.047873568	0.000000000
23	0.085081444	0.065010844	-0.040250436
24	0.000000000	0.188065920	-0.286555399
25	0.188065920	0.000000000	-0.047314945
26	-0.286555399	-0.047314945	0.000000000

Network 2 – Edges between past-month PTSD symptoms at baseline and SCF at follow-up

	SCF at follow-up
1 – Age	0.000000000
2 – Sex	-0.021781867
3 – Education	0.000000000
4 – Lifetime depression	0.000000000
5 – Alcohol use	-0.002169374
6 – B1	0.000000000
7 – B2	0.000000000
8 – B3	0.000000000
9 – B4	0.000000000
10 – B5	0.000000000
11 – C1	0.000000000
12 – C2	0.000000000
13 – D1	0.000000000
14 – D2	-0.057125059
15 – D3	-0.043303871
16 – D4	-0.008194805
17 – D5	0.000000000
18 – D6	0.000000000
19 – D7	-0.040138177
20 – E1	0.000000000
21 – E2	0.022411566
22 – E3	0.000000000
23 – E4	0.000000000
24 – E5	-0.234284710
25 – E6	0.000000000
26 – SCF at follow-up	0.000000000

```
=== Estimated network ===
Number of nodes: 26
Number of non-zero edges: 178 / 325
Mean weight: 0.02670154
Network stored in x$graph
```

```
> N2b$graph
            1           2           3           4           5           6           7           8
1   0.000000000 -0.18566732  0.05150739 -0.062674052 -0.005494505 -0.004444999 0.000000000 0.000000000
2  -0.185667318  0.00000000  0.00000000  0.064118352  0.000000000  0.018771422 0.000000000 0.000000000
3   0.051507390  0.00000000  0.00000000  0.000000000  0.000000000  0.000000000 0.000000000 0.000000000
4  -0.062674052  0.06411835  0.00000000  0.000000000  0.068364519  0.026015514 0.000000000 0.000000000
5  -0.005494505  0.00000000  0.00000000  0.068364519  0.000000000  0.000000000 0.000000000 0.000000000
6  -0.004444999  0.01877142  0.00000000  0.026015514  0.000000000  0.000000000 0.178582917 0.109809076
7   0.000000000  0.00000000  0.00000000  0.000000000  0.000000000  0.178582917 0.000000000 0.195608667
8   0.000000000  0.00000000  0.00000000  0.000000000  0.000000000  0.109809076 0.195608667 0.000000000
9   0.000000000  0.00000000  0.00000000  0.000000000  0.000000000  0.232466371 0.022709211 0.113447996
10  0.000000000  0.00000000  0.00000000  0.000000000  0.000000000  0.080599869 0.132419015 0.125173417
11 -0.008280537  0.00000000  0.00000000  0.018097696  0.029056852  0.099528473 0.033291827 0.044444093
12 -0.002861873  0.00000000  0.00000000  0.000000000  0.000000000  0.025547960 0.050392887 0.043180908
13  0.000000000  0.00000000 -0.01258174  0.000000000  0.000000000  0.000000000 0.058625869 0.000000000
14 -0.034217361  0.00000000  0.00000000  0.042328958  0.000000000  0.000000000 0.000000000 0.000000000
15  0.000000000  0.00000000  0.00000000  0.009556589  0.004855027  0.042470808 0.013172343 0.007765894
16  0.000000000  0.00000000  0.00000000  0.000000000  0.000000000  0.104142657 0.034019862 0.023113113
17  0.000000000  0.00000000 -0.04280532  0.000000000  0.022388373  0.023362234 0.009190369 0.026902564
18 -0.040106130  0.00000000  0.00000000  0.045574777  0.031427112  0.013496361 0.000000000 0.000000000
19 -0.051981565  0.00000000  0.00000000  0.019132825  0.021053641  0.030570653 0.000000000 0.041573809
20 -0.045255742  0.00000000  0.00000000  0.007481584  0.011818599  0.000000000 0.000000000 0.020649945
21  0.000000000  0.00000000  0.00000000  0.000000000  0.006259794  0.000000000 0.056456460 0.000000000
22 -0.016888254  0.00000000 -0.02204253  0.000000000  0.012167434  0.000000000 0.040932750 0.000000000
23  0.000000000  0.00000000 -0.00669008  0.000000000  0.000000000  0.000000000 0.107958472 0.070383514
24  0.000000000  0.00000000  0.00000000  0.063893231  0.000000000  0.011294595 0.000000000 0.012568550
25  0.000000000  0.01968687  0.00000000  0.000000000  0.031441602  0.002970633 0.084758168 0.006290059
26  0.000000000 -0.02178187  0.00000000  0.000000000 -0.002169374  0.000000000 0.000000000 0.000000000

            9          10          11          12          13          14          15
1  0.00000000 0.000000000 -0.008280537 -0.002861873  0.000000000 -0.0342173608  0.000000000
2  0.00000000 0.000000000  0.000000000  0.000000000  0.000000000  0.0000000000  0.000000000
3  0.00000000 0.000000000  0.000000000  0.000000000 -0.012581745  0.0000000000  0.000000000
4  0.00000000 0.000000000  0.018097696  0.000000000  0.000000000  0.0423289584  0.009556589
5  0.00000000 0.000000000  0.029056852  0.000000000  0.000000000  0.0000000000  0.004855027
6  0.23246637 0.080599869  0.099528473  0.025547960  0.000000000  0.0000000000  0.042470808
7  0.02270921 0.132419015  0.033291827  0.050392887  0.058625869  0.0000000000  0.013172343
8  0.11344800 0.125173417  0.044444093  0.043180908  0.000000000  0.0000000000  0.007765894
9  0.00000000 0.182874613  0.149422173  0.132008095  0.000000000  0.0000000000  0.101302601
10 0.18287461 0.000000000  0.046474569  0.112020619  0.000000000  0.0000000000  0.031749601
11 0.14942217 0.046474569  0.000000000  0.267436992  0.097313966  0.0000000000  0.069473624
12 0.13200809 0.112020619  0.267436992  0.000000000  0.147411528  0.0120551798  0.004021992
13 0.00000000 0.000000000  0.097313966  0.147411528  0.000000000  0.0000000000  0.034352162
14 0.00000000 0.000000000  0.000000000  0.012055180  0.000000000  0.0000000000  0.162479250
15 0.10130260 0.031749601  0.069473624  0.004021992  0.034352162  0.1624792505  0.000000000
16 0.03435056 0.104611293  0.000000000  0.039423817  0.017446066  0.2414044479  0.314993216
17 0.00000000 0.033184090  0.000000000  0.096133083  0.055375844  0.0901257037  0.024504020
18 0.00000000 0.000000000  0.000000000  0.024370379  0.007932249  0.1273711654  0.045511298
19 0.00000000 0.000000000  0.064258675  0.024885168  0.000000000  0.0179751879  0.000000000
20 0.03033981 0.027026360  0.033074774  0.000000000  0.022726000  0.0859009528  0.000000000
21 0.00000000 0.025515289  0.000000000  0.023714860  0.005491323  0.0107475463  0.033047345
22 0.00000000 0.018470300  0.054945433  0.057058665  0.002360799  0.0513110479  0.000000000
23 0.00000000 0.045658140  0.008766976  0.027529937  0.000000000  0.0009594989  0.000000000
24 0.00000000 0.000000000  0.000000000  0.000000000  0.083812747  0.0407301017  0.003291944
25 0.01065960 0.001007062  0.019362911  0.000000000  0.000000000  0.0074561761  0.000000000
26 0.00000000 0.000000000  0.000000000  0.000000000  0.000000000 -0.0571250592 -0.043303871
```

	16	17	18	19	20	21	22
1	0.000000000	0.0000000000	-0.040106130	-0.05198156	-0.0452557422	0.000000000	-0.016888254
2	0.000000000	0.0000000000	0.000000000	0.00000000	0.0000000000	0.000000000	0.000000000
3	0.000000000	-0.0428053197	0.000000000	0.00000000	0.0000000000	0.000000000	-0.022042530
4	0.000000000	0.0000000000	0.045574777	0.01913282	0.0074815842	0.000000000	0.000000000
5	0.000000000	0.0223883733	0.031427112	0.02105364	0.0118185993	0.006259794	0.012167434
6	0.104142657	0.0233622335	0.013496361	0.03057065	0.0000000000	0.000000000	0.000000000
7	0.034019862	0.0091903688	0.000000000	0.00000000	0.0000000000	0.056456460	0.040932750
8	0.023113113	0.0269025641	0.000000000	0.04157381	0.0206499451	0.000000000	0.000000000
9	0.034350560	0.0000000000	0.000000000	0.00000000	0.0303398065	0.000000000	0.000000000
10	0.104611293	0.0331840899	0.000000000	0.00000000	0.0270263595	0.025515289	0.018470300
11	0.000000000	0.0000000000	0.000000000	0.06425867	0.0330747739	0.000000000	0.054945433
12	0.039423817	0.0961330834	0.024370379	0.02488517	0.0000000000	0.023714860	0.057058665
13	0.017446066	0.0553758439	0.007932249	0.00000000	0.0227260001	0.005491323	0.002360799
14	0.241404448	0.0901257037	0.127371165	0.01797519	0.0859009528	0.010747546	0.051311048
15	0.314993216	0.0245040202	0.045511298	0.00000000	0.0000000000	0.033047345	0.000000000
16	0.000000000	0.0267434898	0.043828254	0.00000000	0.1148226716	0.000000000	0.050595287
17	0.026743490	0.0000000000	0.129750102	0.07280071	0.0007313013	0.066491115	0.000000000
18	0.043828254	0.1297501022	0.000000000	0.32394809	0.0386161885	0.034175005	0.079209102
19	0.000000000	0.0728007147	0.323948093	0.00000000	0.1869112770	0.021290469	0.000000000
20	0.114822672	0.0007313013	0.038616189	0.18691128	0.0000000000	0.150610471	0.002669704
21	0.000000000	0.0664911153	0.034175005	0.02129047	0.1506104714	0.000000000	0.081488231
22	0.050595287	0.0000000000	0.079209102	0.00000000	0.0026697042	0.081488231	0.000000000
23	0.061453897	0.0269895626	0.019435044	0.05555784	0.0228710077	0.057462289	0.235360964
24	0.000000000	0.1663853948	0.145217740	0.02486835	0.1317529208	0.000000000	0.000000000
25	0.000000000	0.0679061165	0.023169902	0.09280433	0.0271458644	0.000000000	0.047788887
26	-0.008194805	0.0000000000	0.000000000	-0.04013818	0.0000000000	0.022411566	0.000000000

	23	24	25	26
1	0.0000000000	0.000000000	0.000000000	0.000000000
2	0.0000000000	0.000000000	0.019686872	-0.021781867
3	-0.0066900796	0.000000000	0.000000000	0.000000000
4	0.0000000000	0.063893231	0.000000000	0.000000000
5	0.0000000000	0.000000000	0.031441602	-0.002169374
6	0.0000000000	0.011294595	0.002970633	0.000000000
7	0.1079584721	0.000000000	0.084758168	0.000000000
8	0.0703835145	0.012568550	0.006290059	0.000000000
9	0.0000000000	0.000000000	0.010659599	0.000000000
10	0.0456581401	0.000000000	0.001007062	0.000000000
11	0.0087669755	0.000000000	0.019362911	0.000000000
12	0.0275299370	0.000000000	0.000000000	0.000000000
13	0.0000000000	0.083812747	0.000000000	0.000000000
14	0.0009594989	0.040730102	0.007456176	-0.057125059
15	0.0000000000	0.003291944	0.000000000	-0.043303871
16	0.0614538968	0.000000000	0.000000000	-0.008194805
17	0.0269895626	0.166385395	0.067906117	0.000000000
18	0.0194350440	0.145217740	0.023169902	0.000000000
19	0.0555578403	0.024868353	0.092804326	-0.040138177
20	0.0228710077	0.131752921	0.027145864	0.000000000
21	0.0574622887	0.000000000	0.000000000	0.022411566
22	0.2353609635	0.000000000	0.047788887	0.000000000
23	0.0000000000	0.100882166	0.066368685	0.000000000
24	0.1008821665	0.000000000	0.206387279	-0.234284710
25	0.0663686849	0.206387279	0.000000000	0.000000000
26	0.0000000000	-0.234284710	0.000000000	0.000000000

Network 2_{adj} – Edges between past-month PTSD symptoms at baseline and SCF at follow-up, additionally adjusted for SCF at baseline

	SCF at follow-up
1 – Age	-0.01524031
2 – Sex	-0.03880903
3 – Education	0.00000000
4 – Lifetime depression	0.00000000
5 – Alcohol use	0.00000000
6 – B1	0.00000000
7 – B2	0.00000000
8 – B3	0.01899580
9 – B4	0.02648870
10 – B5	0.00000000
11 – C1	0.00000000
12 – C2	0.00000000
13 – D1	0.00000000
14 – D2	-0.05026080
15 – D3	-0.04231443
16 – D4	-0.00207062
17 – D5	0.00000000
18 – D6	0.00000000
19 – D7	-0.00804591
20 – E1	0.00000000
21 – E2	0.05806260
22 – E3	0.00000000
23 – E4	0.00000000
24 – E5	-0.12830229
25 – E6	0.00000000
26 – SCF at baseline	0.33760876
27 – SCF at follow-up	0.00000000

```
=== Estimated network ===
Number of nodes: 27
Number of non-zero edges: 197 / 351
Mean weight: 0.02346115
Network stored in x$graph
```

```
> N2bAdj$graph
             1           2           3           4           5           6           7
1   0.000000000 -0.194800083  0.058386965 -0.065581851 -0.013176771 -0.003637467  0.000000000
2  -0.194800083  0.000000000  0.000000000  0.072819497 -0.012927075  0.027337797  0.000000000
3   0.058386965  0.000000000  0.000000000  0.000000000 -0.002478249  0.000000000  0.000000000
4  -0.065581851  0.072819497  0.000000000  0.000000000  0.070379951  0.026138964  0.000000000
5  -0.013176771 -0.012927075 -0.002478249  0.070379951  0.000000000  0.000000000  0.000000000
6  -0.003637467  0.027337797  0.000000000  0.026138964  0.000000000  0.000000000  0.181035494
7   0.000000000  0.000000000  0.000000000  0.000000000  0.000000000  0.181035494  0.000000000
8   0.000000000  0.000000000  0.000000000  0.000000000  0.000000000  0.110457293  0.198024963
9   0.000000000  0.000000000  0.000000000  0.000000000  0.000000000  0.236045513  0.020564634
10  0.000000000  0.000000000  0.000000000  0.000000000  0.000000000  0.079771497  0.133296822
11 -0.008988690  0.000000000  0.000000000  0.014454354  0.023606532  0.099358872  0.031701989
12 -0.003722758  0.000000000  0.000000000  0.000000000  0.000000000  0.024436918  0.050355112
13  0.000000000  0.000000000 -0.017057247  0.000000000  0.000000000  0.000000000  0.058329374
14 -0.036247631  0.000000000  0.000000000  0.041982024  0.000000000  0.000000000  0.000000000
15  0.000000000  0.000000000  0.000000000  0.009629926  0.002987127  0.041864746  0.012217639
16  0.000000000  0.000000000  0.000000000  0.000000000  0.000000000  0.105307596  0.032838490
17  0.000000000  0.000000000 -0.045250808  0.000000000  0.016349708  0.023731277  0.007055532
18 -0.040719800  0.000000000  0.000000000  0.045432882  0.026757951  0.012845944  0.000000000
19 -0.053418403  0.000000000  0.000000000  0.016795581  0.015535419  0.030412335  0.000000000
20 -0.047976850  0.000000000  0.000000000  0.004415892  0.001128495  0.000000000  0.000000000
21  0.000000000 -0.012960142  0.000000000  0.000000000  0.008812211  0.000000000  0.056400110
22 -0.018936247  0.000000000 -0.025038794  0.000000000  0.012161715  0.000000000  0.040513886
23  0.000000000  0.002192969 -0.008823907  0.000000000  0.000000000  0.000000000  0.108113237
24  0.000000000  0.000000000  0.000000000  0.051329157  0.000000000  0.005895772  0.000000000
25  0.000000000  0.029912883  0.000000000  0.000000000  0.025741259  0.003428844  0.084199881
26  0.000000000  0.026027259  0.000000000 -0.033451206 -0.064476354  0.000000000 -0.007406176
27 -0.015240313 -0.038809032  0.000000000  0.000000000  0.000000000  0.000000000  0.000000000
```

```
             8           9          10          11          12          13          14          15
1  0.000000000  0.00000000  0.00000000 -0.008988690 -0.003722758  0.000000000 -0.03624763  0.000000000
2  0.000000000  0.00000000  0.00000000  0.000000000  0.000000000  0.000000000  0.00000000  0.000000000
3  0.000000000  0.00000000  0.00000000  0.000000000  0.000000000 -0.017057247  0.00000000  0.000000000
4  0.000000000  0.00000000  0.00000000  0.014454354  0.000000000  0.000000000  0.04198202  0.009629926
5  0.000000000  0.00000000  0.00000000  0.023606532  0.000000000  0.000000000  0.00000000  0.002987127
6  0.110457293  0.23604551  0.07977150  0.099358872  0.024436918  0.000000000  0.00000000  0.041864746
7  0.198024963  0.02056463  0.13329682  0.031701989  0.050355112  0.058329374  0.00000000  0.012217639
8  0.000000000  0.11364868  0.12604239  0.044151254  0.042965579  0.000000000  0.00000000  0.008518647
9  0.113648675  0.00000000  0.18502886  0.149931445  0.132848570  0.000000000  0.00000000  0.103639775
10 0.126042394  0.18502886  0.00000000  0.043191763  0.112792752  0.000000000  0.00000000  0.029887939
11 0.044151254  0.14993144  0.04319176  0.000000000  0.270569321  0.092893936  0.00000000  0.066743856
12 0.042965579  0.13284857  0.11279275  0.270569321  0.000000000  0.148982970  0.01031355  0.003546470
13 0.000000000  0.00000000  0.00000000  0.092893936  0.148982970  0.000000000  0.00000000  0.034624135
14 0.000000000  0.00000000  0.00000000  0.000000000  0.010313549  0.000000000  0.00000000  0.162974942
15 0.008518647  0.10363978  0.02988794  0.066743856  0.003546470  0.034624135  0.16297494  0.000000000
16 0.022870467  0.03280107  0.10524746  0.000000000  0.039570119  0.016299856  0.24497575  0.320599177
17 0.027867418  0.00000000  0.02985180  0.000000000  0.095969495  0.054457439  0.09013875  0.023891713
18 0.000000000  0.00000000  0.00000000  0.000000000  0.022859491  0.006460300  0.12893968  0.045176970
19 0.042023867  0.00000000  0.00000000  0.057198428  0.024332239  0.000000000  0.01691043  0.000000000
20 0.021657197  0.02973175  0.02245131  0.022681135  0.000000000  0.018770338  0.08332860  0.000000000
21 0.000000000  0.00000000  0.02494134  0.000000000  0.023197857  0.006816917  0.01227087  0.034281070
22 0.000000000  0.00000000  0.01759996  0.054256788  0.057555569  0.002347608  0.05101943  0.000000000
23 0.071709364  0.00000000  0.04375473  0.002943576  0.027374161  0.000000000  0.00000000  0.000000000
24 0.012614347  0.00000000  0.00000000  0.000000000  0.000000000  0.068266143  0.04066988  0.000000000
25 0.007486066  0.01057774  0.00000000  0.011366749  0.000000000  0.000000000  0.00613184  0.000000000
26 0.000000000 -0.01161475 -0.01811016 -0.056308922  0.000000000 -0.034891092  0.00000000  0.000000000
27 0.018995802  0.02648870  0.00000000  0.000000000  0.000000000  0.000000000 -0.05026080 -0.042314427
```

	16	17	18	19	20	21	22
1	0.00000000	0.000000000	-0.040719800	-0.05341840	-0.047976850	0.000000000	-0.018936247
2	0.00000000	0.000000000	0.000000000	0.00000000	0.000000000	-0.012960142	0.000000000
3	0.00000000	-0.045250808	0.000000000	0.00000000	0.000000000	0.000000000	-0.025038794
4	0.00000000	0.000000000	0.045432882	0.01679558	0.004415892	0.000000000	0.000000000
5	0.00000000	0.016349708	0.026757951	0.01553542	0.001128495	0.008812211	0.012161715
6	0.10530760	0.023731277	0.012845944	0.03041234	0.000000000	0.000000000	0.000000000
7	0.03283849	0.007055532	0.000000000	0.00000000	0.000000000	0.056400110	0.040513886
8	0.02287047	0.027867418	0.000000000	0.04202387	0.021657197	0.000000000	0.000000000
9	0.03280107	0.000000000	0.000000000	0.00000000	0.029731749	0.000000000	0.000000000
10	0.10524746	0.029851803	0.000000000	0.00000000	0.022451313	0.024941342	0.017599963
11	0.00000000	0.000000000	0.000000000	0.05719843	0.022681135	0.000000000	0.054256788
12	0.03957012	0.095969495	0.022859491	0.02433224	0.000000000	0.023197857	0.057555569
13	0.01629986	0.054457439	0.006460300	0.00000000	0.018770338	0.006816917	0.002347608
14	0.24497575	0.090138746	0.128939681	0.01691043	0.083328604	0.012270870	0.051019427
15	0.32059918	0.023891713	0.045176970	0.00000000	0.000000000	0.034281070	0.000000000
16	0.00000000	0.025857834	0.043020437	0.00000000	0.114743650	0.000000000	0.050334553
17	0.02585783	0.000000000	0.130875798	0.07022424	0.000000000	0.067383441	0.000000000
18	0.04302044	0.130875798	0.000000000	0.32921390	0.036143004	0.034471431	0.079074490
19	0.00000000	0.070224239	0.329213901	0.00000000	0.181688750	0.020326238	0.000000000
20	0.11474365	0.000000000	0.036143004	0.18168875	0.000000000	0.152025612	0.001761226
21	0.00000000	0.067383441	0.034471431	0.02032624	0.152025612	0.000000000	0.083060021
22	0.05033455	0.000000000	0.079074490	0.00000000	0.001761226	0.083060021	0.000000000
23	0.06160137	0.025702111	0.018379472	0.05302210	0.018416527	0.058245282	0.238599160
24	0.00000000	0.155221560	0.141842121	0.01050720	0.098195734	0.000000000	0.000000000
25	0.00000000	0.067389409	0.021890860	0.09102003	0.021983507	0.000000000	0.048391423
26	0.00000000	-0.023763512	-0.003070482	-0.05755660	-0.098277478	-0.019678748	0.000000000
27	-0.00207062	0.000000000	0.000000000	-0.00804591	0.000000000	0.058062605	0.000000000

	23	24	25	26	27
1	0.000000000	0.000000000	0.000000000	0.000000000	-0.01524031
2	0.002192969	0.000000000	0.029912883	0.026027259	-0.03880903
3	-0.008823907	0.000000000	0.000000000	0.000000000	0.00000000
4	0.000000000	0.051329157	0.000000000	-0.033451206	0.00000000
5	0.000000000	0.000000000	0.025741259	-0.064476354	0.00000000
6	0.000000000	0.005895772	0.003428844	0.000000000	0.00000000
7	0.108113237	0.000000000	0.084199881	-0.007406176	0.00000000
8	0.071709364	0.012614347	0.007486066	0.000000000	0.01899580
9	0.000000000	0.000000000	0.010577745	-0.011614750	0.02648870
10	0.043754729	0.000000000	0.000000000	-0.018110155	0.00000000
11	0.002943576	0.000000000	0.011366749	-0.056308922	0.00000000
12	0.027374161	0.000000000	0.000000000	0.000000000	0.00000000
13	0.000000000	0.068266143	0.000000000	-0.034891092	0.00000000
14	0.000000000	0.040669884	0.006131840	0.000000000	-0.05026080
15	0.000000000	0.000000000	0.000000000	0.000000000	-0.04231443
16	0.061601372	0.000000000	0.000000000	0.000000000	-0.00207062
17	0.025702111	0.155221560	0.067389409	-0.023763512	0.00000000
18	0.018379472	0.141842121	0.021890860	-0.003070482	0.00000000
19	0.053022105	0.010507198	0.091020032	-0.057556596	-0.00804591
20	0.018416527	0.098195734	0.021983507	-0.098277478	0.00000000
21	0.058245282	0.000000000	0.000000000	-0.019678748	0.05806260
22	0.238599160	0.000000000	0.048391423	0.000000000	0.00000000
23	0.000000000	0.086072410	0.065371534	-0.036766493	0.00000000
24	0.086072410	0.000000000	0.189033001	-0.226927375	-0.12830229
25	0.065371534	0.189033001	0.000000000	-0.044358348	0.00000000
26	-0.036766493	-0.226927375	-0.044358348	0.000000000	0.33760876
27	0.000000000	-0.128302291	0.000000000	0.337608757	0.00000000

Network 3 – Edges between lifetime PTSD symptoms and SCF at baseline

	SCF at baseline
1 – Age	-0.024581544
2 – Sex	0.026936763
3 – Education	0.006148603
4 – Lifetime depression	-0.021366199
5 – Alcohol use	-0.042837412
6 – B1	0.000000000
7 – B2	-0.004925691
8 – B3	-0.044816163
9 – B4	-0.037317908
10 – B5	-0.048502584
11 – C1	-0.053405320
12 – C2	0.000000000
13 – D1	-0.140395669
14 – D2	0.000000000
15 – D3	0.000000000
16 – D4	0.000000000
17 – D5	-0.054252383
18 – D6	0.000000000
19 – D7	-0.035415668
20 – E1	-0.073730275
21 – E2	0.000000000
22 – E3	0.000000000
23 – E4	-0.052049638
24 – E5	-0.245031277
25 – E6	0.000000000
26 – SCF at baseline	0.000000000

```
=== Estimated network ===
Number of nodes: 26
Number of non-zero edges: 201 / 325
Mean weight: 0.02464396
Network stored in x$graph
```

```
> N3b$graph
            1           2           3           4           5           6           7
1   0.00000000 -0.17798222  0.06049630 -0.03205268  0.00000000 -0.02560844  0.00000000
2  -0.17798222  0.00000000  0.00000000  0.06228862 -0.02552740  0.01075370  0.00000000
3   0.06049630  0.00000000  0.00000000 -0.00353032 -0.00556040  0.00000000  0.00000000
4  -0.03205268  0.06228862 -0.00353032  0.00000000  0.04657726  0.00000000  0.00000000
5   0.00000000 -0.02552740 -0.00556040  0.04657726  0.00000000  0.00000000  0.00491641
6   0.00000000  0.01075370  0.00000000  0.00000000  0.00000000  0.00000000  0.17804150
7   0.00000000  0.00000000  0.00000000  0.00000000  0.00491641  0.17804150  0.00000000
8   0.00000000  0.00000000  0.00000000  0.03426672  0.00000000  0.11269167  0.20405598
9   0.00000000  0.01217724  0.00000000  0.00848732  0.00000000  0.24746493  0.04635482
10 -0.04850465  0.00000000  0.00000000  0.00322080  0.00000000  0.02431899  0.14683869
11 -0.02560844  0.00000000  0.00000000  0.02362640  0.00121561  0.11165872  0.07976507
12  0.00000000  0.00263585  0.00000000  0.01244116  0.00000000  0.03890678  0.05581902
13  0.03079590  0.00000000 -0.00144608  0.00000000  0.00000000  0.03075510  0.03120188
14 -0.04654852  0.00000000 -0.00387155  0.05083406  0.00000000  0.02983490  0.00000000
15  0.00000000  0.01702764  0.00000000  0.06578233  0.04020138  0.03544866  0.00644495
16 -0.02279116  0.04237401  0.00000000  0.00000000  0.00000000  0.08862476  0.00273098
17  0.00000000  0.00000000 -0.02508576  0.00607397  0.02867326  0.02500811  0.00000000
18 -0.08684417  0.00000000  0.00000000  0.01298481  0.01523918  0.00000000  0.00000000
19 -0.01664053  0.00000000  0.00000000  0.05008298  0.01940394  0.00808399  0.00000000
20 -0.07337816  0.00000000  0.00164303  0.00545662  0.02656339  0.00341323  0.03387257
21  0.00000000  0.00000000  0.00000000  0.00000000  0.04585706  0.00000000  0.00503039
22 -0.01316540  0.00000000 -0.03134572  0.00000000  0.00000000  0.04973771  0.03515834
23  0.00000000  0.00239992  0.00000000  0.00000000  0.00000000  0.00000000  0.06210532
24  0.00000000  0.00000000  0.00000000  0.04834960  0.02337729  0.00000000  0.00000000
25  0.00000000  0.01563234  0.00000000  0.01092007  0.04505417  0.00166455  0.07082882
26 -0.02458154  0.02693676  0.00614860 -0.02136620 -0.04283741  0.00000000 -0.00492569

            8           9          10          11          12          13          14
1   0.00000000  0.00000000 -0.04850465 -0.02560844  0.00000000  0.03079590 -0.04654852
2   0.00000000  0.01217724  0.00000000  0.00000000  0.00263585  0.00000000  0.00000000
3   0.00000000  0.00000000  0.00000000  0.00000000  0.00000000 -0.00144608 -0.00387155
4   0.03426672  0.00848732  0.00322080  0.02362640  0.01244116  0.00000000  0.05083406
5   0.00000000  0.00000000  0.00000000  0.00121561  0.00000000  0.00000000  0.00000000
6   0.11269167  0.24746493  0.02431899  0.11165872  0.03890678  0.03075510  0.02983490
7   0.20405598  0.04635482  0.14683869  0.07976507  0.05581902  0.03120188  0.00000000
8   0.00000000  0.06645642  0.13953392  0.02045652  0.05893511  0.01787687  0.00000000
9   0.06645642  0.00000000  0.15278869  0.08709127  0.13587077  0.00000000  0.04291065
10  0.13953392  0.15278869  0.00000000  0.04461005  0.11496909  0.00000000  0.00000000
11  0.02045652  0.08709127  0.04461005  0.00000000  0.31962290  0.01238424  0.00000000
12  0.05893511  0.13587077  0.11496909  0.31962290  0.00000000  0.03869411  0.00997951
13  0.01787687  0.00000000  0.00000000  0.01238424  0.03869411  0.00000000  0.02799310
14  0.00000000  0.04291065  0.00000000  0.00000000  0.00997951  0.02799310  0.00000000
15  0.00875234  0.07250268  0.00251817  0.06307747  0.00000000  0.00000000  0.13370257
16  0.01228454  0.05732386  0.06209812  0.03485074  0.03084098  0.00195754  0.24327528
17  0.00975344  0.00000000  0.00115565  0.00000000  0.04620248  0.02052871  0.07337822
18  0.00000000  0.00000000  0.00000000  0.00000000  0.04194474  0.00000000  0.15213782
19  0.05657872  0.01008532  0.00000000  0.06219261  0.03520904  0.00000000  0.05574488
20  0.00000000  0.00786266  0.06546173  0.00000000  0.00000000  0.00586939  0.04682153
21  0.00000000  0.00000000  0.00000000  0.00000000  0.00000000  0.05841900  0.01919433
22  0.03726159  0.00000000  0.01337437  0.03769319  0.06357574  0.00460668  0.05021302
23  0.07983172  0.00000000  0.10671388  0.01900331  0.00518191  0.01853143  0.00000000
24  0.00000000  0.00000000  0.01434107  0.00000000  0.00000000  0.06083925  0.04155025
25  0.00000000  0.01727600  0.00208366  0.00000000  0.01086294  0.00000000  0.00000000
26 -0.04481616 -0.03731791 -0.04850258 -0.05340532  0.00000000 -0.14039567  0.00000000
```

	15	16	17	18	19	20	21
1	0.000000000	-0.022791163	0.000000000	-0.08684417	-0.016640529	-0.073378162	0.000000000
2	0.017027639	0.042374013	0.000000000	0.00000000	0.000000000	0.000000000	0.000000000
3	0.000000000	0.000000000	-0.025085756	0.00000000	0.000000000	0.001643034	0.000000000
4	0.065782327	0.000000000	0.006073969	0.01298481	0.050082982	0.005456621	0.000000000
5	0.040201379	0.000000000	0.028673264	0.01523918	0.019403936	0.026563393	0.045857062
6	0.035448665	0.088624759	0.025008112	0.00000000	0.008083992	0.003413230	0.000000000
7	0.006444953	0.002730977	0.000000000	0.00000000	0.000000000	0.033872567	0.005030392
8	0.008752337	0.012284539	0.009753440	0.00000000	0.056578724	0.000000000	0.000000000
9	0.072502676	0.057323863	0.000000000	0.00000000	0.010085322	0.007862660	0.000000000
10	0.002518170	0.062098119	0.001155649	0.00000000	0.000000000	0.065461732	0.000000000
11	0.063077469	0.034850736	0.000000000	0.00000000	0.062192606	0.000000000	0.000000000
12	0.000000000	0.030840976	0.046202476	0.04194474	0.035209035	0.000000000	0.000000000
13	0.000000000	0.001957543	0.020528712	0.00000000	0.000000000	0.005869394	0.058419004
14	0.133702568	0.243275280	0.073378220	0.15213782	0.055744876	0.046821533	0.019194325
15	0.000000000	0.286189175	0.024578446	0.01904881	0.000000000	0.023340592	0.051819660
16	0.286189175	0.000000000	0.019717618	0.04668585	0.000000000	0.124702304	0.028391290
17	0.024578446	0.019717618	0.000000000	0.15315434	0.068844848	0.006009650	0.025496709
18	0.019048813	0.046685845	0.153154343	0.00000000	0.314717823	0.090786687	0.065662193
19	0.000000000	0.000000000	0.068844848	0.31471782	0.000000000	0.147864917	0.050691263
20	0.023340592	0.124702304	0.006009650	0.09078669	0.147864917	0.000000000	0.156505543
21	0.051819660	0.028391290	0.025496709	0.06566219	0.050691263	0.156505543	0.000000000
22	0.000000000	0.035847549	0.000000000	0.03800158	0.000000000	0.024536969	0.127329657
23	0.000000000	0.022123694	0.000000000	0.07522795	0.000000000	0.024296977	0.067905608
24	0.015368095	0.000000000	0.169518009	0.09643189	0.029338919	0.085756870	0.061897009
25	0.000000000	0.032878884	0.079544435	0.03462630	0.069093930	0.046584356	0.000000000
26	0.000000000	0.000000000	-0.054252383	0.00000000	-0.035415668	-0.073730275	0.000000000

	22	23	24	25	26
1	-0.013165405	0.000000000	0.00000000	0.000000000	-0.024581544
2	0.000000000	0.002399915	0.00000000	0.015632336	0.026936763
3	-0.031345717	0.000000000	0.00000000	0.000000000	0.006148603
4	0.000000000	0.000000000	0.04834960	0.010920073	-0.021366199
5	0.000000000	0.000000000	0.02337729	0.045054168	-0.042837412
6	0.049737709	0.000000000	0.00000000	0.001664546	0.000000000
7	0.035158341	0.062105316	0.00000000	0.070828821	-0.004925691
8	0.037261590	0.079831719	0.00000000	0.000000000	-0.044816163
9	0.000000000	0.000000000	0.00000000	0.017276000	-0.037317908
10	0.013374374	0.106713879	0.01434107	0.002083658	-0.048502584
11	0.037693187	0.019003313	0.00000000	0.000000000	-0.053405320
12	0.063575738	0.005181909	0.00000000	0.010862936	0.000000000
13	0.004606682	0.018531426	0.06083925	0.000000000	-0.140395669
14	0.050213023	0.000000000	0.04155024	0.000000000	0.000000000
15	0.000000000	0.000000000	0.01536809	0.000000000	0.000000000
16	0.035847549	0.022123694	0.00000000	0.032878884	0.000000000
17	0.000000000	0.000000000	0.16951801	0.079544435	-0.054252383
18	0.038001582	0.075227953	0.09643189	0.034626296	0.000000000
19	0.000000000	0.000000000	0.02933892	0.069093930	-0.035415668
20	0.024536969	0.024296977	0.08575687	0.046584356	-0.073730275
21	0.127329657	0.067905608	0.06189701	0.000000000	0.000000000
22	0.000000000	0.270477696	0.00000000	0.000000000	0.000000000
23	0.270477696	0.000000000	0.06676190	0.099531953	-0.052049638
24	0.000000000	0.066761900	0.00000000	0.198895981	-0.245031277
25	0.000000000	0.099531953	0.19889598	0.000000000	0.000000000
26	0.000000000	-0.052049638	-0.24503128	0.000000000	0.000000000

Network 4 – Edges between lifetime PTSD symptoms at baseline and SCF at follow-up

	SCF at follow-up
1 – Age	-0.0261547900
2 – Sex	-0.0171576917
3 – Education	0.0000000000
4 – Lifetime depression	0.0000000000
5 – Alcohol use	0.0000000000
6 – B1	0.0000000000
7 – B2	-0.0008996873
8 – B3	0.0000000000
9 – B4	0.0000000000
10 – B5	0.0000000000
11 – C1	0.0000000000
12 – C2	0.0000000000
13 – D1	-0.0481405197
14 – D2	-0.0374036782
15 – D3	-0.0509237094
16 – D4	-0.0261130143
17 – D5	0.0000000000
18 – D6	0.0000000000
19 – D7	-0.0640856344
20 – E1	-0.0112315746
21 – E2	0.0000000000
22 – E3	0.0000000000
23 – E4	0.0000000000
24 – E5	-0.1869278181
25 – E6	0.0000000000
26 – SCF at follow-up	0.0000000000

```
=== Estimated network ===
Number of nodes: 26
Number of non-zero edges: 195 / 325
Mean weight: 0.02649433
Network stored in x$graph
```

```
> N4b$graph
```

	1	2	3	4	5	6	7
1	0.00000000	-0.174702318	0.057097965	-0.030261283	0.000000000	0.000000000	0.0000000000
2	-0.17470232	0.000000000	0.000000000	0.056940708	-0.018960439	0.007878933	0.0000000000
3	0.05709796	0.000000000	0.000000000	-0.001189659	-0.002284225	0.000000000	0.0000000000
4	-0.03026128	0.056940708	-0.001189659	0.000000000	0.044804569	0.000000000	0.0000000000
5	0.00000000	-0.018960439	-0.002284225	0.044804569	0.000000000	0.000000000	0.0066219528
6	0.00000000	0.007878933	0.000000000	0.000000000	0.000000000	0.000000000	0.1766041693
7	0.00000000	0.000000000	0.000000000	0.000000000	0.006621953	0.176604169	0.0000000000
8	0.00000000	0.000000000	0.000000000	0.035235814	0.000000000	0.112265532	0.2032455617
9	0.00000000	0.008580645	0.000000000	0.010287920	0.000000000	0.246043749	0.0476760646
10	-0.04514503	0.000000000	0.000000000	0.004014931	0.000000000	0.025177922	0.1463343800
11	-0.02349608	0.000000000	0.000000000	0.025905808	0.005640513	0.111610597	0.0803394942
12	0.00000000	0.000000000	0.000000000	0.012384694	0.000000000	0.039143369	0.0557285047
13	0.02298826	0.000000000	0.000000000	0.000000000	0.000000000	0.032403846	0.0331404086
14	-0.04652508	0.000000000	-0.003885079	0.050759575	0.000000000	0.030189636	0.0000000000
15	0.00000000	0.013410725	0.000000000	0.064884240	0.039354568	0.035405215	0.0061755088
16	-0.02427535	0.038621324	0.000000000	0.000000000	0.000000000	0.087875432	0.0029565842
17	0.00000000	0.000000000	-0.024568967	0.006820058	0.030776946	0.027200001	0.0000000000
18	-0.08540459	0.000000000	0.000000000	0.013935150	0.015844279	0.000000000	0.0000000000
19	-0.01618291	0.000000000	0.000000000	0.049667977	0.020792803	0.007311712	0.0000000000
20	-0.06994291	0.000000000	0.000000000	0.007414528	0.030083072	0.004351430	0.0352839637
21	0.00000000	0.000000000	0.000000000	0.000000000	0.045419354	0.000000000	0.0057677470
22	-0.01139893	0.000000000	-0.030079155	0.000000000	0.000000000	0.049817018	0.0350324336
23	0.00000000	0.000000000	0.000000000	0.000000000	0.000000000	0.000000000	0.0626017397
24	0.00000000	0.000000000	0.000000000	0.054613003	0.035695852	0.000000000	0.0000000000
25	0.00000000	0.008170057	0.000000000	0.010727964	0.044002257	0.002075058	0.0708382779
26	-0.02615479	-0.017157692	0.000000000	0.000000000	0.000000000	0.000000000	-0.0008996873

	8	9	10	11	12	13	14
1	0.0000000000	0.000000000	-0.0451450253	-0.023496076	0.0000000000	0.022988259	-0.046525078
2	0.0000000000	0.008580645	0.0000000000	0.000000000	0.0000000000	0.000000000	0.000000000
3	0.0000000000	0.000000000	0.0000000000	0.000000000	0.0000000000	0.000000000	-0.003885079
4	0.0352358145	0.010287920	0.0040149313	0.025905808	0.0123846943	0.000000000	0.050759575
5	0.0000000000	0.000000000	0.0000000000	0.005640513	0.0000000000	0.000000000	0.000000000
6	0.1122655319	0.246043749	0.0251779219	0.111610597	0.0391433693	0.032403846	0.030189636
7	0.2032455617	0.047676065	0.1463343800	0.080339494	0.0557285047	0.033140409	0.000000000
8	0.0000000000	0.069252637	0.1416995886	0.023616814	0.0587560615	0.026295302	0.000000000
9	0.0692526371	0.000000000	0.1546184399	0.090173881	0.1359595927	0.000000000	0.044900518
10	0.1416995886	0.154618440	0.0000000000	0.048623035	0.1144349205	0.000000000	0.000000000
11	0.0236168135	0.090173881	0.0486230350	0.000000000	0.3177297130	0.022749080	0.000000000
12	0.0587560615	0.135959593	0.1144349205	0.317729713	0.0000000000	0.040179939	0.010413384
13	0.0262953018	0.000000000	0.0000000000	0.022749080	0.0401799393	0.000000000	0.025616492
14	0.0000000000	0.044900518	0.0000000000	0.000000000	0.0104133840	0.025616492	0.000000000
15	0.0088175085	0.072629771	0.0026539492	0.063412650	0.0000000000	0.000000000	0.130917439
16	0.0131397741	0.057909917	0.0614204638	0.036580013	0.0301792748	0.000000000	0.239784233
17	0.0148920234	0.000000000	0.0043970608	0.000000000	0.0486239955	0.028052068	0.073438334
18	0.0000000000	0.000000000	0.0000000000	0.000000000	0.0433195495	0.000000000	0.151691847
19	0.0592344075	0.012859904	0.0000000000	0.067033490	0.0338206092	0.000000000	0.052100900
20	0.0000000000	0.013708754	0.0692477494	0.003860823	0.0006847317	0.015807765	0.047063165
21	0.0000000000	0.000000000	0.0000000000	0.000000000	0.0000000000	0.058052131	0.019626140
22	0.0376214347	0.000000000	0.0139230984	0.038519259	0.0629864946	0.004157602	0.050324113
23	0.0832691874	0.000000000	0.1086102211	0.024777069	0.0057495145	0.026236839	0.000000000
24	0.0062692495	0.000000000	0.0343460452	0.000000000	0.0000000000	0.089850875	0.035907148
25	0.0003856289	0.021103658	0.0009970133	0.000000000	0.0115428737	0.000000000	0.000000000
26	0.0000000000	0.000000000	0.0000000000	0.000000000	0.0000000000	-0.048140520	-0.037403678

	15	16	17	18	19	20	21
1	0.000000000	-0.024275347	0.000000000	-0.08540459	-0.016182911	-0.0699429093	0.000000000
2	0.013410725	0.038621324	0.000000000	0.00000000	0.000000000	0.0000000000	0.000000000
3	0.000000000	0.000000000	-0.024568967	0.00000000	0.000000000	0.0000000000	0.000000000
4	0.064884240	0.000000000	0.006820058	0.01393515	0.049667977	0.0074145281	0.000000000
5	0.039354568	0.000000000	0.030776946	0.01584428	0.020792803	0.0300830719	0.045419354
6	0.035405215	0.087875432	0.027200001	0.00000000	0.007311712	0.0043514298	0.000000000
7	0.006175509	0.002956584	0.000000000	0.00000000	0.000000000	0.0352839637	0.005767747
8	0.008817509	0.013139774	0.014892023	0.00000000	0.059234407	0.0000000000	0.000000000
9	0.072629771	0.057909917	0.000000000	0.00000000	0.012859904	0.0137087538	0.000000000
10	0.002653949	0.061420464	0.004397061	0.00000000	0.000000000	0.0692477494	0.000000000
11	0.063412650	0.036580013	0.000000000	0.00000000	0.067033490	0.0038608232	0.000000000
12	0.000000000	0.030179275	0.048623995	0.04331955	0.033820609	0.0006847317	0.000000000
13	0.000000000	0.000000000	0.028052068	0.00000000	0.000000000	0.0158077654	0.058052131
14	0.130917439	0.239784233	0.073438334	0.15169185	0.052100900	0.0470631655	0.019626140
15	0.000000000	0.281982792	0.024333129	0.01859551	0.000000000	0.0224794106	0.051010043
16	0.281982792	0.000000000	0.019417686	0.04622316	0.000000000	0.1228721083	0.028513347
17	0.024333129	0.019417686	0.000000000	0.15270834	0.070647305	0.0106462856	0.025811562
18	0.018595512	0.046223162	0.152708338	0.00000000	0.311180694	0.0914691569	0.065700096
19	0.000000000	0.000000000	0.070647305	0.31118069	0.000000000	0.1486529756	0.050427664
20	0.022479411	0.122872108	0.010646286	0.09146916	0.148652976	0.0000000000	0.155865029
21	0.051010043	0.028513347	0.025811562	0.06570010	0.050427664	0.1558650291	0.000000000
22	0.000000000	0.035755671	0.000000000	0.03874067	0.000000000	0.0251343146	0.126504082
23	0.000000000	0.022183557	0.000000000	0.07552366	0.001889044	0.0285926305	0.067943150
24	0.007611301	0.000000000	0.185471243	0.09757626	0.029411090	0.1029783053	0.062890065
25	0.000000000	0.031817783	0.079394522	0.03518066	0.068139382	0.0465909655	0.000000000
26	-0.050923709	-0.026113014	0.000000000	0.00000000	-0.064085634	-0.0112315746	0.000000000

	22	23	24	25	26
1	-0.011398935	0.000000000	0.000000000	0.0000000000	-0.0261547900
2	0.000000000	0.000000000	0.000000000	0.0081700569	-0.0171576917
3	-0.030079155	0.000000000	0.000000000	0.0000000000	0.0000000000
4	0.000000000	0.000000000	0.054613003	0.0107279641	0.0000000000
5	0.000000000	0.000000000	0.035695852	0.0440022571	0.0000000000
6	0.049817018	0.000000000	0.000000000	0.0020750578	0.0000000000
7	0.035032434	0.062601740	0.000000000	0.0708382779	-0.0008996873
8	0.037621435	0.083269187	0.006269250	0.0003856289	0.0000000000
9	0.000000000	0.000000000	0.000000000	0.0211036579	0.0000000000
10	0.013923098	0.108610221	0.034346045	0.0009970133	0.0000000000
11	0.038519259	0.024777069	0.000000000	0.0000000000	0.0000000000
12	0.062986495	0.005749514	0.000000000	0.0115428737	0.0000000000
13	0.004157602	0.026236839	0.089850875	0.0000000000	-0.0481405197
14	0.050324113	0.000000000	0.035907148	0.0000000000	-0.0374036782
15	0.000000000	0.000000000	0.007611301	0.0000000000	-0.0509237094
16	0.035755671	0.022183557	0.000000000	0.0318177834	-0.0261130143
17	0.000000000	0.000000000	0.185471243	0.0793945218	0.0000000000
18	0.038740669	0.075523662	0.097576257	0.0351806554	0.0000000000
19	0.000000000	0.001889044	0.029411090	0.0681393816	-0.0640856344
20	0.025134315	0.028592631	0.102978305	0.0465909655	-0.0112315746
21	0.126504082	0.067943150	0.062890065	0.0000000000	0.0000000000
22	0.000000000	0.268523616	0.000000000	0.0000000000	0.0000000000
23	0.268523616	0.000000000	0.083442020	0.0989311646	0.0000000000
24	0.000000000	0.083442020	0.000000000	0.2007081891	-0.1869278181
25	0.000000000	0.098931165	0.200708189	0.0000000000	0.0000000000
26	0.000000000	0.000000000	-0.186927818	0.0000000000	0.0000000000

Network 4_{adj} – Edges between lifetime PTSD symptoms at baseline and SCF at follow-up, additionally adjusting for SCF at baseline

	SCF at follow-up
1 – Age	-0.037704197
2 – Sex	-0.037135512
3 – Education	0.000000000
4 – Lifetime depression	0.000000000
5 – Alcohol use	0.000000000
6 – B1	0.000000000
7 – B2	0.000000000
8 – B3	0.000000000
9 – B4	0.000000000
10 – B5	0.000000000
11 – C1	0.000000000
12 – C2	0.000000000
13 – D1	0.000000000
14 – D2	-0.025765633
15 – D3	-0.037821203
16 – D4	-0.007526939
17 – D5	0.000000000
18 – D6	0.000000000
19 – D7	-0.036000947
20 – E1	0.000000000
21 – E2	0.000000000
22 – E3	0.000000000
23 – E4	0.000000000
24 – E5	-0.084898460
25 – E6	0.000000000
26 – SCF at baseline	0.355984903
27 – SCF at follow-up	0.000000000

```
=== Estimated network ===
Number of nodes: 27
Number of non-zero edges: 209 / 351
Mean weight: 0.02340712
Network stored in x$graph
```

```
> N4bAdj$graph
             1           2           3           4           5           6           7
1   0.000000000 -0.178767672  0.060483092 -0.032442023  0.000000000 0.000000000  0.000000000
2  -0.178767672  0.000000000  0.000000000  0.061739087 -0.025736987 0.010551608  0.000000000
3   0.060483092  0.000000000  0.000000000 -0.003545577 -0.005585759 0.000000000  0.000000000
4  -0.032442023  0.061739087 -0.003545577  0.000000000  0.046702692 0.000000000  0.000000000
5   0.000000000 -0.025736987 -0.005585759  0.046702692  0.000000000 0.000000000  0.005050375
6   0.000000000  0.010551608  0.000000000  0.000000000  0.000000000 0.000000000  0.178027554
7   0.000000000  0.000000000  0.000000000  0.000000000  0.005050375 0.178027554  0.000000000
8   0.000000000  0.000000000  0.000000000  0.034445525  0.000000000 0.112683476  0.204113198
9   0.000000000  0.011919662  0.000000000  0.008782572  0.000000000 0.247570000  0.046458839
10 -0.048710513  0.000000000  0.000000000  0.003292675  0.000000000 0.024286330  0.146872470
11 -0.025930057  0.000000000  0.000000000  0.023861571  0.001513977 0.111689368  0.079873303
12  0.000000000  0.002259441  0.000000000  0.012488261  0.000000000 0.038895347  0.055806576
13  0.030252668  0.000000000 -0.001474312  0.000000000  0.000000000 0.030820240  0.031379647
14 -0.048045114  0.000000000 -0.003783700  0.050521178  0.000000000 0.029611822  0.000000000
15  0.000000000  0.015975971  0.000000000  0.065429730  0.039393264 0.035350341  0.006221111
16 -0.023961232  0.041364545  0.000000000  0.000000000  0.000000000 0.088683891  0.002731734
17  0.000000000  0.000000000 -0.025170459  0.006286558  0.028835087 0.025300136  0.000000000
18 -0.087405787  0.000000000  0.000000000  0.013004846  0.015209924 0.000000000  0.000000000
19 -0.017941523  0.000000000  0.000000000  0.049919948  0.019464250 0.007875568  0.000000000
20 -0.073868425  0.000000000  0.001612525  0.005718419  0.026798691 0.003539251  0.034081627
21  0.000000000  0.000000000  0.000000000  0.000000000  0.045876882 0.000000000  0.005116861
22 -0.013395100  0.000000000 -0.031357344  0.000000000  0.000000000 0.049778000  0.035145609
23  0.000000000  0.001865557  0.000000000  0.000000000  0.000000000 0.000000000  0.062171618
24  0.000000000  0.000000000  0.000000000  0.048872467  0.023704768 0.000000000  0.000000000
25  0.000000000  0.014663484  0.000000000  0.011003287  0.045038304 0.001677649  0.070903379
26 -0.009831201  0.040451936  0.005636754 -0.017845343 -0.039056801 0.000000000 -0.003845169
27 -0.037704197 -0.037135512  0.000000000  0.000000000  0.000000000 0.000000000  0.000000000

             8           9          10          11          12           13          14
1   0.000000000  0.000000000 -0.048710513 -0.025930057 0.000000000  0.0302526685 -0.048045114
2   0.000000000  0.011919662  0.000000000  0.000000000 0.002259441  0.0000000000  0.000000000
3   0.000000000  0.000000000  0.000000000  0.000000000 0.000000000 -0.0014743120 -0.003783700
4   0.034445525  0.008782572  0.003292675  0.023861571 0.012488261  0.0000000000  0.050521178
5   0.000000000  0.000000000  0.000000000  0.001513977 0.000000000  0.0000000000  0.000000000
6   0.112683476  0.247570000  0.024286330  0.111689368 0.038895347  0.0308202399  0.029611822
7   0.204113198  0.046458839  0.146872470  0.079873303 0.055806576  0.0313796465  0.000000000
8   0.000000000  0.066731954  0.139645776  0.020635158 0.058913474  0.0181113576  0.000000000
9   0.066731954  0.000000000  0.153078784  0.087448638 0.135987369  0.0000000000  0.042543805
10  0.139645776  0.153078784  0.000000000  0.044827206 0.114936781  0.0000000000  0.000000000
11  0.020635158  0.087448638  0.044827206  0.000000000 0.319689632  0.0128218352  0.000000000
12  0.058913474  0.135987369  0.114936781  0.319689632 0.000000000  0.0387987610  0.009647896
13  0.018111358  0.000000000  0.000000000  0.012821835 0.038798761  0.0000000000  0.026358787
14  0.000000000  0.042543805  0.000000000  0.000000000 0.009647896  0.0263587871  0.000000000
15  0.007822245  0.072010242  0.001691410  0.062113992 0.000000000  0.0000000000  0.132268574
16  0.012093454  0.057340584  0.061750616  0.034682499 0.030870181  0.0009172134  0.242712997
17  0.010078418  0.000000000  0.001371124  0.000000000 0.046479713  0.0209703169  0.072942953
18  0.000000000  0.000000000  0.000000000  0.000000000 0.042086237  0.0000000000  0.152173412
19  0.056683581  0.010257409  0.000000000  0.062412605 0.035081772  0.0000000000  0.053752172
20  0.000000000  0.008633899  0.065688461  0.000000000 0.000000000  0.0065156012  0.046084945
21  0.000000000  0.000000000  0.000000000  0.000000000 0.000000000  0.0583580817  0.019207428
22  0.037264598  0.000000000  0.013319927  0.037726718 0.063590452  0.0046260836  0.049920165
23  0.080003598  0.000000000  0.106835007  0.019340710 0.005196294  0.0187609219  0.000000000
24  0.000000000  0.000000000  0.015228833  0.000000000 0.000000000  0.0610675685  0.036728655
25  0.000000000  0.017682373  0.001975710  0.000000000 0.010907659  0.0000000000  0.000000000
26 -0.041199196 -0.031674234 -0.044105838 -0.047817220 0.000000000 -0.1305399668  0.000000000
27  0.000000000  0.000000000  0.000000000  0.000000000 0.000000000  0.0000000000 -0.025765633
```

	15	16	17	18	19	20	21
1	0.000000000	-0.0239612316	0.000000000	-0.08740579	-0.017941523	-0.073868425	0.000000000
2	0.015975971	0.0413645451	0.000000000	0.00000000	0.000000000	0.000000000	0.000000000
3	0.000000000	0.0000000000	-0.025170459	0.00000000	0.000000000	0.001612525	0.000000000
4	0.065429730	0.0000000000	0.006286558	0.01300485	0.049919948	0.005718419	0.000000000
5	0.039393264	0.0000000000	0.028835087	0.01520992	0.019464250	0.026798691	0.045876882
6	0.035350341	0.0886838908	0.025300136	0.00000000	0.007875568	0.003539251	0.000000000
7	0.006221111	0.0027317341	0.000000000	0.00000000	0.000000000	0.034081627	0.005116861
8	0.007822245	0.0120934537	0.010078418	0.00000000	0.056683581	0.000000000	0.000000000
9	0.072010242	0.0573405843	0.000000000	0.00000000	0.010257409	0.008633899	0.000000000
10	0.001691410	0.0617506160	0.001371124	0.00000000	0.000000000	0.065688461	0.000000000
11	0.062113992	0.0346824988	0.000000000	0.00000000	0.062412605	0.000000000	0.000000000
12	0.000000000	0.0308701809	0.046479713	0.04208624	0.035081772	0.000000000	0.000000000
13	0.000000000	0.0009172134	0.020970317	0.00000000	0.000000000	0.006515601	0.058358082
14	0.132268574	0.2427129973	0.072942953	0.15217341	0.053752172	0.046084945	0.019207428
15	0.000000000	0.2856309734	0.023707825	0.01857732	0.000000000	0.022156695	0.051519611
16	0.285630973	0.0000000000	0.019363415	0.04637668	0.000000000	0.124306468	0.028373438
17	0.023707825	0.0193634146	0.000000000	0.15323659	0.068983516	0.006504088	0.025559861
18	0.018577319	0.0463766773	0.153236591	0.00000000	0.314406113	0.090832394	0.065732356
19	0.000000000	0.0000000000	0.068983516	0.31440611	0.000000000	0.147947448	0.050553054
20	0.022156695	0.1243064677	0.006504088	0.09083239	0.147947448	0.000000000	0.156602543
21	0.051519611	0.0283734378	0.025559861	0.06573236	0.050553054	0.156602543	0.000000000
22	0.000000000	0.0359018461	0.000000000	0.03804037	0.000000000	0.024580950	0.127366042
23	0.000000000	0.0215453525	0.000000000	0.07518459	0.000000000	0.024612952	0.067875282
24	0.008052965	0.0000000000	0.169840804	0.09638024	0.027015438	0.086695271	0.061721597
25	0.000000000	0.0325973174	0.079591127	0.03466866	0.068975898	0.046639961	0.000000000
26	0.000000000	0.0000000000	-0.048055369	0.00000000	-0.017988328	-0.065335926	0.000000000
27	-0.037821203	-0.0075269387	0.000000000	0.00000000	-0.036000947	0.000000000	0.000000000

	22	23	24	25	26	27
1	-0.013395100	0.000000000	0.000000000	0.000000000	-0.009831201	-0.037704197
2	0.000000000	0.001865557	0.000000000	0.014663484	0.040451936	-0.037135512
3	-0.031357344	0.000000000	0.000000000	0.000000000	0.005636754	0.000000000
4	0.000000000	0.000000000	0.048872467	0.011003287	-0.017845343	0.000000000
5	0.000000000	0.000000000	0.023704768	0.045038304	-0.039056801	0.000000000
6	0.049778000	0.000000000	0.000000000	0.001677649	0.000000000	0.000000000
7	0.035145609	0.062171618	0.000000000	0.070903379	-0.003845169	0.000000000
8	0.037264598	0.080003598	0.000000000	0.000000000	-0.041199196	0.000000000
9	0.000000000	0.000000000	0.000000000	0.017682373	-0.031674234	0.000000000
10	0.013319927	0.106835007	0.015228833	0.001975710	-0.044105838	0.000000000
11	0.037726718	0.019340710	0.000000000	0.000000000	-0.047817220	0.000000000
12	0.063590452	0.005196294	0.000000000	0.010907659	0.000000000	0.000000000
13	0.004626084	0.018760922	0.061067568	0.000000000	-0.130539967	0.000000000
14	0.049920165	0.000000000	0.036728655	0.000000000	0.000000000	-0.025765633
15	0.000000000	0.000000000	0.008052965	0.000000000	0.000000000	-0.037821203
16	0.035901846	0.021545352	0.000000000	0.032597317	0.000000000	-0.007526939
17	0.000000000	0.000000000	0.169840804	0.079591127	-0.048055369	0.000000000
18	0.038040370	0.075184586	0.096380237	0.034668664	0.000000000	0.000000000
19	0.000000000	0.000000000	0.027015438	0.068975898	-0.017988328	-0.036000947
20	0.024580950	0.024612952	0.086695271	0.046639961	-0.065335926	0.000000000
21	0.127366042	0.067875282	0.061721597	0.000000000	0.000000000	0.000000000
22	0.000000000	0.270468080	0.000000000	0.000000000	0.000000000	0.000000000
23	0.270468080	0.000000000	0.067108207	0.099558577	-0.047303868	0.000000000
24	0.000000000	0.067108207	0.000000000	0.198241716	-0.196608774	-0.084898460
25	0.000000000	0.099558577	0.198241716	0.000000000	0.000000000	0.000000000
26	0.000000000	-0.047303868	-0.196608774	0.000000000	0.000000000	0.355984903
27	0.000000000	0.000000000	-0.084898460	0.000000000	0.355984903	0.000000000

Based on complete case analyses (CCA)

Network model	**N1**	**N2**	**N2$_{adj}$**	**N3**	**N4**	**N4$_{adj}$**
	SCF at baseline	SCF at follow-up	SCF at follow-up	SCF at baseline	SCF at follow-up	SCF at follow-up
1 – Age	0.000000000	-0.019451132	-0.018601803	-0.04116977	-0.049467036	-0.03163476
2 – Sex	0.000000000	-0.029023640	-0.037005866	0.04142686	-0.027044927	-0.03006110
3 – Education	0.000000000	0.000000000	0.000000000	0.01473843	0.000000000	0.00000000
4 – Lifetime depression	-0.017341746	0.000000000	0.000000000	-0.01977618	0.000000000	0.00000000
5 – Alcohol use	-0.050328376	0.000000000	0.000000000	-0.03624218	0.000000000	0.00000000
6 – B1	0.000000000	0.000000000	0.000000000	0.00000000	0.000000000	0.00000000
7 – B2	-0.016825768	0.000000000	0.000000000	0.00000000	-0.005277909	0.00000000
8 – B3	-0.014595369	0.006927359	0.023040254	-0.04290765	0.000000000	0.00000000
9 – B4	-0.011562540	0.002573735	0.018992842	-0.03959501	0.000000000	0.00000000
10 – B5	-0.030338859	0.000000000	0.000000000	-0.05665157	0.000000000	0.00000000
11 – C1	-0.044846807	0.000000000	0.000000000	-0.05569306	0.000000000	0.00000000
12 – C2	0.000000000	0.000000000	0.007483040	0.00000000	0.000000000	0.00000000
13 – D1	-0.056431343	0.000000000	0.000000000	-0.13331967	-0.047506342	0.00000000
14 – D2	0.000000000	-0.050937555	-0.042292966	0.00000000	-0.036369934	-0.02242984
15 – D3	0.000000000	-0.040995495	-0.034798418	0.00000000	-0.047103170	-0.03220802
16 – D4	0.000000000	-0.020771838	-0.010326767	0.00000000	-0.036339135	-0.01654734
17 – D5	-0.032218181	0.000000000	0.000000000	-0.06266350	0.000000000	0.00000000
18 – D6	-0.008125405	0.000000000	0.000000000	0.00000000	0.000000000	0.00000000
19 – D7	-0.065557994	-0.039283943	-0.002427592	-0.04147089	-0.061782414	-0.02853764
20 – E1	-0.121333351	-0.010436222	0.000000000	-0.06739588	-0.008377292	0.00000000
21 – E2	0.000000000	0.039108884	0.051854335	0.00000000	0.000000000	0.00000000
22 – E3	0.000000000	0.000000000	0.000000000	0.00000000	0.001680389	0.00000000
23 – E4	-0.054889370	0.000000000	0.000000000	-0.04972839	0.000000000	0.00000000
24 – E5	-0.304399888	-0.257129093	-0.143200815	-0.24471612	-0.188807516	-0.08503775
25 – E6	-0.043036572	0.000000000	0.000000000	0.00000000	-0.005903650	0.00000000
26 – SCF at baseline	0.000000000	-	0.322398345	0.00000000	-	0.35546890
27 – SCF at follow-up	-	0.000000000	0.000000000	-	0.00000000	0.00000000

Network 1 – Edges between past-month PTSD symptoms SCF at baseline – CCA

	SCF at baseline
1 – Age	0.000000000
2 – Sex	0.000000000
3 – Education	0.000000000
4 – Lifetime depression	-0.017341746
5 – Alcohol use	-0.050328376
6 – B1	0.000000000
7 – B2	-0.016825768
8 – B3	-0.014595369
9 – B4	-0.011562540
10 – B5	-0.030338859
11 – C1	-0.044846807
12 – C2	0.000000000
13 – D1	-0.056431343
14 – D2	0.000000000
15 – D3	0.000000000
16 – D4	0.000000000
17 – D5	-0.032218181
18 – D6	-0.008125405
19 – D7	-0.065557994
20 – E1	-0.121333351
21 – E2	0.000000000
22 – E3	0.000000000
23 – E4	-0.054889370
24 – E5	-0.304399888
25 – E6	-0.043036572
26 – SCF at baseline	0.000000000

```
=== Estimated network ===
Number of nodes: 26
Number of non-zero edges: 187 / 325
Mean weight: 0.02414713
Network stored in x$graph
```

```
> N1b$graph
             1           2           3           4           5           6           7
1   0.000000000 -0.18551711  0.05261965 -0.054537916  0.000000000 -0.012866545  0.00000000
2  -0.185517107  0.00000000  0.00000000  0.065176743  0.000000000  0.022126915  0.00000000
3   0.052619649  0.00000000  0.00000000  0.000000000  0.000000000  0.000000000  0.00000000
4  -0.054537916  0.06517674  0.00000000  0.000000000  0.059790954  0.039621679  0.00000000
5   0.000000000  0.00000000  0.00000000  0.059790954  0.000000000  0.000000000  0.00000000
6  -0.012866545  0.02212692  0.00000000  0.039621679  0.000000000  0.000000000  0.17235231
7   0.000000000  0.00000000  0.00000000  0.000000000  0.000000000  0.172352314  0.00000000
8   0.000000000  0.00000000  0.00000000  0.000000000  0.000000000  0.107191642  0.18955667
9   0.000000000  0.00000000  0.00000000  0.000000000  0.000000000  0.233444628  0.01291368
10  0.000000000  0.00000000  0.00000000  0.000000000  0.000000000  0.081558965  0.13459060
11 -0.002755425  0.00000000  0.00000000  0.011115383  0.030520395  0.107425011  0.04020584
12 -0.014133898  0.00000000  0.00000000  0.000000000  0.000000000  0.018681047  0.04806942
13  0.000000000  0.00000000 -0.01775855  0.000000000  0.000000000  0.001386680  0.06013854
14 -0.032135023  0.00000000  0.00000000  0.043056733  0.000000000  0.000000000  0.00000000
15  0.000000000  0.00000000  0.00000000  0.016678308  0.001349634  0.026987603  0.00000000
16  0.000000000  0.00000000  0.00000000  0.000000000  0.000000000  0.105730981  0.03768497
17  0.000000000  0.00000000 -0.03922565  0.000000000  0.003112182  0.019393370  0.02668923
18 -0.047004811  0.00000000  0.00000000  0.036598716  0.031739068  0.020602494  0.00000000
19 -0.056693253  0.00000000  0.00000000  0.018386169  0.028529242  0.015870621  0.00000000
20 -0.055700337  0.00000000  0.00000000  0.006468914  0.013170569  0.007609634  0.00000000
21  0.000000000 -0.01264890  0.00000000  0.000000000  0.010741785  0.000000000  0.04174489
22 -0.019046610  0.00000000 -0.01863196  0.000000000  0.020970824  0.000000000  0.05261302
23  0.000000000  0.00000000  0.00000000  0.000000000  0.000000000  0.000000000  0.10216681
24  0.000000000  0.00000000  0.00000000  0.063174989  0.000000000  0.002648168  0.00000000
25  0.000000000  0.02920050  0.00000000  0.005523411  0.025181317  0.017775902  0.06520702
26  0.000000000  0.00000000  0.00000000 -0.017341746 -0.050328376  0.000000000 -0.01682577
```

```
             8           9           10          11           12           13
1   0.000000000  0.000000000  0.000000000 -0.002755425 -0.0141338984  0.000000000
2   0.000000000  0.000000000  0.000000000  0.000000000  0.0000000000  0.000000000
3   0.000000000  0.000000000  0.000000000  0.000000000  0.0000000000 -0.017758549
4   0.000000000  0.000000000  0.000000000  0.011115383  0.0000000000  0.000000000
5   0.000000000  0.000000000  0.000000000  0.030520395  0.0000000000  0.000000000
6   0.107191642  0.233444628  0.081558965  0.107425011  0.0186810468  0.001386680
7   0.189556666  0.012913683  0.134590605  0.040205837  0.0480694182  0.060138537
8   0.000000000  0.116520766  0.135122528  0.062279203  0.0241013735  0.000000000
9   0.116520766  0.000000000  0.178676997  0.161544567  0.1249465095  0.000000000
10  0.135122528  0.178676997  0.000000000  0.016010071  0.1208452412  0.000000000
11  0.062279203  0.161544567  0.016010071  0.000000000  0.2615727744  0.085896698
12  0.024101373  0.124946509  0.120845241  0.261572774  0.0000000000  0.123893966
13  0.000000000  0.000000000  0.000000000  0.085896698  0.1238939660  0.000000000
14  0.000000000  0.000000000  0.000000000  0.000000000  0.0095690468  0.000000000
15  0.008200909  0.110615253  0.022409460  0.078953448  0.0215776419  0.035704987
16  0.003904918  0.027318730  0.125527403  0.010894962  0.0416243471  0.009652515
17  0.018418960  0.000000000  0.010604420  0.000000000  0.1019588591  0.038970360
18  0.000000000  0.000000000  0.000000000  0.001973871  0.0059569110  0.012609565
19  0.025694343  0.000000000  0.000000000  0.054774955  0.0350082637  0.000000000
20  0.027777066  0.015931884  0.033944119  0.028764289  0.0000000000  0.004567333
21  0.000000000  0.000000000  0.036438186  0.000000000  0.0005717033  0.004788751
22  0.000000000  0.000000000  0.004887859  0.035366429  0.0752455875  0.021075159
23  0.057231020  0.000000000  0.039689753  0.003822144  0.0365461673  0.000000000
24  0.002112296  0.000000000  0.000000000  0.000000000  0.0000000000  0.063616672
25  0.009757349  0.005886885  0.005259964  0.030531505  0.0000000000  0.000000000
26 -0.014595369 -0.011562540 -0.030338859 -0.044846807  0.0000000000 -0.056431343
```

	14	15	16	17	18	19	20
1	-0.032135023	0.000000000	0.000000000	0.0000000000	-0.047004811	-0.056693253	-0.0557003367
2	0.000000000	0.000000000	0.000000000	0.0000000000	0.000000000	0.000000000	0.0000000000
3	0.000000000	0.000000000	0.000000000	-0.0392256470	0.000000000	0.000000000	0.0000000000
4	0.043056733	0.016678308	0.000000000	0.0000000000	0.036598716	0.018386169	0.0064689144
5	0.000000000	0.001349634	0.000000000	0.0031121815	0.031739068	0.028529242	0.0131705689
6	0.000000000	0.026987603	0.105730981	0.0193933699	0.020602494	0.015870621	0.0076096335
7	0.000000000	0.000000000	0.037684975	0.0266892343	0.000000000	0.000000000	0.0000000000
8	0.000000000	0.008200909	0.003904918	0.0184189604	0.000000000	0.025694343	0.0277770662
9	0.000000000	0.110615253	0.027318730	0.0000000000	0.000000000	0.000000000	0.0159318843
10	0.000000000	0.022409460	0.125527403	0.0106044197	0.000000000	0.000000000	0.0339441186
11	0.000000000	0.078953448	0.010894962	0.0000000000	0.001973871	0.054774955	0.0287642891
12	0.009569047	0.021577642	0.041624347	0.1019588591	0.005956911	0.035008264	0.0000000000
13	0.000000000	0.035704987	0.009652515	0.0389703597	0.012609565	0.000000000	0.0045673329
14	0.000000000	0.157869687	0.249463726	0.0965706785	0.122458523	0.032191539	0.0843995397
15	0.157869687	0.000000000	0.312428896	0.0417892993	0.043316412	0.000000000	0.0000000000
16	0.249463726	0.312428896	0.000000000	0.0018475400	0.049679715	0.000000000	0.1067666281
17	0.096570678	0.041789299	0.001847540	0.0000000000	0.125435992	0.071495370	0.0005092202
18	0.122458523	0.043316412	0.049679715	0.1254359915	0.000000000	0.325148998	0.0501013742
19	0.032191539	0.000000000	0.000000000	0.0714953704	0.325148998	0.000000000	0.1655020208
20	0.084399540	0.000000000	0.106766628	0.0005092202	0.050101374	0.165502021	0.0000000000
21	0.006146677	0.034887488	0.000000000	0.0692048274	0.027728285	0.021788301	0.1482962236
22	0.047607261	0.000000000	0.051130479	0.0000000000	0.078265385	0.000000000	0.0000000000
23	0.002108307	0.000000000	0.064544627	0.0431683781	0.016872982	0.069776573	0.0100803222
24	0.054668219	0.014330751	0.001812717	0.1595858041	0.137246657	0.004649959	0.0870294176
25	0.000000000	0.000000000	0.000000000	0.0912406544	0.014343292	0.084620291	0.0170846502
26	0.000000000	0.000000000	0.000000000	-0.0322181814	-0.008125405	-0.065557994	-0.1213333514

	21	22	23	24	25	26
1	0.0000000000	-0.019046610	0.000000000	0.000000000	0.000000000	0.000000000
2	-0.0126489018	0.000000000	0.000000000	0.000000000	0.029200504	0.000000000
3	0.0000000000	-0.018631962	0.000000000	0.000000000	0.000000000	0.000000000
4	0.0000000000	0.000000000	0.000000000	0.063174989	0.005523411	-0.017341746
5	0.0107417854	0.020970824	0.000000000	0.000000000	0.025181317	-0.050328376
6	0.0000000000	0.000000000	0.000000000	0.002648168	0.017775902	0.000000000
7	0.0417448863	0.052613016	0.102166812	0.000000000	0.065207023	-0.016825768
8	0.0000000000	0.000000000	0.057231020	0.002112296	0.009757349	-0.014595369
9	0.0000000000	0.000000000	0.000000000	0.000000000	0.005886885	-0.011562540
10	0.0364381864	0.004887859	0.039689753	0.000000000	0.005259964	-0.030338859
11	0.0000000000	0.035366429	0.003822144	0.000000000	0.030531505	-0.044846807
12	0.0005717033	0.075245587	0.036546167	0.000000000	0.000000000	0.000000000
13	0.0047887512	0.021075159	0.000000000	0.063616672	0.000000000	-0.056431343
14	0.0061466771	0.047607261	0.002108307	0.054668219	0.000000000	0.000000000
15	0.0348874885	0.000000000	0.000000000	0.014330751	0.000000000	0.000000000
16	0.0000000000	0.051130479	0.064544627	0.001812717	0.000000000	0.000000000
17	0.0692048274	0.000000000	0.043168378	0.159585804	0.091240654	-0.032218181
18	0.0277282851	0.078265385	0.016872982	0.137246657	0.014343292	-0.008125405
19	0.0217883014	0.000000000	0.069776573	0.004649959	0.084620291	-0.065557994
20	0.1482962236	0.000000000	0.010080322	0.087029418	0.017084650	-0.121333351
21	0.0000000000	0.080001152	0.057322656	0.000000000	0.000000000	0.000000000
22	0.0800011519	0.000000000	0.235852170	0.000000000	0.041516380	0.000000000
23	0.0573226560	0.235852170	0.000000000	0.083801746	0.068999627	-0.054889370
24	0.0000000000	0.000000000	0.083801746	0.000000000	0.173378073	-0.304399888
25	0.0000000000	0.041516380	0.068999627	0.173378073	0.000000000	-0.043036572
26	0.0000000000	0.000000000	-0.054889370	-0.304399888	-0.043036572	0.000000000

Network 2 – Edges between past-month PTSD symptoms at baseline and SCF at follow-up – CCA

	SCF at follow-up
1 – Age	-0.019451132
2 – Sex	-0.029023640
3 – Education	0.000000000
4 – Lifetime depression	0.000000000
5 – Alcohol use	0.000000000
6 – B1	0.000000000
7 – B2	0.000000000
8 – B3	0.006927359
9 – B4	0.002573735
10 – B5	0.000000000
11 – C1	0.000000000
12 – C2	0.000000000
13 – D1	0.000000000
14 – D2	-0.050937555
15 – D3	-0.040995495
16 – D4	-0.020771838
17 – D5	0.000000000
18 – D6	0.000000000
19 – D7	-0.039283943
20 – E1	-0.010436222
21 – E2	0.039108884
22 – E3	0.000000000
23 – E4	0.000000000
24 – E5	-0.257129093
25 – E6	0.000000000
26 – SCF at follow-up	0.000000000

```
=== Estimated network ===
Number of nodes: 26
Number of non-zero edges: 185 / 325
Mean weight: 0.02645491
Network stored in x$graph
```

```
> N2b$graph
              1           2           3           4           5           6          7
1   0.000000000 -0.191940000  0.058164729 -0.057334580 -0.001720713 -0.013086155 0.00000000
2  -0.191940000  0.000000000  0.000000000  0.069870912 -0.012349281  0.025094564 0.00000000
3   0.058164729  0.000000000  0.000000000  0.000000000 -0.002902915  0.000000000 0.00000000
4  -0.057334580  0.069870912  0.000000000  0.000000000  0.067093213  0.040390631 0.00000000
5  -0.001720713 -0.012349281 -0.002902915  0.067093213  0.000000000  0.000000000 0.00000000
6  -0.013086155  0.025094564  0.000000000  0.040390631  0.000000000  0.000000000 0.17404018
7   0.000000000  0.000000000  0.000000000  0.000000000  0.000000000  0.174040178 0.00000000
8   0.000000000  0.000000000  0.000000000  0.000000000  0.000000000  0.107086661 0.19189981
9   0.000000000  0.000000000  0.000000000  0.000000000  0.000000000  0.236348745 0.01182196
10  0.000000000  0.000000000  0.000000000  0.000000000  0.000000000  0.081207385 0.13657879
11 -0.003274712  0.000000000  0.000000000  0.013782758  0.036021856  0.107911065 0.04100438
12 -0.014871880  0.000000000  0.000000000  0.000000000  0.000000000  0.016904084 0.04769698
13  0.000000000  0.000000000 -0.021882899  0.000000000  0.000000000  0.001257729 0.06352462
14 -0.033908491  0.000000000  0.000000000  0.043509443  0.000000000  0.000000000 0.00000000
15  0.000000000  0.000000000  0.000000000  0.016951269  0.003241455  0.025140666 0.00000000
16  0.000000000  0.000000000  0.000000000  0.000000000  0.000000000  0.106021213 0.03770150
17  0.000000000  0.000000000 -0.041627845  0.000000000  0.008450008  0.018349814 0.02859856
18 -0.047830301  0.000000000  0.000000000  0.036401417  0.034532790  0.019656477 0.00000000
19 -0.058082315  0.000000000  0.000000000  0.019264113  0.033126708  0.015447289 0.00000000
20 -0.059123974 -0.004962551  0.000000000  0.009038603  0.022327145  0.006185013 0.00000000
21  0.000000000 -0.025260994  0.000000000  0.000000000  0.013959113  0.000000000 0.04293168
22 -0.020781229  0.000000000 -0.021627067  0.000000000  0.024334596  0.000000000 0.05259891
23  0.000000000  0.000000000  0.000000000  0.000000000  0.000000000  0.000000000 0.10480417
24  0.000000000  0.000000000  0.000000000  0.071459193  0.003846462  0.009223935 0.00000000
25  0.000000000  0.032205635  0.000000000  0.006854432  0.032965046  0.015250765 0.06813260
26 -0.019451132 -0.029023640  0.000000000  0.000000000  0.000000000  0.000000000 0.00000000
```

```
              8           9           10          11          12          13          14
1   0.000000000 0.000000000 0.000000000 -0.003274712 -0.014871880  0.000000000 -0.033908491
2   0.000000000 0.000000000 0.000000000  0.000000000  0.000000000  0.000000000  0.000000000
3   0.000000000 0.000000000 0.000000000  0.000000000  0.000000000 -0.021882899  0.000000000
4   0.000000000 0.000000000 0.000000000  0.013782758  0.000000000  0.000000000  0.043509443
5   0.000000000 0.000000000 0.000000000  0.036021856  0.000000000  0.000000000  0.000000000
6   0.107086661 0.236348745 0.081207385  0.107911065  0.016904084  0.001257729  0.000000000
7   0.191899808 0.011821957 0.136578788  0.041004378  0.047696979  0.063524616  0.000000000
8   0.000000000 0.117510882 0.136702230  0.063171811  0.023146573  0.000000000  0.000000000
9   0.117510882 0.000000000 0.181091995  0.163734217  0.125895539  0.000000000  0.000000000
10  0.136702230 0.181091995 0.000000000  0.016785267  0.122233622  0.000000000  0.000000000
11  0.063171811 0.163734217 0.016785267  0.000000000  0.265193224  0.091425589  0.000000000
12  0.023146573 0.125895539 0.122233622  0.265193224  0.000000000  0.125703917  0.008989282
13  0.000000000 0.000000000 0.000000000  0.091425589  0.125703917  0.000000000  0.000000000
14  0.000000000 0.000000000 0.000000000  0.000000000  0.008989282  0.000000000  0.000000000
15  0.007573520 0.111963398 0.021478035  0.079423810  0.020213486  0.035992574  0.155280157
16  0.002847793 0.026480684 0.127323765  0.010047968  0.041289486  0.009240113  0.250525263
17  0.017834311 0.000000000 0.014263029  0.000000000  0.103657736  0.040956461  0.097034141
18  0.000000000 0.000000000 0.000000000  0.004617477  0.005350534  0.013871932  0.123522669
19  0.027283485 0.000000000 0.000000000  0.059087944  0.035142997  0.000000000  0.028069873
20  0.029281429 0.018108012 0.040249422  0.035891093  0.000000000  0.011812135  0.084027582
21  0.000000000 0.000000000 0.037135481  0.000000000  0.000000000  0.007551942  0.009069515
22  0.000000000 0.000000000 0.004484194  0.034782725  0.075230786  0.022393106  0.047331708
23  0.057375533 0.000000000 0.042741864  0.007768509  0.036492469  0.000000000  0.001208962
24  0.014495019 0.000000000 0.000000000  0.000000000  0.000000000  0.087453357  0.042203422
25  0.008911766 0.007335908 0.008449920  0.035398822  0.000000000  0.000000000  0.000000000
26  0.006927359 0.002573735 0.000000000  0.000000000  0.000000000  0.000000000 -0.050937555
```

	15	16	17	18	19	20	21
1	0.000000000	0.000000000	0.000000000	-0.047830301	-0.05808231	-0.059123974	0.000000000
2	0.000000000	0.000000000	0.000000000	0.000000000	0.00000000	-0.004962551	-0.025260994
3	0.000000000	0.000000000	-0.041627845	0.000000000	0.00000000	0.000000000	0.000000000
4	0.016951269	0.000000000	0.000000000	0.036401417	0.01926411	0.009038603	0.000000000
5	0.003241455	0.000000000	0.008450008	0.034532790	0.03312671	0.022327145	0.013959113
6	0.025140666	0.106021213	0.018349814	0.019656477	0.01544729	0.006185013	0.000000000
7	0.000000000	0.037701503	0.028598560	0.000000000	0.00000000	0.000000000	0.042931676
8	0.007573520	0.002847793	0.017834311	0.000000000	0.02728349	0.029281429	0.000000000
9	0.111963398	0.026480684	0.000000000	0.000000000	0.00000000	0.018108012	0.000000000
10	0.021478035	0.127323765	0.014263029	0.000000000	0.00000000	0.040249422	0.037135481
11	0.079423810	0.010047968	0.000000000	0.004617477	0.05908794	0.035891093	0.000000000
12	0.020213486	0.041289486	0.103657736	0.005350534	0.03514300	0.000000000	0.000000000
13	0.035992574	0.009240113	0.040956461	0.013871932	0.00000000	0.011812135	0.007551942
14	0.155280157	0.250525263	0.097034141	0.123522669	0.02806987	0.084027582	0.009069515
15	0.000000000	0.314803840	0.041044275	0.041361614	0.00000000	0.000000000	0.036639499
16	0.314803840	0.000000000	0.000000000	0.048700178	0.00000000	0.106363439	0.000000000
17	0.041044275	0.000000000	0.000000000	0.125829044	0.07336848	0.002361766	0.072098795
18	0.041361614	0.048700178	0.125829044	0.000000000	0.32978523	0.049578839	0.029499153
19	0.000000000	0.000000000	0.073368478	0.329785232	0.00000000	0.175553627	0.023673821
20	0.000000000	0.106363439	0.002361766	0.049578839	0.17555363	0.000000000	0.152984208
21	0.036639499	0.000000000	0.072098795	0.029499153	0.02367382	0.152984208	0.000000000
22	0.000000000	0.050468370	0.000000000	0.077916411	0.00000000	0.000000000	0.081095158
23	0.000000000	0.063860177	0.043847723	0.016411804	0.07381062	0.015637732	0.059263857
24	0.005868643	0.000000000	0.175572346	0.144121204	0.01584761	0.128587655	0.000000000
25	0.000000000	0.000000000	0.092344426	0.012764062	0.08771557	0.021363289	0.000000000
26	-0.040995495	-0.020771838	0.000000000	0.000000000	-0.03928394	-0.010436222	0.039108884

	22	23	24	25	26
1	-0.020781229	0.000000000	0.000000000	0.000000000	-0.019451132
2	0.000000000	0.000000000	0.000000000	0.032205635	-0.029023640
3	-0.021627067	0.000000000	0.000000000	0.000000000	0.000000000
4	0.000000000	0.000000000	0.071459193	0.006854432	0.000000000
5	0.024334596	0.000000000	0.003846462	0.032965046	0.000000000
6	0.000000000	0.000000000	0.009223935	0.015250765	0.000000000
7	0.052598914	0.104804170	0.000000000	0.068132597	0.000000000
8	0.000000000	0.057375533	0.014495019	0.008911766	0.006927359
9	0.000000000	0.000000000	0.000000000	0.007335908	0.002573735
10	0.004484194	0.042741864	0.000000000	0.008449920	0.000000000
11	0.034782725	0.007768509	0.000000000	0.035398822	0.000000000
12	0.075230786	0.036492469	0.000000000	0.000000000	0.000000000
13	0.022393106	0.000000000	0.087453357	0.000000000	0.000000000
14	0.047331708	0.001208962	0.042203422	0.000000000	-0.050937555
15	0.000000000	0.000000000	0.005868643	0.000000000	-0.040995495
16	0.050468370	0.063860177	0.000000000	0.000000000	-0.020771838
17	0.000000000	0.043847723	0.175572346	0.092344426	0.000000000
18	0.077916411	0.016411804	0.144121204	0.012764062	0.000000000
19	0.000000000	0.073810618	0.015847615	0.087715568	-0.039283943
20	0.000000000	0.015637732	0.128587655	0.021363289	-0.010436222
21	0.081095158	0.059263857	0.000000000	0.000000000	0.039108884
22	0.000000000	0.238680911	0.000000000	0.041467957	0.000000000
23	0.238680911	0.000000000	0.106358714	0.071014041	0.000000000
24	0.000000000	0.106358714	0.000000000	0.192816461	-0.257129093
25	0.041467957	0.071014041	0.192816461	0.000000000	0.000000000
26	0.000000000	0.000000000	-0.257129093	0.000000000	0.000000000

Network 2_{adj} – Edges between past-month PTSD symptoms at baseline and SCF at follow-up, additionally adjusted for SCF at baseline – CCA

	SCF at follow-up
1 – Age	-0.018601803
2 – Sex	-0.037005866
3 – Education	0.000000000
4 – Lifetime depression	0.000000000
5 – Alcohol use	0.000000000
6 – B1	0.000000000
7 – B2	0.000000000
8 – B3	0.023040254
9 – B4	0.018992842
10 – B5	0.000000000
11 – C1	0.000000000
12 – C2	0.007483040
13 – D1	0.000000000
14 – D2	-0.042292966
15 – D3	-0.034798418
16 – D4	-0.010326767
17 – D5	0.000000000
18 – D6	0.000000000
19 – D7	-0.002427592
20 – E1	0.000000000
21 – E2	0.051854335
22 – E3	0.000000000
23 – E4	0.000000000
24 – E5	-0.143200815
25 – E6	0.000000000
26 – SCF at baseline	0.322398345
27 – SCF at follow-up	0.000000000

```
=== Estimated network ===
Number of nodes: 27
Number of non-zero edges: 203 / 351
Mean weight: 0.02297792
Network stored in x$graph
```

```
> N2bAdj$graph
             1           2           3           4           5           6           7
1   0.000000000 -0.192405100  0.058226476 -0.057662022 -0.0024383996 -0.013070032  0.00000000
2  -0.192405100  0.000000000  0.000000000  0.071172329 -0.0112039172  0.026835651  0.00000000
3   0.058226476  0.000000000  0.000000000  0.000000000 -0.0027839135  0.000000000  0.00000000
4  -0.057662022  0.071172329  0.000000000  0.000000000  0.0647848817  0.039988674  0.00000000
5  -0.002438400 -0.011203917 -0.002783914  0.064784882  0.0000000000  0.000000000  0.00000000
6  -0.013070032  0.026835651  0.000000000  0.039988674  0.0000000000  0.000000000  0.17405324
7   0.000000000  0.000000000  0.000000000  0.000000000  0.0000000000  0.174053242  0.00000000
8   0.000000000  0.000000000  0.000000000  0.000000000  0.0000000000  0.107413549  0.19136736
9   0.000000000  0.002267381  0.000000000  0.000000000  0.0000000000  0.236189412  0.01128765
10  0.000000000  0.000000000  0.000000000  0.000000000  0.0000000000  0.081065758  0.13573789
11 -0.004303906  0.000000000  0.000000000  0.011447102  0.0315656924  0.107945938  0.03983502
12 -0.015341925  0.000000000  0.000000000  0.000000000  0.0000000000  0.017317159  0.04792032
13  0.000000000  0.000000000 -0.021882856  0.000000000  0.0000000000  0.001119803  0.06083199
14 -0.034436067  0.000000000  0.000000000  0.043006602  0.0000000000  0.000000000  0.00000000
15  0.000000000  0.000000000  0.000000000  0.016786908  0.0009120129  0.025460764  0.00000000
16  0.000000000  0.000000000  0.000000000  0.000000000  0.0000000000  0.106590459  0.03676057
17  0.000000000  0.000000000 -0.041675494  0.000000000  0.0032841932  0.019153052  0.02634158
18 -0.048817648  0.000000000  0.000000000  0.036404591  0.0317452853  0.020290332  0.00000000
19 -0.059063520  0.000000000  0.000000000  0.018149521  0.0286523352  0.015002370  0.00000000
20 -0.060384211  0.000000000  0.000000000  0.006594345  0.0133734336  0.006785708  0.00000000
21  0.000000000 -0.023544906  0.000000000  0.000000000  0.0136029244  0.000000000  0.04209430
22 -0.021302491  0.000000000 -0.021606272  0.000000000  0.0224551551  0.000000000  0.05247730
23  0.000000000  0.000000000  0.000000000  0.000000000  0.0000000000  0.000000000  0.10286852
24  0.000000000  0.000000000  0.000000000  0.063288214  0.0000000000  0.003760892  0.00000000
25  0.000000000  0.036100935  0.000000000  0.005930214  0.0273032586  0.016840247  0.06582765
26 -0.007661392  0.024809127  0.000000000 -0.017731606 -0.0487640591  0.000000000 -0.01484503
27 -0.018601803 -0.037005866  0.000000000  0.000000000  0.0000000000  0.000000000  0.00000000

             8           9           10          11          12          13
1   0.000000000  0.000000000  0.000000000 -0.004303906 -0.015341925  0.000000000
2   0.000000000  0.002267381  0.000000000  0.000000000  0.000000000  0.000000000
3   0.000000000  0.000000000  0.000000000  0.000000000  0.000000000 -0.021882856
4   0.000000000  0.000000000  0.000000000  0.011447102  0.000000000  0.000000000
5   0.000000000  0.000000000  0.000000000  0.031565692  0.000000000  0.000000000
6   0.107413549  0.236189412  0.081065758  0.107945938  0.017317159  0.001119803
7   0.191367362  0.011287652  0.135737890  0.039835020  0.047920318  0.060831990
8   0.000000000  0.116804650  0.136086439  0.062407363  0.023234805  0.000000000
9   0.116804650  0.000000000  0.180613633  0.162915217  0.125490923  0.000000000
10  0.136086439  0.180613633  0.000000000  0.014861121  0.121970988  0.000000000
11  0.062407363  0.162915217  0.014861121  0.000000000  0.265078359  0.086517054
12  0.023234805  0.125490923  0.121970988  0.265078359  0.000000000  0.125263657
13  0.000000000  0.000000000  0.000000000  0.086517054  0.125263657  0.000000000
14  0.000000000  0.000000000  0.000000000  0.000000000  0.008817317  0.000000000
15  0.008187151  0.112248729  0.020483505  0.078380220  0.020922122  0.035203059
16  0.003462881  0.026485348  0.126748502  0.009569166  0.042012427  0.008585713
17  0.018367056  0.000000000  0.010492925  0.000000000  0.103492004  0.038779646
18  0.000000000  0.000000000  0.000000000  0.001591508  0.005892521  0.012427498
19  0.025538028  0.000000000  0.000000000  0.054778314  0.034713139  0.000000000
20  0.027808688  0.016155225  0.034078941  0.028675857  0.000000000  0.004343556
21  0.000000000  0.000000000  0.036720712  0.000000000  0.000000000  0.007084293
22  0.000000000  0.000000000  0.004142159  0.034918594  0.075531387  0.021453845
23  0.057341372  0.000000000  0.039742905  0.003296400  0.036747976  0.000000000
24  0.006485103  0.000000000  0.000000000  0.000000000  0.000000000  0.064335829
25  0.009730073  0.006416203  0.005136737  0.030547711  0.000000000  0.000000000
26 -0.020664334 -0.015203540 -0.026783743 -0.041130160  0.000000000 -0.053320358
27  0.023040254  0.018992842  0.000000000  0.000000000  0.007483040  0.000000000
```

	14	15	16	17	18	19
1	-0.0344360672	0.0000000000	0.0000000000	0.0000000000	-0.048817648	-0.059063520
2	0.0000000000	0.0000000000	0.0000000000	0.0000000000	0.000000000	0.000000000
3	0.0000000000	0.0000000000	0.0000000000	-0.0416754939	0.000000000	0.000000000
4	0.0430066017	0.0167869083	0.0000000000	0.0000000000	0.036404591	0.018149521
5	0.0000000000	0.0009120129	0.0000000000	0.0032841932	0.031745285	0.028652335
6	0.0000000000	0.0254607641	0.1065904589	0.0191530519	0.020290332	0.015002370
7	0.0000000000	0.0000000000	0.0367605669	0.0263415782	0.000000000	0.000000000
8	0.0000000000	0.0081871514	0.0034628814	0.0183670563	0.000000000	0.025538028
9	0.0000000000	0.1122487285	0.0264853485	0.0000000000	0.000000000	0.000000000
10	0.0000000000	0.0204835047	0.1267485023	0.0104929249	0.000000000	0.000000000
11	0.0000000000	0.0783802198	0.0095691658	0.0000000000	0.001591508	0.054778314
12	0.0088173173	0.0209221221	0.0420124265	0.1034920040	0.005892521	0.034713139
13	0.0000000000	0.0352030589	0.0085857125	0.0387796460	0.012427498	0.000000000
14	0.0000000000	0.1557680047	0.2512859097	0.0966010795	0.123352745	0.029104811
15	0.1557680047	0.0000000000	0.3156621610	0.0410197660	0.042016717	0.000000000
16	0.2512859097	0.3156621610	0.0000000000	0.0003399022	0.049106303	0.000000000
17	0.0966010795	0.0410197660	0.0003399022	0.0000000000	0.126114997	0.071238643
18	0.1233527453	0.0420167172	0.0491063029	0.1261149975	0.000000000	0.329481903
19	0.0291048111	0.0000000000	0.0000000000	0.0712386429	0.329481903	0.000000000
20	0.0820691264	0.0000000000	0.1060412224	0.0000000000	0.049111369	0.166775064
21	0.0090534928	0.0366311679	0.0000000000	0.0718428980	0.029163232	0.022126668
22	0.0471805915	0.0000000000	0.0507365452	0.0000000000	0.078006302	0.000000000
23	0.0002846719	0.0000000000	0.0641862491	0.0428261959	0.016323299	0.069945356
24	0.0433999168	0.0051643295	0.0000000000	0.1613111859	0.139227156	0.003164594
25	0.0000000000	0.0000000000	0.0000000000	0.0916072700	0.013024879	0.085112426
26	0.0000000000	0.0000000000	0.0000000000	-0.0270955152	-0.002948077	-0.061801170
27	-0.0422929662	-0.0347984179	-0.0103267669	0.0000000000	0.000000000	-0.002427592

	20	21	22	23	24	25
1	-0.060384211	0.000000000	-0.021302491	0.0000000000	0.000000000	0.000000000
2	0.000000000	-0.023544906	0.000000000	0.0000000000	0.000000000	0.036100935
3	0.000000000	0.000000000	-0.021606272	0.0000000000	0.000000000	0.000000000
4	0.006594345	0.000000000	0.000000000	0.0000000000	0.063288214	0.005930214
5	0.013373434	0.013602924	0.022455155	0.0000000000	0.000000000	0.027303259
6	0.006785708	0.000000000	0.000000000	0.0000000000	0.003760892	0.016840247
7	0.000000000	0.042094298	0.052477297	0.1028685209	0.000000000	0.065827653
8	0.027808688	0.000000000	0.000000000	0.0573413723	0.006485103	0.009730073
9	0.016155225	0.000000000	0.000000000	0.0000000000	0.000000000	0.006416203
10	0.034078941	0.036720712	0.004142159	0.0397429052	0.000000000	0.005136737
11	0.028675857	0.000000000	0.034918594	0.0032964005	0.000000000	0.030547711
12	0.000000000	0.000000000	0.075531387	0.0367479762	0.000000000	0.000000000
13	0.004343556	0.007084293	0.021453845	0.0000000000	0.064335829	0.000000000
14	0.082069126	0.009053493	0.047180592	0.0002846719	0.043399917	0.000000000
15	0.000000000	0.036631168	0.000000000	0.0000000000	0.005164330	0.000000000
16	0.106041222	0.000000000	0.050736545	0.0641862491	0.000000000	0.000000000
17	0.000000000	0.071842898	0.000000000	0.0428261959	0.161311186	0.091607270
18	0.049111369	0.029163232	0.078006302	0.0163232992	0.139227156	0.013024879
19	0.166775064	0.022126668	0.000000000	0.0699453559	0.003164594	0.085112426
20	0.000000000	0.151560020	0.000000000	0.0093854722	0.089127509	0.016512928
21	0.151560020	0.000000000	0.081143455	0.0590659429	0.000000000	0.000000000
22	0.000000000	0.081143455	0.000000000	0.2384048115	0.000000000	0.041694004
23	0.009385472	0.059065943	0.238404812	0.0000000000	0.084830965	0.069326654
24	0.089127509	0.000000000	0.000000000	0.0848309645	0.000000000	0.173241631
25	0.016512928	0.000000000	0.041694004	0.0693266541	0.173241631	0.000000000
26	-0.113419968	-0.013552817	0.000000000	-0.0507767538	-0.241378871	-0.040708490
27	0.000000000	0.051854335	0.000000000	0.0000000000	-0.143200815	0.000000000

	26	27
1	-0.007661392	-0.018601803
2	0.024809127	-0.037005866
3	0.000000000	0.000000000
4	-0.017731606	0.000000000
5	-0.048764059	0.000000000
6	0.000000000	0.000000000
7	-0.014845032	0.000000000
8	-0.020664334	0.023040254
9	-0.015203540	0.018992842
10	-0.026783743	0.000000000
11	-0.041130160	0.000000000
12	0.000000000	0.007483040
13	-0.053320358	0.000000000
14	0.000000000	-0.042292966
15	0.000000000	-0.034798418
16	0.000000000	-0.010326767
17	-0.027095515	0.000000000
18	-0.002948077	0.000000000
19	-0.061801170	-0.002427592
20	-0.113419968	0.000000000
21	-0.013552817	0.051854335
22	0.000000000	0.000000000
23	-0.050776754	0.000000000
24	-0.241378871	-0.143200815
25	-0.040708490	0.000000000
26	0.000000000	0.322398345
27	0.322398345	0.000000000

Network 3 – Edges between lifetime PTSD symptoms and SCF at baseline – CCA

	SCF at baseline
1 – Age	-0.04116977
2 – Sex	0.04142686
3 – Education	0.01473843
4 – Lifetime depression	-0.01977618
5 – Alcohol use	-0.03624218
6 – B1	0.00000000
7 – B2	0.00000000
8 – B3	-0.04290765
9 – B4	-0.03959501
10 – B5	-0.05665157
11 – C1	-0.05569306
12 – C2	0.00000000
13 – D1	-0.13331967
14 – D2	0.00000000
15 – D3	0.00000000
16 – D4	0.00000000
17 – D5	-0.06266350
18 – D6	0.00000000
19 – D7	-0.04147089
20 – E1	-0.06739588
21 – E2	0.00000000
22 – E3	0.00000000
23 – E4	-0.04972839
24 – E5	-0.24471612
25 – E6	0.00000000
26 – SCF at baseline	0.00000000

```
=== Estimated network ===
Number of nodes: 26
Number of non-zero edges: 206 / 325
Mean weight: 0.02488427
Network stored in x$graph
```

```
> N3b$graph
              1            2           3           4           5           6           7
1   0.000000000 -0.181705404  0.072638739 -0.030307189  0.000000000 0.026201094 0.0000000000
2  -0.181705404  0.000000000  0.000000000  0.066523214 -0.040724230 0.016587091 0.0000000000
3   0.072638739  0.000000000  0.000000000 -0.010776974 -0.013016686 0.000000000 0.0000000000
4  -0.030307189  0.066523214 -0.010776974  0.000000000  0.046049605 0.000000000 0.0000000000
5   0.000000000 -0.040724230 -0.013016686  0.046049605  0.000000000 0.000000000 0.0035853030
6   0.026201094  0.016587091  0.000000000  0.000000000  0.000000000 0.000000000 0.1798084792
7   0.000000000  0.000000000  0.000000000  0.000000000  0.003585303 0.179808479 0.0000000000
8  -0.012004636  0.000000000  0.000000000  0.039777052  0.000000000 0.114199473 0.1985959416
9   0.000000000  0.005385924  0.000000000  0.010645006  0.000000000 0.249758762 0.0432703436
10 -0.059977811  0.000000000  0.000000000  0.004759357  0.000000000 0.027056973 0.1561096770
11 -0.031169871  0.000000000 -0.003313508  0.016895019  0.010222074 0.128377894 0.0769193993
12  0.000000000  0.004553601  0.000000000  0.013551978  0.000000000 0.028154766 0.0560359247
13  0.046632849  0.000000000 -0.006735088  0.000000000  0.000000000 0.037834729 0.0330691385
14 -0.046209442  0.000000000  0.000000000  0.050690664  0.000000000 0.020389663 0.0000000000
15  0.000000000  0.029014505  0.000000000  0.063596799  0.038204134 0.037171889 0.0056217669
16 -0.030631589  0.043413479  0.000000000  0.000000000  0.000000000 0.102921199 0.0002877571
17  0.009371078  0.000000000 -0.046755791  0.000000000  0.029171928 0.021628465 0.0000000000
18 -0.092309196  0.000000000  0.006870357  0.024373274  0.023027409 0.000000000 0.0000000000
19 -0.017839641  0.000000000  0.000000000  0.050951254  0.016894898 0.000000000 0.0000000000
20 -0.080466215  0.000000000  0.026380718  0.003625686  0.030561016 0.008243744 0.0193379833
21  0.000000000 -0.012387465  0.000000000  0.000000000  0.048290855 0.000000000 0.0201178867
22 -0.018479718  0.000000000 -0.028698718  0.000000000  0.000000000 0.041043769 0.0444191039
23  0.000000000  0.014762434  0.000000000  0.000000000  0.000000000 0.000000000 0.0575952732
24  0.000000000  0.000000000  0.000000000  0.049420557  0.029699278 0.000000000 0.0000000000
25  0.000000000  0.021347718  0.000000000  0.016358251  0.041795001 0.006948511 0.0808615765
26 -0.041169770  0.041426856  0.014738434 -0.019776181 -0.036242176 0.000000000 0.0000000000


              8            9            10          11          12           13          14
1  -0.012004636  0.000000000 -0.0599778112 -0.031169871 0.000000000  0.046632849 -0.046209442
2   0.000000000  0.005385924  0.0000000000  0.000000000 0.004553601  0.000000000  0.000000000
3   0.000000000  0.000000000  0.0000000000 -0.003313508 0.000000000 -0.006735088  0.000000000
4   0.039777052  0.010645006  0.0047593567  0.016895019 0.013551978  0.000000000  0.050690664
5   0.000000000  0.000000000  0.0000000000  0.010222074 0.000000000  0.000000000  0.000000000
6   0.114199473  0.249758762  0.0270569726  0.128377894 0.028154766  0.037834729  0.020389663
7   0.198595942  0.043270344  0.1561096770  0.076919399 0.056035925  0.033069139  0.000000000
8   0.000000000  0.071575718  0.1453503577  0.029726444 0.048763136  0.021159459  0.000000000
9   0.071575718  0.000000000  0.1465217089  0.082336955 0.141053038  0.000000000  0.043203986
10  0.145350358  0.146521709  0.0000000000  0.040138058 0.106140889  0.000000000  0.000000000
11  0.029726444  0.082336955  0.0401380579  0.000000000 0.333805323  0.011666382  0.000000000
12  0.048763136  0.141053038  0.1061408888  0.333805323 0.000000000  0.023488683  0.003164718
13  0.021159459  0.000000000  0.0000000000  0.011666382 0.023488683  0.000000000  0.026525564
14  0.000000000  0.043203986  0.0000000000  0.000000000 0.003164718  0.026525564  0.000000000
15  0.002722143  0.068383605  0.0046022186  0.067622180 0.000000000  0.000000000  0.141177754
16  0.006503824  0.062619436  0.0635196601  0.028303170 0.038084299  0.000000000  0.250534624
17  0.011222570  0.000000000  0.0004685151  0.000000000 0.050988106  0.022321342  0.079426770
18  0.000000000  0.000000000  0.0000000000  0.000000000 0.038794204  0.000000000  0.154403675
19  0.057629918  0.008840331  0.0000000000  0.055973246 0.041817115  0.000000000  0.049749941
20  0.000000000  0.004345895  0.0573223331  0.004299508 0.000000000  0.010965473  0.053417171
21  0.000000000  0.000000000  0.0000000000  0.000000000 0.000000000  0.059688689  0.019754649
22  0.031354718  0.000000000  0.0061467210  0.031744748 0.060448237  0.000000000  0.051356926
23  0.089033745  0.000000000  0.1101641954  0.007854134 0.016605123  0.036835962  0.000000000
24  0.000000000  0.000000000  0.0087278132  0.000000000 0.000000000  0.067695404  0.037818295
25  0.000000000  0.013196779  0.0018418601  0.000000000 0.003415276  0.000000000  0.000000000
26 -0.042907653 -0.039595005 -0.0566515713 -0.055693062 0.000000000 -0.133319672  0.000000000
```

	15	16	17	18	19	20	21
1	0.000000000	-0.0306315885	0.0093710783	-0.092309196	-0.017839641	-0.080466215	0.00000000
2	0.029014505	0.0434134786	0.0000000000	0.000000000	0.000000000	0.000000000	-0.01238746
3	0.000000000	0.0000000000	-0.0467557911	0.006870357	0.000000000	0.026380718	0.00000000
4	0.063596799	0.0000000000	0.0000000000	0.024373274	0.050951254	0.003625686	0.00000000
5	0.038204134	0.0000000000	0.0291719285	0.023027409	0.016894898	0.030561016	0.04829086
6	0.037171889	0.1029211990	0.0216284648	0.000000000	0.000000000	0.008243744	0.00000000
7	0.005621767	0.0002877571	0.0000000000	0.000000000	0.000000000	0.019337983	0.02011789
8	0.002722143	0.0065038245	0.0112225701	0.000000000	0.057629918	0.000000000	0.00000000
9	0.068383605	0.0626194360	0.0000000000	0.000000000	0.008840331	0.004345895	0.00000000
10	0.004602219	0.0635196601	0.0004685151	0.000000000	0.000000000	0.057322333	0.00000000
11	0.067622180	0.0283031704	0.0000000000	0.000000000	0.055973246	0.004299508	0.00000000
12	0.000000000	0.0380842988	0.0509881064	0.038794204	0.041817115	0.000000000	0.00000000
13	0.000000000	0.0000000000	0.0223213417	0.000000000	0.000000000	0.010965473	0.05968869
14	0.141177754	0.2505346238	0.0794267701	0.154403675	0.049749941	0.053417171	0.01975465
15	0.000000000	0.2736460140	0.0201836092	0.022828282	0.000000000	0.026844619	0.06472508
16	0.273646014	0.0000000000	0.0047806044	0.033193904	0.011526811	0.120133192	0.03451468
17	0.020183609	0.0047806044	0.0000000000	0.163031570	0.062205958	0.023125106	0.01944338
18	0.022828282	0.0331939035	0.1630315704	0.000000000	0.314019251	0.095617382	0.06336644
19	0.000000000	0.0115268106	0.0622059583	0.314019251	0.000000000	0.136545669	0.05227750
20	0.026844619	0.1201331920	0.0231251056	0.095617382	0.136545669	0.000000000	0.14357630
21	0.064725080	0.0345146769	0.0194433788	0.063366437	0.052277495	0.143576298	0.00000000
22	0.000000000	0.0409806767	0.0000000000	0.040434624	0.006229072	0.016111074	0.12291634
23	0.000000000	0.0174336268	0.0000000000	0.067310911	0.009111983	0.034436263	0.07511742
24	0.014038871	0.0029808217	0.1803487788	0.105977819	0.025457505	0.084539381	0.05724072
25	0.000000000	0.0257897063	0.0846617568	0.027089466	0.076245562	0.055869263	0.00000000
26	0.000000000	0.0000000000	-0.0626634952	0.000000000	-0.041470890	-0.067395877	0.00000000

	22	23	24	25	26
1	-0.018479718	0.000000000	0.000000000	0.000000000	-0.04116977
2	0.000000000	0.014762434	0.000000000	0.021347718	0.04142686
3	-0.028698718	0.000000000	0.000000000	0.000000000	0.01473843
4	0.000000000	0.000000000	0.049420557	0.016358251	-0.01977618
5	0.000000000	0.000000000	0.029699278	0.041795001	-0.03624218
6	0.041043769	0.000000000	0.000000000	0.006948511	0.00000000
7	0.044419104	0.057595273	0.000000000	0.080861576	0.00000000
8	0.031354718	0.089033745	0.000000000	0.000000000	-0.04290765
9	0.000000000	0.000000000	0.000000000	0.013196779	-0.03959501
10	0.006146721	0.110164195	0.008727813	0.001841860	-0.05665157
11	0.031744748	0.007854134	0.000000000	0.000000000	-0.05569306
12	0.060448237	0.016605123	0.000000000	0.003415276	0.00000000
13	0.000000000	0.036835962	0.067695404	0.000000000	-0.13331967
14	0.051356926	0.000000000	0.037818295	0.000000000	0.00000000
15	0.000000000	0.000000000	0.014038871	0.000000000	0.00000000
16	0.040980677	0.017433627	0.002980822	0.025789706	0.00000000
17	0.000000000	0.000000000	0.180348779	0.084661757	-0.06266350
18	0.040434624	0.067310911	0.105977819	0.027089466	0.00000000
19	0.006229072	0.009111983	0.025457505	0.076245562	-0.04147089
20	0.016111074	0.034436263	0.084539381	0.055869263	-0.06739588
21	0.122916340	0.075117418	0.057240719	0.000000000	0.00000000
22	0.000000000	0.275716164	0.000000000	0.000000000	0.00000000
23	0.275716164	0.000000000	0.058069975	0.087989804	-0.04972839
24	0.000000000	0.058069975	0.000000000	0.196406770	-0.24471612
25	0.000000000	0.087989804	0.196406770	0.000000000	0.00000000
26	0.000000000	-0.049728390	-0.244716119	0.000000000	0.00000000

Network 4 – Edges between lifetime PTSD symptoms at baseline and SCF at follow-up – CCA

	SCF at follow-up
1 – Age	-0.049467036
2 – Sex	-0.027044927
3 – Education	0.000000000
4 – Lifetime depression	0.000000000
5 – Alcohol use	0.000000000
6 – B1	0.000000000
7 – B2	-0.005277909
8 – B3	0.000000000
9 – B4	0.000000000
10 – B5	0.000000000
11 – C1	0.000000000
12 – C2	0.000000000
13 – D1	-0.047506342
14 – D2	-0.036369934
15 – D3	-0.047103170
16 – D4	-0.036339135
17 – D5	0.000000000
18 – D6	0.000000000
19 – D7	-0.061782414
20 – E1	-0.008377292
21 – E2	0.000000000
22 – E3	0.001680389
23 – E4	0.000000000
24 – E5	-0.188807516
25 – E6	-0.005903650
26 – SCF at follow-up	0.000000000

```
=== Estimated network ===
Number of nodes: 26
Number of non-zero edges: 203 / 325
Mean weight: 0.02650716
Network stored in x$graph
```

```
> N4b$graph
```

	1	2	3	4	5	6	7
1	0.000000000	-0.181705486	0.068136191	-0.029158407	0.000000000	0.018517338	0.000000000
2	-0.181705486	0.000000000	0.000000000	0.061699287	-0.040142749	0.012370566	0.000000000
3	0.068136191	0.000000000	0.000000000	-0.009179000	-0.011128225	0.000000000	0.000000000
4	-0.029158407	0.061699287	-0.009179000	0.000000000	0.045602196	0.000000000	0.000000000
5	0.000000000	-0.040142749	-0.011128225	0.045602196	0.000000000	0.000000000	0.005093536
6	0.018517338	0.012370566	0.000000000	0.000000000	0.000000000	0.000000000	0.178878293
7	0.000000000	0.000000000	0.000000000	0.000000000	0.005093536	0.178878293	0.000000000
8	-0.008146658	0.000000000	0.000000000	0.041413368	0.000000000	0.113748261	0.198210902
9	0.000000000	0.001119189	0.000000000	0.012386563	0.000000000	0.249463614	0.044119841
10	-0.055145546	0.000000000	0.000000000	0.005555153	0.000000000	0.027090882	0.155765778
11	-0.026598741	0.000000000	-0.003281371	0.019167298	0.014473818	0.128076706	0.077165209
12	0.000000000	0.000442503	0.000000000	0.013653654	0.000000000	0.028102089	0.055671550
13	0.046536350	0.000000000	-0.006600371	0.000000000	0.000000000	0.039788802	0.034008139
14	-0.046614958	0.000000000	0.000000000	0.050718397	0.000000000	0.019889461	0.000000000
15	0.000000000	0.025023978	0.000000000	0.063214319	0.037739948	0.036959085	0.004833830
16	-0.032650953	0.038623829	0.000000000	0.000000000	0.000000000	0.102015151	0.000000000
17	0.005919645	0.000000000	-0.044532212	0.000000000	0.031872543	0.023793373	0.000000000
18	-0.089563494	0.000000000	0.000000000	0.024954864	0.023218962	0.000000000	0.000000000
19	-0.017584906	0.000000000	0.000000000	0.050870204	0.018491468	0.000000000	0.000000000
20	-0.075559181	0.000000000	0.019467862	0.005011717	0.033297500	0.007548577	0.019575121
21	0.000000000	-0.011246556	0.000000000	0.000000000	0.048469571	0.000000000	0.020401350
22	-0.017027507	0.000000000	-0.026739704	0.000000000	0.000000000	0.040979190	0.044152013
23	0.000000000	0.006586429	0.000000000	0.000000000	0.000000000	0.000000000	0.057507596
24	0.000000000	0.000000000	0.000000000	0.055475556	0.040959305	0.000000000	0.000000000
25	0.000000000	0.012910340	0.000000000	0.016602137	0.041090962	0.007202804	0.080589853
26	-0.049467036	-0.027044927	0.000000000	0.000000000	0.000000000	0.000000000	-0.005277909

	8	9	10	11	12	13	14
1	-0.008146658	0.000000000	-0.0551455457	-0.026598741	0.000000000	0.046536350	-0.046614958
2	0.000000000	0.001119189	0.0000000000	0.000000000	0.000442503	0.000000000	0.000000000
3	0.000000000	0.000000000	0.0000000000	-0.003281371	0.000000000	-0.006600371	0.000000000
4	0.041413368	0.012386563	0.0055551534	0.019167298	0.013653654	0.000000000	0.050718397
5	0.000000000	0.000000000	0.0000000000	0.014473818	0.000000000	0.000000000	0.000000000
6	0.113748261	0.249463614	0.0270908825	0.128076706	0.028102089	0.039788802	0.019889461
7	0.198210902	0.044119841	0.1557657778	0.077165209	0.055671550	0.034008139	0.000000000
8	0.000000000	0.074438372	0.1485849164	0.032789268	0.048658643	0.029913816	0.000000000
9	0.074438372	0.000000000	0.1493776511	0.085519748	0.141455307	0.000000000	0.045168501
10	0.148584916	0.149377651	0.0000000000	0.044414718	0.105971054	0.000000000	0.000000000
11	0.032789268	0.085519748	0.0444147175	0.000000000	0.333236983	0.022032802	0.000000000
12	0.048658643	0.141455307	0.1059710536	0.333236983	0.000000000	0.024976186	0.003363152
13	0.029913816	0.000000000	0.0000000000	0.022032802	0.024976186	0.000000000	0.023873685
14	0.000000000	0.045168501	0.0000000000	0.000000000	0.003363152	0.023873685	0.000000000
15	0.003073660	0.068762823	0.0045759015	0.067934683	0.000000000	0.000000000	0.138739079
16	0.007709072	0.063063955	0.0630296926	0.029380863	0.037642079	0.000000000	0.247678957
17	0.018152370	0.000000000	0.0039091693	0.000000000	0.053892203	0.031234126	0.079287076
18	0.000000000	0.000000000	0.0000000000	0.001072182	0.039488860	0.000000000	0.154081704
19	0.061236582	0.012057056	0.0000000000	0.060397247	0.040650197	0.000000000	0.047012578
20	0.000000000	0.009807131	0.0613905195	0.011154657	0.000000000	0.019619498	0.053400708
21	0.000000000	0.000000000	0.0000000000	0.000000000	0.000000000	0.059768303	0.019997628
22	0.031928904	0.000000000	0.0065606245	0.032367140	0.060126460	0.000000000	0.051597886
23	0.092960757	0.000000000	0.1128255148	0.013075042	0.016978039	0.043949200	0.000000000
24	0.001002194	0.000000000	0.0316963662	0.000000000	0.000000000	0.095516040	0.032227842
25	0.000000000	0.017320087	0.0007057533	0.000000000	0.004212007	0.000000000	0.000000000
26	0.000000000	0.000000000	0.0000000000	0.000000000	0.000000000	-0.047506342	-0.036369934

	15	16	17	18	19	20	21
1	0.000000000	-0.032650953	0.005919645	-0.089563494	-0.017584906	-0.075559181	0.00000000
2	0.025023978	0.038623829	0.000000000	0.000000000	0.000000000	0.000000000	-0.01124656
3	0.000000000	0.000000000	-0.044532212	0.000000000	0.000000000	0.019467862	0.00000000
4	0.063214319	0.000000000	0.000000000	0.024954864	0.050870204	0.005011717	0.00000000
5	0.037739948	0.000000000	0.031872543	0.023218962	0.018491468	0.033297500	0.04846957
6	0.036959085	0.102015151	0.023793373	0.000000000	0.000000000	0.007548577	0.00000000
7	0.004833830	0.000000000	0.000000000	0.000000000	0.000000000	0.019575121	0.02040135
8	0.003073660	0.007709072	0.018152370	0.000000000	0.061236582	0.000000000	0.00000000
9	0.068762823	0.063063955	0.000000000	0.000000000	0.012057056	0.009807131	0.00000000
10	0.004575901	0.063029693	0.003909169	0.000000000	0.000000000	0.061390520	0.00000000
11	0.067934683	0.029380863	0.000000000	0.001072182	0.060397247	0.011154657	0.00000000
12	0.000000000	0.037642079	0.053892203	0.039488860	0.040650197	0.000000000	0.00000000
13	0.000000000	0.000000000	0.031234126	0.000000000	0.000000000	0.019619498	0.05976830
14	0.138739079	0.247678957	0.079287076	0.154081704	0.047012578	0.053400708	0.01999763
15	0.000000000	0.270462374	0.019940088	0.022037739	0.000000000	0.025739868	0.06401626
16	0.270462374	0.000000000	0.004333485	0.033459814	0.007919393	0.119043218	0.03436165
17	0.019940088	0.004333485	0.000000000	0.162123224	0.064723387	0.026930203	0.01982018
18	0.022037739	0.033459814	0.162123224	0.000000000	0.312030430	0.096214845	0.06328782
19	0.000000000	0.007919393	0.064723387	0.312030430	0.000000000	0.138418933	0.05206966
20	0.025739868	0.119043218	0.026930203	0.096214845	0.138418933	0.000000000	0.14341098
21	0.064016262	0.034361652	0.019820176	0.063287817	0.052069662	0.143410982	0.00000000
22	0.000000000	0.040997307	0.000000000	0.040746601	0.006312069	0.016370301	0.12262354
23	0.000000000	0.017628462	0.000000000	0.067548394	0.011199554	0.037955897	0.07508282
24	0.006999622	0.000000000	0.199596295	0.107251938	0.027489492	0.100813040	0.05847211
25	0.000000000	0.024753752	0.084487625	0.027286215	0.075022236	0.055688867	0.00000000
26	-0.047103170	-0.036339135	0.000000000	0.000000000	-0.061782414	-0.008377292	0.00000000

	22	23	24	25	26
1	-0.0170275074	0.000000000	0.000000000	0.0000000000	-0.049467036
2	0.0000000000	0.006586429	0.000000000	0.0129103404	-0.027044927
3	-0.0267397042	0.000000000	0.000000000	0.0000000000	0.000000000
4	0.0000000000	0.000000000	0.055475556	0.0166021366	0.000000000
5	0.0000000000	0.000000000	0.040959305	0.0410909624	0.000000000
6	0.0409791902	0.000000000	0.000000000	0.0072028038	0.000000000
7	0.0441520134	0.057507596	0.000000000	0.0805898528	-0.005277909
8	0.0319289039	0.092960757	0.001002194	0.0000000000	0.000000000
9	0.0000000000	0.000000000	0.000000000	0.0173200872	0.000000000
10	0.0065606245	0.112825515	0.031696366	0.0007057533	0.000000000
11	0.0323671404	0.013075042	0.000000000	0.0000000000	0.000000000
12	0.0601264596	0.016978039	0.000000000	0.0042120071	0.000000000
13	0.0000000000	0.043949200	0.095516040	0.0000000000	-0.047506342
14	0.0515978861	0.000000000	0.032227842	0.0000000000	-0.036369934
15	0.0000000000	0.000000000	0.006999622	0.0000000000	-0.047103170
16	0.0409973067	0.017628462	0.000000000	0.0247537522	-0.036339135
17	0.0000000000	0.000000000	0.199596295	0.0844876248	0.000000000
18	0.0407466010	0.067548394	0.107251938	0.0272862154	0.000000000
19	0.0063120694	0.011199554	0.027489492	0.0750222361	-0.061782414
20	0.0163703007	0.037955897	0.100813040	0.0556888666	-0.008377292
21	0.1226235446	0.075082816	0.058472113	0.0000000000	0.000000000
22	0.0000000000	0.274863925	0.000000000	0.0001323152	0.001680389
23	0.2748639251	0.000000000	0.074510922	0.0878524703	0.000000000
24	0.0000000000	0.074510922	0.000000000	0.1974538125	-0.188807516
25	0.0001323152	0.087852470	0.197453812	0.0000000000	-0.005903650
26	0.0016803887	0.000000000	-0.188807516	-0.0059036498	0.000000000

Network 4_{adj} – Edges between lifetime PTSD symptoms at baseline and SCF at follow-up, additionally adjusting for SCF at baseline – CCA

	SCF at follow-up
1 – Age	-0.03163476
2 – Sex	-0.03006110
3 – Education	0.00000000
4 – Lifetime depression	0.00000000
5 – Alcohol use	0.00000000
6 – B1	0.00000000
7 – B2	0.00000000
8 – B3	0.00000000
9 – B4	0.00000000
10 – B5	0.00000000
11 – C1	0.00000000
12 – C2	0.00000000
13 – D1	0.00000000
14 – D2	-0.02242984
15 – D3	-0.03220802
16 – D4	-0.01654734
17 – D5	0.00000000
18 – D6	0.00000000
19 – D7	-0.02853764
20 – E1	0.00000000
21 – E2	0.00000000
22 – E3	0.00000000
23 – E4	0.00000000
24 – E5	-0.08503775
25 – E6	0.00000000
26 – SCF at baseline	0.35546890
27 – SCF at follow-up	0.00000000

```
=== Estimated network ===
Number of nodes: 27
Number of non-zero edges: 208 / 351
Mean weight: 0.02357819
Network stored in x$graph
```

```
> N4bAdj$graph
```

	1	2	3	4	5	6	7
1	0.000000000	-0.175701153	0.058658347	-0.026951325	0.000000000	0.000000000	0.000000000
2	-0.175701153	0.000000000	0.000000000	0.058108024	-0.021907598	0.009079529	0.000000000
3	0.058658347	0.000000000	0.000000000	-0.002050523	-0.002364440	0.000000000	0.000000000
4	-0.026951325	0.058108024	-0.002050523	0.000000000	0.039826818	0.000000000	0.000000000
5	0.000000000	-0.021907598	-0.002364440	0.039826818	0.000000000	0.000000000	0.002273259
6	0.000000000	0.009079529	0.000000000	0.000000000	0.000000000	0.000000000	0.177176479
7	0.000000000	0.000000000	0.000000000	0.000000000	0.002273259	0.177176479	0.000000000
8	-0.003367648	0.000000000	0.000000000	0.039082909	0.000000000	0.113116795	0.195949469
9	0.000000000	0.002704441	0.000000000	0.010861220	0.000000000	0.245387473	0.044972387
10	-0.052975120	0.000000000	0.000000000	0.005484454	0.000000000	0.027466699	0.154006268
11	-0.022140511	0.000000000	0.000000000	0.017554373	0.009337046	0.126273448	0.076963661
12	0.000000000	0.001349270	0.000000000	0.013510618	0.000000000	0.030046664	0.056559181
13	0.026771200	0.000000000	0.000000000	0.000000000	0.000000000	0.037971516	0.032236134
14	-0.043249868	0.000000000	0.000000000	0.050527354	0.000000000	0.020202873	0.000000000
15	0.000000000	0.023457510	0.000000000	0.062492501	0.034847985	0.037721944	0.006011964
16	-0.027960509	0.040812070	0.000000000	0.000000000	0.000000000	0.100500101	0.001491237
17	0.000000000	0.000000000	-0.035792891	0.000000000	0.028398197	0.021875478	0.000000000
18	-0.087015001	0.000000000	0.000000000	0.026051498	0.023132539	0.000000000	0.000000000
19	-0.015600150	0.000000000	0.000000000	0.050433227	0.016864025	0.000000000	0.000000000
20	-0.071916078	0.000000000	0.000000000	0.004691110	0.029748917	0.006671206	0.020297572
21	0.000000000	0.000000000	0.000000000	0.000000000	0.046091542	0.000000000	0.020645803
22	-0.014268734	0.000000000	-0.019362968	0.000000000	0.000000000	0.040544719	0.044248632
23	0.000000000	0.007166737	0.000000000	0.000000000	0.000000000	0.000000000	0.058136455
24	0.000000000	0.000000000	0.000000000	0.049575182	0.030384161	0.000000000	0.000000000
25	0.000000000	0.012098037	0.000000000	0.015765857	0.038664499	0.007430467	0.079840137
26	-0.007518360	0.032762645	0.003897491	-0.012480718	-0.032327934	0.000000000	0.000000000
27	-0.031634758	-0.030061103	0.000000000	0.000000000	0.000000000	0.000000000	0.000000000

	8	9	10	11	12	13	14
1	-0.003367648	0.000000000	-0.052975120	-0.022140511	0.000000000	0.02677120	-0.043249868
2	0.000000000	0.002704441	0.000000000	0.000000000	0.001349270	0.00000000	0.000000000
3	0.000000000	0.000000000	0.000000000	0.000000000	0.000000000	0.00000000	0.000000000
4	0.039082909	0.010861220	0.005484454	0.017554373	0.013510618	0.00000000	0.050527354
5	0.000000000	0.000000000	0.000000000	0.009337046	0.000000000	0.00000000	0.000000000
6	0.113116795	0.245387473	0.027466699	0.126273448	0.030046664	0.03797152	0.020202873
7	0.195949469	0.044972387	0.154006268	0.076963661	0.056559181	0.03223613	0.000000000
8	0.000000000	0.072221025	0.144571731	0.031161992	0.049139329	0.01995649	0.000000000
9	0.072221025	0.000000000	0.145039511	0.083479062	0.139635520	0.00000000	0.043726203
10	0.144571731	0.145039511	0.000000000	0.042101461	0.105350304	0.00000000	0.000000000
11	0.031161992	0.083479062	0.042101461	0.000000000	0.327515996	0.01087826	0.000000000
12	0.049139329	0.139635520	0.105350304	0.327515996	0.000000000	0.02261415	0.004756042
13	0.019956490	0.000000000	0.000000000	0.010878257	0.022614145	0.00000000	0.022056030
14	0.000000000	0.043726203	0.000000000	0.000000000	0.004756042	0.02205603	0.000000000
15	0.002662134	0.067672640	0.005084460	0.066753519	0.000000000	0.00000000	0.139609332
16	0.007868353	0.062798918	0.063108149	0.029478317	0.038263752	0.00000000	0.245955760
17	0.012473420	0.000000000	0.001226349	0.000000000	0.050994628	0.02201528	0.078192987
18	0.000000000	0.000000000	0.000000000	0.000000000	0.040169227	0.00000000	0.152680120
19	0.058371925	0.009997153	0.000000000	0.056956246	0.041585840	0.00000000	0.049847911
20	0.000000000	0.006095357	0.058550747	0.007016083	0.000000000	0.00906431	0.054332949
21	0.000000000	0.000000000	0.000000000	0.000000000	0.000000000	0.05712369	0.020566720
22	0.031934791	0.000000000	0.007844433	0.032505710	0.059744572	0.00000000	0.051657480
23	0.088965100	0.000000000	0.109115216	0.009419055	0.017565833	0.03567849	0.000000000
24	0.000000000	0.000000000	0.011496949	0.000000000	0.000000000	0.06722359	0.034686643
25	0.000000000	0.013921802	0.002420166	0.000000000	0.004000733	0.00000000	0.000000000
26	-0.039176742	-0.033387236	-0.048962829	-0.048723771	0.000000000	-0.12287103	0.000000000
27	0.000000000	0.000000000	0.000000000	0.000000000	0.000000000	0.00000000	-0.022429836

	15	16	17	18	19	20	21
1	0.000000000	-0.0279605092	0.000000000	-0.08701500	-0.015600150	-0.071916078	0.00000000
2	0.023457510	0.0408120700	0.000000000	0.00000000	0.000000000	0.000000000	0.00000000
3	0.000000000	0.0000000000	-0.035792891	0.00000000	0.000000000	0.000000000	0.00000000
4	0.062492501	0.0000000000	0.000000000	0.02605150	0.050433227	0.004691110	0.00000000
5	0.034847985	0.0000000000	0.028398197	0.02313254	0.016864025	0.029748917	0.04609154
6	0.037721944	0.1005001005	0.021875478	0.00000000	0.000000000	0.006671206	0.00000000
7	0.006011964	0.0014912367	0.000000000	0.00000000	0.000000000	0.020297572	0.02064580
8	0.002662134	0.0078683532	0.012473420	0.00000000	0.058371925	0.000000000	0.00000000
9	0.067672640	0.0627989177	0.000000000	0.00000000	0.009997153	0.006095357	0.00000000
10	0.005084460	0.0631081495	0.001226349	0.00000000	0.000000000	0.058550747	0.00000000
11	0.066753519	0.0294783170	0.000000000	0.00000000	0.056956246	0.007016083	0.00000000
12	0.000000000	0.0382637523	0.050994628	0.04016923	0.041585840	0.000000000	0.00000000
13	0.000000000	0.0000000000	0.022015278	0.00000000	0.000000000	0.009064310	0.05712369
14	0.139609332	0.2459557602	0.078192987	0.15268012	0.049847911	0.054332949	0.02056672
15	0.000000000	0.2685429062	0.019300375	0.02398276	0.000000000	0.027027579	0.06314015
16	0.268542906	0.0000000000	0.004996779	0.03475854	0.011596738	0.118196061	0.03445252
17	0.019300375	0.0049967788	0.000000000	0.16010017	0.063093675	0.022928410	0.01997505
18	0.023982762	0.0347585446	0.160100173	0.00000000	0.307926373	0.096683127	0.06333115
19	0.000000000	0.0115967385	0.063093675	0.30792637	0.000000000	0.135795121	0.05235485
20	0.027027579	0.1181960605	0.022928410	0.09668313	0.135795121	0.000000000	0.14159474
21	0.063140152	0.0344525154	0.019975051	0.06333115	0.052354850	0.141594736	0.00000000
22	0.000000000	0.0412650621	0.000000000	0.04147772	0.006980003	0.016597629	0.12084975
23	0.000000000	0.0180306739	0.000000000	0.06740633	0.010420612	0.035353177	0.07470479
24	0.008644323	0.0009057035	0.178679987	0.10465840	0.025775174	0.085362571	0.05743147
25	0.000000000	0.0263806054	0.084001293	0.02900237	0.075463023	0.055977405	0.00000000
26	0.000000000	0.0000000000	-0.056750113	0.00000000	-0.025104219	-0.056050220	0.00000000
27	-0.032208016	-0.0165473380	0.000000000	0.00000000	-0.028537644	0.000000000	0.00000000

	22	23	24	25	26	27
1	-0.0142687336	0.000000000	0.0000000000	0.0000000000	-0.007518360	-0.03163476
2	0.0000000000	0.007166737	0.0000000000	0.0120980373	0.032762645	-0.03006110
3	-0.0193629683	0.000000000	0.0000000000	0.0000000000	0.003897491	0.00000000
4	0.0000000000	0.000000000	0.0495751822	0.0157658570	-0.012480718	0.00000000
5	0.0000000000	0.000000000	0.0303841614	0.0386644992	-0.032327934	0.00000000
6	0.0405447186	0.000000000	0.0000000000	0.0074304674	0.000000000	0.00000000
7	0.0442486323	0.058136455	0.0000000000	0.0798401366	0.000000000	0.00000000
8	0.0319347911	0.088965100	0.0000000000	0.0000000000	-0.039176742	0.00000000
9	0.0000000000	0.000000000	0.0000000000	0.0139218025	-0.033387236	0.00000000
10	0.0078444332	0.109115216	0.0114969489	0.0024201662	-0.048962829	0.00000000
11	0.0325057098	0.009419055	0.0000000000	0.0000000000	-0.048723771	0.00000000
12	0.0597445718	0.017565833	0.0000000000	0.0040007333	0.000000000	0.00000000
13	0.0000000000	0.035678494	0.0672235875	0.0000000000	-0.122871034	0.00000000
14	0.0516574804	0.000000000	0.0346866426	0.0000000000	0.000000000	-0.02242984
15	0.0000000000	0.000000000	0.0086443234	0.0000000000	0.000000000	-0.03220802
16	0.0412650621	0.018030674	0.0009057035	0.0263806054	0.000000000	-0.01654734
17	0.0000000000	0.000000000	0.1786799872	0.0840012930	-0.056750113	0.00000000
18	0.0414777241	0.067406328	0.1046584000	0.0290023668	0.000000000	0.00000000
19	0.0069800035	0.010420612	0.0257751736	0.0754630232	-0.025104219	-0.02853764
20	0.0165976286	0.035353177	0.0853625713	0.0559774054	-0.056050220	0.00000000
21	0.1208497532	0.074704786	0.0574314703	0.0000000000	0.000000000	0.00000000
22	0.0000000000	0.270755530	0.0000000000	0.0002095979	0.000000000	0.00000000
23	0.2707555302	0.000000000	0.0591234619	0.0869238726	-0.044280393	0.00000000
24	0.0000000000	0.059123462	0.0000000000	0.1929591725	-0.193037339	-0.08503775
25	0.0002095979	0.086923873	0.1929591725	0.0000000000	0.000000000	0.00000000
26	0.0000000000	-0.044280393	-0.1930373393	0.0000000000	0.000000000	0.35546890
27	0.0000000000	0.000000000	-0.0850377468	0.0000000000	0.355468898	0.00000000

6. R-packages and versions used

R SessionInfo()

```
> sessionInfo()
R version 4.2.0 (2022-04-22)
Platform: x86_64-apple-darwin17.0 (64-bit)
Running under: macOS Monterey 12.4

Matrix products: default
LAPACK: /Library/Frameworks/R.framework/Versions/4.2/Resources/lib/libRlapack.dylib

locale:
[1] de_DE.UTF-8/de_DE.UTF-8/de_DE.UTF-8/C/de_DE.UTF-8/de_DE.UTF-8

attached base packages:
[1] stats     graphics  grDevices utils     datasets  methods   base

other attached packages:
[1] psych_2.2.5               NetworkComparisonTest_2.2.1 dplyr_1.0.9
[4] mgm_1.2-12                OpenMx_2.20.6               qgraph_1.9.2
[7] bootnet_1.5               ggplot2_3.3.6               haven_2.5.0

loaded via a namespace (and not attached):
  [1] minqa_1.2.4         colorspace_2.0-3    pryr_0.1.5          ellipsis_0.3.2
  [5] class_7.3-20        htmlTable_2.4.0     corpcor_1.6.10      base64enc_0.1-3
  [9] rstudioapi_0.13     proxy_0.4-26        mice_3.14.0         farver_2.1.0
 [13] lavaan_0.6-11       IsingFit_0.3.1      lubridate_1.8.0     mvtnorm_1.1-3
 [17] fansi_1.0.3         codetools_0.2-18    splines_4.2.0       R.methodsS3_1.8.1
 [21] mnormt_2.0.2        doParallel_1.0.17   knitr_1.39          glasso_1.11
 [25] networktools_1.4.0  Formula_1.2-4       polynom_1.4-1       nloptr_2.0.2
 [29] broom_0.8.0         cluster_2.1.3       png_0.1-7           R.oo_1.24.0
 [33] readr_2.1.2         compiler_4.2.0      backports_1.4.1     Matrix_1.4-1
 [37] fastmap_1.1.0       cli_3.3.0           htmltools_0.5.2     tools_4.2.0
 [41] igraph_1.3.1        gtable_0.3.0        glue_1.6.2          reshape2_1.4.4
 [45] Rcpp_1.0.8.3        carData_3.0-5       vctrs_0.4.1         gdata_2.18.0.1
 [49] nlme_3.1-157        iterators_1.0.14    eigenmodel_1.11     xfun_0.31
 [53] stringr_1.4.0       lme4_1.1-29         lifecycle_1.0.1     weights_1.0.4
 [57] gtools_3.9.2.1      candisc_0.8-6       MASS_7.3-56         scales_1.2.0
 [61] heplots_1.3-9       hms_1.1.1           parallel_4.2.0      NetworkToolbox_1.4.2
 [65] smacof_2.1-5        RColorBrewer_1.1-3  pbapply_1.5-0       gridExtra_2.3
 [69] pander_0.6.5        IsingSampler_0.2.1  rpart_4.1.16        latticeExtra_0.6-29
 [73] stringi_1.7.6       foreach_1.5.2       plotrix_3.8-2       e1071_1.7-9
 [77] checkmate_2.1.0     boot_1.3-28         shape_1.4.6         matrixStats_0.62.0
 [81] rlang_1.0.2         pkgconfig_2.0.3     lattice_0.20-45     purrr_0.3.4
 [85] labeling_0.4.2      rapportools_1.1     htmlwidgets_1.5.4   tidyselect_1.1.2
 [89] plyr_1.8.7          magrittr_2.0.3      R6_2.5.1            magick_2.7.3
 [93] snow_0.4-4          generics_0.1.2      nnls_1.4            Hmisc_4.7-0
 [97] pillar_1.7.0        foreign_0.8-82      withr_2.5.0         survival_3.3-1
[101] abind_1.4-5         nnet_7.3-17         tibble_3.1.7        crayon_1.5.1
[105] car_3.0-13          wordcloud_2.6       fdrtool_1.2.17      utf8_1.2.2
[109] ellipse_0.4.2       tmvnsim_1.0-2       tzdb_0.3.0          jpeg_0.1-9
[113] grid_4.2.0          pbivnorm_0.6.0      data.table_1.14.2   forcats_0.5.1
[117] digest_0.6.29       tidyr_1.2.0         R.utils_2.11.0      RcppParallel_5.1.5
[121] glmnet_4.1-4        stats4_4.2.0        munsell_0.5.0
```

7. References

Epskamp, S. (2018). *New featues in qgraph 1.5*. PsychoSystems Project. http://psychosystems.org/qgraph_1.5

Epskamp, S., Borsboom, D., & Fried, E. I. (2018). Estimating psychological networks and their accuracy: A tutorial paper. *Behavior Research Methods*, *50*(1), 195–212. https://doi.org/10.3758/s13428-017-0862-1

Epskamp, S., & Fried, E. I. (2018). A tutorial on regularized partial correlation networks. *Psychological Methods*. https://doi.org/https://doi.org/10.1037/met0000167

Muthén, B. (1984). A general structural equation model with dichotomous, ordered categorical, and continuous latent variable indicators. *Psychometrika*. https://doi.org/10.1007/BF02294210

Williams, D. R., Rhemtulla, M., Wysocki, A. C., & Rast, P. (2019). On Nonregularized Estimation of Psychological Networks. *Multivariate Behavioral Research*. https://doi.org/10.1080/00273171.2019.1575716

Appendix B: Supplementary Materials Study II

eTable B1. Adverse Childhood Experiences (ACEs) by Group

	Overall (n = 434 215)	Comparison group (n = 389 516)[a]	ACEs (n = 45 536)[b]	PTSD (n = 941)	Dissociative disorders (n = 325)	Depression (n = 44 140)	Depression only (n = 43 452)[c]
Types of ACEs n (%)	45 536 / 137 631 (33.09)	40 081 / 126 577 (31.67)	45 536 / 45 536 (100.00)	111 / 189 (58.73)	47 / 79 (59.49)	5381 / 10 914 (49.30)	5301 / 10 790 (49.13)
0	92 095 / 137 631 (66.91)	86 496 / 126 577 (68.33)	0 / 45 536 (0.00)	78 / 189 (41.27)	32 / 79 (40.51)	5533 / 10 914 (50.70)	5489 / 10 790 (50.87)
1	27 975 / 137 631 (20.33)	25 286 / 126 577 (19.98)	27 975 / 45 536 (61.43)	35 / 189 (18.52)	18 / 79 (22.78)	2660 / 10 914 (24.37)	2636 / 10 790 (24.43)
2	10 422 / 137 631 (7.57)	9014 / 126 577 (7.12)	10 422 / 45 536 (22.89)	24 / 189 (12.70)	10 / 79 (12.66)	1385 / 10 914 (12.69)	1374 / 10 790 (12.73)
3	4636 / 137 631 (3.37)	3860 / 126 577 (3.05)	4636 / 45 536 (10.18)	21 / 189 (11.11)	11 / 79 (13.92)	766 / 10,914 (7.02)	747 / 10 790 (6.92)
4	1898 / 137 631 (1.38)	1485 / 126 577 (1.17)	1898 / 45 536 (4.17)	17 / 189 (8.99)	3 / 79 (3.80)	408 / 10 914 (3.74)	394 / 10 790 (3.65)
5	605 / 137 631 (0.44)	436 / 126 577 (0.34)	605 / 45 536 (1.33)	14 / 189 (7.41)	5 / 79 (6.33)	162 / 10 914 (1.48)	150 / 10 790 (1.39)
Physical abuse	11 426 / 140 478 (8.13)	9735 / 129 036 (7.54)	10 914 / 45 536 (23.97)	54 / 200 (27.00)	18 / 82 (21.95)	1660 / 11 297 (14.69)	1620 / 11 164 (14.51)
Emotional abuse	13 215 / 140 412 (9.41)	10 955 / 128 980 (8.49)	12 667 / 45 536 (27.82)	64 / 200 (32.00)	21 / 81 (25.93)	2226 / 11 288 (19.72)	2178 / 11 155 (19.52)
Sexual abuse	12 161 / 139 202 (8.74)	10 524 / 127 956 (8.22)	12 006 / 45 536 (26.37)	52 / 194 (26.80)	26 / 81 (32.10)	1604 / 11 102 (14.45)	1562 / 10 975 (14.23)
Physical neglect	7876 / 139 856 (5.63)	6782 / 128 464 (5.28)	7586 / 45 536 (16.66)	40 / 201 (19.90)	13 / 82 (15.85)	1078 / 11 247 (9.58)	1044 / 11 113 (9.39)
Emotional neglect	31 222 / 140 259 (22.26)	27 020 / 128 831 (20.97)	30 171 / 45 536 (66.26)	87 / 202 (43.07)	33 / 83 (39.76)	4152 / 11 283 (36.80)	4085 / 11 147 (36.65)

ACEs = adverse childhood experiences; PTSD = post-traumatic stress disorder; N = sample size.
The categories are not mutually exclusive. Only available at follow-up, in 2017, as part of the mental health survey.
[a] "Comparison group" refers to participants without PTSD dissociative disorders or depression (PTSD–/Dissociative disorders–/Depression–).
[b] "ACEs" group refers to participants who self-reported that they had at least one type of ACEs as part of the online mental health survey (ACEs+).
[c] "Depression only" group refers to participants with depression but without PTSD or dissociative disorders (Depression+/ PTSD–/Dissociative disorders–).

	Overall (n = 434 215)	Comparison group[a] (n = 389 516)	Comparison group 2[b] (n = 86 496)	ACEs[c] (n = 45 536)	PTSD (n = 941)	Dissociative disorders (n = 325)	Depression (n = 44 140)	Depression only[d] (n = 43 452)	Depression only 2[e] (n = 5489)
Dementia (n, %)	8118 (1.87)	6703 (1.72)	454 (0.52)	266 (0.58)	22 (2.34)	20 (6.15)	1397 (3.16)	1373 (3.16)	48 (0.87)

N = sample size; ACEs = adverse childhood experiences; PTSD = post-traumatic stress disorder. The categories are not mutually exclusive.

[a]"Comparison group" refers to participants without PTSD, dissociative disorders, or depression (PTSD–/Dissociative disorders–/Depression–).

[b]"Comparison group 2" refers to participants without PTSD, dissociative disorders, or depression, who self-reported as part of the online mental health survey that they had no ACEs (ACEs–/PTSD–/Dissociative disorders–/Depression–).

[c]"ACEs" group refers to participants who self-reported that they had at least one type of ACEs, as part of the online mental health survey (ACEs+).

[d]"Depression only" group refers to participants with depression but without PTSD or dissociative disorders (Depression+/ PTSD–/Dissociative disorders–).

[e]"Depression only 2" group refers to participants without PTSD, dissociative disorders, or depression, who self-reported as part of the online mental health survey that they had no ACEs (Depression+/ACEs–/PTSD–/Dissociative disorders–).

eTable B3. Dementia Outcome by Number of Types of Adverse Childhood Experiences (ACEs) (n = 137 631)

Number of ACE types	0 (n = 92 095)	1 (n = 27 975)	2 (n = 10 422)	3 (n = 4636)	4 (n = 1898)	5 (n = 605)
Dementia (n, %)	503 (0.55)	158 (0.56)	64 (0.61)	30 (0.65)	12 (0.63)	2 (0.33)

ACEs = adverse childhood experiences; N = sample size.

The following types of ACEs are included: emotional neglect, physical neglect, emotional abuse, physical abuse, and sexual abuse.

eMethods. Used R Packages and Versions

```
R version 4.2.0 (2022-04-22)

Platform: x86_64-apple-darwin17.0 (64-bit)

Running under: macOS 14.4


Matrix products: default

LAPACK: /Library/Frameworks/R.framework/Versions/4.2/Resources/lib/libRlapa
ck.dylib


locale:

[1] de_DE.UTF-8/de_DE.UTF-8/de_DE.UTF-8/C/de_DE.UTF-8/de_DE.UTF-8


attached base packages:

[1] stats     graphics  grDevices utils     datasets  methods   base


other attached packages:

[1] dplyr_1.1.2    CMAverse_0.1.0


loaded via a namespace (and not attached):

 [1] Rcpp_1.0.8.3      MetaUtility_2.1.2 msm_1.7           mvtnorm_1.1-3

 [5] lattice_0.20-45   tidyr_1.3.0       zoo_1.8-10        digest_0.6.29

 [9] utf8_1.2.2        R6_2.5.1          backports_1.4.1   survey_4.1-1

[13] evaluate_0.15     ggplot2_3.4.2     pillar_1.9.0      rlang_1.1.1

[17] multcomp_1.4-20   rstudioapi_0.13   car_3.0-13        Matrix_1.4-1

[21] rmarkdown_2.19    mathjaxr_1.6-0    splines_4.2.0     stringr_1.5.0

[25] igraph_1.3.1      munsell_0.5.0     broom_1.0.3       compiler_4.2.0

[29] xfun_0.31         pkgconfig_2.0.3   EValue_4.1.3      mitools_2.4

[33] htmltools_0.5.4   nnet_7.3-17       tidyselect_1.2.0  tibble_3.2.1

[37] expm_0.999-7      codetools_0.2-18  simex_1.8         fansi_1.0.3

[41] withr_2.5.0       MASS_7.3-56       SuppDists_1.1-9.7 grid_4.2.0

[45] DBI_1.1.3         nlme_3.1-157      gtable_0.3.0      lifecycle_1.0.3

[49] magrittr_2.0.3    metafor_3.8-1     scales_1.2.0      metadat_1.2-0

[53] cli_3.6.0         stringi_1.7.6     carData_3.0-5     mice_3.14.0

[57] generics_0.1.2    vctrs_0.6.2       boot_1.3-28       sandwich_3.0-2

[61] TH.data_1.1-1     tools_4.2.0       ggdag_0.2.7       medflex_0.6-7

[65] glue_1.6.2        purrr_1.0.1       abind_1.4-5       fastmap_1.1.0

[69] survival_3.5-0    yaml_2.3.5        colorspace_2.0-3  tidygraph_1.2.2

[73] knitr_1.39
```

```
R version 4.2.0 (2022-04-22)

Platform: x86_64-apple-darwin17.0 (64-bit)

Running under: macOS 14.4


Matrix products: default

LAPACK: /Library/Frameworks/R.framework/Versions/4.2/Resources/lib/libRlapa
ck.dylib


locale:

[1] de_DE.UTF-8/de_DE.UTF-8/de_DE.UTF-8/C/de_DE.UTF-8/de_DE.UTF-8


attached base packages:

[1] stats     graphics  grDevices utils     datasets  methods   base


other attached packages:

 [1] ggfortify_0.4.15 ranger_0.14.1    survival_3.5-0   forcats_0.5.1    st
ringr_1.5.0

 [6] purrr_1.0.1      readr_2.1.2      tidyr_1.3.0      tibble_3.2.1     gg
plot2_3.4.2

[11] tidyverse_1.3.2  gtsummary_1.7.0  psych_2.2.5      dplyr_1.1.2      CM
Averse_0.1.0


loaded via a namespace (and not attached):

 [1] TH.data_1.1-1        googledrive_2.0.0    colorspace_2.0-3     ellipsi
s_0.3.2

 [5] fs_1.5.2             rstudioapi_0.13      mice_3.14.0          fansi_1
.0.3

 [9] mvtnorm_1.1-3        lubridate_1.8.0      mathjaxr_1.6-0       xml2_1.
3.3

[13] codetools_0.2-18     splines_4.2.0        simex_1.8            mnormt_
2.0.2

[17] medflex_0.6-7        knitr_1.39           SuppDists_1.1-9.7    jsonlit
e_1.8.0

[21] gt_0.8.0             broom_1.0.3          dbplyr_2.3.0         compile
r_4.2.0

[25] httr_1.4.3           backports_1.4.1      assertthat_0.2.1     Matrix_
1.4-1

[29] fastmap_1.1.0        gargle_1.2.1         survey_4.1-1         cli_3.6
.0

[33] htmltools_0.5.4      tools_4.2.0          igraph_1.3.1         gtable_
0.3.0
```

```
[37] glue_1.6.2           Rcpp_1.0.8.3         msm_1.7              carData
_3.0-5

[41] cellranger_1.1.0     vctrs_0.6.2          ggdag_0.2.7          nlme_3.
1-157

[45] broom.helpers_1.11.0 EValue_4.1.3         xfun_0.31            rvest_1
.0.3

[49] lifecycle_1.0.3      googlesheets4_1.0.1  MASS_7.3-56          zoo_1.8
-10

[53] scales_1.2.0         tidygraph_1.2.2      hms_1.1.1            paralle
l_4.2.0

[57] sandwich_3.0-2       expm_0.999-7         metafor_3.8-1        yaml_2.
3.5

[61] gridExtra_2.3        sass_0.4.4           labelled_2.10.0      stringi
_1.7.6

[65] boot_1.3-28          rlang_1.1.1          pkgconfig_2.0.3      commonm
ark_1.8.1

[69] evaluate_0.15        lattice_0.20-45      tidyselect_1.2.0     magritt
r_2.0.3

[73] R6_2.5.1             generics_0.1.2       multcomp_1.4-20      DBI_1.1
.3

[77] pillar_1.9.0         haven_2.5.0          withr_2.5.0          abind_1
.4-5

[81] nnet_7.3-17          modelr_0.1.10        crayon_1.5.1         car_3.0
-13

[85] utf8_1.2.2           tmvnsim_1.0-2        tzdb_0.3.0           rmarkdo
wn_2.19

[89] grid_4.2.0           metadat_1.2-0        readxl_1.4.1         reprex_
2.0.2

[93] digest_0.6.29        MetaUtility_2.1.2    munsell_0.5.0        mitools
_2.4
```

*The analytic code is available online (*https://osf.io/b28y3/).

Appendix C: Supplementary Materials Study III

eMethods. Further Information on Main Predictor Diagnoses.

PTSD, Dissociative Disorders, and Depression

PTSD, dissociative disorders and depression were identified through linked health records using codes from the *International Classification of Diseases, Tenth Revision* (ICD-10) (PTSD, F43.1; any dissociative disorder, including the following: dissociative amnesia, F44.0; dissociative fugue, F44.1; dissociative stupor, F44.2; trance and possession disorders, F44.3; dissociative motor disorders, F44.4; dissociative convulsions, F44.5; dissociative anesthesia and sensory loss, F44.6; mixed dissociative [conversion] disorders, F44.7; other dissociative [conversion] disorders, F44.80 – F44.88; dissociative [conversion] disorder, unspecified, F44.9; depersonalization-derealization syndrome, F48.1; any depression, including the following: mild depressive episode, F32.0; moderate depressive episode, F32.1; severe depressive episode without psychotic symptoms, F32.2; severe depressive episode with psychotic symptoms, F32.3; other depressive episodes, F32.8; depressive episode, unspecified, F32.9; recurrent depressive episode, current episode mild, F33.0; recurrent depressive episode, current episode moderate, F33.1; recurrent depressive episode, current episode severe without psychotic symptoms, F33.2; recurrent depressive episode, current episode severe with psychotic symptoms, F33.3; other recurrent depressive disorders, F33.8; recurrent depressive disorder, unspecified; F33.9).

eTable C1. Types of Adverse Childhood Experiences (ACEs).

	ACEs* **(n = 44,515)**
Type of ACEs **N (%)**	44,515 (100.00)
Physical abuse	10,682 (24.00)
Emotional abuse	12,435 (27.93)
Sexual abuse	11,786 (26.48)
Physical neglect	7,355 (16.52)
Emotional neglect	29,498 (66.27)

ACEs = Adverse childhood experiences; N = sample size.

*Including participants that have had at least one ACE.

eTable C2. Dementia Outcome by Number of Types of Adverse Childhood Experiences (ACEs) (n = 134,316).

Number of ACE types	0 (n = 89,808)	1 (n = 27,344)	2 (n = 10,157)	3 (n = 4,548)	4 (n = 1,856)	5 (n = 603)
Dementia (n, %)	474 (0.53)	149 (0.54)	58 (0.57)	29 (0.64)	11 (0.59)	2 (0.33)

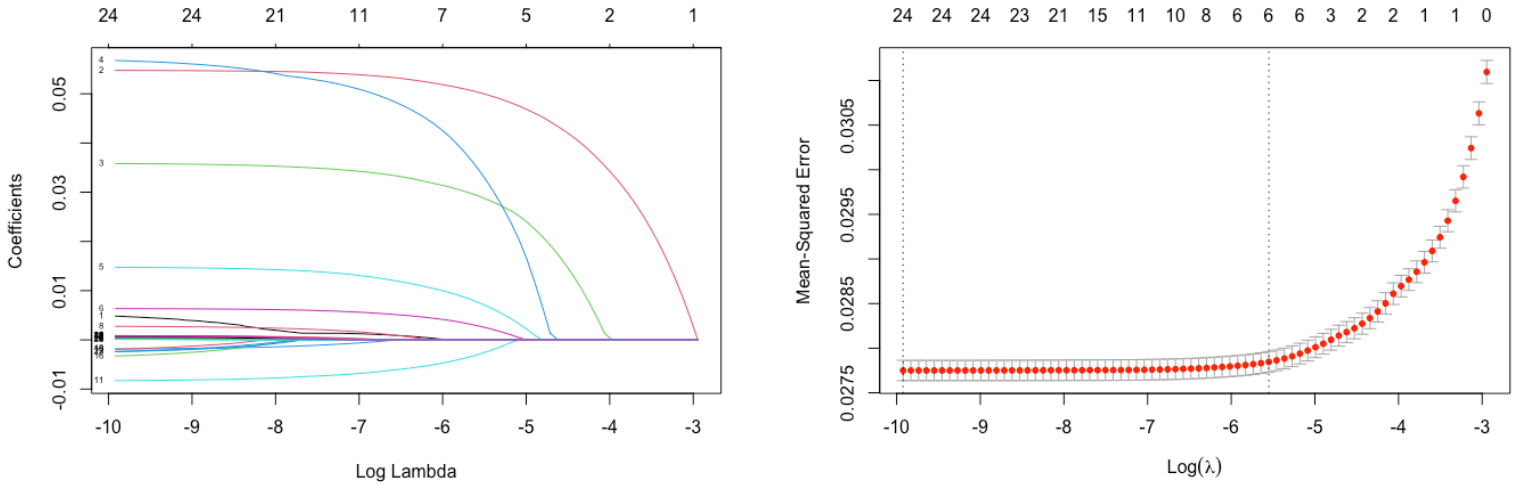
ACEs = adverse childhood experiences; N = sample size.

The following types of ACEs are included: emotional neglect, physical neglect, emotional abuse, physical abuse, and sexual abuse. Dementia cases that were diagnosed before baseline were excluded.

LASSO-Models with Adverse Childhood Experiences (ACEs) as the Main Predictor

LASSO-Model with ACEs and Log Reaction Time

eFigure C1. Regularization Path for the LASSO-Model (left) and Cross-Validation Error Plot (right).



The regularization path for the LASSO-Model (left) illustrates how the regression coefficients of all predictors change as the penalty term (i.e., regularization strength, λ) varies. As λ increases, more coefficients shrink toward zero, resulting in a sparser model with fewer selected predictors. The cross-validation error plot (right) displays the model's cross-validation error (i.e., mean squared error) across different values of λ, aiming to identify the optimal penalty term that minimizes prediction error while avoiding overfitting. The lowest point on the curve represents the chosen λ, ensuring an optimal balance-off between sparsity and accuracy.

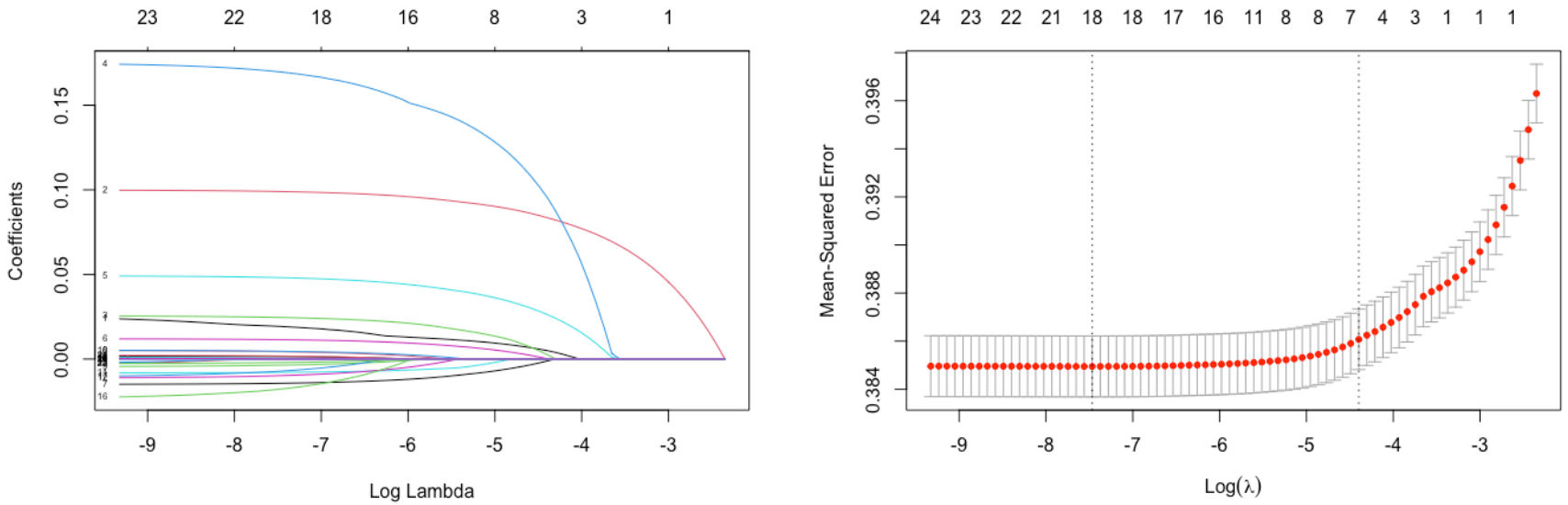
Non-Zero Coefficients from the LASSO-Model at the Optimal Penalty Term (λ = 0.00005).

```
## 26 x 1 sparse Matrix of class "dgCMatrix"
##                                    s1
## (Intercept)                6.2577898025
## ace.nc_scaled              0.0048348789
## age_scaled                 0.0547589008
## sex_numeric                0.0358238618
## ethn                       0.0567613119
## edubinary                  0.0147520396
## deprivation_scaled         0.0063511636
## met.tot.log_rec_scaled     0.0005630100
## soc.visi_recoded_scaled    0.0027452756
## soc.conf_recoded_scaled    0.0004624754
## soc.acti_recoded_scaled   -0.0018375785
## alc.ut_cat2               -0.0082776629
## smoking_status             0.0008652514
## hyt                        0.0007247233
## ACEs_age                   .
## ACEs_sex                  -0.0019093827
## ACEs_ethn                 -0.0032937996
## ACEs_education            -0.0024121242
## ACEs_deprivation           0.0001246286
## ACEs_physical_activity     0.0007499773
## ACEs_social_visits         0.0002418781
## ACEs_social_confiding      0.0008168592
## ACEs_social_acti           0.0002294606
## ACEs_alcohol              -0.0023558332
## ACEs_smoking               0.0001446434
## ACEs_hypertension          0.0008363270
```

***Note*:** ACEs = adverse childhood experiences; age_scaled = age (scaled); sex_numeric = male vs. female; ethn = White vs. Asian, Black, Mixed, or Other; edubinary = university or college vs. below, dichotomized; deprivation_scaled = Townsend deprivation index (scaled); met.tot.log_rec_scaled = total metabolic equivalent of task (log-transformed and scaled); soc.visi_recoded_scaled = frequency of family or friends' visits (scaled); soc.conf_recoded_scaled = perceived ability to confide in others (scaled); soc.acti_recoded_scaled = engagement in leisure activities (scaled); alc.ut_cat2 = low vs. increasing/high risk of alcohol consumption; smoking_status = never vs. former/current smoker; hypertension = absent vs. present. Interaction terms (e.g., "ACEs x Age") indicate the interaction between ACEs and the respective variable.

LASSO-Model with ACEs and Log Visual Memory Errors

eFigure C2. Regularization Path for the LASSO-Model (left) and Cross-Validation Error Plot (right).



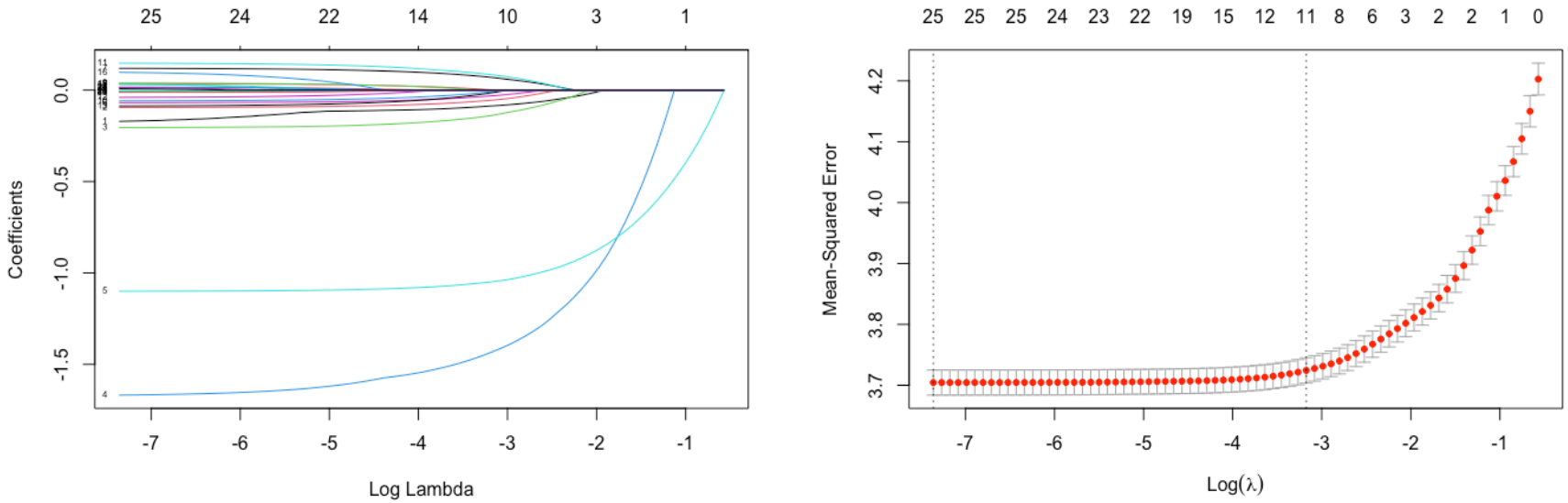
Non-Zero Coefficients from the LASSO-Model at the Optimal Penalty Term (λ = 0.00057).

```
## 26 x 1 sparse Matrix of class "dgCMatrix"
##                                    s1
## (Intercept)              1.4375235305
## ace.nc_scaled            0.0192892418
## age_scaled               0.0989979806
## sex_numeric              0.0245977457
## ethn                     0.1696372092
## edubinary                0.0481061204
## deprivation_scaled       0.0114679912
## met.tot.log_rec_scaled  -0.0142842283
## soc.visi_recoded_scaled  0.0043862907
## soc.conf_recoded_scaled -0.0036150135
## soc.acti_recoded_scaled  0.0046019549
## alc.ut_cat2             -0.0078073718
## smoking_status          -0.0097806475
## hyt                      .
## ACEs_age                 .
## ACEs_sex                 .
## ACEs_ethn               -0.0177343401
## ACEs_education          -0.0071288139
## ACEs_deprivation         0.0005334985
## ACEs_physical_activity   .
## ACEs_social_visits       0.0014451683
## ACEs_social_confiding    0.0018167203
## ACEs_social_acti        -0.0020576902
## ACEs_alcohol             .
## ACEs_smoking             .
## ACEs_hypertension        .
```

***Note*:** ACEs = adverse childhood experiences; age_scaled = age (scaled); sex_numeric = male vs. female; ethn = White vs. Asian, Black, Mixed, or Other; edubinary = university or college vs. below, dichotomized; deprivation_scaled = Townsend deprivation index (scaled); met.tot.log_rec_scaled = total metabolic equivalent of task (log-transformed and scaled); soc.visi_recoded_scaled = frequency of family or friends' visits (scaled); soc.conf_recoded_scaled = perceived ability to confide in others (scaled); soc.acti_recoded_scaled = engagement in leisure activities (scaled); alc.ut_cat2 = low vs. increasing/high risk of alcohol consumption; smoking_status = never vs. former/current smoker; hypertension = absent vs. present. Interaction terms (e.g., "ACEs x Age") indicate the interaction between ACEs and the respective variable.

LASSO-Model with ACEs and Reasoning Ability

eFigure C3. Regularization Path for the LASSO-Model (left) and Cross-Validation Error Plot (right).



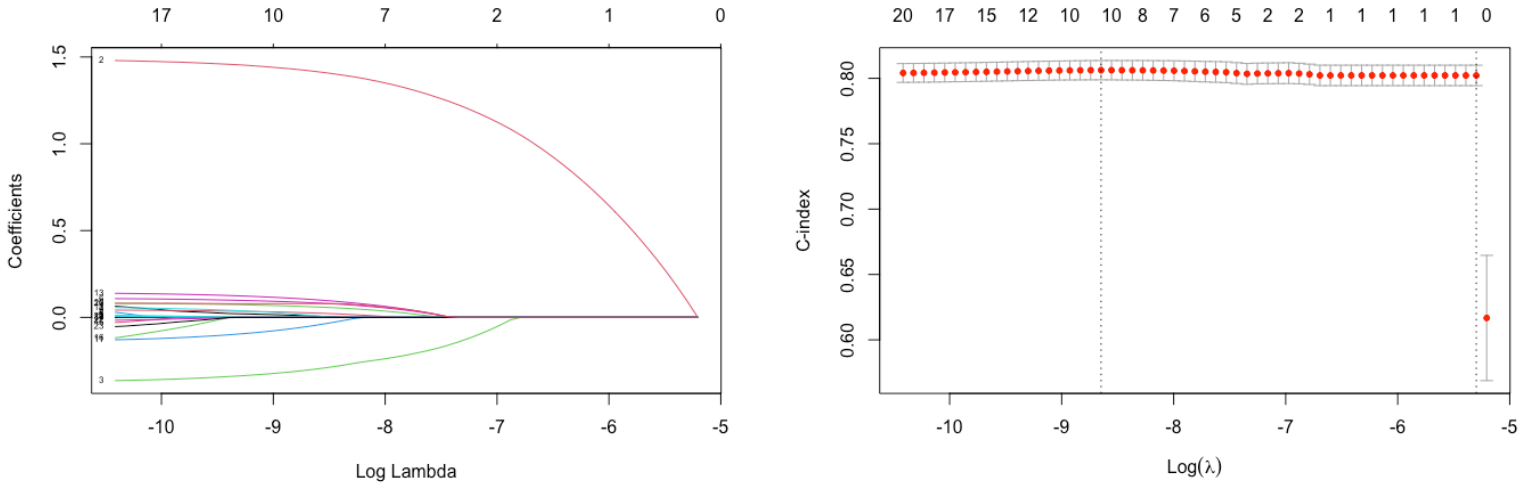
Non-Zero Coefficients from the LASSO-Model at the Optimal Penalty Term (λ = 0.00064).

```
## 26 x 1 sparse Matrix of class "dgCMatrix"
##                                    s1
## (Intercept)                7.477607969
## ace.nc_scaled             -0.170955592
## age_scaled                -0.095100079
## sex_numeric               -0.205185595
## ethn                      -1.668329048
## edubinary                 -1.100220197
## deprivation_scaled        -0.068848731
## met.tot.log_rec_scaled     0.119195524
## soc.visi_recoded_scaled    0.035016674
## soc.conf_recoded_scaled    0.038570901
## soc.acti_recoded_scaled   -0.058626243
## alc.ut_cat2                0.147047210
## smoking_status            -0.040016496
## hyt                       -0.086800962
## ACEs_age                   0.015083156
## ACEs_sex                   0.032179527
## ACEs_ethn                  0.097088584
## ACEs_education             0.030853914
## ACEs_deprivation          -0.011228933
## ACEs_physical_activity    -0.009493614
## ACEs_social_visits        -0.011977326
## ACEs_social_confiding     -0.006859295
## ACEs_social_acti           0.015315490
## ACEs_alcohol              -0.001809645
## ACEs_smoking               0.013774101
## ACEs_hypertension          0.007639019
```

***Note*:** ACEs = adverse childhood experiences; age_scaled = age (scaled); sex_numeric = male vs. female; ethn = White vs. Asian, Black, Mixed, or Other; edubinary = university or college vs. below, dichotomized; deprivation_scaled = Townsend deprivation index (scaled); met.tot.log_rec_scaled = total metabolic equivalent of task (log-transformed and scaled); soc.visi_recoded_scaled = frequency of family or friends' visits (scaled); soc.conf_recoded_scaled = perceived ability to confide in others (scaled); soc.acti_recoded_scaled = engagement in leisure activities (scaled); alc.ut_cat2 = low vs. increasing/high risk of alcohol consumption; smoking_status = never vs. former/current smoker; hypertension = absent vs. present. Interaction terms (e.g., "ACEs x Age") indicate the interaction between ACEs and the respective variable.

LASSO-Model with ACEs and Dementia

eFigure C4. Regularization Path for the LASSO-Model (left) and Cross-Validation Error Plot (right).



The regularization path for the LASSO-Model (left) illustrates how the regression coefficients of all predictors change as the penalty term (i.e., regularization strength, λ) varies. As λ increases, more coefficients shrink toward zero, resulting in a sparser model with fewer selected predictors. The cross-validation error plot (right) displays the 1-C-index across different values of λ, where the optimal penalty term is selected at the minimum cross-validation error, corresponding to the highest C-index. This ensures an optimal balance between sparsity and predictive performance.

Non-Zero Coefficients from the LASSO-Model at the Optimal Penalty Term (λ = 0.00018).

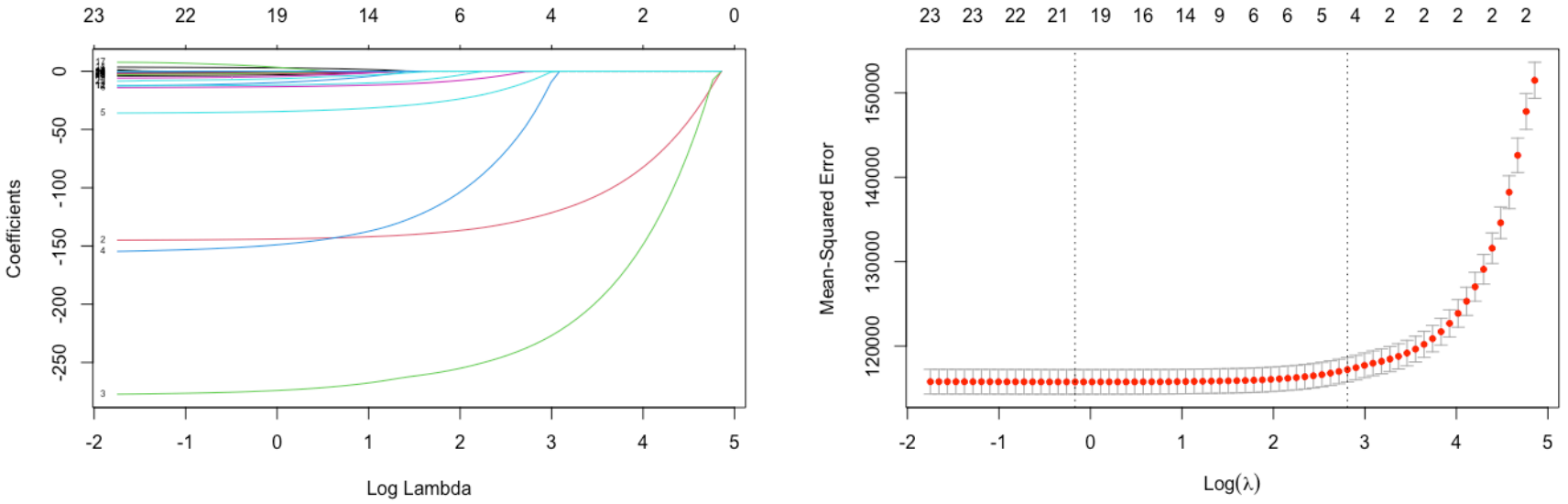
```
## 25 x 1 sparse Matrix of class "dgCMatrix"
##                                    1
## ace.nc_scaled            0.007840885
## age_scaled               1.418409435
## sex_numeric             -0.300122328
## ethn                     .
## edubinary                .
## deprivation_scaled       0.084140193
## met.tot.log_rec_scaled   .
## soc.visi_recoded_scaled  .
## soc.conf_recoded_scaled  0.025354095
## soc.acti_recoded_scaled  0.060970097
## alc.ut_cat2             -0.048263901
## smoking_status           0.010935518
## hyt                      0.102667373
## ACEs_age                 .
## ACEs_sex                 .
## ACEs_ethn                .
## ACEs_education           .
## ACEs_deprivation         .
## ACEs_physical_activity   .
## ACEs_social_visits       .
## ACEs_social_confiding    .
## ACEs_social_acti         .
## ACEs_alcohol             .
## ACEs_smoking             .
## ACEs_hypertension        0.079363121
```

***Note*:** ACEs = adverse childhood experiences; age_scaled = age (scaled); sex_numeric = male vs. female; ethn = White vs. Asian, Black, Mixed, or Other; edubinary = university or college vs. below, dichotomized; deprivation_scaled = Townsend deprivation index (scaled); met.tot.log_rec_scaled = total metabolic equivalent of task (log-transformed and scaled); soc.visi_recoded_scaled = frequency of family or friends' visits (scaled); soc.conf_recoded_scaled = perceived ability to confide in others (scaled); soc.acti_recoded_scaled = engagement in leisure activities (scaled); alc.ut_cat2 = low vs. increasing/high risk of alcohol consumption; smoking_status = never vs. former/current smoker; hypertension = absent vs. present. Interaction terms (e.g., "ACEs x Age") indicate the interaction between ACEs and the respective variable.

The values are in log-hazard ratio format (i.e., raw coefficients before exponentiation).

LASSO-Model with ACEs and Left Hippocampal Volume

eFigure C5. Regularization Path for the LASSO-Model (left) and Cross-Validation Error Plot (right).



The regularization path for the LASSO-Model (left) illustrates how the regression coefficients of all predictors change as the penalty term (i.e., regularization strength, λ) varies. As λ increases, more coefficients shrink toward zero, resulting in a sparser model with fewer selected predictors. The cross-validation error plot (right) displays the model's cross-validation error (i.e., mean squared error) across different values of λ, aiming to identify the optimal penalty term that minimizes prediction error while avoiding overfitting. The lowest point on the curve represents the chosen λ, ensuring an optimal balance-off between sparsity and accuracy.

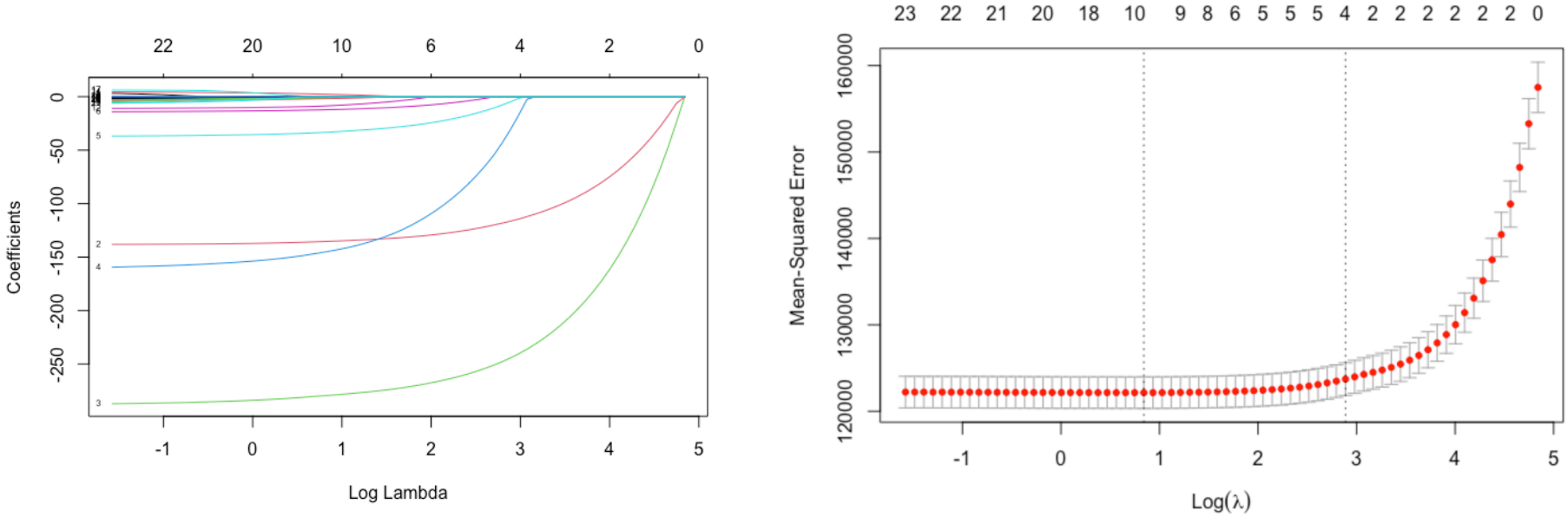
Non-Zero Coefficients from the LASSO-Model at the Optimal Penalty Term (λ = 0.845).

```
## 26 x 1 sparse Matrix of class "dgCMatrix"
##                                      s1
## (Intercept)              3863.72549568
## ace.nc_scaled               .
## age_scaled               -144.18361677
## sex_numeric              -274.63715494
## ethn                     -149.98346247
## edubinary                 -34.86928081
## deprivation_scaled        -13.43381131
## met.tot.log_rec_scaled      .
## soc.visi_recoded_scaled    -3.27665557
## soc.conf_recoded_scaled    -2.21489400
## soc.acti_recoded_scaled    -0.06346392
## alc.ut_cat2               -10.17954154
## smoking_status            -11.96975293
## hyt                        -4.68128251
## ACEs_age                    3.00242010
## ACEs_sex                   -0.97313177
## ACEs_ethn                   .
## ACEs_education              4.23187199
## ACEs_deprivation           -1.05986898
## ACEs_physical_activity      .
## ACEs_social_visits         -1.31119840
## ACEs_social_confiding      -0.99124060
## ACEs_social_acti           -1.19505610
## ACEs_alcohol               -1.62964705
## ACEs_smoking                .
## ACEs_hypertension          -6.71165177
```

***Note*:** ACEs = adverse childhood experiences; age_scaled = age (scaled); sex_numeric = male vs. female; ethn = White vs. Asian, Black, Mixed, or Other; edubinary = university or college vs. below, dichotomized; deprivation_scaled = Townsend deprivation index (scaled); met.tot.log_rec_scaled = total metabolic equivalent of task (log-transformed and scaled); soc.visi_recoded_scaled = frequency of family or friends' visits (scaled); soc.conf_recoded_scaled = perceived ability to confide in others (scaled); soc.acti_recoded_scaled = engagement in leisure activities (scaled); alc.ut_cat2 = low vs. increasing/high risk of alcohol consumption; smoking_status = never vs. former/current smoker; hypertension = absent vs. present. Interaction terms (e.g., "ACEs x Age") indicate the interaction between ACEs and the respective variable.

LASSO-Model with ACEs and Right Hippocampal Volume

eFigure C6. Regularization Path for the LASSO-Model (left) and Cross-Validation Error Plot (right).



Non-Zero Coefficients from the LASSO-Model at the Optimal Penalty Term (λ = 2.318).

```
## 26 x 1 sparse Matrix of class "dgCMatrix"
##                                    s1
## (Intercept)              3973.2697966
## ace.nc_scaled               .
## age_scaled               -135.3059725
## sex_numeric              -279.3921717
## ethn                     -144.7929832
## edubinary                 -33.1629152
## deprivation_scaled        -12.1258347
## met.tot.log_rec_scaled      .
## soc.visi_recoded_scaled    -1.0557885
## soc.conf_recoded_scaled     .
## soc.acti_recoded_scaled     .
## alc.ut_cat2                 .
## smoking_status             -8.4977010
## hyt                         .
## ACEs_age                    2.3495185
## ACEs_sex                    .
## ACEs_ethn                   .
## ACEs_education              .
## ACEs_deprivation            .
## ACEs_physical_activity      .
## ACEs_social_visits         -1.7487438
## ACEs_social_confiding      -0.8658161
## ACEs_social_acti            .
## ACEs_alcohol                .
## ACEs_smoking                .
## ACEs_hypertension           .
```

***Note*:** ACEs = adverse childhood experiences; age_scaled = age (scaled); sex_numeric = male vs. female; ethn = White vs. Asian, Black, Mixed, or Other; edubinary = university or college vs. below, dichotomized; deprivation_scaled = Townsend deprivation index (scaled); met.tot.log_rec_scaled = total metabolic equivalent of task (log-transformed and scaled); soc.visi_recoded_scaled = frequency of family or friends' visits (scaled); soc.conf_recoded_scaled = perceived ability to confide in others (scaled); soc.acti_recoded_scaled = engagement in leisure activities (scaled); alc.ut_cat2 = low vs. increasing/high risk of alcohol consumption; smoking_status = never vs. former/current smoker; hypertension = absent vs. present. Interaction terms (e.g., "ACEs x Age") indicate the interaction between ACEs and the respective variable.

eTable C3. Associations between ACEs, Moderators, Cognitive Functioning, Dementia, and Hippocampal Volumes of the Selected Predictors.

	Standardized β (95% CI)	*P*
Cognitive functioning		
Log reaction time*		
ACEs†	0.0063 (0.0041, 0.0084)	< .001
Age†	0.0550 (0.0541, 0.0559)	< .001
Sex (reference category: Male)	0.0358 (0.0339, 0.0377)	< .001
Ethnicity (reference category: White)	0.0572 (0.0513, 0.0632)	< .001
Education (reference category: University or College degree)	0.0150 (0.0132, 0.0168)	< .001
Deprivation†	0.0065 (0.0056, 0.0074)	< .001
Smoking status (reference category: Never)		
Alcohol consumption (reference category: Lower-risk consumption)	-0.0082 (-0.0101, -0.0063)	< .001
Log physical activity†		
Hypertension (reference category: absent)		
Frequency of family or friends' visits†	0.0029 (0.0020, 0.0038)	< .001
Ability to confide in others†		
Engagement in leisure activities†	-0.0018 (-0.0027, -0.0009)	< .001
ACEs x Age		
ACEs x Sex	-0.0026 (-0.0046, -0.0007)	.009
ACEs x Ethnicity	-0.0037 (-0.0078, 0.0003)	.073
ACEs x Education	-0.0027 (-0.0045, -0.0009)	.003
ACEs x Deprivation		
ACEs x Smoking status		
ACEs x Alcohol consumption	-0.0028 (-0.0047, -0.0008)	.005
ACEs x Physical activity	0.0009 (0.0001, 0.0017)	.030
ACEs x Hypertension		
ACEs x Frequency of family or friends' visits		
ACEs x Ability to confide in others	0.0009 (0.0001, 0.0018)	.031
ACEs x Engagement in leisure activities		
Log visual memory errors*		
ACEs†	0.0224 (0.0172, 0.0276)	< .001
Age†	0.0999 (0.0965, 0.1033)	< .001
Sex	0.0256 (0.0184, 0.0328)	< .001
Ethnicity	0.1751 (0.1529, 0.1973)	< .001
Education	0.0493 (0.0426, 0.0561)	< .001
Deprivation†	0.0121 (0.0087, 0.0155)	< .001
Smoking status	-0.0113 (-0.0183, -0.0044)	.001
Alcohol consumption	-0.0082 (-0.0155, -0.0009)	.027
Log physical activity†	-0.0150 (-0.0184, -0.0116)	< .001
Hypertension		
Frequency of family or friends' visits†	0.0029 (0.0020, 0.0038)	< .001
Ability to confide in others†	-0.0045 (-0.0078, -0.0011)	.010
Engagement in leisure activities†	0.0052 (0.0018, 0.0087)	.003
ACEs x Age		
ACEs x Sex		
ACEs x Ethnicity	-0.0220 (-0.0371, -0.0069)	.004
ACEs x Education	-0.0112 (-0.0179, -0.0045)	.001
ACEs x Deprivation		
ACEs x Smoking status		
ACEs x Alcohol consumption		
ACEs x Physical activity		
ACEs x Hypertension		
ACEs x Frequency of family or friends' visits		

ACEs x Ability to confide in others	0.0026 (-0.0006, 0.0057)	.107
ACEs x Engagement in leisure activities		
Reasoning ability‡		
ACEs†	-0.1677 (-0.2025, -0.1329)	< .001
Age†	-0.0958 (-0.1137, -0.0779)	< .001
Sex	-0.2060 (-0.2418, -0.1703)	< .001
Ethnicity	-1.6738 (-1.7639, -1.5837)	< .001
Education	-1.1008 (-1.1343, -1.0673)	< .001
Deprivation†	-0.0694 (-0.0862, -0.0526)	< .001
Smoking status	-0.0410 (-0.0753, -0.0067)	.019
Alcohol consumption	0.1477 (0.1112, 0.1842)	< .001
Log physical activity†	0.1191 (0.1025, 0.1357)	< .001
Hypertension	-0.0881 (-0.1235, -0.0526)	< .001
Frequency of family or friends' visits†	0.0355 (0.0185, 0.0525)	.003
Ability to confide in others†	0.0387 (0.0220, 0.0554)	< .001
Engagement in leisure activities†	-0.0593 (-0.0762, -0.0424)	< .001
ACEs x Age	0.0170 (0.0003, 0.0338)	.047
ACEs x Sex	0.0357 (0.0009, 0.0705)	.044
ACEs x Ethnicity	0.1010 (0.0361, 0.1660)	.002
ACEs x Education	0.0353 (0.0018, 0.0687)	.039
ACEs x Deprivation	-0.0118 (-0.0271, 0.0036)	.134
ACEs x Smoking status		
ACEs x Alcohol consumption		
ACEs x Physical activity		
ACEs x Hypertension		
ACEs x Frequency of family or friends' visits	-0.0137 (-0.0293, 0.0018)	.083
ACEs x Ability to confide in others		
ACEs x Engagement in leisure activities	0.0148 (-0.0018, 0.0314)	.080

	HR (95% CI)	***P***
Dementia		
ACEs†		
Age†	4.4879 (3.9682, 5.0756)	< .001
Sex	0.6806 (0.5814, 0.7966)	< .001
Ethnicity		
Education		
Deprivation†	1.1268 (1.0479, 1.2115)	0.001
Smoking status		
Alcohol consumption	0.8726 (0.7460, 1.0207)	.088
Log physical activity†		
Hypertension	1.1604 (0.9919, 1.3574)	.063
Frequency of family or friends' visits†		
Ability to confide in others†		
Engagement in leisure activities†	1.0933 (1.0149, 1.1777)	.019
ACEs x Age		
ACEs x Sex		
ACEs x Ethnicity		
ACEs x Education		
ACEs x Deprivation		
ACEs x Smoking status		
ACEs x Alcohol consumption		
ACEs x Physical activity		
ACEs x Hypertension	1.1264 (1.0315, 1.2300)	.008
ACEs x Frequency of family or friends' visits		
ACEs x Ability to confide in others		
ACEs x Engagement in leisure activities		
	Standardized β (95% CI)	***P***

Hippocampal volume‡		
Left		
ACEs†		
Age†	-146.07 (-151.12, -141.03)	< .001
Sex	-276.74 (-287.31, -266.17)	< .001
Ethnicity	-156.76 (-191.22, -122.30)	< .001
Education	-37.13 (-47.06, -27.20)	< .001
Deprivation†	-14.35 (-19.33, -9.37)	< .001
Smoking status	-12.77 (-23.18, -2.36)	.0162
Alcohol consumption	-12.84 (-23.52, -2.16)	.0184
Log physical activity†		
Hypertension		
Frequency of family or friends' visits†	-4.71 (-9.72, 0.29)	.0651
Ability to confide in others†		
Engagement in leisure activities†		
ACEs x Age	4.36 (-0.63, 9.35)	.0870
ACEs x Sex		
ACEs x Ethnicity		
ACEs x Education		
ACEs x Deprivation		
ACEs x Smoking status		
ACEs x Alcohol consumption		
ACEs x Physical activity		
ACEs x Hypertension	-7.60 (-15.38, 0.18)	.0556
ACEs x Frequency of family or friends' visits		
ACEs x Ability to confide in others		
ACEs x Engagement in leisure activities		
Right		
ACEs†		
Age†	-138.29 (-143.47, -133.11)	< .001
Sex	-285.43 (-295.72, -275.13)	< .001
Ethnicity	-160.01 (-195.34, -124.67)	< .001
Education	-37.64 (-47.84, -27.45)	< .001
Deprivation†	-14.21 (-19.32, -9.10)	< .001
Smoking status	-12.29 (-22.78, -1.80)	.0216
Alcohol consumption		
Log physical activity†		
Hypertension		
Frequency of family or friends' visits†	-4.03 (-9.18, 1.12)	.1249
Ability to confide in others†		
Engagement in leisure activities†		
ACEs x Age	4.16 (-0.93, 9.25)	.1093
ACEs x Sex		
ACEs x Ethnicity		
ACEs x Education		
ACEs x Deprivation		
ACEs x Smoking status		
ACEs x Alcohol consumption		
ACEs x Physical activity		
ACEs x Hypertension		
ACEs x Frequency of family or friends' visits	-3.53 (-8.35, 1.29)	0.1508
ACEs x Ability to confide in others		
ACEs x Engagement in leisure activities		

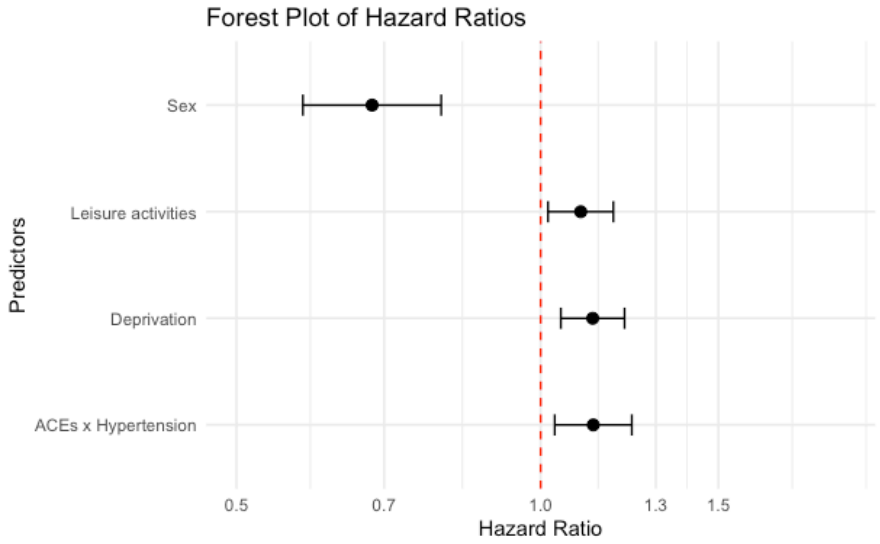
CI = confidence interval; P = p-value; ACEs = adverse childhood experiences; HR = hazard ratio.
Based on the final model, after stepwise selection of the LASSO-selected predictors.
*Positive coefficients indicate a worse outcome.
†Variables were standardized to have a mean of 0 and a standard deviation of 1.
‡Negative coefficients indicate a worse outcome.

eTable C4. Associations between ACEs, Moderators, and Dementia in the Stratified Model.

Dementia	HR (95% CI)	*P*
ACEs*		
Age*		
Sex	0.6809 (0.5817, 0.7971)	< .001
Ethnicity		
Education		
Deprivation*	1.1260 (1.0471, 1.2107)	0.001
Smoking status		
Alcohol consumption	0.8742 (0.7473, 1.0227)	.093
Log weekly physical activity*		
Hypertension	1.1607 (0.9921, 1.3581)	.063
Frequency of family or friends' visits*		
Ability to confide in others*		
Engagement in leisure activities*	1.0956 (1.0170, 1.1803)	.016
ACEs x Age		
ACEs x Sex		
ACEs x Ethnicity		
ACEs x Education		
ACEs x Deprivation		
ACEs x Smoking status		
ACEs x Alcohol consumption		
ACEs x Physical activity		
ACEs x Hypertension	1.1274 (1.0326, 1.2310)	.007
ACEs x Frequency of family or friends' visits		
ACEs x Ability to confide in others		
ACEs x Engagement in leisure activities		

CI = confidence interval; P = p-value; ACEs = adverse childhood experiences; HR = hazard ratio.
*Variables were standardized to have a mean of 0 and a standard deviation of 1.

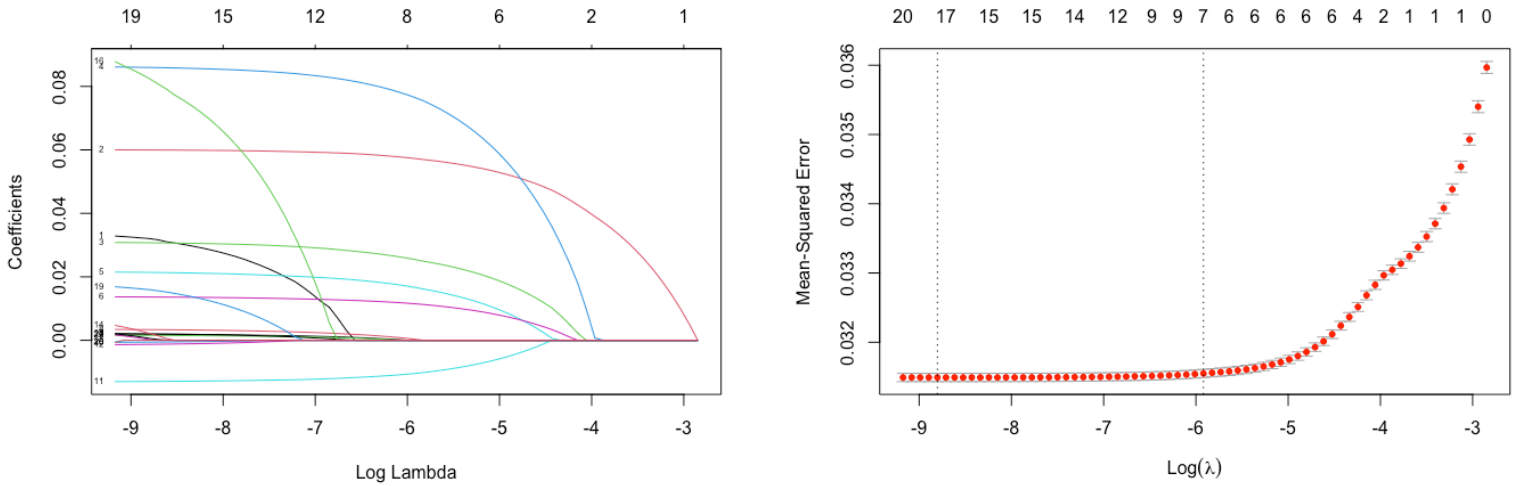
eFigure C7. Forest Plot of the Stratified Stepwise Model ACEs – Dementia.



LASSO-Models with Posttraumatic Stress Disorder (PTSD) Diagnosis as the Main Predictor

LASSO-Model with PTSD Diagnosis and Log Reaction Time

eFigure C8. Regularization Path for the LASSO-Model (left) and Cross-Validation Error Plot (right).



The regularization path for the LASSO-Model (left) illustrates how the regression coefficients of all predictors change as the penalty term (i.e., regularization strength, λ) varies. As λ increases, more coefficients shrink toward zero, resulting in a sparser model with fewer selected predictors. The cross-validation error plot (right) displays the model's cross-validation error (i.e., mean squared error) across different values of λ, aiming to identify the optimal penalty term that minimizes prediction error while avoiding overfitting. The lowest point on the curve represents the chosen λ, ensuring an optimal balance-off between sparsity and accuracy.

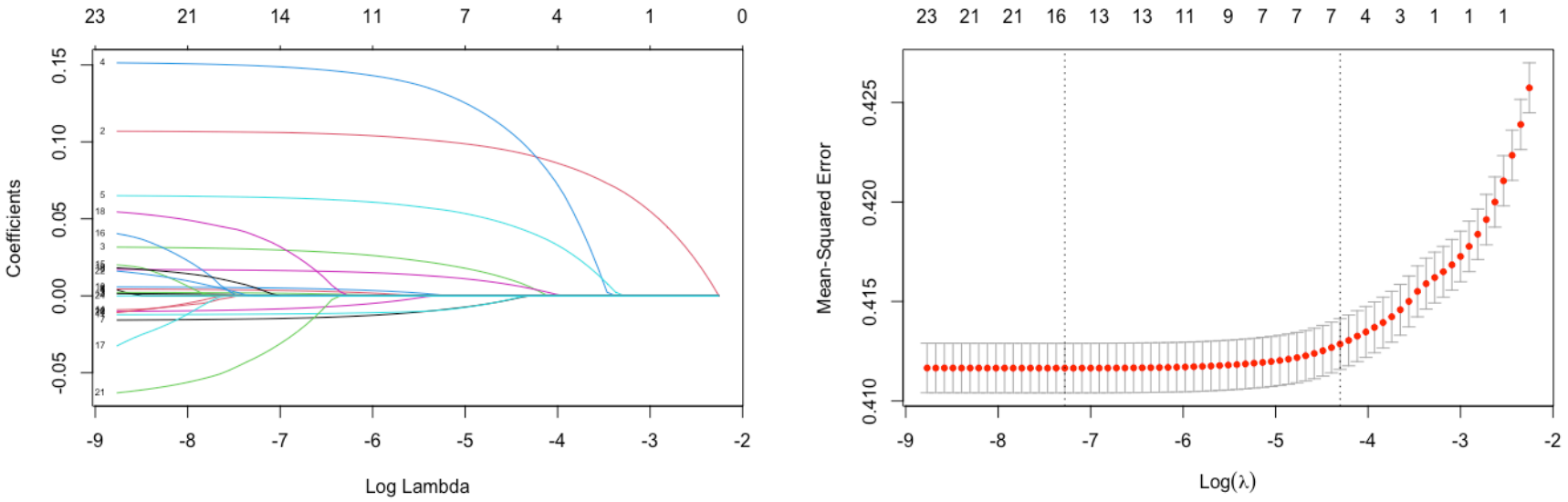
Non-Zero Coefficients from the LASSO-Model at the Optimal Penalty Term (λ = 0.00015).

```
## 26 x 1 sparse Matrix of class "dgCMatrix"
##                                    s1
## (Intercept)                6.2773674424
## ptsd                       0.0320618693
## age_scaled                 0.0599689973
## sex_numeric                0.0307360641
## ethn                       0.0859730002
## edubinary                  0.0213936270
## deprivation_scaled         0.0136386903
## met.tot.log_rec_scaled     0.0019396419
## soc.visi_recoded_scaled    0.0033670499
## soc.conf_recoded_scaled    0.0015275267
## soc.acti_recoded_scaled -0.0005610580
## alc.ut_cat2             -0.0129652164
## smoking_status          -0.0012758340
## hyt                        0.0020244977
## PTSD_age                   0.0021922516
## PTSD_sex                   .
## PTSD_ethn                  0.0824821218
## PTSD_education             .
## PTSD_deprivation           .
## PTSD_physical_activity     0.0159661893
## PTSD_social_visits         .
## PTSD_social_confiding      .
## PTSD_social_acti           0.0002457639
## PTSD_alcohol               .
## PTSD_smoking               0.0006118350
## PTSD_hypertension          .
```

***Note*:** PTSD = posttraumatic stress disorder; age_scaled = age (scaled); sex_numeric = male vs. female; ethn = White vs. Asian, Black, Mixed, or Other; edubinary = university or college vs. below, dichotomized; deprivation_scaled = Townsend deprivation index (scaled); met.tot.log_rec_scaled = total metabolic equivalent of task (log-transformed and scaled); soc.visi_recoded_scaled = frequency of family or friends' visits (scaled); soc.conf_recoded_scaled = perceived ability to confide in others (scaled); soc.acti_recoded_scaled = engagement in leisure activities (scaled); alc.ut_cat2 = low vs. increasing/high risk of alcohol consumption; smoking_status = never vs. former/current smoker; hypertension = absent vs. present. Interaction terms (e.g., "PTSD x Age") indicate the interaction between PTSD and the respective variable.

LASSO-Model with PTSD Diagnosis and Log Visual Memory Errors

eFigure C9. Regularization Path for the LASSO-Model (left) and Cross-Validation Error Plot (right).



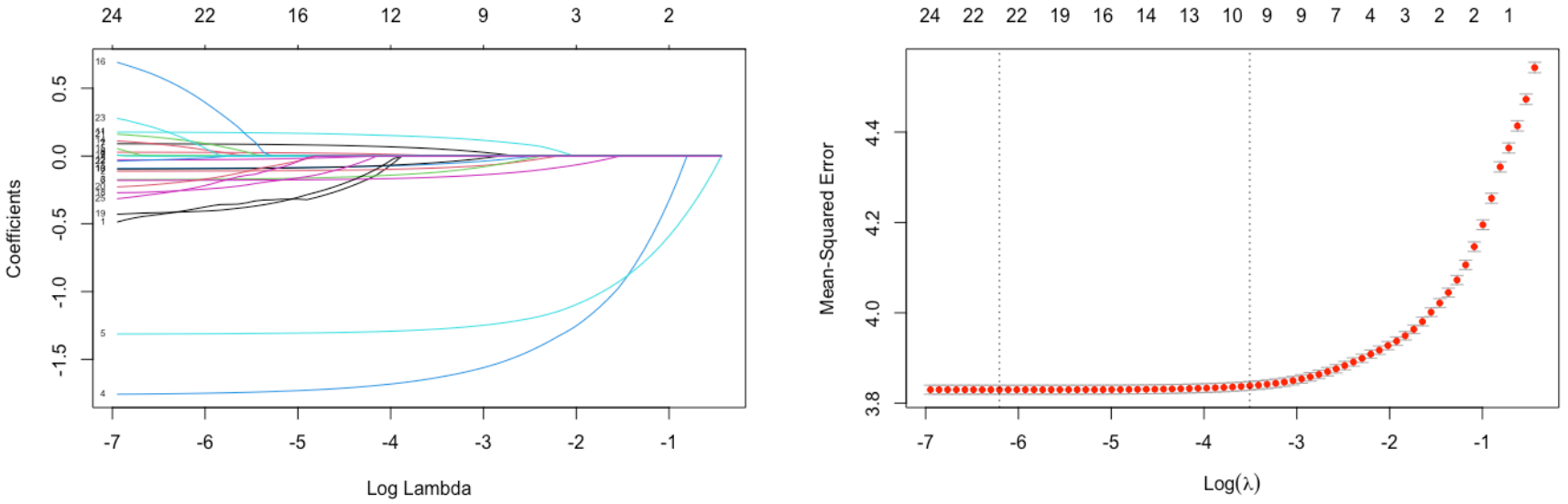
Non-Zero Coefficients from the LASSO-Model at the Optimal Penalty Term (λ = 0.00069).

```
## 26 x 1 sparse Matrix of class "dgCMatrix"
##                                    s1
## (Intercept)              1.4816427699
## ptsd                     .
## age_scaled               0.1062989270
## sex_numeric              0.0302885333
## ethn                     0.1495385631
## edubinary                0.0640721975
## deprivation_scaled       0.0166006124
## met.tot.log_rec_scaled  -0.0150634348
## soc.visi_recoded_scaled  0.0037399534
## soc.conf_recoded_scaled  0.0017778108
## soc.acti_recoded_scaled  0.0052234349
## alc.ut_cat2             -0.0119511788
## smoking_status          -0.0089913230
## hyt                      0.0004969468
## PTSD_age                 .
## PTSD_sex                 .
## PTSD_ethn                .
## PTSD_education           .
## PTSD_deprivation         0.0393630297
## PTSD_physical_activity   0.0053988876
## PTSD_social_visits       .
## PTSD_social_confiding   -0.0406667740
## PTSD_social_acti         .
## PTSD_alcohol             .
## PTSD_smoking             .
## PTSD_hypertension        .
```

Note: PTSD = posttraumatic stress disorder; age_scaled = age (scaled); sex_numeric = male vs. female; ethn = White vs. Asian, Black, Mixed, or Other; edubinary = university or college vs. below, dichotomized; deprivation_scaled = Townsend deprivation index (scaled); met.tot.log_rec_scaled = total metabolic equivalent of task (log-transformed and scaled); soc.visi_recoded_scaled = frequency of family or friends' visits (scaled); soc.conf_recoded_scaled = perceived ability to confide in others (scaled); soc.acti_recoded_scaled = engagement in leisure activities (scaled); alc.ut_cat2 = low vs. increasing/high risk of alcohol consumption; smoking_status = never vs. former/current smoker; hypertension = absent vs. present. Interaction terms (e.g., "PTSD x Age") indicate the interaction between PTSD and the respective variable.

LASSO-Model with PTSD Diagnosis and Reasoning Ability

eFigure C10. Regularization Path for the LASSO-Model (left) and Cross-Validation Error Plot (right)



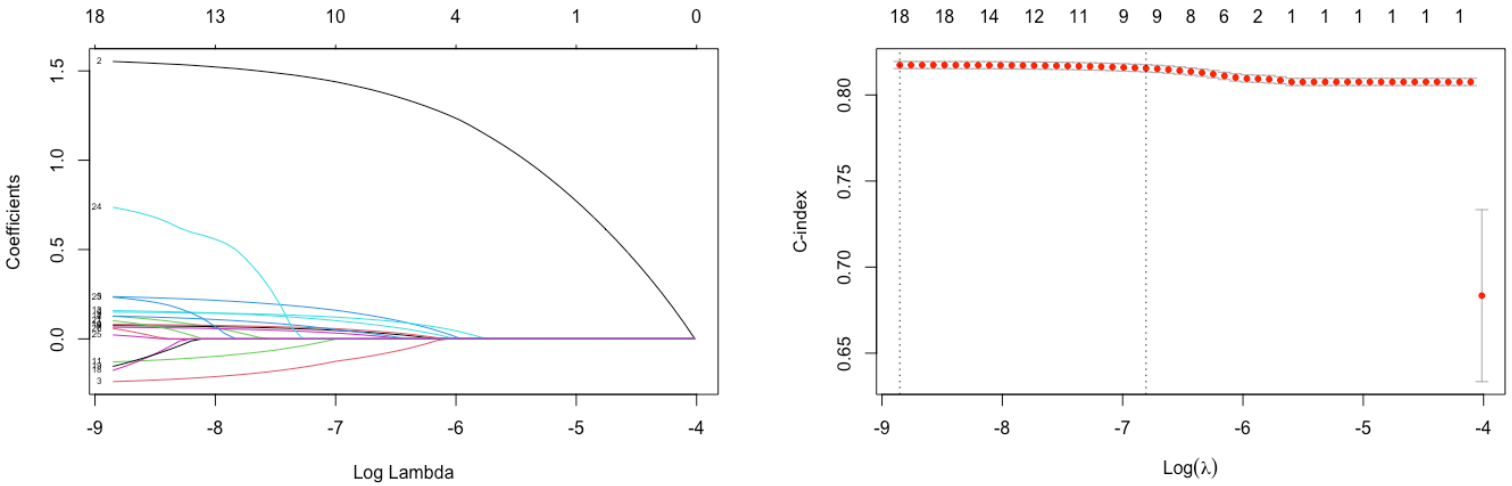
Non-Zero Coefficients from the LASSO-Model at the Optimal Penalty Term (λ = 0.00202).

```
## 26 x 1 sparse Matrix of class "dgCMatrix"
##                                    s1
## (Intercept)                7.121635600
## ptsd                      -0.400988326
## age_scaled                -0.111418655
## sex_numeric               -0.171995292
## ethn                      -1.752087994
## edubinary                 -1.311695271
## deprivation_scaled        -0.178869461
## met.tot.log_rec_scaled     0.089426598
## soc.visi_recoded_scaled    0.027004234
## soc.conf_recoded_scaled    0.003375671
## soc.acti_recoded_scaled   -0.090626795
## alc.ut_cat2                0.174971384
## smoking_status            -0.027692558
## hyt                       -0.094433218
## PTSD_age                   0.065028178
## PTSD_sex                   .
## PTSD_ethn                  0.484133232
## PTSD_education             .
## PTSD_deprivation          -0.252898560
## PTSD_physical_activity    -0.411557240
## PTSD_social_visits        -0.187829324
## PTSD_social_confiding      0.113570896
## PTSD_social_acti          -0.020496179
## PTSD_alcohol               0.123427027
## PTSD_smoking               .
## PTSD_hypertension         -0.246509603
```

Note: PTSD = posttraumatic stress disorder; age_scaled = age (scaled); sex_numeric = male vs. female; ethn = White vs. Asian, Black, Mixed, or Other; edubinary = university or college vs. below, dichotomized; deprivation_scaled = Townsend deprivation index (scaled); met.tot.log_rec_scaled = total metabolic equivalent of task (log-transformed and scaled); soc.visi_recoded_scaled = frequency of family or friends' visits (scaled); soc.conf_recoded_scaled = perceived ability to confide in others (scaled); soc.acti_recoded_scaled = engagement in leisure activities (scaled); alc.ut_cat2 = low vs. increasing/high risk of alcohol consumption; smoking_status = never vs. former/current smoker; hypertension = absent vs. present. Interaction terms (e.g., "PTSD x Age") indicate the interaction between PTSD and the respective variable.

LASSO-Model with PTSD Diagnosis and Dementia

eFigure C11. Regularization Path for the LASSO-Model (left) and Cross-Validation Error Plot (right).



The regularization path for the LASSO-Model (left) illustrates how the regression coefficients of all predictors change as the penalty term (i.e., regularization strength, λ) varies. As λ increases, more coefficients shrink toward zero, resulting in a sparser model with fewer selected predictors. The cross-validation error plot (right) displays the 1-C-index across different values of λ, where the optimal penalty term is selected at the minimum cross-validation error, corresponding to the highest C-index. This ensures an optimal balance between sparsity and predictive performance.

Non-Zero Coefficients from the LASSO-Model at the Optimal Penalty Term (λ = 0.00014).

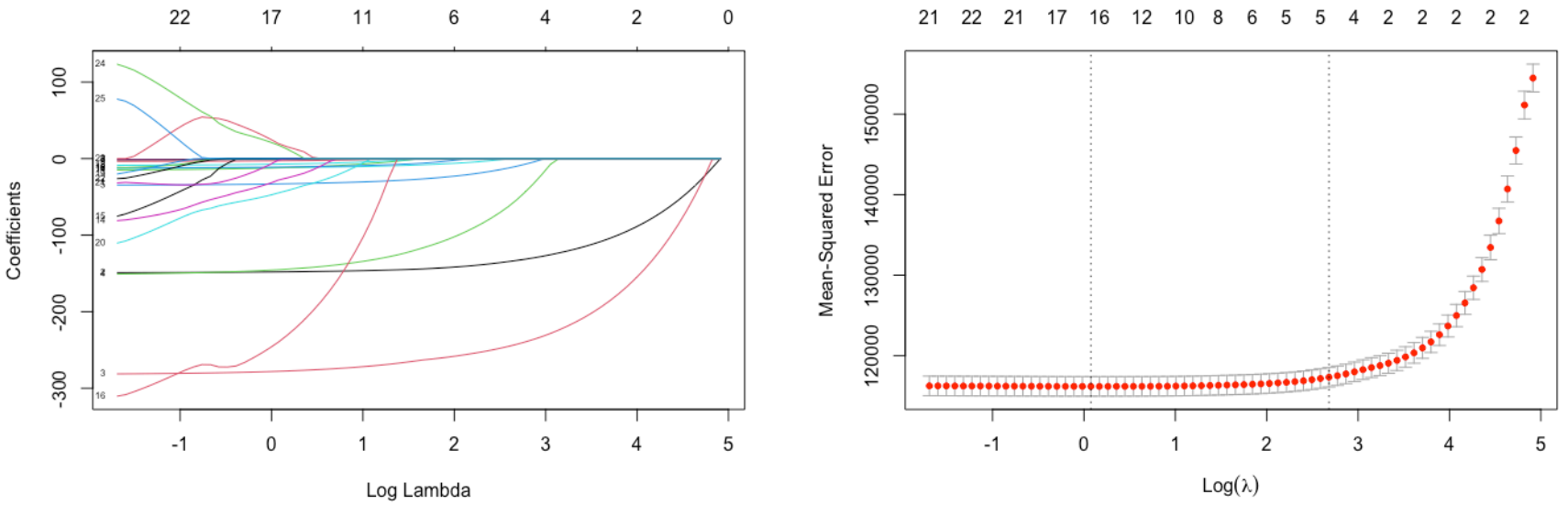
```
## 25 x 1 sparse Matrix of class "dgCMatrix"
##                                1
## ptsddem                .
## age_scaled              1.55255737
## sex_numeric            -0.23909669
## ethn                    0.12759761
## edubinary               0.23633537
## deprivation_scaled      0.14973764
## met.tot.log_rec_scaled  0.06539819
## soc.visi_recoded_scaled .
## soc.conf_recoded_scaled 0.07453699
## soc.acti_recoded_scaled 0.08139673
## alc.ut_cat2            -0.12905013
## smoking_status          0.12783286
## hyt                     0.15827222
## PTSD_age                .
## PTSD_sex                .
## PTSD_ethn               .
## PTSD_education          .
## PTSD_deprivation       -0.17663703
## PTSD_physical_activity -0.15440016
## PTSD_social_visits      0.05846880
## PTSD_social_confiding   0.10149939
## PTSD_social_acti        .
## PTSD_alcohol            0.23348515
## PTSD_smoking            0.73623392
## PTSD_hypertension       0.02206842
```

Note: PTSD = posttraumatic stress disorder; age_scaled = age (scaled); sex_numeric = male vs. female; ethn = White vs. Asian, Black, Mixed, or Other; edubinary = university or college vs. below, dichotomized; deprivation_scaled = Townsend deprivation index (scaled); met.tot.log_rec_scaled = total metabolic equivalent of task (log-transformed and scaled); soc.visi_recoded_scaled = frequency of family or friends' visits (scaled); soc.conf_recoded_scaled = perceived ability to confide in others (scaled); soc.acti_recoded_scaled = engagement in leisure activities (scaled); alc.ut_cat2 = low vs. increasing/high risk of alcohol consumption; smoking_status = never vs. former/current smoker; hypertension = absent vs. present. Interaction terms (e.g., "PTSD x Age") indicate the interaction between PTSD and the respective variable.

The values are in log-hazard ratio format (i.e., raw coefficients before exponentiation).

LASSO-Model with PTSD Diagnosis and Left Hippocampal Volume

eFigure C12. Regularization Path for the LASSO-Model (left) and Cross-Validation Error Plot (right).



The regularization path for the LASSO-Model (left) illustrates how the regression coefficients of all predictors change as the penalty term (i.e., regularization strength, λ) varies. As λ increases, more coefficients shrink toward zero, resulting in a sparser model with fewer selected predictors. The cross-validation error plot (right) displays the model's cross-validation error (i.e., mean squared error) across different values of λ, aiming to identify the optimal penalty term that minimizes prediction error while avoiding overfitting. The lowest point on the curve represents the chosen λ, ensuring an optimal balance-off between sparsity and accuracy.

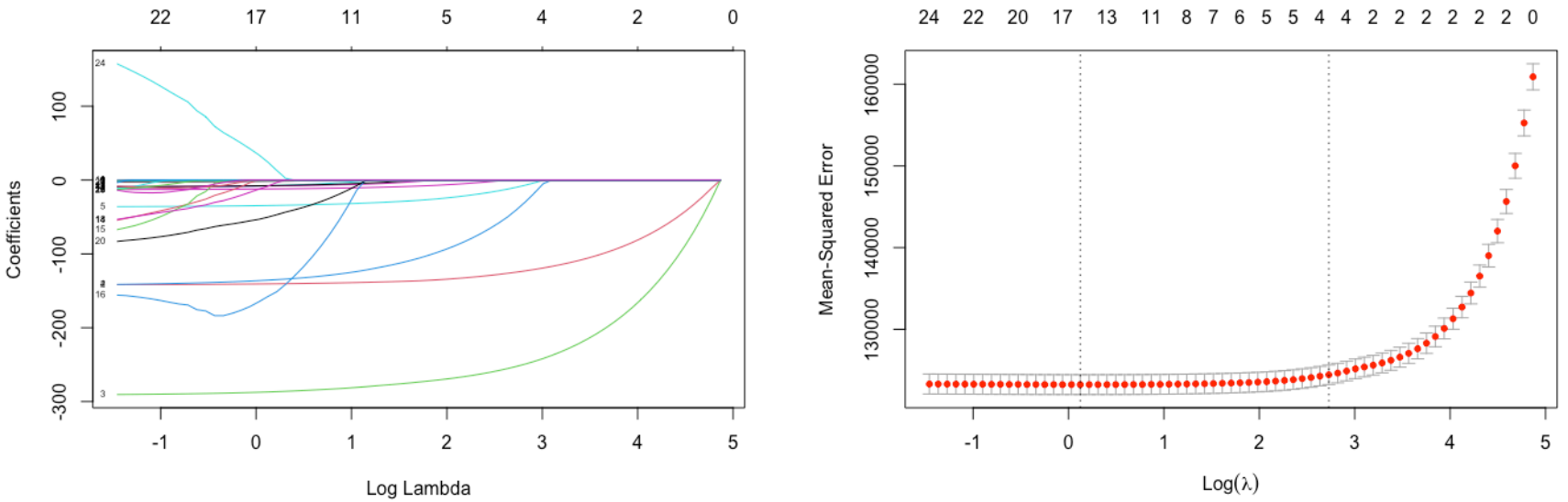
Non-Zero Coefficients from the LASSO-Model at the Optimal Penalty Term (λ = 1.079).

```
## 26 x 1 sparse Matrix of class "dgCMatrix"
##                                    s1
## (Intercept)             3862.0188798
## ptsd                       .
## age_scaled              -148.0249075
## sex_numeric             -277.8937602
## ethn                    -145.1174954
## edubinary                -33.0910814
## deprivation_scaled       -11.7533468
## met.tot.log_rec_scaled    -0.4046325
## soc.visi_recoded_scaled   -0.6711777
## soc.conf_recoded_scaled   -2.9931684
## soc.acti_recoded_scaled    .
## alc.ut_cat2              -12.0524007
## smoking_status           -11.0119046
## hyt                       -7.2462546
## PTSD_age                 -27.9799265
## PTSD_sex                   .
## PTSD_ethn               -239.6557561
## PTSD_education             .
## PTSD_deprivation           .
## PTSD_physical_activity     .
## PTSD_social_visits       -44.7995907
## PTSD_social_confiding     -1.8422856
## PTSD_social_acti           .
## PTSD_alcohol              19.5643709
## PTSD_smoking              17.5985835
## PTSD_hypertension          .
```

Note: PTSD = posttraumatic stress disorder; age_scaled = age (scaled); sex_numeric = male vs. female; ethn = White vs. Asian, Black, Mixed, or Other; edubinary = university or college vs. below, dichotomized; deprivation_scaled = Townsend deprivation index (scaled); met.tot.log_rec_scaled = total metabolic equivalent of task (log-transformed and scaled); soc.visi_recoded_scaled = frequency of family or friends' visits (scaled); soc.conf_recoded_scaled = perceived ability to confide in others (scaled); soc.acti_recoded_scaled = engagement in leisure activities (scaled); alc.ut_cat2 = low vs. increasing/high risk of alcohol consumption; smoking_status = never vs. former/current smoker; hypertension = absent vs. present. Interaction terms (e.g., "PTSD x Age") indicate the interaction between PTSD and the respective variable.

LASSO-Model with PTSD and Right Hippocampal Volume

eFigure C13. Regularization Path for the LASSO-Model (left) and Cross-Validation Error Plot (right).



Non-Zero Coefficients from the LASSO-Model at the Optimal Penalty Term (λ = 1.132).

```
## 26 x 1 sparse Matrix of class "dgCMatrix"
##                                    s1
## (Intercept)              3980.6328447
## ptsd                        .
## age_scaled               -140.6305496
## sex_numeric              -287.0042938
## ethn                     -135.5870218
## edubinary                 -34.5256645
## deprivation_scaled        -12.0201899
## met.tot.log_rec_scaled     -1.7080511
## soc.visi_recoded_scaled    -0.7524826
## soc.conf_recoded_scaled    -0.6356637
## soc.acti_recoded_scaled     .
## alc.ut_cat2                -7.6962947
## smoking_status             -7.9000507
## hyt                        -7.5382114
## PTSD_age                    .
## PTSD_sex                    .
## PTSD_ethn                -157.7331329
## PTSD_education              .
## PTSD_deprivation           -8.3409974
## PTSD_physical_activity      .
## PTSD_social_visits        -50.2469808
## PTSD_social_confiding       .
## PTSD_social_acti            .
## PTSD_alcohol                .
## PTSD_smoking               24.2826691
## PTSD_hypertension           .
```

Note: PTSD = posttraumatic stress disorder; age_scaled = age (scaled); sex_numeric = male vs. female; ethn = White vs. Asian, Black, Mixed, or Other; edubinary = university or college vs. below, dichotomized; deprivation_scaled = Townsend deprivation index (scaled); met.tot.log_rec_scaled = total metabolic equivalent of task (log-transformed and scaled); soc.visi_recoded_scaled = frequency of family or friends' visits (scaled); soc.conf_recoded_scaled = perceived ability to confide in others (scaled); soc.acti_recoded_scaled = engagement in leisure activities (scaled); alc.ut_cat2 = low vs. increasing/high risk of alcohol consumption; smoking_status = never vs. former/current smoker; hypertension = absent vs. present. Interaction terms (e.g., "PTSD x Age") indicate the interaction between PTSD and the respective variable.

eTable C5. Associations between PTSD Diagnosis, Moderators, Cognitive Functioning, Dementia, and Hippocampal Volumes of the Selected Predictors.

	Standardized β (95% CI)	*P*
Cognitive functioning		
Log reaction time*		
PTSD diagnosis	0.0352 (0.0158, 0.0546)	<.001
Age†	0.0601 (0.0595, 0.0607)	<.001
Sex (reference category: Male)	0.031 (0.0299, 0.0322)	<.001
Ethnicity (reference category: White)	0.0865 (0.0838, 0.0891)	<.001
Education (reference category: University or College degree)	0.0217 (0.0206, 0.0229)	<.001
Deprivation†	0.0138 (0.0132, 0.0143)	<.001
Smoking status (reference category: never)	-0.0016 (-0.0027, -0.0005)	.005
Alcohol consumption (reference category: Lower-risk consumption)	-0.0131 (-0.0143, -0.0119)	<.001
Log physical activity†	0.0021 (0.0015, 0.0026)	<.001
Hypertension (reference category: absent)	0.0023 (0.0011, 0.0034)	<.001
Frequency of family or friends' visits†	0.0036 (0.0030, 0.0041)	<.001
Ability to confide in others†	0.0016 (0.0011, 0.0022)	<.001
Engagement in leisure activities†	-0.0008 (-0.0013, -0.0002)	.006
PTSD diagnosis x Age		
PTSD diagnosis x Sex		
PTSD diagnosis x Ethnicity	0.0939 (0.0311, 0.1566)	.003
PTSD diagnosis x Education		
PTSD diagnosis x Deprivation		
PTSD diagnosis x Smoking status		
PTSD diagnosis x Alcohol consumption		
PTSD diagnosis x Physical activity	0.0198 (0.0046, 0.0351)	.011
PTSD diagnosis x Hypertension		
PTSD diagnosis x Frequency of family or friends' visits		
PTSD diagnosis x Ability to confide in others		
PTSD diagnosis x Engagement in leisure activities		
Log visual memory errors*		
PTSD diagnosis		
Age†	0.1073 (0.1053, 0.1093)	< .001
Sex	0.0318 (0.0276, 0.036)	< .001
Ethnicity	0.1521 (0.1425, 0.1616)	< .001
Education	0.0654 (0.0612, 0.0696)	< .001
Deprivation†	0.0172 (0.0152, 0.0192)	< .001
Smoking status	-0.0106 (-0.0146, -0.0065)	< .001
Alcohol consumption	-0.0123 (-0.0166, -0.0079)	< .001
Log physical activity†	-0.016 (-0.0179, -0.014)	< .001
Hypertension		
Frequency of family or friends' visits†	0.0045 (0.0025, 0.0066)	< .001
Ability to confide in others†	0.0023 (0.0003, 0.0043)	.022
Engagement in leisure activities†	0.0059 (0.0039, 0.0079)	< .001
PTSD diagnosis x Age		
PTSD diagnosis x Sex		
PTSD diagnosis x Ethnicity		
PTSD diagnosis x Education		
PTSD diagnosis x Deprivation	0.0646 (0.0075, 0.1218)	.027
PTSD diagnosis x Smoking status		
PTSD diagnosis x Alcohol consumption		
PTSD diagnosis x Physical activity		
PTSD diagnosis x Hypertension		
PTSD diagnosis x Frequency of family or friends' visits		

PTSD diagnosis x Ability to confide in others	-0.0692 (-0.1328, -0.0055)	.033
PTSD diagnosis x Engagement in leisure activities		
Reasoning ability‡		
PTSD diagnosis	-0.5596 (-0.8986, -0.2206)	.001
Age†	-0.1128 (-0.1236, -0.102)	< .001
Sex	-0.1764 (-0.1978, -0.155)	
Ethnicity	-1.7606 (-1.8018, -1.7194)	
Education	-1.3137 (-1.3349, -1.2926)	
Deprivation†	-0.1801 (-0.1903, -0.17)	
Smoking status	-0.0319 (-0.0525, -0.0113)	.002
Alcohol consumption	0.1781 (0.1557, 0.2005)	
Log physical activity†	0.0922 (0.0822, 0.1023)	
Hypertension	-0.0981 (-0.1195, -0.0767)	
Frequency of family or friends' visits†	0.0294 (0.0192, 0.0395)	
Ability to confide in others†		
Engagement in leisure activities†	-0.0928 (-0.103, -0.0826)	
PTSD diagnosis x Age		
PTSD diagnosis x Sex		
PTSD diagnosis x Ethnicity	0.8513 (-0.1728, 1.8754)	.103
PTSD diagnosis x Education		
PTSD diagnosis x Deprivation	-0.3069 (-0.5948, -0.0190)	.037
PTSD diagnosis x Smoking status		
PTSD diagnosis x Alcohol consumption		
PTSD diagnosis x Physical activity	-0.4328 (-0.6883, -0.1773)	.001
PTSD diagnosis x Hypertension		
PTSD diagnosis x Frequency of family or friends' visits	-0.2325 (-0.5078, 0.0429)	.098
PTSD diagnosis x Ability to confide in others		
PTSD diagnosis x Engagement in leisure activities		

	HR (95% CI)	***P***
Dementia		
PTSD diagnosis		
Age†	4.8443 (4.6444, 5.0527)	< .001
Sex	0.7712 (0.7339, 0.8103)	< .001
Ethnicity	1.19 (1.0503, 1.3483)	.006
Education	1.2866 (1.2163, 1.361)	< .001
Deprivation†	1.1672 (1.1415, 1.1935)	< .001
Smoking status	1.1528 (1.0994, 1.2088)	< .001
Alcohol consumption	0.8596 (0.8162, 0.9052)	< .001
Log physical activity†	1.0741 (1.052, 1.0967)	< .001
Hypertension	1.1842 (1.1251, 1.2464)	< .001
Frequency of family or friends' visits†		
Ability to confide in others†	1.0828 (1.0601, 1.1061)	< .001
Engagement in leisure activities†	1.0899 (1.064, 1.1164)	< .001
PTSD diagnosis x Age		
PTSD diagnosis x Sex		
PTSD diagnosis x Ethnicity		
PTSD diagnosis x Education		
PTSD diagnosis x Deprivation	0.6943 (0.4444, 1.0849)	.109
PTSD diagnosis x Smoking status	2.9281 (1.7472, 4.9072)	< .001
PTSD diagnosis x Alcohol consumption		
PTSD diagnosis x Physical activity	0.6981 (0.422, 1.1548)	.162
PTSD diagnosis x Hypertension		
PTSD diagnosis x Frequency of family or friends' visits		
PTSD diagnosis x Ability to confide in others		
PTSD diagnosis x Engagement in leisure activities		

Hippocampal volume‡	Standardized β (95% CI)	*P*
Left		
PTSD diagnosis		
Age†	-148.942 (-153.301, -144.583)	< .001
Sex	-281.563 (-290.37, -272.756)	< .001
Ethnicity	-152.612 (-178.727, -126.496)	< .001
Education	-34.63 (-42.909, -26.351)	< .001
Deprivation†	-12.687 (-16.84, -8.534)	< .001
Smoking status	-12.324 (-20.973, -3.674)	.005
Alcohol consumption	-15.147 (-24.054, -6.241)	.001
Log physical activity†		
Hypertension	-9.125 (-17.962, -0.289)	.043
Frequency of family or friends' visits†		
Ability to confide in others†	-4.096 (-8.217, 0.026)	.051
Engagement in leisure activities†		
PTSD diagnosis x Age		
PTSD diagnosis x Sex		
PTSD diagnosis x Ethnicity	-344.337 (-730.766, 42.092)	.081
PTSD diagnosis x Education		
PTSD diagnosis x Deprivation		
PTSD diagnosis x Smoking status		
PTSD diagnosis x Alcohol consumption		
PTSD diagnosis x Physical activity		
PTSD diagnosis x Hypertension		
PTSD diagnosis x Frequency of family or friends' visits		
PTSD diagnosis x Ability to confide in others		
PTSD diagnosis x Engagement in leisure activities		
Right		
PTSD diagnosis		
Age†	-141.587 (-146.075, -137.100)	< .001
Sex	-290.702 (-299.741, -281.662)	< .001
Ethnicity	-145.019 (-171.847, -118.191)	< .001
Education	-36.312 (-44.827, -27.797)	< .001
Deprivation†	-13.076 (-17.349, -8.802)	< .001
Smoking status	-9.174 (-18.083, -0.266)	.044
Alcohol consumption	-10.85 (-20.023, -1.676)	.020
Log physical activity†		
Hypertension	-9.555 (-18.656, -0.453)	.040
Frequency of family or friends' visits†		
Ability to confide in others†		
Engagement in leisure activities†		
PTSD diagnosis x Age		
PTSD diagnosis x Sex		
PTSD diagnosis x Ethnicity		
PTSD diagnosis x Education		
PTSD diagnosis x Deprivation		
PTSD diagnosis x Smoking status		
PTSD diagnosis x Alcohol consumption		
PTSD diagnosis x Physical activity		
PTSD diagnosis x Hypertension		

	PTSD diagnosis x Frequency of family or friends' visits	-78.232 (-182.276, 25.811)	.141
	PTSD diagnosis x Ability to confide in others		
	PTSD diagnosis x Engagement in leisure activities		

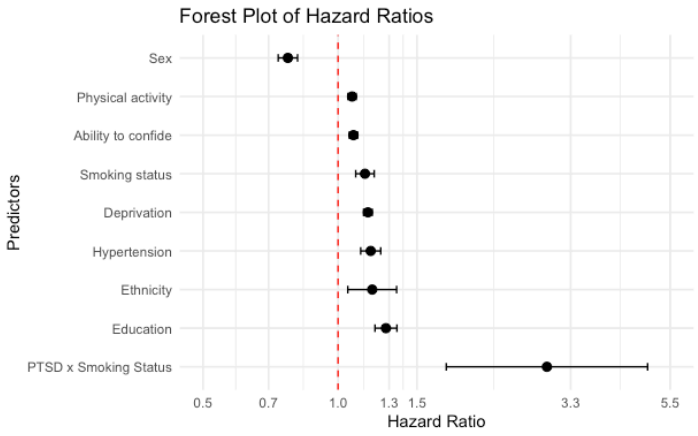
CI = confidence interval; P = p-value; PTSD = posttraumatic stress disorder; HR = hazard ratio.
Based on the final model, after stepwise selection of the LASSO-selected predictors.
*Positive coefficients indicate a worse outcome.
†Variables were standardized to have a mean of 0 and a standard deviation of 1.
‡Negative coefficients indicate a worse outcome.

eTable C6. Associations between PTSD Diagnosis, Moderators, and Dementia in the Stratified Model.

Dementia	HR (95% CI)	*P*
PTSD diagnosis		
Age*		
Sex	0.773 (0.7356, 0.8124)	< .001
Ethnicity	1.1918 (1.0515, 1.3507)	.006
Education	1.2788 (1.2087, 1.353)	< .001
Deprivation*	1.1657 (1.14, 1.1921)	< .001
Smoking status	1.1483 (1.0951, 1.2041)	< .001
Alcohol consumption		
Log weekly physical activity*	1.0747 (1.0526, 1.0973)	< .001
Hypertension	1.1826 (1.1235, 1.2449)	< .001
Frequency of family or friends' visits*		
Ability to confide in others*	1.0823 (1.0596, 1.1056)	< .001
Engagement in leisure activities*		
PTSD diagnosis x Age		
PTSD diagnosis x Sex		
PTSD diagnosis x Ethnicity		
PTSD diagnosis x Education		
PTSD diagnosis x Deprivation	0.7088 (0.4554, 1.1033)	.127
PTSD diagnosis x Smoking status	2.9217 (1.7427, 4.8983)	< .001
PTSD diagnosis x Alcohol consumption		
PTSD diagnosis x Physical activity	0.7062 (0.4271, 1.1677)	.175
PTSD diagnosis x Hypertension		
PTSD diagnosis x Frequency of family or friends' visits		
PTSD diagnosis x Ability to confide in others		
PTSD diagnosis x Engagement in leisure activities		

CI = confidence interval; P = p-value; PTSD = posttraumatic stress disorder; HR = hazard ratio.
*Variables were standardized to have a mean of 0 and a standard deviation of 1.

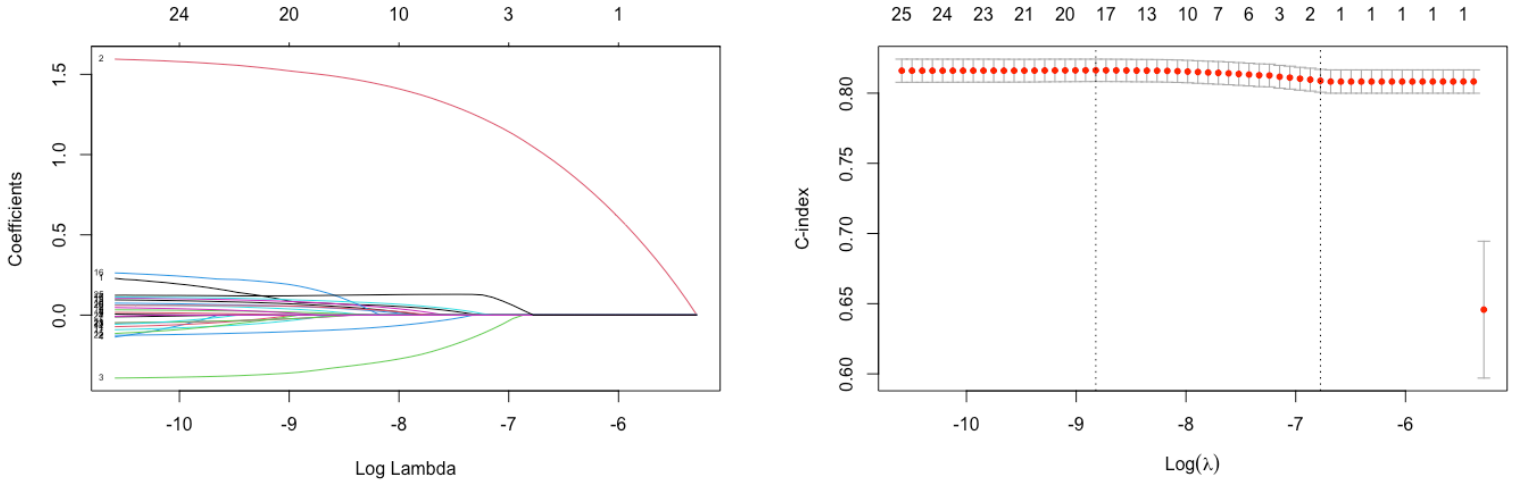
eFigure C14. Forest Plot of the Stratified Stepwise Model PTSD Diagnosis – Dementia.



LASSO-Models with Posttraumatic Stress Disorder (PTSD) Symptoms as the Main Predictor

LASSO-Model with PTSD Symptoms and Dementia

eFigure C15. Regularization Path for the LASSO-Model (left) and Cross-Validation Error Plot (right).



The regularization path for the LASSO-Model (left) illustrates how the regression coefficients of all predictors change as the penalty term (i.e., regularization strength, λ) varies. As λ increases, more coefficients shrink toward zero, resulting in a sparser model with fewer selected predictors. The cross-validation error plot (right) displays the 1-C-index across different values of λ, where the optimal penalty term is selected at the minimum cross-validation error, corresponding to the highest C-index. This ensures an optimal balance between sparsity and predictive performance.

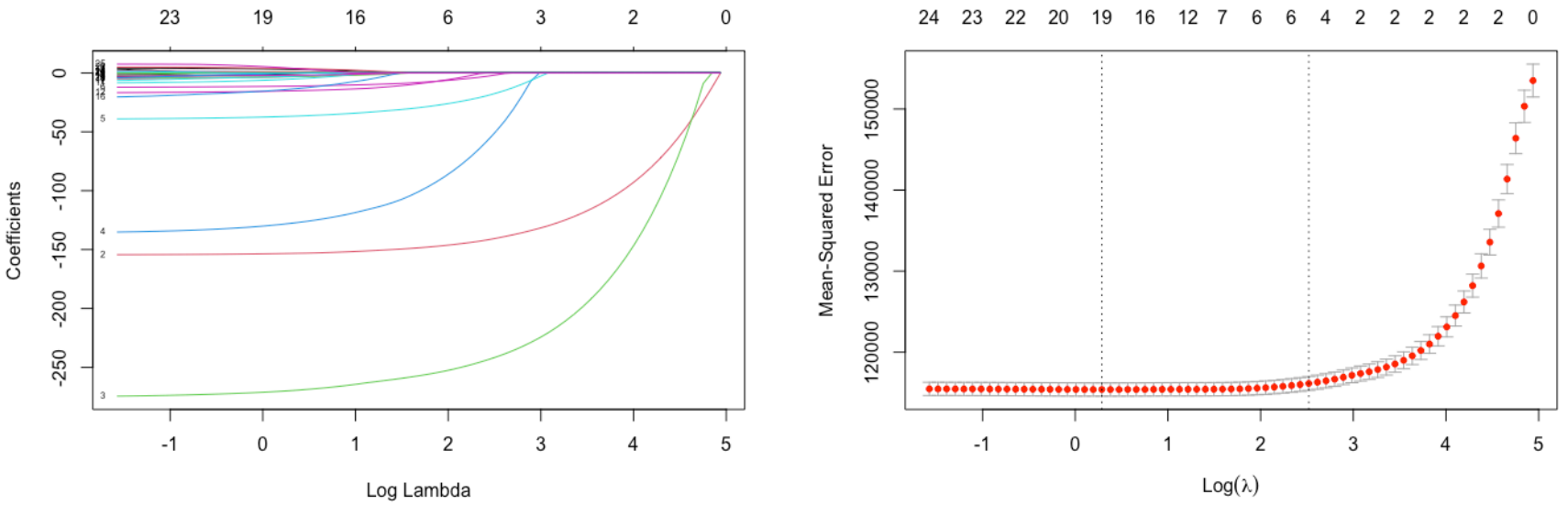
Non-Zero Coefficients from the LASSO-Model at the Optimal Penalty Term (λ = 0.00015).

```
## 25 x 1 sparse Matrix of class "dgCMatrix"
##                                1
## pcl_scaled              0.07673801
## age_scaled              1.50809980
## sex_numeric            -0.34907659
## ethn                    .
## edubinary               0.03147326
## deprivation_scaled      0.07969321
## met.tot.log_rec_scaled  .
## soc.visi_recoded_scaled .
## soc.conf_recoded_scaled 0.01551441
## soc.acti_recoded_scaled 0.05045681
## alc.ut_cat2            -0.01998410
## smoking_status          0.00501659
## hyt                     0.06425878
## PTSD_age                .
## PTSD_sex                .
## PTSD_ethn               0.16747712
## PTSD_education          0.09202844
## PTSD_deprivation       -0.01736032
## PTSD_physical_activity  .
## PTSD_social_visits      0.05283664
## PTSD_social_confiding  -0.01664324
## PTSD_social_acti       -0.09872740
## PTSD_alcohol            .
## PTSD_smoking            .
## PTSD_hypertension       0.12148777
```

Note: pcl_scaled = self-reported PTSD symptoms (scaled); PTSD = posttraumatic stress disorder; age_scaled = age (scaled); sex_numeric = male vs. female; ethn = White vs. Asian, Black, Mixed, or Other; edubinary = university or college vs. below, dichotomized; deprivation_scaled = Townsend deprivation index (scaled); met.tot.log_rec_scaled = total metabolic equivalent of task (log-transformed and scaled); soc.visi_recoded_scaled = frequency of family or friends' visits (scaled); soc.conf_recoded_scaled = perceived ability to confide in others (scaled); soc.acti_recoded_scaled = engagement in leisure activities (scaled); alc.ut_cat2 = low vs. increasing/high risk of alcohol consumption; smoking_status = never vs. former/current smoker; hypertension = absent vs. present. Interaction terms (e.g., "PTSD x Age") indicate the interaction between PTSD symptoms and the respective variable.
The values are in log-hazard ratio format (i.e., raw coefficients before exponentiation).

LASSO-Model with PTSD Symptoms and Left Hippocampal Volume

eFigure C16. Regularization Path for the LASSO-Model (left) and Cross-Validation Error Plot (right).



The regularization path for the LASSO-Model (left) illustrates how the regression coefficients of all predictors change as the penalty term (i.e., regularization strength, λ) varies. As λ increases, more coefficients shrink toward zero, resulting in a sparser model with fewer selected predictors. The cross-validation error plot (right) displays the model's cross-validation error (i.e., mean squared error) across different values of λ, aiming to identify the optimal penalty term that minimizes prediction error while avoiding overfitting. The lowest point on the curve represents the chosen λ, ensuring an optimal balance-off between sparsity and accuracy.

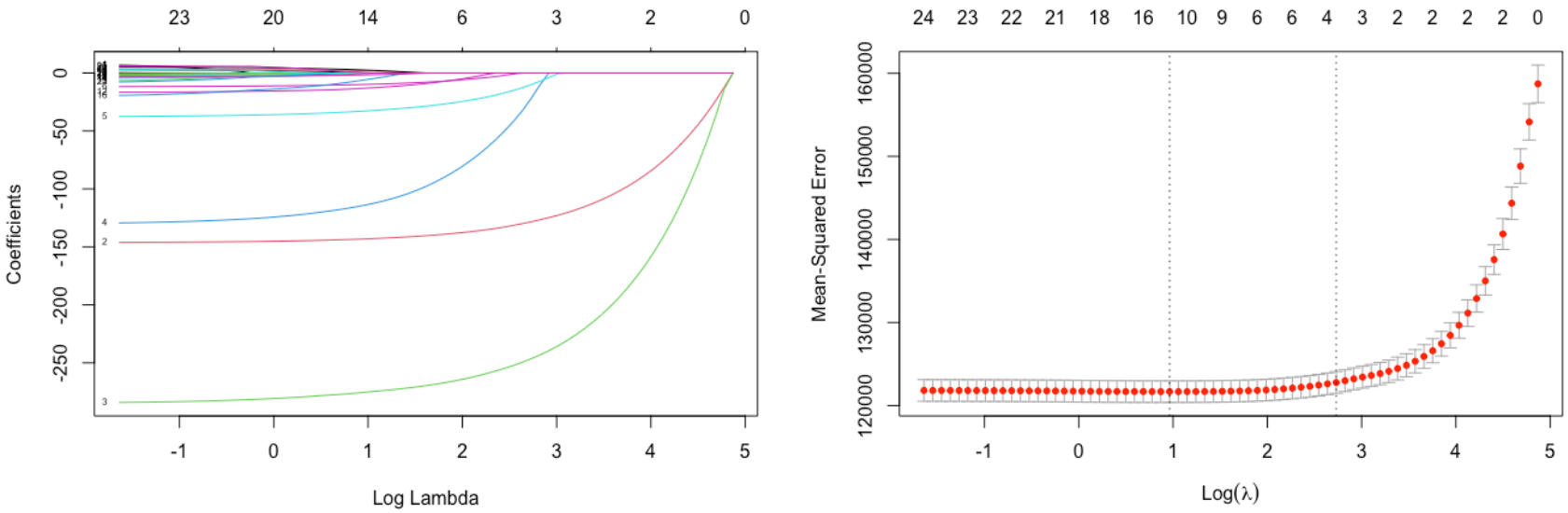
Non-Zero Coefficients from the LASSO-Model at the Optimal Penalty Term (λ = 1.332).

```
## 26 x 1 sparse Matrix of class "dgCMatrix"
##                                    s1
## (Intercept)              3857.3268401
## pcl_scaled                  .
## age_scaled               -153.2898141
## sex_numeric              -269.9087374
## ethn                     -127.8654284
## edubinary                 -36.8464320
## deprivation_scaled        -11.2495843
## met.tot.log_rec_scaled      3.0513289
## soc.visi_recoded_scaled    -3.2528961
## soc.conf_recoded_scaled    -3.0737770
## soc.acti_recoded_scaled     0.5349036
## alc.ut_cat2                -5.2778808
## smoking_status            -15.2523205
## hyt                        -0.7793078
## PTSD_age                    0.8217345
## PTSD_sex                    .
## PTSD_ethn                 -13.8384079
## PTSD_education             -2.9903572
## PTSD_deprivation           -1.9787311
## PTSD_physical_activity      .
## PTSD_social_visits          3.8561107
## PTSD_social_confiding       .
## PTSD_social_acti            .
## PTSD_alcohol               -0.2811099
## PTSD_smoking                .
## PTSD_hypertension           4.1232417
```

Note: pcl_scaled = self-reported PTSD symptoms (scaled); PTSD = posttraumatic stress disorder; age_scaled = age (scaled); sex_numeric = male vs. female; ethn = White vs. Asian, Black, Mixed, or Other; edubinary = university or college vs. below, dichotomized; deprivation_scaled = Townsend deprivation index (scaled); met.tot.log_rec_scaled = total metabolic equivalent of task (log-transformed and scaled); soc.visi_recoded_scaled = frequency of family or friends' visits (scaled); soc.conf_recoded_scaled = perceived ability to confide in others (scaled); soc.acti_recoded_scaled = engagement in leisure activities (scaled); alc.ut_cat2 = low vs. increasing/high risk of alcohol consumption; smoking_status = never vs. former/current smoker; hypertension = absent vs. present. Interaction terms (e.g., "PTSD x Age") indicate the interaction between PTSD symptoms and the respective variable.

LASSO-Model with PTSD Symptoms and Right Hippocampal Volume

eFigure C17. Regularization Path for the LASSO-Model (left) and Cross-Validation Error Plot (right).



Non-Zero Coefficients from the LASSO-Model at the Optimal Penalty Term (λ = 2.619).

```
## 26 x 1 sparse Matrix of class "dgCMatrix"
##                                    s1
## (Intercept)             3973.39139299
## pcl_scaled                 .
## age_scaled              -143.13501725
## sex_numeric             -275.40553229
## ethn                    -114.07206925
## edubinary                -32.84794010
## deprivation_scaled        -9.88332169
## met.tot.log_rec_scaled     0.19909934
## soc.visi_recoded_scaled   -0.54872739
## soc.conf_recoded_scaled   -0.02604787
## soc.acti_recoded_scaled    .
## alc.ut_cat2                .
## smoking_status          -13.14752837
## hyt                        .
## PTSD_age                   2.03125961
## PTSD_sex                   .
## PTSD_ethn                 -5.96969468
## PTSD_education             .
## PTSD_deprivation          -1.69523925
## PTSD_physical_activity     .
## PTSD_social_visits         2.56933584
## PTSD_social_confiding      .
## PTSD_social_acti           .
## PTSD_alcohol               .
## PTSD_smoking               .
## PTSD_hypertension          0.17704945
```

Note: pcl_scaled = self-reported PTSD symptoms (scaled); PTSD = posttraumatic stress disorder; age_scaled = age (scaled); sex_numeric = male vs. female; ethn = White vs. Asian, Black, Mixed, or Other; edubinary = university or college vs. below, dichotomized; deprivation_scaled = Townsend deprivation index (scaled); met.tot.log_rec_scaled = total metabolic equivalent of task (log-transformed and scaled); soc.visi_recoded_scaled = frequency of family or friends' visits (scaled); soc.conf_recoded_scaled = perceived ability to confide in others (scaled); soc.acti_recoded_scaled = engagement in leisure activities (scaled); alc.ut_cat2 = low vs. increasing/high risk of alcohol consumption; smoking_status = never vs. former/current smoker; hypertension = absent vs. present. Interaction terms (e.g., "PTSD x Age") indicate the interaction between PTSD symptoms and the respective variable.

eTable C7. Associations between PTSD Symptoms, Moderators, Dementia, and Hippocampal Volumes of the Selected Predictors.

Dementia	**HR (95% CI)**	***P***
PTSD Symptoms†		
Age†	5.0226 (4.4137, 5.7154)	< .001
Sex (reference category: Male)	0.6691 (0.5727, 0.7818)	< .001
Ethnicity (reference category: White)		
Education (reference category: University or College degree)		
Deprivation†	1.1225 (1.0401, 1.2115)	.003
Smoking status (reference category: Never)		
Alcohol consumption (reference category: Lower-risk consumption)		
Log physical activity†		
Hypertension (reference category: absent)		
Frequency of family or friends' visits†		
Ability to confide in others†		
Engagement in leisure activities†	1.092 (1.0106, 1.1799)	
PTSD symptoms x Age		
PTSD symptoms x Sex		
PTSD symptoms x Ethnicity	1.387 (1.0111, 1.9025)	.043
PTSD symptoms x Education	1.189 (1.0531, 1.3424)	.005
PTSD symptoms x Deprivation	0.953 (0.8914, 1.0188)	.158
PTSD symptoms x Smoking status		
PTSD symptoms x Alcohol consumption		
PTSD symptoms x Physical activity		
PTSD symptoms x Hypertension	1.1923 (1.0568, 1.3452)	.004
PTSD symptoms x Frequency of family or friends' visits	1.0854 (1.0221, 1.1527)	.008
PTSD symptoms x Ability to confide in others	0.9508 (0.8912, 1.0143)	.126
PTSD symptoms x Engagement in leisure activities	0.8805 (0.8251, 0.9396)	< .001

Hippocampal volume‡	**Standardized β (95% CI)**	***P***
Left		
PTSD symptoms†		
Age†	-154.986 (-161.105, -148.867)	< .001
Sex	-271.474 (-283.677, -259.27)	< .001
Ethnicity	-139.18 (-180.624, -97.735)	< .001
Education	-40.006 (-52.092, -27.92)	< .001
Deprivation†	-12.894 (-18.942, -6.847)	< .001
Smoking status	-18.356 (-30.843, -5.869)	.004
Alcohol consumption		
Log physical activity†	4.566 (-1.423, 10.556)	.135
Hypertension		
Frequency of family or friends' visits†	-5.417 (-11.517, 0.683)	.082
Ability to confide in others†		
Engagement in leisure activities†		
PTSD symptoms x Age		
PTSD symptoms x Sex		
PTSD symptoms x Ethnicity		
PTSD symptoms x Education		
PTSD symptoms x Deprivation		
PTSD symptoms x Smoking status		
PTSD symptoms x Alcohol consumption		
PTSD symptoms x Physical activity		
PTSD symptoms x Hypertension		

	PTSD symptoms x Frequency of family or friends' visits	5.089 (-0.616, 10.794)	.080
	PTSD symptoms x Ability to confide in others		
	PTSD symptoms x Engagement in leisure activities		
Right			
	PTSD symptoms[†]		
	Age[†]	-145.994 (-152.247, -139.742)	< .001
	Sex	-281.385 (-293.793, -268.977)	< .001
	Ethnicity	-134.819 (-177.345, -92.293)s	< .001
	Education	-37.177 (-49.529, -24.825)	< .001
	Deprivation[†,‡]	-12.382 (-18.594, -6.17)	< .001
	Smoking status	-17.597 (-30.42, -4.774)	.007
	Alcohol consumption		
	Log physical activity[†]		
	Hypertension		
	Frequency of family or friends' visits[†]		
	Ability to confide in others[†]		
	Engagement in leisure activities[†]		
	PTSD symptoms x Age	5.224 (-0.983, 11.431)	.099
	PTSD symptoms x Sex		
	PTSD symptoms x Ethnicity		
	PTSD symptoms x Education		
	PTSD symptoms x Deprivation		
	PTSD symptoms x Smoking status		
	PTSD symptoms x Alcohol consumption		
	PTSD symptoms x Physical activity		
	PTSD symptoms x Hypertension		
	PTSD symptoms x Frequency of family or friends' visits		
	PTSD symptoms x Ability to confide in others		
	PTSD symptoms x Engagement in leisure activities	5.328 (-0.561, 11.217)	.076

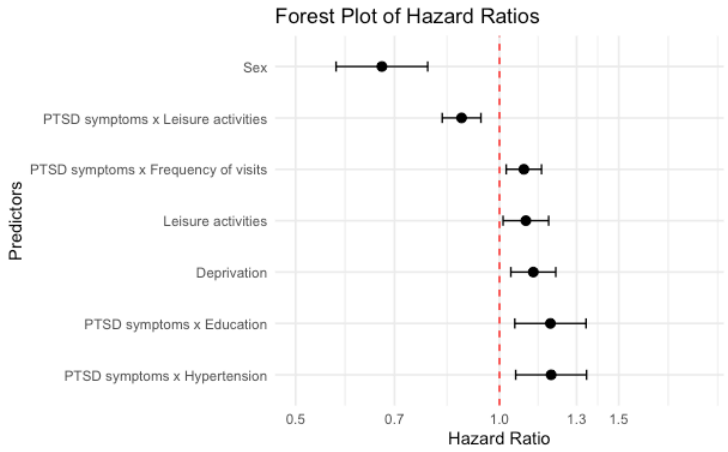
CI = confidence interval; P = p-value; PTSD = posttraumatic stress disorder; HR = hazard ratio.
Based on the final model, after stepwise selection of the LASSO-selected predictors.
[*]Positive coefficients indicate a worse outcome.
[†]Variables were standardized to have a mean of 0 and a standard deviation of 1.
[‡]Negative coefficients indicate a worse outcome.

eTable C8. Associations between PTSD symptoms, Moderators, and Dementia in the Stratified Model.

Dementia	HR (95% CI)	*P*
PTSD Symptoms*		
Age*		
Sex	0.6704 (0.5738, 0.7834)	< .001
Ethnicity		
Education		
Deprivation*	1.122 (1.0395, 1.211)	.003
Smoking status		
Alcohol consumption		
Log weekly physical activity*		
Hypertension		
Frequency of family or friends' visits*		
Ability to confide in others*		
Engagement in leisure activities*	1.0939 (1.0123, 1.182)	.023
PTSD symptoms x Age		
PTSD symptoms x Sex		
PTSD symptoms x Ethnicity	1.3719 (0.9993, 1.8836)	.051
PTSD symptoms x Education	1.1892 (1.0536, 1.3422)	.005
PTSD symptoms x Deprivation	0.953 (0.8913, 1.0188)	.158
PTSD symptoms x Smoking status		
PTSD symptoms x Alcohol consumption		
PTSD symptoms x Physical activity		
PTSD symptoms x Hypertension	1.192 (1.0567, 1.3447)	.004
PTSD symptoms x Frequency of family or friends' visits	1.0865 (1.0232, 1.1536)	.007
PTSD symptoms x Ability to confide in others	0.9525 (0.893, 1.016)	.139
PTSD symptoms x Engagement in leisure activities	0.8791 (0.8231, 0.9389)	< .001

CI = confidence interval; P = p-value; PTSD = posttraumatic stress disorder; HR = hazard ratio.
*Variables were standardized to have a mean of 0 and a standard deviation of 1.

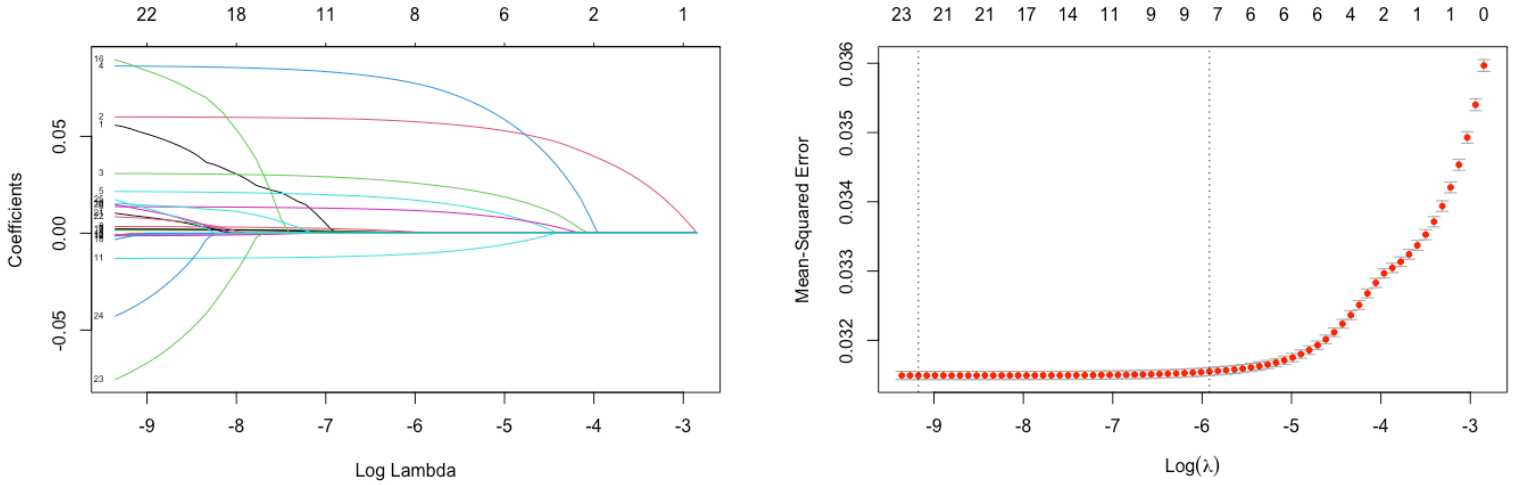
eFigure C18. Forest Plot of the Stratified Stepwise Model PTSD Symptoms – Dementia.



LASSO-Models with Dissociative Disorders as the Main Predictor

LASSO-Model with Dissociative Disorders and Log Reaction Time

eFigure C19. Regularization Path for the LASSO-Model (left) and Cross-Validation Error Plot (right).



The regularization path for the LASSO-Model (left) illustrates how the regression coefficients of all predictors change as the penalty term (i.e., regularization strength, λ) varies. As λ increases, more coefficients shrink toward zero, resulting in a sparser model with fewer selected predictors. The cross-validation error plot (right) displays the model's cross-validation error (i.e., mean squared error) across different values of λ, aiming to identify the optimal penalty term that minimizes prediction error while avoiding overfitting. The lowest point on the curve represents the chosen λ, ensuring an optimal balance-off between sparsity and accuracy.

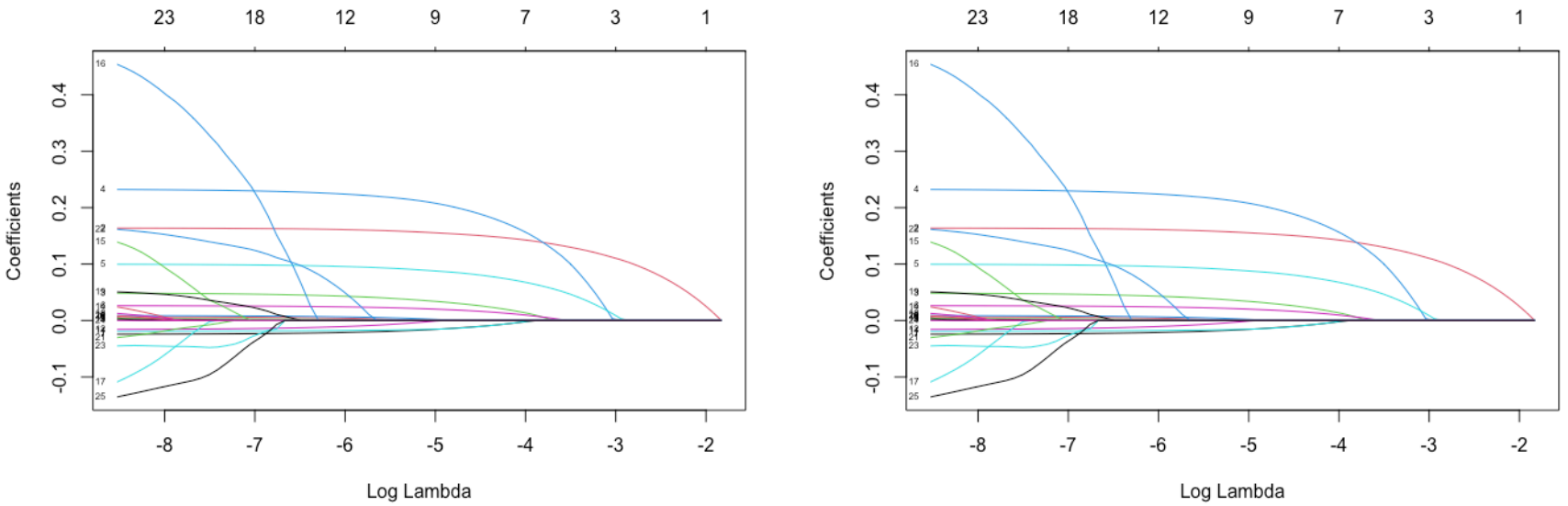
Non-Zero Coefficients from the LASSO-Model at the Optimal Penalty Term (λ = 0.00010).

```
## 26 x 1 sparse Matrix of class "dgCMatrix"
##                                    s1
## (Intercept)                6.2772820967
## diss                       0.0537605714
## age_scaled                 0.0600007903
## sex_numeric                0.0308012435
## ethn                       0.0862748618
## edubinary                  0.0214944921
## deprivation_scaled         0.0136876951
## met.tot.log_rec_scaled     0.0019894949
## soc.visi_recoded_scaled    0.0034203422
## soc.conf_recoded_scaled    0.0015643927
## soc.acti_recoded_scaled   -0.0006302216
## alc.ut_cat2               -0.0129999104
## smoking_status            -0.0013502853
## hyt                        0.0021000034
## diss_age                   .
## diss_sex                   .
## diss_ethn                  0.0868290804
## diss_education             .
## diss_deprivation          -0.0015025834
## diss_physical_activity     0.0149620049
## diss_social_visits         0.0132033027
## diss_social_confiding      0.0092004804
## diss_social_acti           0.0080996468
## diss_alcohol              -0.0715745275
## diss_smoking              -0.0387262416
## diss_hypertension          0.0147857508
```

Note: Diss = dissociative disorders; age_scaled = age (scaled); sex_numeric = male vs. female; ethn = White vs. Asian, Black, Mixed, or Other; edubinary = university or college vs. below, dichotomized; deprivation_scaled = Townsend deprivation index (scaled); met.tot.log_rec_scaled = total metabolic equivalent of task (log-transformed and scaled); soc.visi_recoded_scaled = frequency of family or friends' visits (scaled); soc.conf_recoded_scaled = perceived ability to confide in others (scaled); soc.acti_recoded_scaled = engagement in leisure activities (scaled); alc.ut_cat2 = low vs. increasing/high risk of alcohol consumption; smoking_status = never vs. former/current smoker; hypertension = absent vs. present. Interaction terms (e.g., "Diss x Age") indicate the interaction between dissociative disorders and the respective variable.

LASSO-Model with Dissociative Disorders and Log Visual Memory Errors

eFigure C20. Regularization Path for the LASSO-Model (left) and Cross-Validation Error Plot (right).



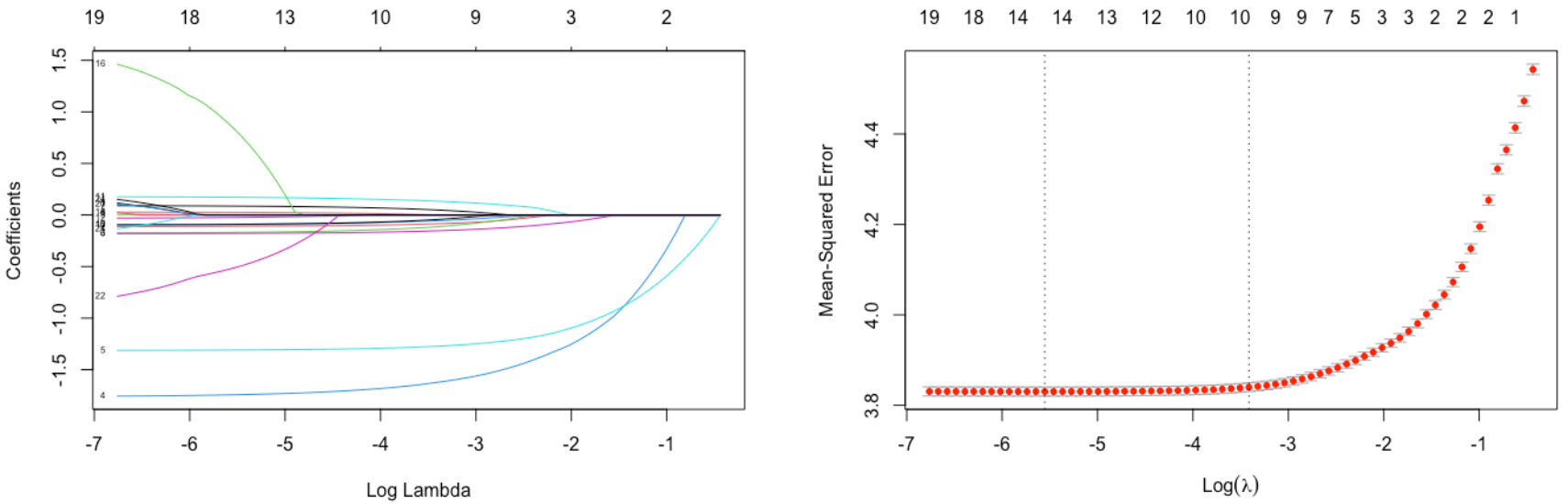
Non-Zero Coefficients from the LASSO-Model at the Optimal Penalty Term (λ = 0.00127).

```
## 26 x 1 sparse Matrix of class "dgCMatrix"
##                                    s1
## (Intercept)             -0.0864867155
## diss                     .
## age_scaled               0.1626770245
## sex_numeric              0.0458556542
## ethn                     0.2283887570
## edubinary                0.0978144638
## deprivation_scaled       0.0253049674
## met.tot.log_rec_scaled  -0.0227908684
## soc.visi_recoded_scaled  0.0054828543
## soc.conf_recoded_scaled  0.0025112212
## soc.acti_recoded_scaled  0.0077481883
## alc.ut_cat2             -0.0181963751
## smoking_status          -0.0132946205
## hyt                      0.0003865989
## diss_age                 .
## diss_sex                 .
## diss_ethn                0.1246864408
## diss_education           .
## diss_deprivation         .
## diss_physical_activity   0.0073613291
## diss_social_visits       .
## diss_social_confiding    .
## diss_social_acti         0.1070099215
## diss_alcohol             .
## diss_smoking             .
## diss_hypertension        .
```

Note: Diss = dissociative disorders; age_scaled = age (scaled); sex_numeric = male vs. female; ethn = White vs. Asian, Black, Mixed, or Other; edubinary = university or college vs. below, dichotomized; deprivation_scaled = Townsend deprivation index (scaled); met.tot.log_rec_scaled = total metabolic equivalent of task (log-transformed and scaled); soc.visi_recoded_scaled = frequency of family or friends' visits (scaled); soc.conf_recoded_scaled = perceived ability to confide in others (scaled); soc.acti_recoded_scaled = engagement in leisure activities (scaled); alc.ut_cat2 = low vs. increasing/high risk of alcohol consumption; smoking_status = never vs. former/current smoker; hypertension = absent vs. present. Interaction terms (e.g., "Diss x Age") indicate the interaction between dissociative disorders and the respective variable.

LASSO-Model with Dissociative Disorders and Reasoning Ability

eFigure C21. Regularization Path for the LASSO-Model (left) and Cross-Validation Error Plot (right).



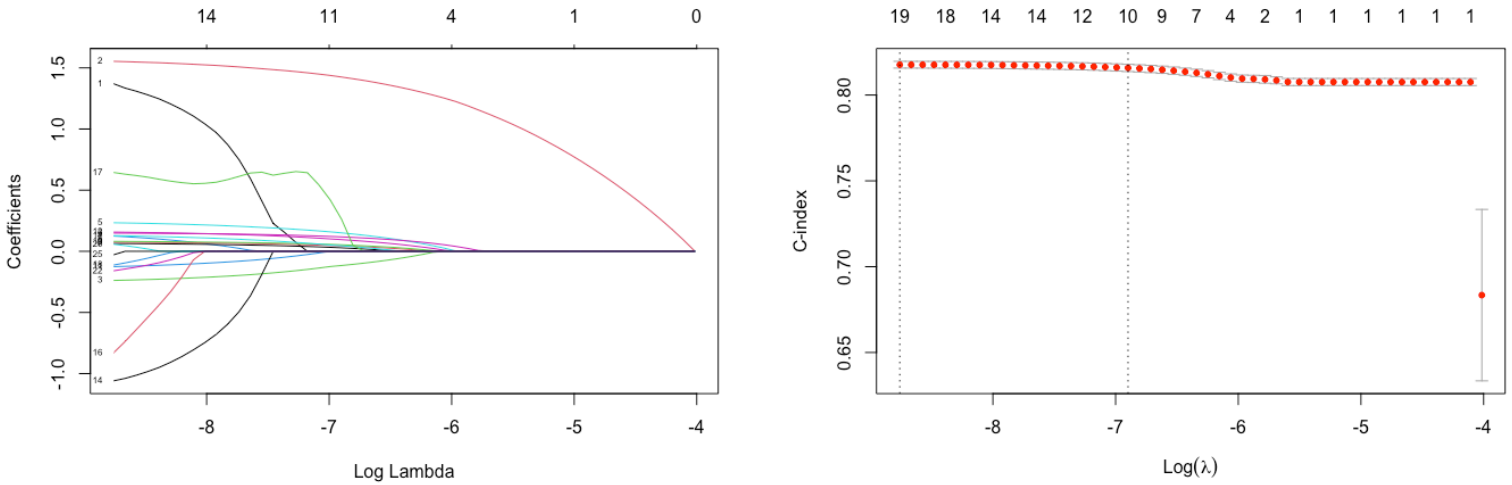
Non-Zero Coefficients from the LASSO-Model at the Optimal Penalty Term (λ = 0.00387).

```
## 26 x 1 sparse Matrix of class "dgCMatrix"
##                                    s1
## (Intercept)              7.114917203
## diss                     .
## age_scaled              -0.109606911
## sex_numeric             -0.168346866
## ethn                    -1.743335414
## edubinary               -1.309449131
## deprivation_scaled      -0.177833252
## met.tot.log_rec_scaled   0.086459208
## soc.visi_recoded_scaled  0.025380405
## soc.conf_recoded_scaled  0.001481935
## soc.acti_recoded_scaled -0.088426428
## alc.ut_cat2              0.172444838
## smoking_status          -0.024099009
## hyt                     -0.091543624
## diss_age                 .
## diss_sex                 .
## diss_ethn                0.852768889
## diss_education           .
## diss_deprivation         .
## diss_physical_activity   .
## diss_social_visits       .
## diss_social_confiding    .
## diss_social_acti        -0.517348204
## diss_alcohol             .
## diss_smoking             .
## diss_hypertension        .
```

Note: Diss = dissociative disorders; age_scaled = age (scaled); sex_numeric = male vs. female; ethn = White vs. Asian, Black, Mixed, or Other; edubinary = university or college vs. below, dichotomized; deprivation_scaled = Townsend deprivation index (scaled); met.tot.log_rec_scaled = total metabolic equivalent of task (log-transformed and scaled); soc.visi_recoded_scaled = frequency of family or friends' visits (scaled); soc.conf_recoded_scaled = perceived ability to confide in others (scaled); soc.acti_recoded_scaled = engagement in leisure activities (scaled); alc.ut_cat2 = low vs. increasing/high risk of alcohol

LASSO-Model with Dissociative Disorders and Dementia

eFigure C22. Regularization Path for the LASSO-Model (left) and Cross-Validation Error Plot (right).



The regularization path for the LASSO-Model (left) illustrates how the regression coefficients of all predictors change as the penalty term (i.e., regularization strength, λ) varies. As λ increases, more coefficients shrink toward zero, resulting in a sparser model with fewer selected predictors. The cross-validation error plot (right) displays the 1-C-index across different values of λ, where the optimal penalty term is selected at the minimum cross-validation error, corresponding to the highest C-index. This ensures an optimal balance between sparsity and predictive performance.

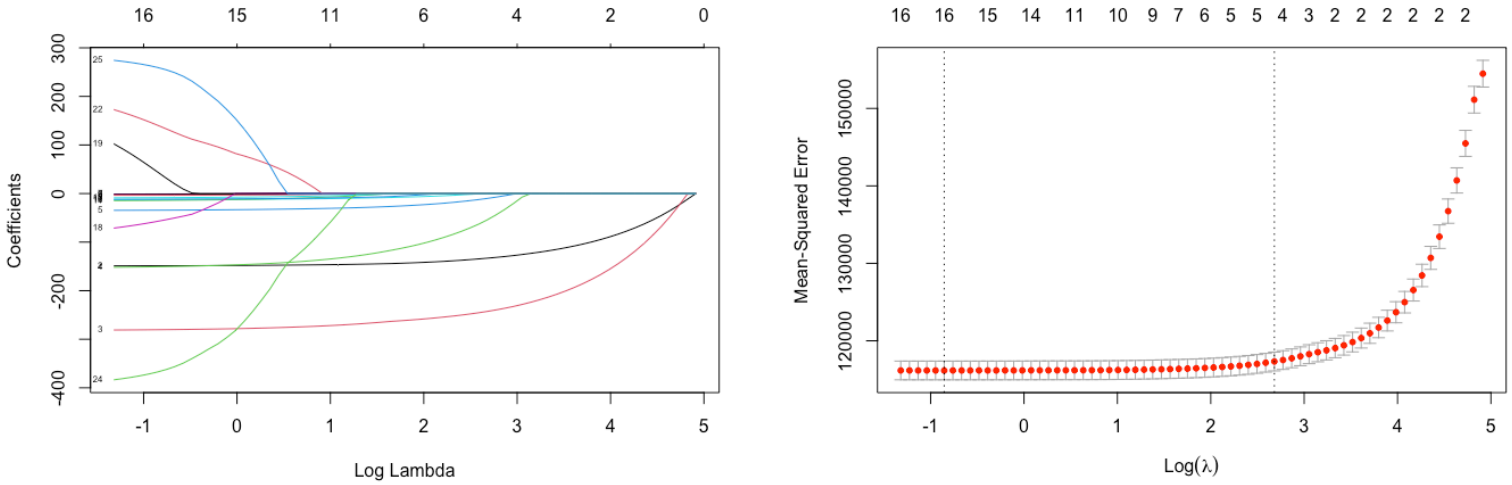
Non-Zero Coefficients from the LASSO-Model at the Optimal Penalty Term (λ = 0.00016).

```
## 25 x 1 sparse Matrix of class "dgCMatrix"
##                                1
## dissdem                 1.37019343
## age_scaled              1.55360208
## sex_numeric            -0.23824686
## ethn                    0.12484062
## edubinary               0.23356098
## deprivation_scaled      0.14886082
## met.tot.log_rec_scaled  0.06401875
## soc.visi_recoded_scaled .
## soc.conf_recoded_scaled 0.07443124
## soc.acti_recoded_scaled 0.08109488
## alc.ut_cat2            -0.12544695
## smoking_status          0.12758342
## hyt                     0.15711608
## diss_age               -1.05926534
## diss_sex                .
## diss_ethn              -0.82954306
## diss_education          0.64460415
## diss_deprivation       -0.11239342
## diss_physical_activity  .
## diss_social_visits      0.05772338
## diss_social_confiding   .
## diss_social_acti       -0.15936269
## diss_alcohol            .
## diss_smoking            .
## diss_hypertension      -0.02841858
```

Note: Diss = dissociative disorders; age_scaled = age (scaled); sex_numeric = male vs. female; ethn = White vs. Asian, Black, Mixed, or Other; edubinary = university or college vs. below, dichotomized; deprivation_scaled = Townsend deprivation index (scaled); met.tot.log_rec_scaled = total metabolic equivalent of task (log-transformed and scaled); soc.visi_recoded_scaled = frequency of family or friends' visits (scaled); soc.conf_recoded_scaled = perceived ability to confide in others (scaled); soc.acti_recoded_scaled = engagement in leisure activities (scaled); alc.ut_cat2 = low vs. increasing/high risk of alcohol consumption; smoking_status = never vs. former/current smoker; hypertension = absent vs. present. Interaction terms (e.g., "Diss x Age") indicate the interaction between dissociative disorders and the respective variable.
The values are in log-hazard ratio format (i.e., raw coefficients before exponentiation).

LASSO-Model with Dissociative Disorders and Left Hippocampal Volume

eFigure C23. Regularization Path for the LASSO-Model (left) and Cross-Validation Error Plot (right).



The regularization path for the LASSO-Model (left) illustrates how the regression coefficients of all predictors change as the penalty term (i.e., regularization strength, λ) varies. As λ increases, more coefficients shrink toward zero, resulting in a sparser model with fewer selected predictors. The cross-validation error plot (right) displays the model's cross-validation error (i.e., mean squared error) across different values of λ, aiming to identify the optimal penalty term that minimizes prediction error while avoiding overfitting. The lowest point on the curve represents the chosen λ, ensuring an optimal balance-off between sparsity and accuracy.

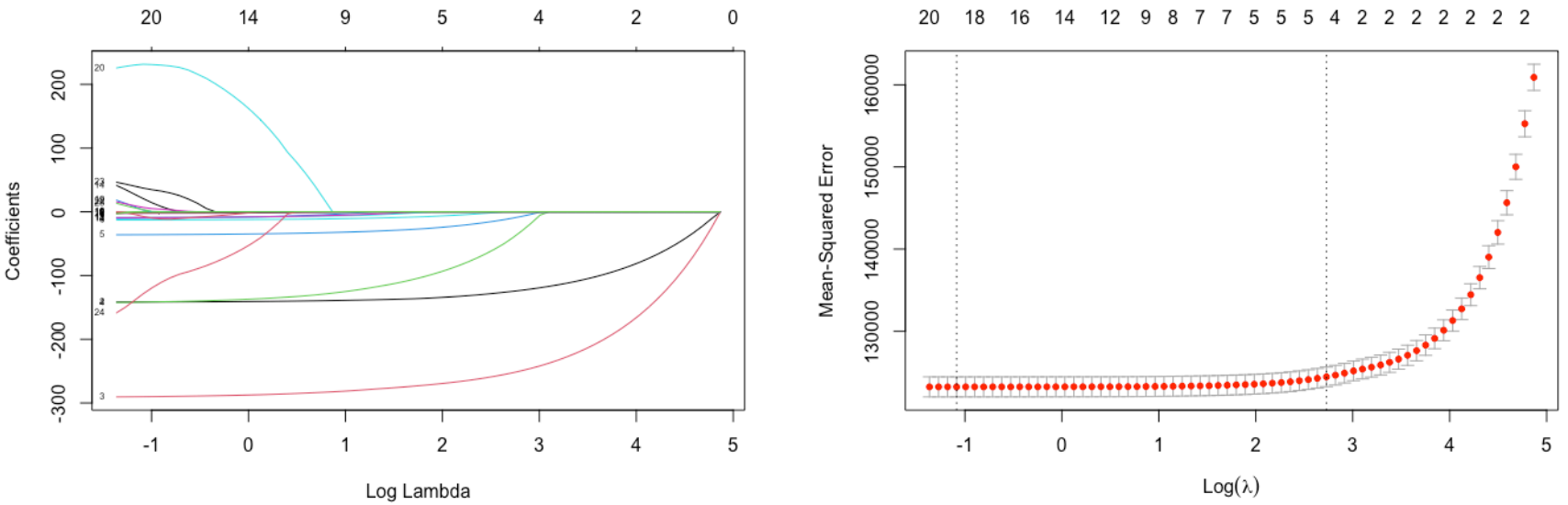
Non-Zero Coefficients from the LASSO-Model at the Optimal Penalty Term (λ = 0.426).

```
## 26 x 1 sparse Matrix of class "dgCMatrix"
##                                    s1
## (Intercept)              3865.7288146
## diss                        .
## age_scaled               -148.7622787
## sex_numeric              -280.3839905
## ethn                     -150.6728596
## edubinary                 -34.2937614
## deprivation_scaled        -12.3212722
## met.tot.log_rec_scaled     -0.9557508
## soc.visi_recoded_scaled    -1.5642995
## soc.conf_recoded_scaled    -3.4177132
## soc.acti_recoded_scaled     .
## alc.ut_cat2              -14.1016924
## smoking_status           -11.6143840
## hyt                       -8.4443652
## diss_age                    .
## diss_sex                    .
## diss_ethn                   .
## diss_education              .
## diss_deprivation         -57.3272600
## diss_physical_activity    44.8442562
## diss_social_visits          .
## diss_social_confiding       .
## diss_social_acti         140.9045711
## diss_alcohol                .
## diss_smoking             -367.5284647
## diss_hypertension         259.7637011
```

Note: Diss = dissociative disorders; age_scaled = age (scaled); sex_numeric = male vs. female; ethn = White vs. Asian, Black, Mixed, or Other; edubinary = university or college vs. below, dichotomized; deprivation_scaled = Townsend deprivation index (scaled); met.tot.log_rec_scaled = total metabolic equivalent of task (log-transformed and scaled); soc.visi_recoded_scaled = frequency of family or friends' visits (scaled); soc.conf_recoded_scaled = perceived ability to confide in others (scaled); soc.acti_recoded_scaled = engagement in leisure activities (scaled); alc.ut_cat2 = low vs. increasing/high risk of alcohol consumption; smoking_status = never vs. former/current smoker; hypertension = absent vs. present. Interaction terms (e.g., "Diss x Age") indicate the interaction between dissociative disorders and the respective variable

LASSO-Model with Dissociative Disorders and Right Hippocampal Volume

eFigure C24. Regularization Path for the LASSO-Model (left) and Cross-Validation Error Plot (right).



Non-Zero Coefficients from the LASSO-Model at the Optimal Penalty Term (λ = 0.338).

```
## 26 x 1 sparse Matrix of class "dgCMatrix"
##                                    s1
## (Intercept)             3985.1339395
## diss                       .
## age_scaled              -141.5664745
## sex_numeric             -290.0701782
## ethn                    -141.6873410
## edubinary                -35.9318985
## deprivation_scaled       -12.7496937
## met.tot.log_rec_scaled    -2.3174029
## soc.visi_recoded_scaled   -1.7930678
## soc.conf_recoded_scaled   -1.2149381
## soc.acti_recoded_scaled   -0.4586853
## alc.ut_cat2              -10.2457265
## smoking_status            -8.7404504
## hyt                       -8.9066215
## diss_age                  20.7489622
## diss_sex                  -7.2012702
## diss_ethn                  .
## diss_education             .
## diss_deprivation           .
## diss_physical_activity     2.7809138
## diss_social_visits       231.5771505
## diss_social_confiding      .
## diss_social_acti           6.8411951
## diss_alcohol              37.1908576
## diss_smoking            -128.5729963
## diss_hypertension          3.3239026
```

Note: Diss = dissociative disorders; age_scaled = age (scaled); sex_numeric = male vs. female; ethn = White vs. Asian, Black, Mixed, or Other; edubinary = university or college vs. below, dichotomized; deprivation_scaled = Townsend deprivation index (scaled); met.tot.log_rec_scaled = total metabolic equivalent of task (log-transformed and scaled); soc.visi_recoded_scaled = frequency of family or friends' visits (scaled); soc.conf_recoded_scaled = perceived ability to confide in others (scaled); soc.acti_recoded_scaled = engagement in leisure activities (scaled); alc.ut_cat2 = low vs. increasing/high risk of alcohol consumption; smoking_status = never vs. former/current smoker; hypertension = absent vs. present. Interaction terms (e.g., "Diss x Age") indicate the interaction between dissociative disorders and the respective variable.

eTable C9. Associations between Dissociative Disorders, Moderators, Cognitive Functioning, Dementia, and Hippocampal Volumes of the Selected Predictors.

	Standardized β (95% CI)	*P*
Cognitive functioning		
Log reaction time*		
Dissociative disorders	0.0789 (0.0371, 0.1207)	< .001
Age†	0.0601 (0.0595, 0.0607)	< .001
Sex (reference category: Male)	0.0310 (0.0298, 0.0322)	< .001
Ethnicity (reference category: White)	0.0866 (0.0840, 0.0893)	< .001
Education (reference category: University or College degree)	0.0217 (0.0206, 0.0229)	< .001
Deprivation†	0.0138 (0.0132, 0.0143)	< .001
Smoking status (reference category: Never)	-0.0016 (-0.0027, -0.0004)	.006
Alcohol consumption (reference category: Lower-risk consumption)	-0.0131 (-0.0143, -0.0119)	< .001
Log physical activity†	0.0021 (0.0015, 0.0026)	< .001
Hypertension (reference category: absent)	0.0023 (0.0011, 0.0034)	< .001
Frequency of family or friends' visits†	0.0036 (0.0030, 0.0041)	< .001
Ability to confide in others†	0.0016 (0.0011, 0.0022)	< .001
Engagement in leisure activities†	-0.0008 (-0.0013, -0.0002)	.006
Dissociative disorders x Age		
Dissociative disorders x Sex		
Dissociative disorders x Ethnicity	0.1106 (-0.0360, 0.2573)	.139
Dissociative disorders x Education		
Dissociative disorders x Deprivation		
Dissociative disorders x Smoking status	-0.0632 (-0.1266, 0.0002)	.051
Dissociative disorders x Alcohol consumption	-0.0845 (-0.1640, -0.0049)	.037
Dissociative disorders x Physical activity	0.0173 (-0.0026, 0.0372)	.089
Dissociative disorders x Hypertension		
Dissociative disorders x Frequency of family or friends' visits	0.0207 (-0.0056, 0.0470)	.123
Dissociative disorders x Ability to confide in others		
Dissociative disorders x Engagement in leisure activities		
Log visual memory errors*		
Dissociative disorders		
Age†	0.1645 (0.1614, 0.1675)	< .001
Sex	0.0487 (0.0422, 0.0552)	< .001
Ethnicity	0.2331 (0.2185, 0.2478)	< .001
Education	0.1002 (0.0937, 0.1066)	< .001
Deprivation†	0.0265 (0.0234, 0.0296)	< .001
Smoking status	-0.0162 (-0.0224, -0.0100)	< .001
Alcohol consumption	-0.0188 (-0.0255, -0.0122)	< .001
Log physical activity†	-0.0245 (-0.0275, -0.0214)	< .001
Hypertension		
Frequency of family or friends' visits†	0.0069 (0.0038, 0.0100)	< .001
Ability to confide in others†	0.0034 (0.0004, 0.0065)	.026
Engagement in leisure activities†	0.0090 (0.0059, 0.0121)	< .001
Dissociative disorders x Age		
Dissociative disorders x Sex		
Dissociative disorders x Ethnicity		
Dissociative disorders x Education		
Dissociative disorders x Deprivation		
Dissociative disorders x Smoking status		
Dissociative disorders x Alcohol consumption		
Dissociative disorders x Physical activity		

Dissociative disorders x Hypertension		
Dissociative disorders x Frequency of family or friends' visits		
Dissociative disorders x Ability to confide in others		
Dissociative disorders x Engagement in leisure activities	0.1764 (0.0198, 0.3330)	.027
Reasoning ability‡		
Dissociative disorders		
Age†	-0.1126 (-0.1234, -0.1017)	< .001
Sex	-0.1760 (-0.1974, -0.1545)	< .001
Ethnicity	-1.7599 (-1.8010, -1.7187)	< .001
Education	-1.3138 (-1.3349, -1.2926)	< .001
Deprivation†	-0.1807 (-0.1909, -0.1706)	< .001
Smoking status	-0.0323 (-0.0529, -0.0117)	.002
Alcohol consumption	0.1784 (0.1560, 0.2008)	< .001
Log physical activity†	0.0916 (0.0815, 0.1016)	< .001
Hypertension	-0.0980 (-0.1194, -0.0766)	< .001
Frequency of family or friends' visits†	0.0291 (0.0189, 0.0393)	< .001
Ability to confide in others†		
Engagement in leisure activities†	-0.0926 (-0.1028, -0.0824)	< .001
Dissociative disorders x Age		
Dissociative disorders x Sex		
Dissociative disorders x Ethnicity	1.7467 (-0.4682, 3.9616)	.122
Dissociative disorders x Education		
Dissociative disorders x Deprivation		
Dissociative disorders x Smoking status		
Dissociative disorders x Alcohol consumption		
Dissociative disorders x Physical activity		
Dissociative disorders x Hypertension		
Dissociative disorders x Frequency of family or friends' visits		
Dissociative disorders x Ability to confide in others		
Dissociative disorders x Engagement in leisure activities	-0.7678 (-1.4114, -0.1243)	.019

Dementia	**HR (95% CI)**	***P***
Dissociative disorders	5.6710 (1.3528, 23.7739)	.018
Age†	4.8683 (4.6668, 5.0784)	< .001
Sex	0.7702 (0.7330, 0.8093)	< .001
Ethnicity	1.1910 (1.0511, 1.3494)	.006
Education	1.2844 (1.2141, 1.3586)	< .001
Deprivation†	1.1665 (1.1408, 1.1928)	< .001
Smoking status	1.1550 (1.1016, 1.2111)	< .001
Alcohol consumption	0.8604 (0.8170, 0.9061)	< .001
Log physical activity†	1.0727 (1.0506, 1.0952)	< .001
Hypertension	1.1857 (1.1265, 1.2481)	< .001
Frequency of family or friends' visits†		
Ability to confide in others†	1.0830 (1.0602, 1.1063)	< .001
Engagement in leisure activities†	1.0904 (1.0645, 1.1169)	< .001
Dissociative disorders x Age	0.3100 (0.1834, 0.5240)	< .001
Dissociative disorders x Sex		
Dissociative disorders x Ethnicity		
Dissociative disorders x Education	2.3104 (0.5053, 10.5639)	.280
Dissociative disorders x Deprivation	0.7240 (0.4686, 1.1186)	.146
Dissociative disorders x Smoking status		
Dissociative disorders x Alcohol consumption		
Dissociative disorders x Physical activity		

Dissociative disorders x Hypertension	0.5230 (0.1896, 1.4429)	.211
Dissociative disorders x Frequency of family or friends' visits	1.1787 (0.7725, 1.7984)	.446
Dissociative disorders x Ability to confide in others		
Dissociative disorders x Engagement in leisure activities	0.7322 (0.4737, 1.1318)	.161

Hippocampal volume‡	**Standardized β (95% CI)**	***P***
Left		
Dissociative disorders		
Age†	-148.928 (-153.2867, -144.5688)	< .001
Sex	-281.559 (-290.3664, -272.7520)	
Ethnicity	-154.154 (-180.2142, -128.0929)	
Education	-34.654 (-42.9326, -26.3749)	
Deprivation†	-12.675 (-16.8287, -8.5223)	
Smoking status	-12.133 (-20.7834, -3.4836)	.006
Alcohol consumption	-15.186 (-24.0933, -6.2795)	
Log physical activity†		
Hypertension	-9.268 (-18.1055, -0.4313)	.040
Frequency of family or friends' visits†		
Ability to confide in others†	-4.035 (-8.1568, 0.0867)	.055
Engagement in leisure activities†		
Dissociative disorders x Age		
Dissociative disorders x Sex		
Dissociative disorders x Ethnicity		
Dissociative disorders x Education		
Dissociative disorders x Deprivation		
Dissociative disorders x Smoking status	-463.712 (-872.7787, -54.6449	.026
Dissociative disorders x Alcohol consumption		
Dissociative disorders x Physical activity		
Dissociative disorders x Hypertension	379.931 (-92.3465, 852.2093)	.115
Dissociative disorders x Frequency of family or friends' visits		
Dissociative disorders x Ability to confide in others		
Dissociative disorders x Engagement in leisure activities		
Right		
Dissociative disorders		
Age†	-141.579 (-146.0671, -137.0918)	< .001
Sex	-290.635 (-299.6742, -281.5952)	< .001
Ethnicity	-145.045 (-171.8738, -118.2170)	< .001
Education	-36.345 (-44.8598, -27.8304)	< .001
Deprivation†	-13.096 (-17.3696, -8.8229)	< .001
Smoking status	-9.226 (-18.1348, -0.3176)	.042
Alcohol consumption	-10.782 (-19.9548, -1.6084)	.021
Log physical activity†		
Hypertension	-9.226 (-18.1348, -0.3176)	.039
Frequency of family or friends' visits†		
Ability to confide in others†		
Engagement in leisure activities†		
Dissociative disorders x Age		
Dissociative disorders x Sex		
Dissociative disorders x Ethnicity		
Dissociative disorders x Education		
Dissociative disorders x Deprivation		
Dissociative disorders x Smoking status		
Dissociative disorders x Alcohol consumption		
Dissociative disorders x Physical activity		
Dissociative disorders x Hypertension		

	Dissociative disorders x Frequency of family or friends' visits
	Dissociative disorders x Ability to confide in others
	Dissociative disorders x Engagement in leisure activities

CI = confidence interval; P = p-value; HR = hazard ratio.
Based on the final model, after stepwise selection of the LASSO-selected predictors.
*Positive coefficients indicate a worse outcome.
†Variables were standardized to have a mean of 0 and a standard deviation of 1.
‡Negative coefficients indicate a worse outcome.

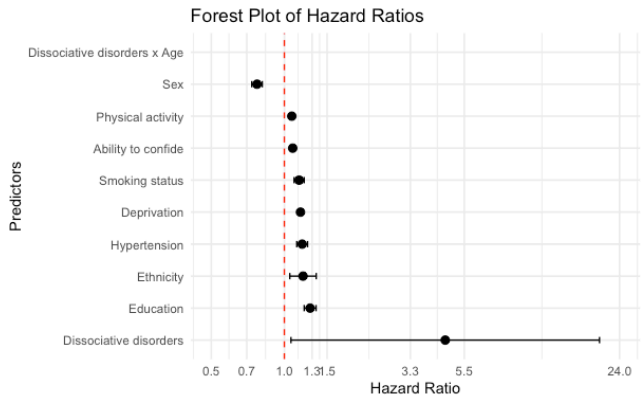
eTable C10. Associations between Dissociative Disorders, Moderators, and Dementia in the Stratified Model.

Dementia	HR (95% CI)	*P*
Dissociative disorders	4.5953 (1.0649, 19.8307)	.041
Age*		
Sex	0.7719 (0.7345, 0.8112)	< .001
Ethnicity	1.1937 (1.0532, 1.3529)	.006
Education	1.2767 (1.2067, 1.3508)	< .001
Deprivation*	1.1652 (1.1394, 1.1915)	< .001
Smoking status	1.1505 (1.0972, 1.2063)	< .001
Alcohol consumption		
Log weekly physical activity*	1.0733 (1.0512, 1.0958)	< .001
Hypertension	1.1840 (1.1247, 1.2464)	< .001
Frequency of family or friends' visits*		
Ability to confide in others*	1.0825 (1.0597, 1.1057)	< .001
Engagement in leisure activities*		
Dissociative disorders x Age	0.3347 (0.1978, 0.5663)	< .001
Dissociative disorders x Sex		
Dissociative disorders x Ethnicity		
Dissociative disorders x Education	2.7126 (0.5712, 12.8816)	.209
Dissociative disorders x Deprivation	0.7766 (0.4996, 1.2071)	.261
Dissociative disorders x Smoking status		
Dissociative disorders x Alcohol consumption		
Dissociative disorders x Physical activity		
Dissociative disorders x Hypertension	0.5327 (0.1907, 1.4883)	.230
Dissociative disorders x Frequency of family or friends' visits	1.2742 (0.8231, 1.9726)	.277
Dissociative disorders x Ability to confide in others		
Dissociative disorders x Engagement in leisure activities	0.7019 (0.4358, 1.1304)	.145

CI = confidence interval; P = p-value; HR = hazard ratio.

*Variables were standardized to have a mean of 0 and a standard deviation of 1.

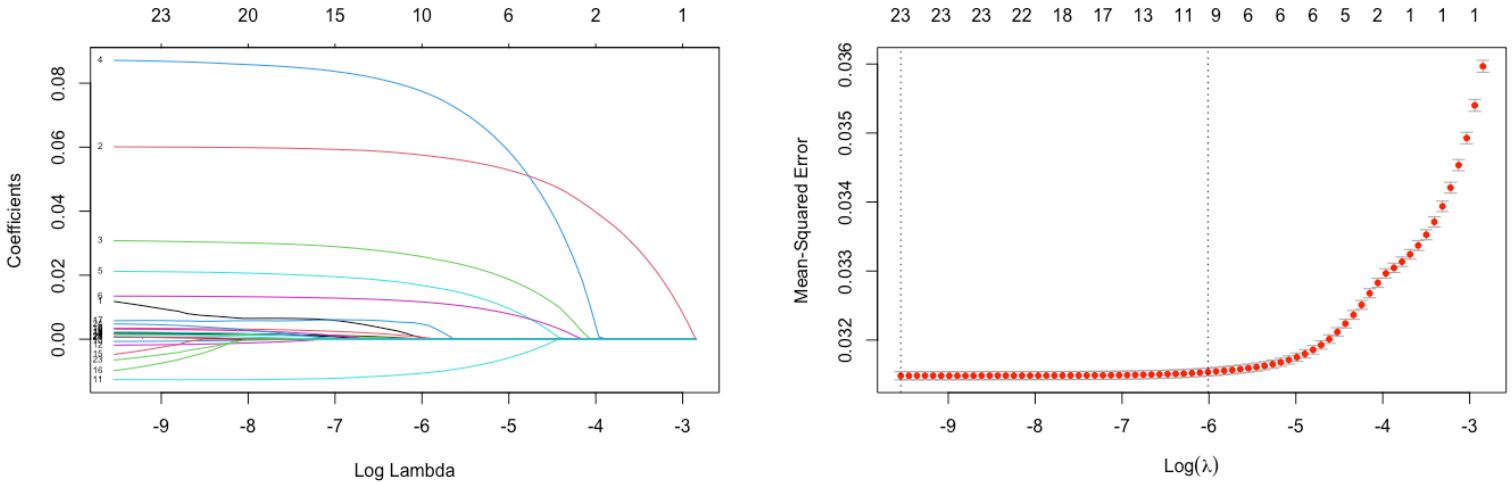
eFigure C25. Forest Plot of the Stratified Stepwise Model Dissociative Disorders – Dementia.



LASSO-Models with Depression as the Main Predictor

LASSO-Model with Depression and Log Reaction Time

eFigure C26. Regularization Path for the LASSO-Model (left) and Cross-Validation Error Plot (right).



The regularization path for the LASSO-Model (left) illustrates how the regression coefficients of all predictors change as the penalty term (i.e., regularization strength, λ) varies. As λ increases, more coefficients shrink toward zero, resulting in a sparser model with fewer selected predictors. The cross-validation error plot (right) displays the model's cross-validation error (i.e., mean squared error) across different values of λ, aiming to identify the optimal penalty term that minimizes prediction error while avoiding overfitting. The lowest point on the curve represents the chosen λ, ensuring an optimal balance-off between sparsity and accuracy.

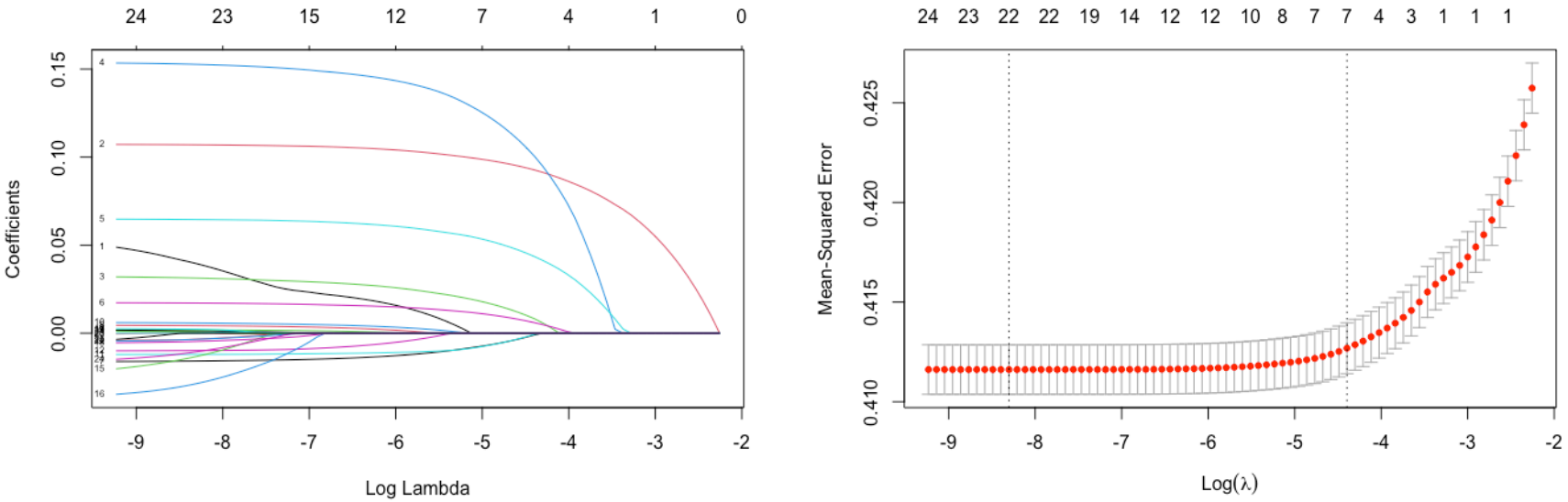
Non-Zero Coefficients from the LASSO-Model at the Optimal Penalty Term (λ = 0.00007).

```
## 26 x 1 sparse Matrix of class "dgCMatrix"
##                                    s1
## (Intercept)                6.2768656464
## depression                 0.0117995776
## age_scaled                 0.0601080493
## sex_numeric                0.0308037113
## ethn                       0.0871487874
## edubinary                  0.0212123467
## deprivation_scaled         0.0134766903
## met.tot.log_rec_scaled     0.0017610203
## soc.visi_recoded_scaled    0.0034475844
## soc.conf_recoded_scaled    0.0014466368
## soc.acti_recoded_scaled -0.0006950950
## alc.ut_cat2             -0.0126372019
## smoking_status          -0.0018472250
## hyt                        0.0021015871
## dep_age                    .
## dep_sex                 -0.0047559540
## dep_ethn                -0.0098269458
## dep_education              0.0057587581
## dep_deprivation            0.0022490533
## dep_physical_activity      0.0031897789
## dep_social_visits          0.0006144558
## dep_social_confiding       0.0006138173
## dep_social_acti            .
## dep_alcohol             -0.0065236339
## dep_smoking                0.0047793563
## dep_hypertension           0.0009708037
```

Note: Dep = depression; age_scaled = age (scaled); sex_numeric = male vs. female; ethn = White vs. Asian, Black, Mixed, or Other; edubinary = university or college vs. below, dichotomized; deprivation_scaled = Townsend deprivation index (scaled); met.tot.log_rec_scaled = total metabolic equivalent of task (log-transformed and scaled); soc.visi_recoded_scaled = frequency of family or friends' visits (scaled); soc.conf_recoded_scaled = perceived ability to confide in others (scaled); soc.acti_recoded_scaled = engagement in leisure activities (scaled); alc.ut_cat2 = low vs. increasing/high risk of alcohol consumption; smoking_status = never vs. former/current smoker; hypertension = absent vs. present. Interaction terms (e.g., "Dep x Age") indicate the interaction between depression and the respective variable.

LASSO-Model with Depression and Log Visual Memory Errors

eFigure C27. Regularization Path for the LASSO-Model (left) and Cross-Validation Error Plot (right).



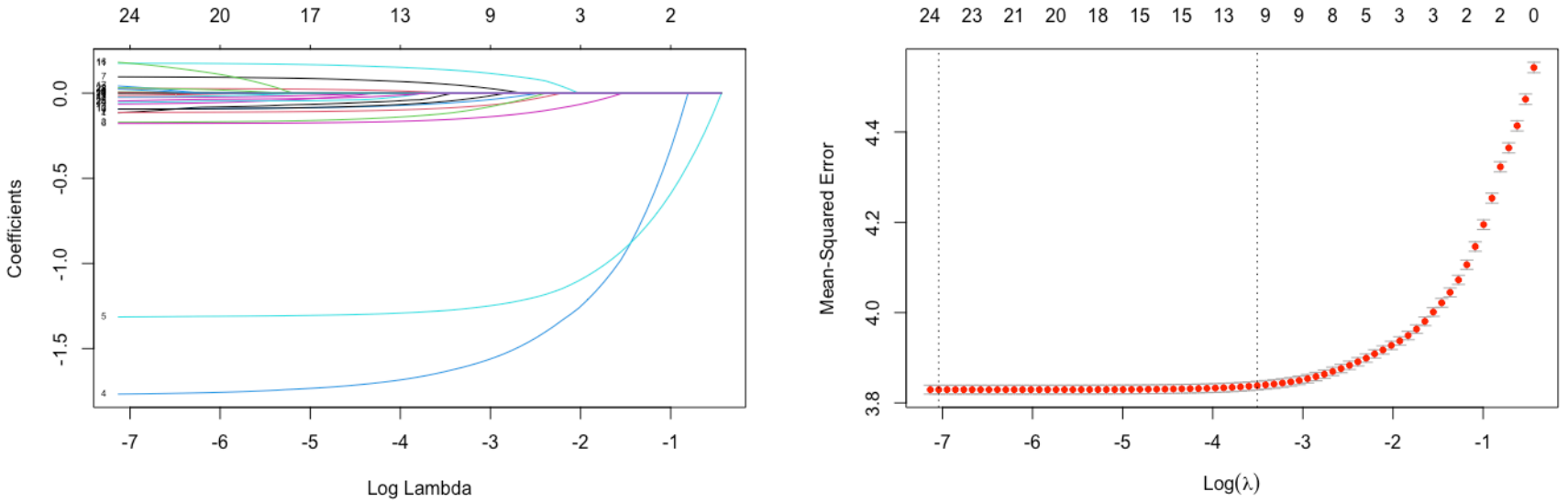
Non-Zero Coefficients from the LASSO-Model at the Optimal Penalty Term (λ = 0.00025).

```
## 26 x 1 sparse Matrix of class "dgCMatrix"
##                                      s1
## (Intercept)                1.4794917265
## depression                 0.0395187954
## age_scaled                 0.1070151445
## sex_numeric                0.0313232084
## ethn                       0.1526598426
## edubinary                  0.0645476420
## deprivation_scaled         0.0171042617
## met.tot.log_rec_scaled    -0.0158076532
## soc.visi_recoded_scaled    0.0042697581
## soc.conf_recoded_scaled    0.0018620480
## soc.acti_recoded_scaled    0.0058023422
## alc.ut_cat2               -0.0120274994
## smoking_status            -0.0098375860
## hyt                        0.0012620473
## dep_age                   -0.0034025287
## dep_sex                   -0.0132284180
## dep_ethn                  -0.0286299821
## dep_education              0.0022450909
## dep_deprivation           -0.0046486981
## dep_physical_activity      0.0006445621
## dep_social_visits          .
## dep_social_confiding       0.0006133142
## dep_social_acti           -0.0034689902
## dep_alcohol                .
## dep_smoking               -0.0105191247
## dep_hypertension           .
```

Note: Dep = depression; age_scaled = age (scaled); sex_numeric = male vs. female; ethn = White vs. Asian, Black, Mixed, or Other; edubinary = university or college vs. below, dichotomized; deprivation_scaled = Townsend deprivation index (scaled); met.tot.log_rec_scaled = total metabolic equivalent of task (log-transformed and scaled); soc.visi_recoded_scaled = frequency of family or friends' visits (scaled); soc.conf_recoded_scaled = perceived ability to confide in others (scaled); soc.acti_recoded_scaled = engagement in leisure activities (scaled); alc.ut_cat2 = low vs. increasing/high risk of alcohol consumption; smoking_status = never vs. former/current smoker; hypertension = absent vs. present. Interaction terms (e.g., "Dep x Age") indicate the interaction between depression and the respective variable.

LASSO-Model with Depression and Reasoning Ability

eFigure C28. Regularization Path for the LASSO-Model (left) and Cross-Validation Error Plot (right).



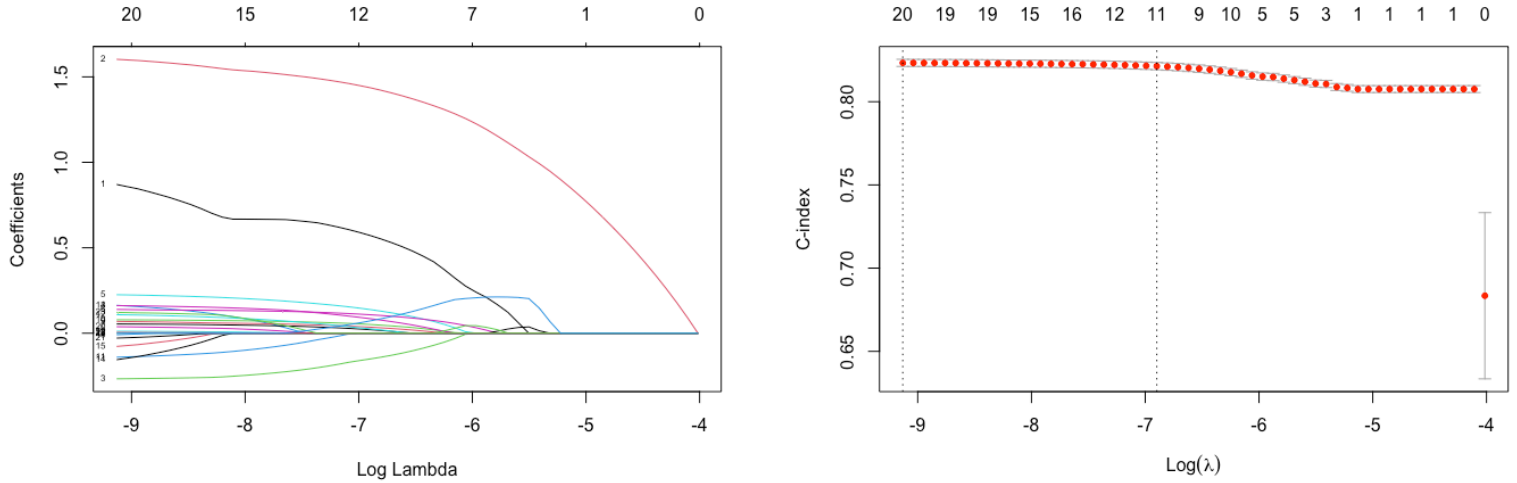
Non-Zero Coefficients from the LASSO-Model at the Optimal Penalty Term (λ = 0.00088).

```
## 26 x 1 sparse Matrix of class "dgCMatrix"
##                                  s1
## (Intercept)              7.1284848471
## depression              -0.1128988927
## age_scaled              -0.1132823043
## sex_numeric             -0.1708521644
## ethn                    -1.7668739889
## edubinary               -1.3139868889
## deprivation_scaled      -0.1777551437
## met.tot.log_rec_scaled   0.0956417251
## soc.visi_recoded_scaled  0.0275004054
## soc.conf_recoded_scaled    0.0065065655
## soc.acti_recoded_scaled    -0.0932694303
## alc.ut_cat2                         0.1750490117
## smoking_status             -0.0251017862
## hyt                                 -0.0936116669
## dep_age                             0.0043644501
## dep_sex                  .
## dep_ethn                 0.1773078733
## dep_education            0.0391031140
## dep_deprivation         -0.0218155318
## dep_physical_activity   -0.0636317215
## dep_social_visits       -0.0003880039
## dep_social_confiding    -0.0136637883
## dep_social_acti          0.0302677571
## dep_alcohol              0.0218952087
## dep_smoking             -0.0540492058
## dep_hypertension        -0.0448696503
```

Note: Dep = depression; age_scaled = age (scaled); sex_numeric = male vs. female; ethn = White vs. Asian, Black, Mixed, or Other; edubinary = university or college vs. below, dichotomized; deprivation_scaled = Townsend deprivation index (scaled); met.tot.log_rec_scaled = total metabolic equivalent of task (log-transformed and scaled); soc.visi_recoded_scaled = frequency of family or friends' visits (scaled); soc.conf_recoded_scaled = perceived ability to confide in others (scaled); soc.acti_recoded_scaled = engagement in leisure activities (scaled); alc.ut_cat2 = low vs. increasing/high risk of alcohol consumption; smoking_status = never vs. former/current smoker; hypertension = absent vs. present. Interaction terms (e.g., "Dep x Age") indicate the interaction between depression and the respective variable.

LASSO-Model with Depression and Dementia

eFigure C29. Regularization Path for the LASSO-Model (left) and Cross-Validation Error Plot (right).



The regularization path for the LASSO-Model (left) illustrates how the regression coefficients of all predictors change as the penalty term (i.e., regularization strength, λ) varies. As λ increases, more coefficients shrink toward zero, resulting in a sparser model with fewer selected predictors. The cross-validation error plot (right) displays the 1-C-index across different values of λ, where the optimal penalty term is selected at the minimum cross-validation error, corresponding to the highest C-index. This ensures an optimal balance between sparsity and predictive performance.

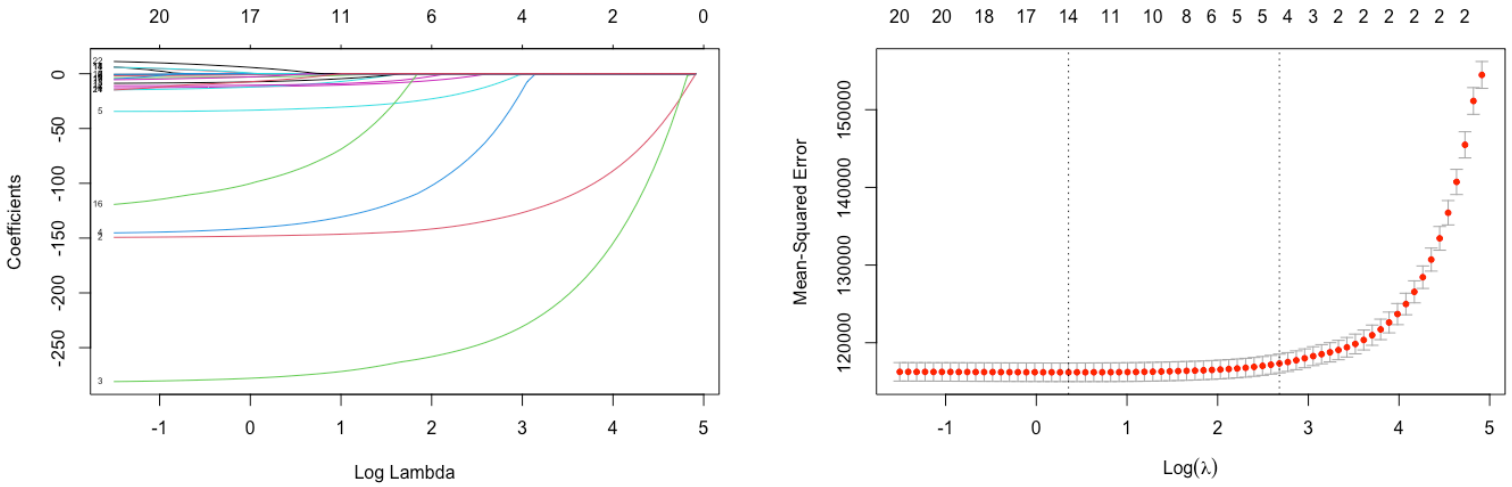
Non-Zero Coefficients from the LASSO-Model at the Optimal Penalty Term (λ = 0.00011).

```
## 25 x 1 sparse Matrix of class "dgCMatrix"
##                                    1
## depdem                     0.870435321
## age_scaled                 1.602666133
## sex_numeric               -0.266905096
## ethn                       0.162931139
## edubinary                  0.225273752
## deprivation_scaled         0.139092667
## met.tot.log_rec_scaled     0.054099840
## soc.visi_recoded_scaled    .
## soc.conf_recoded_scaled    0.068995540
## soc.acti_recoded_scaled    0.078618291
## alc.ut_cat2               -0.140174068
## smoking_status             0.108416360
## hyt                        0.161815312
## dep_age                   -0.154967205
## dep_sex                   -0.077333224
## dep_ethn                   .
## dep_education              .
## dep_deprivation           -0.009019308
## dep_physical_activity      0.011810479
## dep_social_visits          0.038055274
## dep_social_confiding      -0.028449549
## dep_social_acti            0.004991051
## dep_alcohol                0.121496592
## dep_smoking                .
## dep_hypertension           .
```

Note: Dep = depression; age_scaled = age (scaled); sex_numeric = male vs. female; ethn = White vs. Asian, Black, Mixed, or Other; edubinary = university or college vs. below, dichotomized; deprivation_scaled = Townsend deprivation index (scaled); met.tot.log_rec_scaled = total metabolic equivalent of task (log-transformed and scaled); soc.visi_recoded_scaled = frequency of family or friends' visits (scaled); soc.conf_recoded_scaled = perceived ability to confide in others (scaled); soc.acti_recoded_scaled = engagement in leisure activities (scaled); alc.ut_cat2 = low vs. increasing/high risk of alcohol consumption; smoking_status = never vs. former/current smoker; hypertension = absent vs. present. Interaction terms (e.g., "Dep x Age") indicate the interaction between depression and the respective variable.
The values are in log-hazard ratio format (i.e., raw coefficients before exponentiation).

LASSO-Model with Depression and Left Hippocampal Volume

eFigure C30. Regularization Path for the LASSO-Model (left) and Cross-Validation Error Plot (right).



The regularization path for the LASSO-Model (left) illustrates how the regression coefficients of all predictors change as the penalty term (i.e., regularization strength, λ) varies. As λ increases, more coefficients shrink toward zero, resulting in a sparser model with fewer selected predictors. The cross-validation error plot (right) displays the model's cross-validation error (i.e., mean squared error) across different values of λ, aiming to identify the optimal penalty term that minimizes prediction error while avoiding overfitting. The lowest point on the curve represents the chosen λ, ensuring an optimal balance-off between sparsity and accuracy.

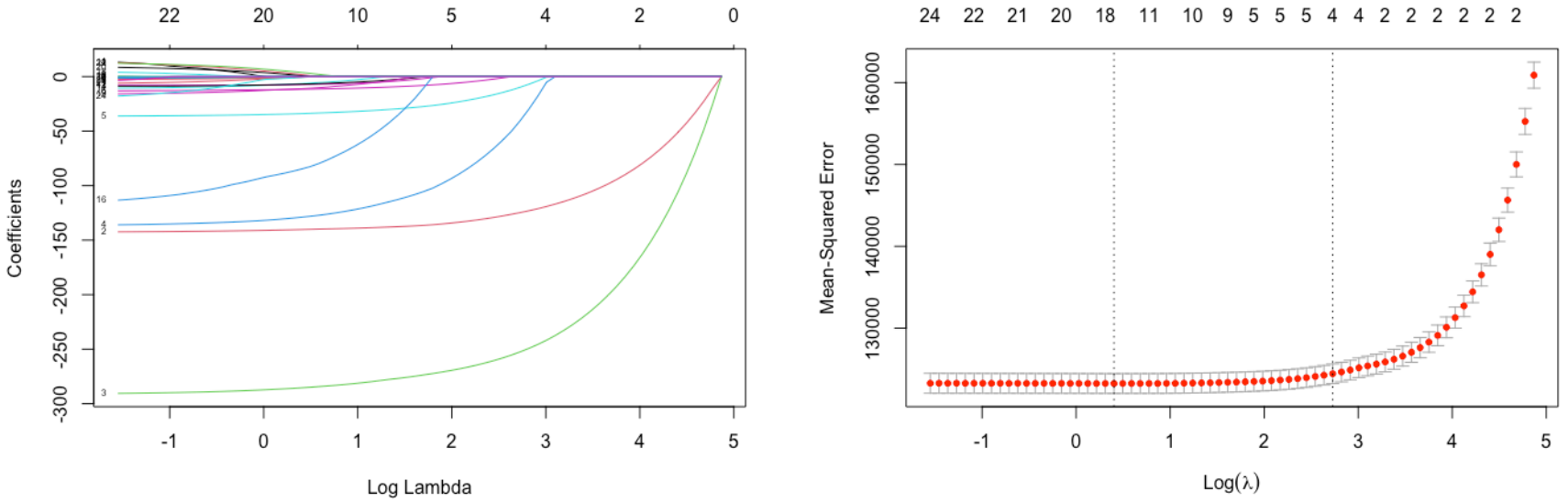
Non-Zero Coefficients from the LASSO-Model at the Optimal Penalty Term (λ = 1.426).

```
## 26 x 1 sparse Matrix of class "dgCMatrix"
##                                    s1
## (Intercept)              3859.9499441
## depression                  .
## age_scaled               -147.6519415
## sex_numeric              -276.3334688
## ethn                     -138.5288531
## edubinary                 -32.5323831
## deprivation_scaled        -11.3880036
## met.tot.log_rec_scaled      .
## soc.visi_recoded_scaled    -0.3773001
## soc.conf_recoded_scaled    -2.6511352
## soc.acti_recoded_scaled     .
## alc.ut_cat2              -10.8932627
## smoking_status           -10.1286816
## hyt                       -6.7185267
## dep_age                     .
## dep_sex                     .
## dep_ethn                 -92.1346851
## dep_education               .
## dep_deprivation             .
## dep_physical_activity     -1.5270436
## dep_social_visits           .
## dep_social_confiding        .
## dep_social_acti             3.5475609
## dep_alcohol                 .
## dep_smoking               -5.3400259
## dep_hypertension            .
```

Note: Dep = depression; age_scaled = age (scaled); sex_numeric = male vs. female; ethn = White vs. Asian, Black, Mixed, or Other; edubinary = university or college vs. below, dichotomized; deprivation_scaled = Townsend deprivation index (scaled); met.tot.log_rec_scaled = total metabolic equivalent of task (log-transformed and scaled); soc.visi_recoded_scaled = frequency of family or friends' visits (scaled); soc.conf_recoded_scaled = perceived ability to confide in others (scaled); soc.acti_recoded_scaled = engagement in leisure activities (scaled); alc.ut_cat2 = low vs. increasing/high risk of alcohol consumption; smoking_status = never vs. former/current smoker; hypertension = absent vs. present. Interaction terms (e.g., "Dep x Age") indicate the interaction between depression and the respective variable.

LASSO-Model with Depression and Right Hippocampal Volume

eFigure C31. Regularization Path for the LASSO-Model (left) and Cross-Validation Error Plot (right).



Non-Zero Coefficients from the LASSO-Model at the Optimal Penalty Term (λ = 1.496).

```
## 26 x 1 sparse Matrix of class "dgCMatrix"
##                                    s1
## (Intercept)              3978.6143736
## depression                  .
## age_scaled               -140.2983695
## sex_numeric              -285.4413280
## ethn                     -128.9733362
## edubinary                 -33.9656600
## deprivation_scaled        -11.6618081
## met.tot.log_rec_scaled     -0.2748645
## soc.visi_recoded_scaled    -0.4840869
## soc.conf_recoded_scaled    -0.2561794
## soc.acti_recoded_scaled     .
## alc.ut_cat2                -6.4408832
## smoking_status             -7.3628261
## hyt                        -6.9617019
## dep_age                     1.7832300
## dep_sex                     .
## dep_ethn                  -84.7652013
## dep_education               .
## dep_deprivation             .
## dep_physical_activity     -11.1174907
## dep_social_visits           0.7256045
## dep_social_confiding       -0.4790956
## dep_social_acti             3.7617412
## dep_alcohol                 .
## dep_smoking                -0.7244935
## dep_hypertension            .
```

Note: Dep = depression; age_scaled = age (scaled); sex_numeric = male vs. female; ethn = White vs. Asian, Black, Mixed, or Other; edubinary = university or college vs. below, dichotomized; deprivation_scaled = Townsend deprivation index (scaled); met.tot.log_rec_scaled = total metabolic equivalent of task (log-transformed and scaled); soc.visi_recoded_scaled = frequency of family or friends' visits (scaled); soc.conf_recoded_scaled = perceived ability to confide in others (scaled); soc.acti_recoded_scaled = engagement in leisure activities (scaled); alc.ut_cat2 = low vs. increasing/high risk of alcohol consumption; smoking_status = never vs. former/current smoker; hypertension = absent vs. present. Interaction terms (e.g., "Dep x Age") indicate the interaction between depression and the respective variable.

eTable C11. Associations between Depression, Moderators, Cognitive Functioning, Dementia, and Hippocampal Volumes of the Selected Predictors

	Standardized β (95% CI)	*P*
Cognitive functioning		
Log reaction time*		
Depression	0.0164 (0.0093, 0.0235)	< .001
Age†	0.0602 (0.0596, 0.0608)	< .001
Sex (reference category: Male)	0.0311 (0.0299, 0.0323)	< .001
Ethnicity (reference category: White)	0.0875 (0.0848, 0.0902)	< .001
Education (reference category: University or College degree)	0.0214 (0.0202, 0.0226)	< .001
Deprivation†	0.0135 (0.0130, 0.0141)	< .001
Smoking status (reference category: Never)	-0.0020 (-0.0032, -0.0009)	< .001
Alcohol consumption (reference category: Lower-risk consumption)	-0.0126 (-0.0138, -0.0113)	< .001
Log physical activity†	0.0018 (0.0013, 0.0024)	< .001
Hypertension (reference category: absent)	0.0023 (0.0011, 0.0034)	< .001
Frequency of family or friends' visits†	0.0036 (0.0030, 0.0041)	< .001
Ability to confide in others†	0.0015 (0.0010, 0.0021)	< .001
Engagement in leisure activities†	-0.0008 (-0.0014, -0.0002)	.005
Depression x Age		
Depression x Sex	-0.0086 (-0.0143, -0.0030)	.003
Depression x Ethnicity	-0.0129 (-0.0270, 0.0012)	.073
Depression x Education	0.0053 (-0.0004, 0.0109)	.068
Depression x Deprivation	0.0025 (0.00003, 0.0049)	.047
Depression x Smoking status	0.0051 (-0.0002, 0.0103)	.060
Depression x Alcohol consumption	-0.0091 (-0.0148, -0.0034)	.002
Depression x Physical activity	0.0034 (0.0012, 0.0056)	.003
Depression x Hypertension		
Depression x Frequency of family or friends' visits		
Depression x Ability to confide in others		
Depression x Engagement in leisure activities		
Log visual memory errors*		
Depression	0.0541 (0.0347, 0.0734)	< .001
Age†	0.1074 (0.1054, 0.1094)	< .001
Sex	0.0322 (0.0279, 0.0365)	< .001
Ethnicity	0.1542 (0.1445, 0.1639)	< .001
Education	0.0652 (0.0609, 0.0694)	< .001
Deprivation†	0.0171 (0.0151, 0.0191)	< .001
Smoking status	-0.0100 (-0.0141, -0.0058)	< .001
Alcohol consumption	-0.0120 (-0.0164, -0.0077)	< .001
Log physical activity†	-0.0161 (-0.0181, -0.0141)	< .001
Hypertension		
Frequency of family or friends' visits†	0.0045 (0.0025, 0.0066)	< .001
Ability to confide in others†	0.0021 (0.0001, 0.0040)	.042
Engagement in leisure activities†	0.0059 (0.0039, 0.0079)	< .001
Depression x Age		
Depression x Sex	-0.0230 (-0.0426, -0.0035)	.021
Depression x Ethnicity	-0.0415 (-0.0919, 0.0089)	.107
Depression x Education		
Depression x Deprivation		
Depression x Smoking status	-0.0203 (-0.0389, -0.0017)	.033
Depression x Alcohol consumption		
Depression x Physical activity		
Depression x Hypertension		
Depression x Frequency of family or friends' visits		

Depression x Ability to confide in others		
Depression x Engagement in leisure activities		
Reasoning ability‡		
Depression	-0.1366 (-0.1820, -0.0913)	< .001
Age†	-0.1134 (-0.1243, -0.1026)	< .001
Sex	-0.1732 (-0.1947, -0.1518)	< .001
Ethnicity	-1.7693 (-1.8111, -1.7274)	< .001
Education	-1.3127 (-1.3339, -1.2916)	< .001
Deprivation†	-0.1795 (-0.1897, -0.1693)	< .001
Smoking status	-0.0299 (-0.0505, -0.0093)	.004
Alcohol consumption	0.1775 (0.1551, 0.1998)	< .001
Log physical activity†	0.0974 (0.0870, 0.1078)	< .001
Hypertension	-0.0976 (-0.1190, -0.0763)	< .001
Frequency of family or friends' visits†	0.0290 (0.0188, 0.0391)	< .001
Ability to confide in others†		
Engagement in leisure activities†	-0.0943 (-0.1048, -0.0838)	< .001
Depression x Age		
Depression x Sex		
Depression x Ethnicity	0.1837 (-0.0384, 0.4057)	.105
Depression x Education		
Depression x Deprivation		
Depression x Smoking status		
Depression x Alcohol consumption		
Depression x Physical activity	-0.0710 (-0.1093, -0.0327)	< .001
Depression x Hypertension		
Depression x Frequency of family or friends' visits		
Depression x Ability to confide in others		
Depression x Engagement in leisure activities	0.0323 (-0.0119, 0.0764)	.152

Dementia	**HR (95% CI)**	***P***
Depression	2.7335 (2.3641, 3.1606)	< .001
Age†	5.1818 (4.9409, 5.4345)	< .001
Sex	0.7613 (0.7209, 0.8039)	.002
Ethnicity	1.2199 (1.0766, 1.3822)	< .001
Education	1.2666 (1.1974, 1.3399)	< .001
Deprivation†	1.1503 (1.1249, 1.1763)	< .001
Smoking status	1.1270 (1.0747, 1.1817)	< .001
Alcohol consumption	0.8545 (0.8075, 0.9043)	< .001
Log physical activity†	1.0627 (1.0408, 1.0850)	< .001
Hypertension	1.1852 (1.1260, 1.2474)	< .001
Frequency of family or friends' visits†		
Ability to confide in others†	1.0793 (1.0543, 1.1049)	< .001
Engagement in leisure activities†	1.0864 (1.0606, 1.1128)	< .001
Depression x Age	0.7784 (0.7055, 0.8588)	< .001
Depression x Sex	0.8748 (0.7689, 0.9952)	.042
Depression x Ethnicity		
Depression x Education		
Depression x Deprivation		
Depression x Smoking status		
Depression x Alcohol consumption	1.1329 (0.9917, 1.2942)	.066
Depression x Physical activity		
Depression x Hypertension		
Depression x Frequency of family or friends' visits	1.0457 (0.9936, 1.1005)	.087
Depression x Ability to confide in others	0.9492 (0.8972, 1.0043)	.070
Depression x Engagement in leisure activities		

Hippocampal volume‡	Standardized β (95% CI)	*P*
Left		
Depression		
Age†	-148.932 (-153.291, -144.573)	< .001
Sex	-281.396 (-290.205, -272.587)	< .001
Ethnicity	-147.086 (-173.899, -120.273)	< .001
Education	-34.599 (-42.878, -26.321)	< .001
Deprivation†	-12.631 (-16.785, -8.478)	< .001
Smoking status	-12.205 (-20.854, -3.556)	.006
Alcohol consumption	-15.091 (-23.997, -6.184)	< .001
Log physical activity†		
Hypertension	-9.136 (-17.972, -0.300)	.043
Frequency of family or friends' visits†		
Ability to confide in others†	-4.064 (-8.188, 0.060	.053
Engagement in leisure activities†		
Depression x Age		
Depression x Sex		
Depression x Ethnicity	-121.256 (-230.078, -12.433)	.029
Depression x Education		
Depression x Deprivation		
Depression x Smoking status		
Depression x Alcohol consumption		
Depression x Physical activity		
Depression x Hypertension		
Depression x Frequency of family or friends' visits		
Depression x Ability to confide in others		
Depression x Engagement in leisure activities		
Right		
Depression		
Age†	-141.614 (-146.101, -137.126)	< .001
Sex	-290.337 (-299.376, -281.297)	< .001
Ethnicity	-138.500 (-166.102, -110.898)	< .001
Education	-36.294 (-44.807, -27.780)	< .001
Deprivation†	-13.022 (-17.295, -8.749)	< .001
Smoking status	-9.156 (-18.063, -0.248)	.044
Alcohol consumption	-10.837 (-20.010, -1.665)	.021
Log physical activity†		
Hypertension	-9.453 (-18.554, -0.352)	.042
Frequency of family or friends' visits†		
Ability to confide in others†		
Engagement in leisure activities†		
Depression x Age		
Depression x Sex		
Depression x Ethnicity	-112.720 (-224.856, -0.584)	.049
Depression x Education		
Depression x Deprivation		
Depression x Smoking status		
Depression x Alcohol consumption		
Depression x Physical activity	-15.583 (-29.161, -2.006)	.025
Depression x Hypertension		
Depression x Frequency of family or friends' visits		
Depression x Ability to confide in others		
Depression x Engagement in leisure activities		

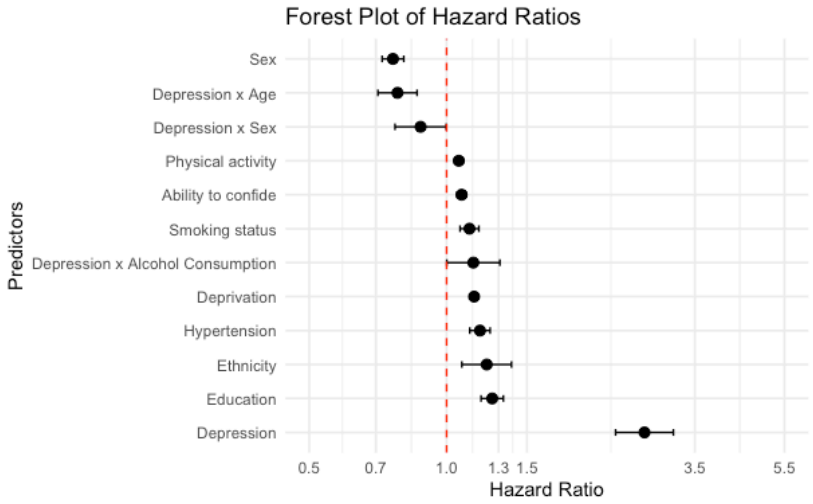
CI = confidence interval; P = p-value; HR = hazard ratio.
Based on the final model, after stepwise selection of the LASSO-selected predictors.
*Positive coefficients indicate a worse outcome.
†Variables were standardized to have a mean of 0 and a standard deviation of 1.
‡Negative coefficients indicate a worse outcome.

eTable C12. Associations between Depression, Moderators, and Dementia in the Stratified Model.

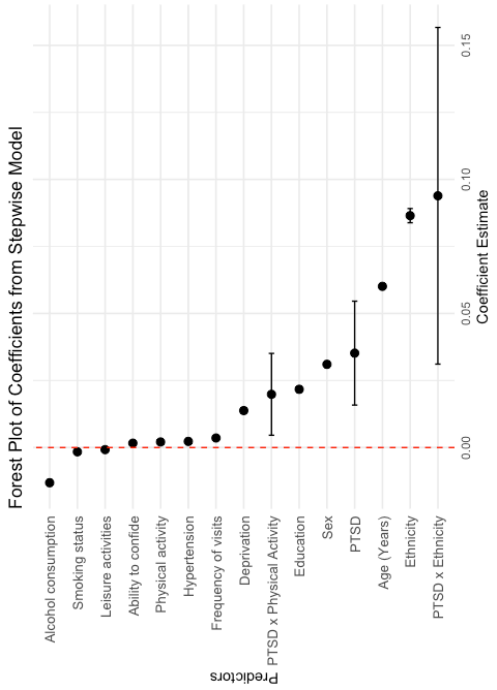
Dementia	HR (95% CI)	*P*
Depression	2.7136 (2.3453, 3.1398)	< .001
Age*		
Sex	0.7629 (0.7223, 0.8058)	< .001
Ethnicity	1.2241 (1.0801, 1.3874)	.002
Education	1.2587 (1.1897, 1.3318)	< .001
Deprivation*	1.1489 (1.1235, 1.1749)	< .001
Smoking status	1.1223 (1.0702, 1.1769)	< .001
Alcohol consumption		
Log weekly physical activity*	1.0635 (1.0416, 1.0859)	< .001
Hypertension	1.1834 (1.1242, 1.2457)	< .001
Frequency of family or friends' visits*		
Ability to confide in others*	1.0787 (1.0538, 1.1043)	< .001
Engagement in leisure activities*		
Depression x Age	0.7805 (0.7071, 0.8616)	< .001
Depression x Sex	0.8771 (0.7708, 0.9980)	.047
Depression x Ethnicity		
Depression x Education		
Depression x Deprivation		
Depression x Smoking status		
Depression x Alcohol consumption	1.1443 (1.0009, 1.3083)	.049
Depression x Physical activity		
Depression x Hypertension		
Depression x Frequency of family or friends' visits	1.0461 (0.9940, 1.1010)	.084
Depression x Ability to confide in others	0.9495 (0.8974, 1.0046)	.072
Depression x Engagement in leisure activities		

CI = confidence interval; P = p-value; HR = hazard ratio.
*Variables were standardized to have a mean of 0 and a standard deviation of 1.

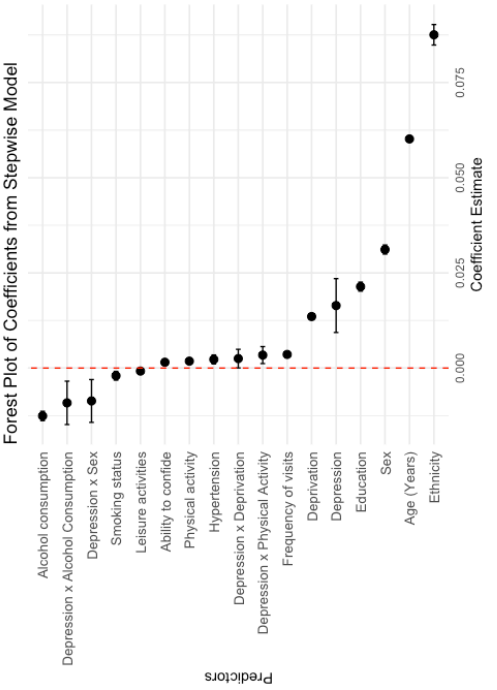
eFigure C32. Forest Plot of the Stratified Stepwise Model Depression – Dementia.



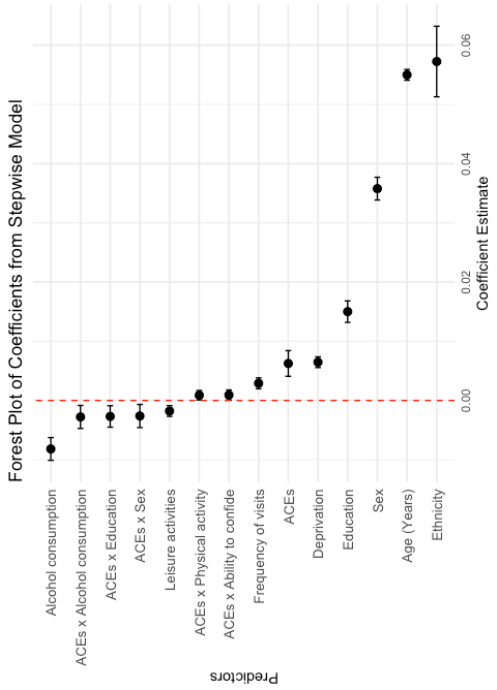
eFigure C33. Forest Plots of Selected Variables and Log Reaction Time.



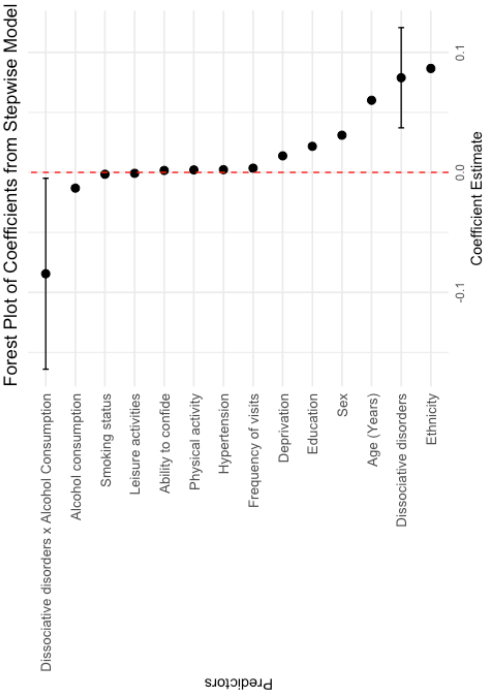
PTSD – Log Reaction Time



Depression – Log Reaction Time

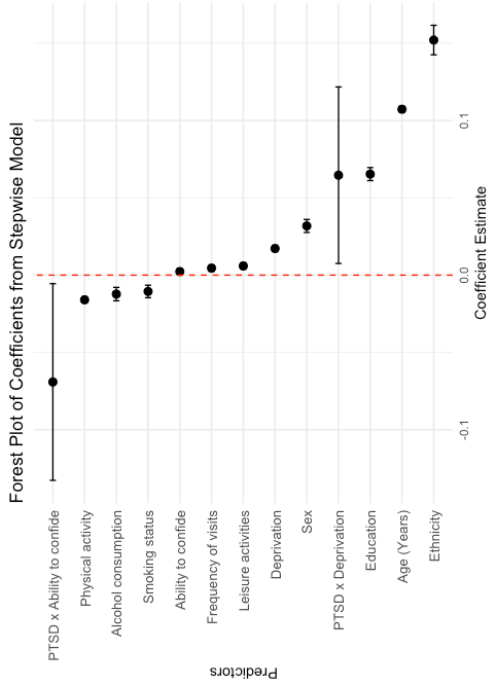


ACEs – Log Reaction Time

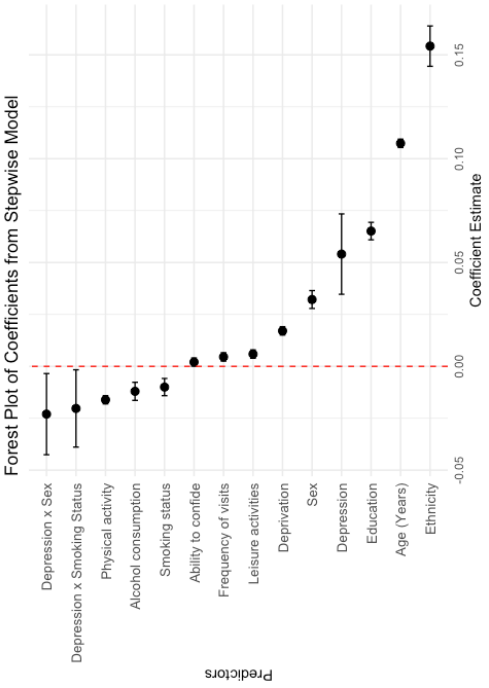


Dissociative Disorders – Log Reaction Time

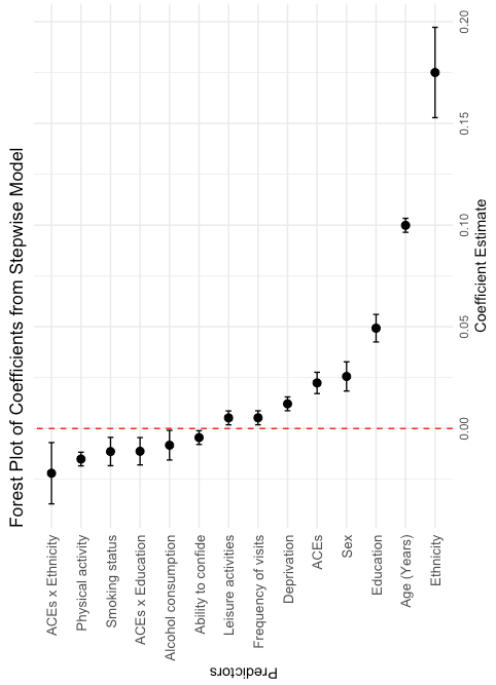
eFigure C34. Forest Plots of Selected Variables and Log Visual Memory Errors.



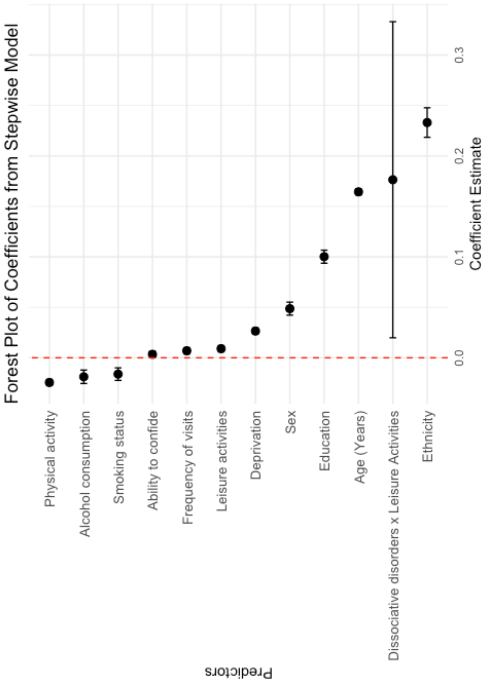
PTSD Diagnosis – Log Visual Memory Errors



Depression – Log Visual Memory Errors

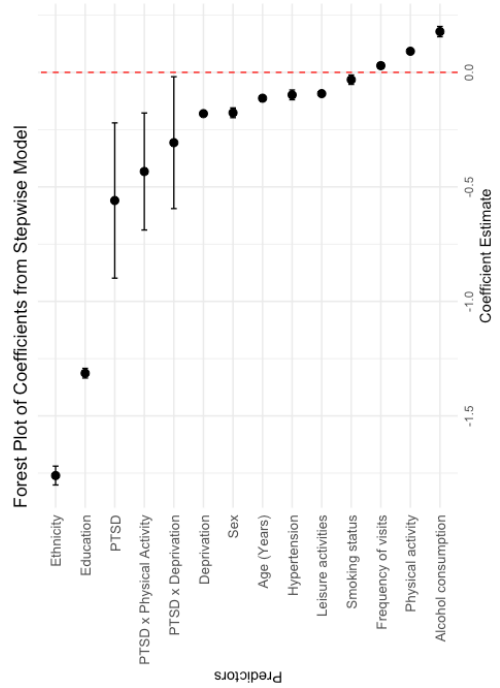


ACEs – Log Visual Memory Errors

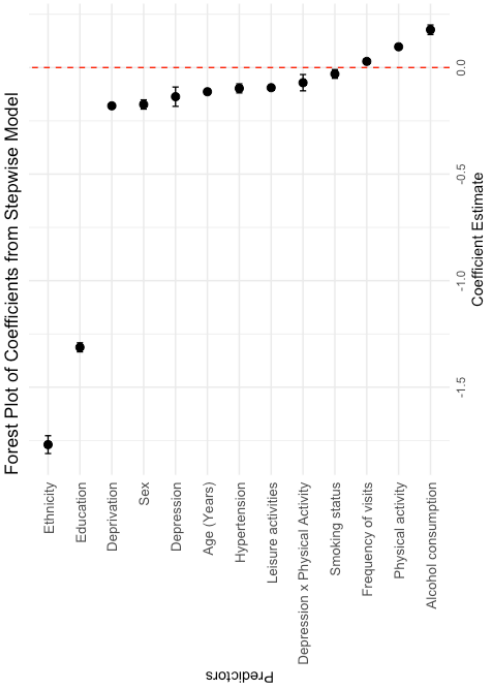


Dissociative Disorders – Log Visual Memory Errors

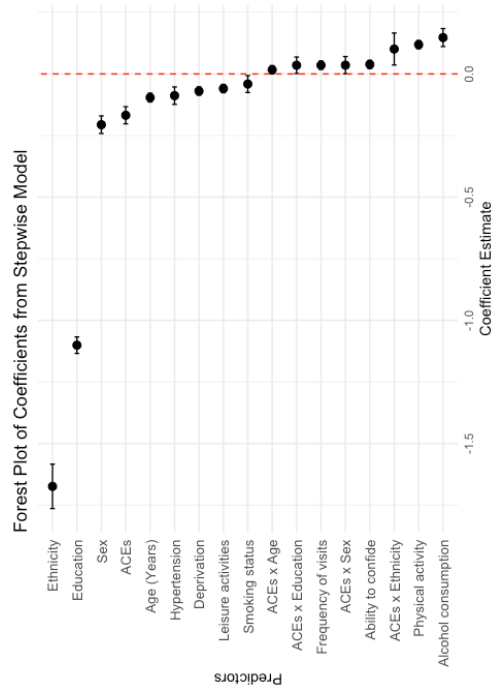
eFigure C35. Forest Plots of Selected Variables and Reasoning Ability.



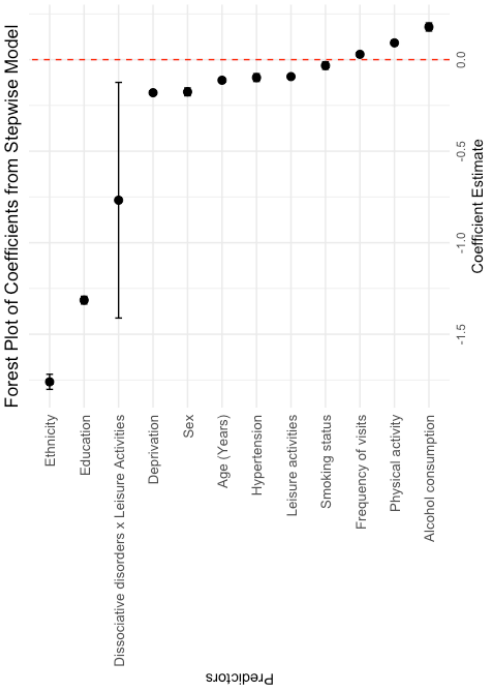
PTSD Diagnosis – Reasoning



Depression – Reasoning

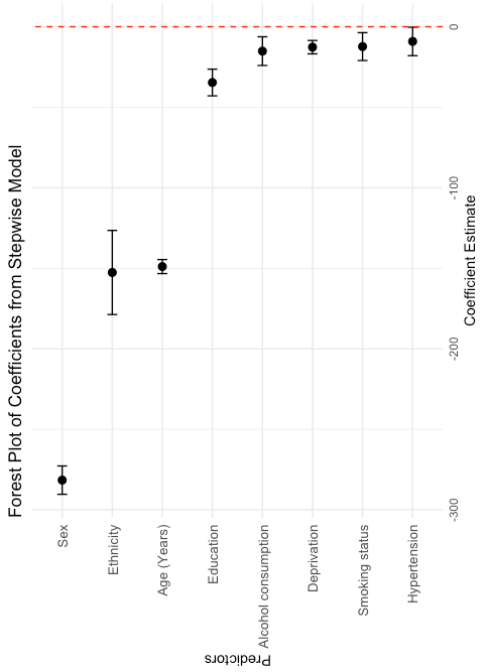


ACEs – Reasoning

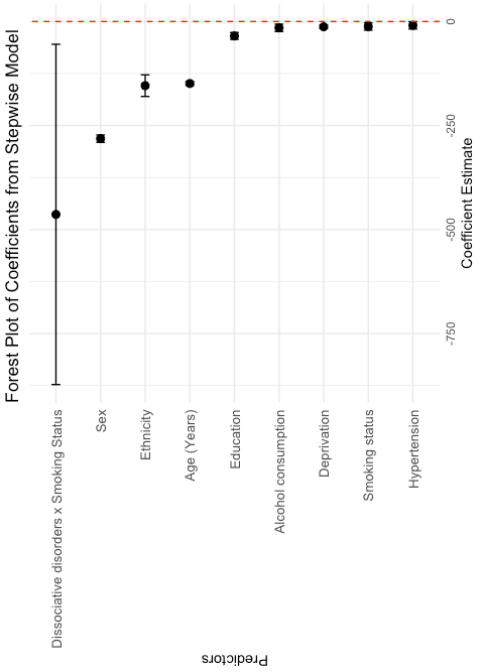


Dissociative Disorders – Reasoning

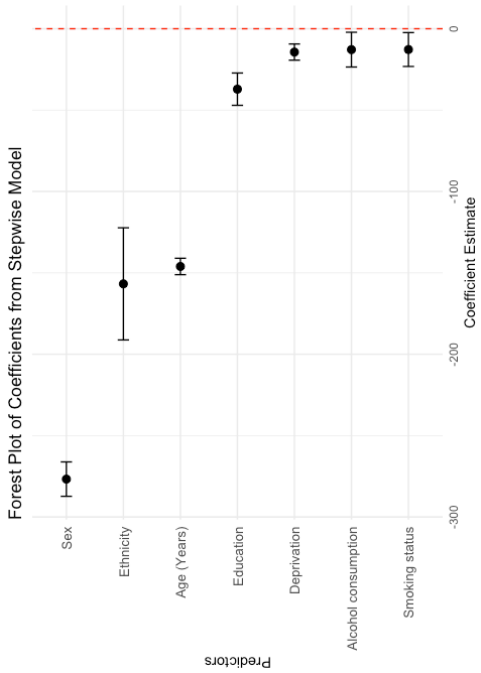
eFigure C36. Forest Plots of Selected Variables and Hippocampal Volume (Left).



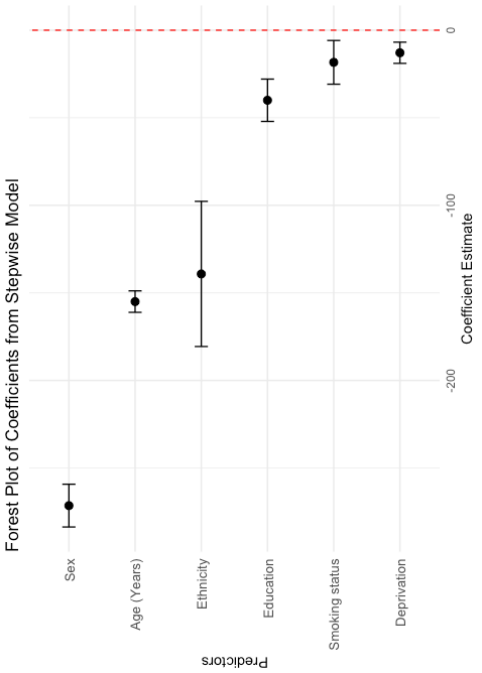
PTSD Diagnosis – Hippocampal Volume (Left)



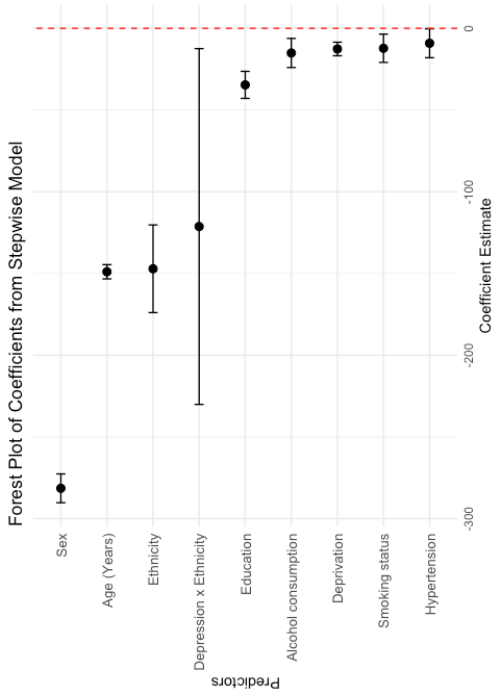
Dissociative Disorders – Hippocampal Volume (Left)



ACEs – Hippocampal Volume (Left)

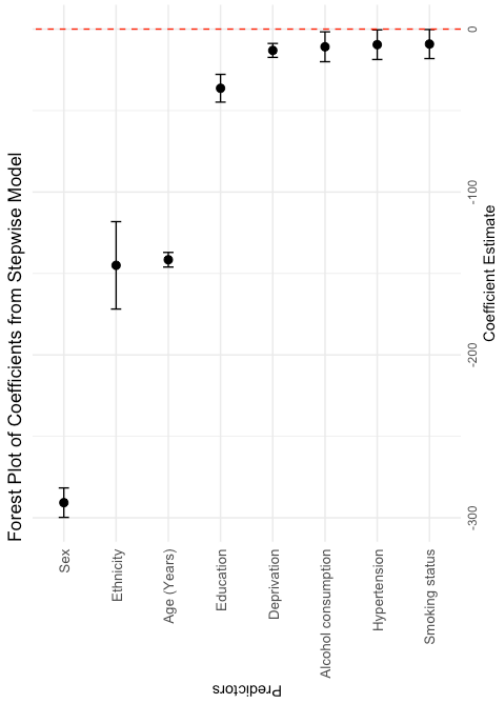


PTSD Symptoms – Hippocampal Volume (Left)

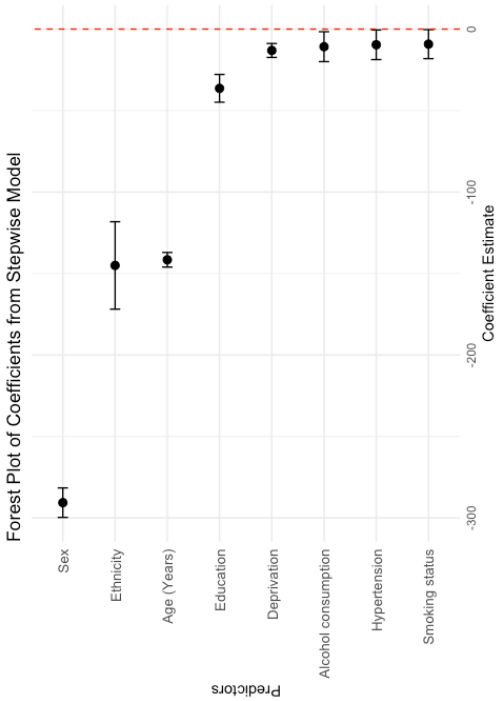


Depression – Hippocampal Volume (Left)

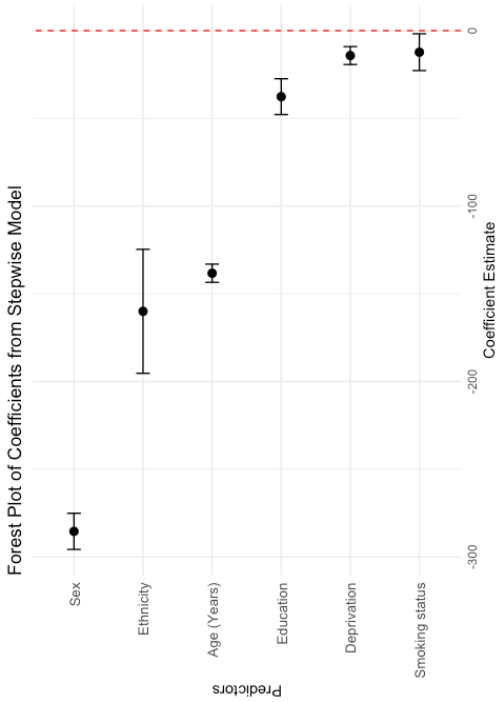
eFigure C37. Forest Plots of Selected Variables and Hippocampal Volume (Right).



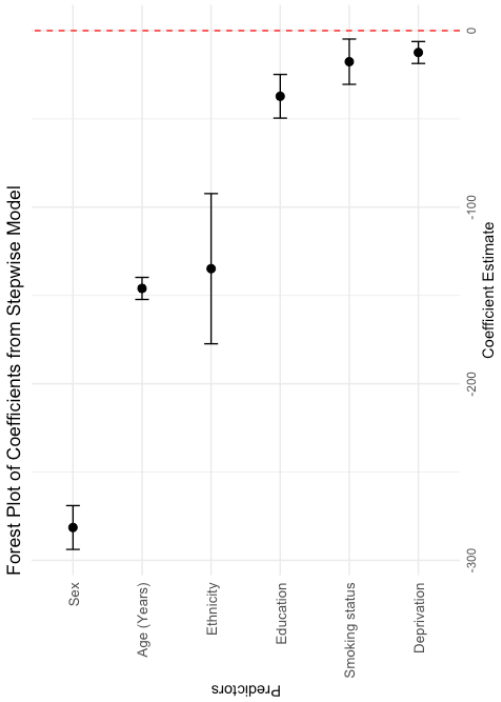
PTSD Diagnosis – Hippocampal Volume (Right)



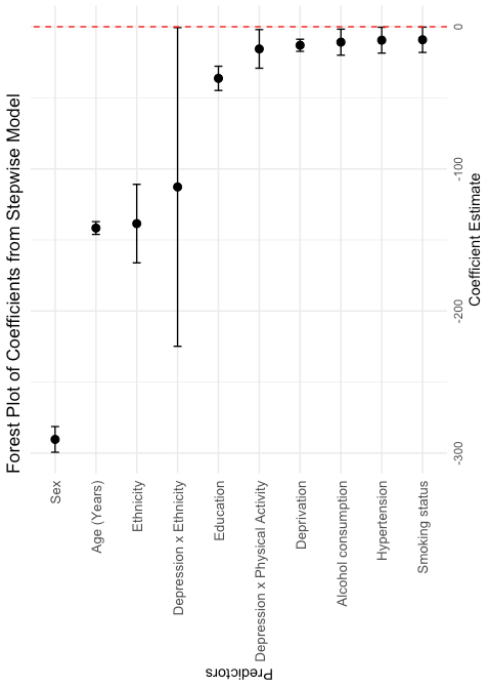
Dissociative Disorders – Hippocampal Volume (Right)



ACEs – Hippocampal Volume (Right)



PTSD Symptoms – Hippocampal Volume (Right)



Depression – Hippocampal Volume (Right)

eMethods. Used R Packages and Versions.

```
R version 4.4.1 (2024-06-14)

Platform: aarch64-apple-darwin20

Running under: macOS Sonoma 14.6


Matrix products: default

BLAS:   /Library/Frameworks/R.framework/Versions/4.4-arm64/Resources/lib/li
bRblas.0.dylib

LAPACK: /Library/Frameworks/R.framework/Versions/4.4-arm64/Resources/lib/li
bRlapack.dylib;  LAPACK version 3.12.0


locale:

[1] en_US.UTF-8/en_US.UTF-8/en_US.UTF-8/C/en_US.UTF-8/en_US.UTF-8


time zone: Europe/Berlin

tzcode source: internal


attached base packages:

[1] stats     graphics  grDevices utils     datasets  methods   base


other attached packages:

[1] lubridate_1.9.4 foreign_0.8-88  haven_2.5.4     nortest_1.0-4

[5] goftest_1.2-3   gtsummary_2.0.4 dplyr_1.1.4     psych_2.4.12


loaded via a namespace (and not attached):

 [1] jsonlite_1.8.9    compiler_4.4.1    tidyselect_1.2.1  parallel_4.4.1

 [5] jquerylib_0.1.4   yaml_2.3.10       fastmap_1.2.0     lattice_0.22-6

 [9] R6_2.5.1          generics_0.1.3    knitr_1.49        forcats_1.0.0

[13] tibble_3.2.1      bslib_0.8.0       pillar_1.10.1     rlang_1.1.5

[17] cachem_1.1.0      xfun_0.50         sass_0.4.9        timechange_0.3.0

[21] cli_3.6.3         withr_3.0.2       magrittr_2.0.3    digest_0.6.37

[25] grid_4.4.1        rstudioapi_0.17.1 hms_1.1.3         lifecycle_1.0.4

[29] nlme_3.1-167      vctrs_0.6.5       mnormt_2.1.1      evaluate_1.0.3

[33] glue_1.8.0        rmarkdown_2.29    tools_4.4.1       pkgconfig_2.0.3

[37] htmltools_0.5.8.1


---
```

```
R version 4.4.1 (2024-06-14)

Platform: aarch64-apple-darwin20

Running under: macOS Sonoma 14.6


Matrix products: default

BLAS:   /Library/Frameworks/R.framework/Versions/4.4-arm64/Resources/lib/li
bRblas.0.dylib

LAPACK: /Library/Frameworks/R.framework/Versions/4.4-arm64/Resources/lib/li
bRlapack.dylib;  LAPACK version 3.12.0


locale:

[1] en_US.UTF-8/en_US.UTF-8/en_US.UTF-8/C/en_US.UTF-8/en_US.UTF-8


time zone: Europe/Berlin

tzcode source: internal


attached base packages:

[1] stats     graphics  grDevices utils     datasets  methods   base


other attached packages:

[1] lavaan_0.6-19   ggplot2_3.5.1   devtools_2.4.5  usethis_3.1.0

[5] nortest_1.0-4   gtsummary_2.0.4 dplyr_1.1.4     psych_2.4.12

loaded via a namespace (and not attached):

 [1] gt_0.11.1          tidyr_1.3.1        sass_0.4.9         generics_0.1.3

 [5] xml2_1.3.6         lattice_0.22-6     digest_0.6.37      magrittr_2.0.3

 [9] evaluate_1.0.3     grid_4.4.1         cards_0.4.0        pkgload_1.4.0

[13] fastmap_1.2.0      jsonlite_1.8.9     pkgbuild_1.4.6     sessioninfo_1.2.
2

[17] urlchecker_1.0.1   promises_1.3.2     purrr_1.0.2        scales_1.3.0

[21] pbivnorm_0.6.0     jquerylib_0.1.4    mnormt_2.1.1       cli_3.6.3

[25] shiny_1.10.0       rlang_1.1.5        commonmark_1.9.2   munsell_0.5.1

[29] ellipsis_0.3.2     withr_3.0.2        remotes_2.5.0      cachem_1.1.0

[33] yaml_2.3.10        tools_4.4.1        parallel_4.4.1     memoise_2.0.1

[37] colorspace_2.1-1   httpuv_1.6.15      vctrs_0.6.5        R6_2.5.1

[41] mime_0.12          stats4_4.4.1       lifecycle_1.0.4    fs_1.6.5

[45] htmlwidgets_1.6.4 miniUI_0.1.1.1     pkgconfig_2.0.3    gtable_0.3.6

[49] pillar_1.10.1      bslib_0.8.0        later_1.4.1        glue_1.8.0

[53] profvis_0.4.0      Rcpp_1.0.14        xfun_0.50          tibble_3.2.1
```

```
[57] tidyselect_1.2.1  rstudioapi_0.17.1 knitr_1.49        xtable_1.8-4
[61] htmltools_0.5.8.1 nlme_3.1-167      rmarkdown_2.29    compiler_4.4.1
[65] quadprog_1.5-8    markdown_1.13

---



R version 4.4.1 (2024-06-14)
Platform: aarch64-apple-darwin20
Running under: macOS Sonoma 14.6


Matrix products: default
BLAS:   /Library/Frameworks/R.framework/Versions/4.4-arm64/Resources/lib/li
bRblas.0.dylib
LAPACK: /Library/Frameworks/R.framework/Versions/4.4-arm64/Resources/lib/li
bRlapack.dylib;  LAPACK version 3.12.0


locale:
[1] en_US.UTF-8/en_US.UTF-8/en_US.UTF-8/C/en_US.UTF-8/en_US.UTF-8


time zone: Europe/Berlin
tzcode source: internal


attached base packages:
[1] stats     graphics  grDevices utils     datasets  methods   base


other attached packages:
 [1] survminer_0.5.0      ggpubr_0.6.0         emmeans_1.10.7
 [4] broom_1.0.7          GGally_2.2.1         glmnet_4.1-8
 [7] Matrix_1.7-2         lmtest_0.9-40        zoo_1.8-12
[10] QuantPsyc_1.6        MASS_7.3-64          purrr_1.0.2
[13] boot_1.3-31          corrplot_0.95        car_3.1-3
[16] carData_3.0-5        interactionR_0.1.7   broom.helpers_1.18.0
[19] survival_3.8-3       factoextra_1.0.7     FactoMineR_2.11
[22] ggplot2_3.5.1        devtools_2.4.5       usethis_3.1.0
[25] nortest_1.0-4        gtsummary_2.0.4      dplyr_1.1.4
[28] psych_2.4.12
```

```
loaded via a namespace (and not attached):
  [1] RColorBrewer_1.1-3      rstudioapi_0.17.1       jsonlite_1.8.9
  [4] shape_1.4.6.1           magrittr_2.0.3          estimability_1.5.1
  [7] farver_2.1.2            rmarkdown_2.29          fs_1.6.5
 [10] ragg_1.3.3              vctrs_0.6.5             memoise_2.0.1
 [13] askpass_1.2.1           rstatix_0.7.2           htmltools_0.5.8.1
 [16] Formula_1.2-5           sass_0.4.9              bslib_0.8.0
 [19] htmlwidgets_1.6.4       plyr_1.8.9              cachem_1.1.0
 [22] uuid_1.2-1              mime_0.12               lifecycle_1.0.4
 [25] iterators_1.0.14        pkgconfig_2.0.3         R6_2.5.1
 [28] fastmap_1.2.0           shiny_1.10.0            digest_0.6.37
 [31] colorspace_2.1-1        pkgload_1.4.0           textshaping_1.0.0
 [34] labeling_0.4.3          km.ci_0.5-6             abind_1.4-8
 [37] compiler_4.4.1          remotes_2.5.0           fontquiver_0.2.1
 [40] withr_3.0.2             backports_1.5.0         ggstats_0.8.0
 [43] pkgbuild_1.4.6          ggsignif_0.6.4          openssl_2.3.1
 [46] sessioninfo_1.2.2       scatterplot3d_0.3-44    flashClust_1.01-2
 [49] tools_4.4.1             zip_2.3.1               httpuv_1.6.15
 [52] glue_1.8.0              nlme_3.1-167            promises_1.3.2
 [55] grid_4.4.1              cluster_2.1.8           generics_0.1.3
 [58] gtable_0.3.6            KMsurv_0.1-5            tidyr_1.3.1
 [61] data.table_1.16.4       utf8_1.2.4              xml2_1.3.6
 [64] ggrepel_0.9.6           foreach_1.5.2           pillar_1.10.1
 [67] later_1.4.1             splines_4.4.1           lattice_0.22-6
 [70] tidyselect_1.2.1        fontLiberation_0.1.0    miniUI_0.1.1.1
 [73] knitr_1.49              fontBitstreamVera_0.1.1 gridExtra_2.3
 [76] xfun_0.50               expm_1.0-0              DT_0.33
 [79] yaml_2.3.10             evaluate_1.0.3          codetools_0.2-20
 [82] officer_0.6.7           msm_1.8.2               gdtools_0.4.1
 [85] tibble_3.2.1            multcompView_0.1-10     cli_3.6.3
 [88] xtable_1.8-4            systemfonts_1.2.1       munsell_0.5.1
 [91] jquerylib_0.1.4         survMisc_0.5.6          Rcpp_1.0.14
 [94] coda_0.19-4.1           parallel_4.4.1          leaps_3.2
 [97] ellipsis_0.3.2          profvis_0.4.0           urlchecker_1.0.1
[100] mvtnorm_1.3-3           scales_1.3.0            flextable_0.9.7
[103] rlang_1.1.5             mnormt_2.1.1
```

The analytic code is available online (https://osf.io/k4b5w/).