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Clinical Features of dementia cases ascertained by ICD coding in LIMBIC-CENC multicenter study of mild traumatic brain injury

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Abstract

Objective: Describe dementia cases identified through International Classification of Diseases (ICD) coding in the Long-term Impact of Military-relevant Brain Injury Consortium – Chronic Effects of Neurotrauma Consortium (LIMBIC-CENC) multicenter prospective longitudinal study (PLS) of mild traumatic brain injury (mTBI).

Design: Descriptive case series using cross-sectional data.

Methods: Veterans Affairs (VA) health system data including ICD codes were obtained for 1563 PLS participants through the VA Informatics and Computing Infrastructure (VINCI). Demographic, injury, and clinical characteristics of Dementia positive and negative cases are described.

Results: Five cases of dementia were identified, all under 65 years old. The dementia cases all had a history of blast-related mTBI and all had self-reported functional problems and four had PTSD symptomatology at the clinical disorder range. Cognitive testing revealed some deficits especially in the visual memory and verbal learning and memory domains, and that two of the cases might be false positives.

Conclusions: ICD codes for early dementia in the VA system have specificity concerns, but could be indicative of cognitive performance and self-reported cognitive function. Further research

is needed to better determine links to blast exposure, blast-related mTBI, and PTSD to early dementia in the military population.

INTRODUCTION

Dementia is a syndrome characterized by progressive deterioration of cognitive function in at least 2 domains (e.g., memory, language, visual spatial, executive function) that affects one's ability to function independently. For decades, emerging data from epidemiological studies,[1]–[3] systematic reviews,[4] and meta-analyses[5] have suggested that traumatic brain injury (TBI) is a risk factor for dementia [6]. More recent population-based studies suggest that all TBI severities, including mild TBI (mTBI), increase risk for dementia in a dose-dependent fashion. Because military Service Members (SMs) and Veterans have a significantly higher risk for mTBI due to activities inherent to military service in both deployed and garrison settings (e.g., blast, accidents) [7], there is a growing concern that this population could be at higher risk for dementia compared to their civilian counterparts. Additionally, SMs are often subject to repetitive subconcussive forces from blast exposure and other mechanisms. Repeated blunt head impacts have been recognized as a source of brain insult in contact sports athletes[8]–[12]. Similar findings have been documented with military breacher and heavy weapons training [13]–[15].

Using Veterans Affairs (VA) health system data, identifying mTBI and dementia using International Classification of Disease (ICD) supports earlier epidemiological reports that even mTBI without loss of consciousness may be associated with a small but increased risk of incident dementia later in life [16]. However, significant limitations in study methodologies leave questions regarding the risk of mTBI particularly for early onset dementia (EOD), defined as onset before age 65 years. First, ICD classification that were used to identify dementia has low positive predictive value in patients under the age of 65 (and especially under the age of 55 years) in both VA and non-VA settings [17], [18]. Second, studies employing both VA and non-VA data have also found that diagnosis of mTBI itself has decreased accuracy with both false-positive and false-negative code assignments [19], [20]. As such, a prospective longitudinal study of a large cohort of Service Members and Veterans with and without combat-related mTBI in which a diagnosis of mTBI and dementia is confirmed using a combination of clinical assessments and other validated diagnostic tools is a promising approach to examine the association of mTBI and incident dementia later in life.

The Long-Term Impact of Military-Relevant Brain Injury Consortium (LIMBIC) multicenter prospective longitudinal study (PLS) is uniquely positioned to link prospectively collected standardized research data with VA ICD code data. The overall objective of the study is to longitudinally follow our enrolled participants to identify incident dementia as well as evidence of neurodegenerative disorders [21], [22]. None of the participants enrolled in the study had previously been identified as having dementia at the time of enrollment. However, when we linked our enrollment data to administrative claims data from VA Informatics and Computing Infrastructure (VINCI), we found that some participants were assigned ICD codes for dementia during their clinical care encounters at VA medical centers. This unexpected finding was the impetus to conduct this analysis, which aims to provide an

in-depth characterization of these participants with assigned ICD dementia codes using standardized functional status and cognitive performance assessments. This would serve to inform and confirm our case definition of dementia in future research in and outside the LIMBIC consortium. This work could also mitigate "attribution error" in subsequent research to examine the association between dementia and health outcomes utilizing similar administrative data.

The VINCI contains administrative inpatient and outpatient VA facility and non-VA facility care paid for by the VA. The PLS developed a process for requesting VINCI data for their study participants and linking it to their prospectively collected research database. When we linked this administrative data from VINCI, we surprisingly found a small number of participants who had received ICD codes for dementia during their clinical care encounters at a VAMC. This secondary analysis aims to provide an in-depth characterization of these participants to help determine whether the dementia codes typically used for older adults apply to these younger adults. The objective of this study was to identify cases with ICD dementia codes [16] in the VA system among LIMBIC PLS participants and describe their dementia risk factors (age, Apo E status, lifetime TBI history and PTSD), self-reported functional status, quality of life and objective cognitive performance. The goal was to inform the case definition of dementia in outcomes research utilizing similar administrative data including future research in LIMBIC. By characterizing the functional status and cognitive performance of those with and without ICD dementia codes, we can learn the utility of using these codes as an indicator for dementia within our prospective study cohort as well as the broader population.

MATERIALS and METHODS:

Design:

This descriptive case series study analyzed data from the ongoing LIMBIC-CENC multicenter prospective longitudinal study (PLS). At the time of this data extraction, eight PLS sites across the United States (US) had been actively engaged in participant recruitment/enrollment. Details of the LIMBIC-CENC PLS purpose, recruitment processes, eligibility criteria, and overall methods have been previously described [21]–[23]. Briefly, the PLS enrolls current and former US SMs with combat exposure and a range of number of mTBIs during their lifetime, including those with an entirely negative TBI history. Participants are primarily recruited through mass mailings and non-paid advertisements. Eligibility criteria are: adult (18+) of any sex (with the exception of females for hypogonadism analyses), race or ethnicity; history of post-911 deployment and combat exposure; and absence of history of moderate to severe TBI, schizophrenia, or major neurologic disorder. This parent study, including the database registry and all secondary analyses, was approved by the local Institutional Review Boards at each of the eight PLS enrollment sites. Before any study procedures, all participants provided written consent. For the current set of analyses, participants were included if they had linkable records in the VA Informatics and Computing Infrastructure (VINCI).

Lifetime Mild TBI history:

The LIMBIC-CENC PLS obtains a clinical diagnosis of all lifetime mTBI(s) through a rigorous, standardized, and validated process. Each participant's potential concussive events (PCEs) are catalogued using a modified version of the Ohio State University TBI Identification (OSU TBI-ID) [24]. Each PCE is then assessed via a validated retrospective Concussion Diagnostic Interview, yielding a preliminary algorithm-generated TBI diagnosis (No mTBI, mTBI with posttraumatic amnesia (PTA), or mTBI without PTA) [25]. Every algorithm rating is then reviewed, checked against available medical records, and vetted with a centralized expert committee to yield a final determination that adheres to the VA/DoD common definition of mTBI [26]. Mechanism of each mTBI diagnosed is also categorized as blast-related or not, and if blast-related, then whether a blunt mechanism was also present (mixed blast-blunt) or not (pure blast). From this TBI level data, positive lifetime mTBI histories were subclassified for these analyses as follows: 1) 1–2 mTBIs versus 3+ (repetitive mTBI), 2) any mTBIs having PTA or none having PTA, 3) any mTBIs were blast-related or none were blast-related, and 4) all lifetime mTBIs were of pure blast or any were either non-blast related or mixed blast-blunt mTBIs.

ICD code extraction:

With regulatory approval and while maintaining information security, social security numbers of participants were used to extract linked VINCI ICD-9 and ICD-10 codes for Dementia along with the date of code entry from 2000 until most recent VINCI data pull. Dates of dementia diagnosis were also obtained to examine time between TBI diagnosis and first dementia diagnosis within VA. We obtained all IRB and VA R&D regulatory approvals to request real Social Security Numbers (SSNs) from each of the 7 participating VAs represented by veterans in the Longitudinal Study. These real SSNs were then uploaded into the VA Informatics and Computing Infrastructure (VINCI). A request was made from VINCI for all inpatient and outpatient records either in VA facilities or community care reimbursed by VA from enrollment date in VA from 2000 until 2019. The first dementia diagnosis was June 2012 and the last was July 2019. After removal of real SSN, records were then transferred along with Longitudinal Study ID to VCU server via a Data Use Agreement (DUA). Study team members then merged the VINCI inpatient and outpatient records with Longitudinal Study data by Study ID.

Dementia Case Definition:

The VINCI inpatient and outpatient records were used to extract ICD9 and ICD-10 codes for Dementia along with the date of code entry. The number of dementia code entries, date of entry, and type of dementia diagnoses based on VINCI records were recorded. Using the algorithm applied in recent studies examining dementia risk among Veterans, dementia cases were selected if encounters contained ICD diagnosis codes for dementia at two or more visits at least 7 days apart [16], [27]. Both 9th Revision (ICD-9) and 10th Revision (ICD-10) codes were extracted. This essentially consist of the non-infectious Dementia ICD codes and included the following ICD-9 codes: 290.X, 291.2, 294.1X, 331.0, 331.1X, 331.2, 331.7, 331.82, 331.9, 294.0, 294.2, 294.8; and the following ICD-10 codes: A8100, A8101, A8109, A812, A8182, A8189, A819, F0150, F0151, F0280, F0281, F0390, F0391, F1027,

F1097, F1327, F1397, F1817, F1827, F1897, F1917, F1927, F1997, G231, G300, G301, G308, G309, G3101, G3109, G3183, G903. Participants with no ICD dementia diagnoses were classified as Dementia Negative. Those with any dementia ICD code entries present but not meeting the above dementia case criteria were classified as questionable dementia cases, and excluded from analysis (n=4).

Cognitive and Global Functioning:

A parsimonious set of measures were preselected from the extensive LIMBIC-CENC cognitive test battery that are characteristic of clinical dementia. This included neurocognitive performance tests, self-reported cognitive function, executive function, social participation, and global functional status.

The performance tests of neurocognition concentrated on tasks of executive function and memory which are the earliest affected in Alzheimer's disease, as well as language (verbal fluency) and complex attention (working memory, and processing speed).[28] Additionally, a composite test of overall cognition and a test of performance validity were included. All instruments are well-validated and recommended as part of the NIH TBI Common Data Elements [29]. Standardized scores were used for all cognitive measures in this study. The specific tests chosen are described below. The Medical Symptom Validity Test (MSVT), applying the developer recommended cut-off scores, was used to detect invalid neuropsychological test performance and non-credible self-reported symptom [30]. Visual memory and learning were assessed using the Brief Visuospatial Memory Test-Revised (BVMT-R) Trials 1–3 Total and Delayed Recall [31].

Verbal learning and memory was measured using the California Verbal Learning Test-II (CVLT-II) Trials 1–5 Total Recall score and the Long Delay Free Recall score [32]. Cued verbal fluency was evaluated using the Delis–Kaplan Executive Function System (D-KEFS) Letter Fluency and Category Fluency [33]. Processing speed and working memory were measured by the Wechsler Adult Intelligence Scale 4th Edition (WAIS-IV) Processing Speed Index (PSI), a composite of the timed tasks of Symbol Search and Coding, and the Working Memory Index, a composite of the digit span and letter-number sequencing task [34]. Additionally, the NIH Toolbox cognition battery (NIHTB-CB) Fluid Composite score was used as an estimate of global functioning and capacity for new learning and information processing in novel situations[35]. The NIHTB-CB subtests that comprise the Fluid Composite span various cognitive domains including language, memory, and executive functioning [35].

Several short-forms of the Quality of Life (TBI-QOL) instrument were used to assess cognitive and social participation aspects of health-related functional status and quality of life [36]. These forms are self-ratings with total scores ranging from 10 – 50. For the TBI-QOL Cognition General Concerns and Executive Function short forms, higher scores indicate better function with less difficulty endorsed for general cognition or executive function, respectively. For the social participation form, higher scores indicate greater participation in social activities [36]. The Glasgow Outcome Scale Extended (GOS-E) was used to assess global function through a structured interview [37], [38] The GOS-E [39] is a modification of the original GOS[40] with upper and lower subdivisions for severe

disability, moderate disability and good recovery; a higher score on the 1–8 point ordinal scale indicates better global function with less need for assistance in daily life.

Other Health Status and Risk Factor Measures:

Lists of current medications were obtained through a combination of participant interview and medical record abstraction. These medications were first categorized by pharmacologic class, and then further categorized into psychoactive or not. Psychoactive subcategories of interest for this study were developed to include medications that might be used to treat dementia patients or could be contributing to cognitive impairment. Additional measures were included that might contribute to the risk of early onset dementia and/or confound the clinical picture of dementia. These included: combat intensity via the Deployment Risk and Resiliency Inventory, Version 2, Section D (DRRI-2-D) [41]; PTSD status via the PTSD Checklist for the Diagnostic and Statistical Manual, 5th edition (PCL-5) with total score > 33 indicating clinical PTSD [42]; The Patient Health Questionnaire (PHQ-9), a widely used 9-item rating of current (prior two-week) depression symptoms with total scores ranging from 0 (None) to 27 (Severe) [43]; hypertension; diabetes; cigarette use history as queried in the CDC developed Behavioral Risk Factor Surveillance System (BRFSS); illicit drug abuse using a cut-point of 2.5 on the Drug Abuse Screening Test 10 (DAST10) questionnaire [44]; alcohol use (using the Alcohol Use Disorders Test Consumption (AUDIT-C) questionnaire); total number of months combat deployed; age; and time since first and most recent TBI.

Dementia case identification.

Five participants (0.032% of the sample) met all the criteria for dementia classification, with target ICD code applied in at least two separate clinical encounters on separate dates. Four participants (0.026% of the sample) received a dementia ICD code on only a single clinical encounter; these were classified as ‘possible’ dementia and excluded from analysis. The remaining 99.4% of the sample (n=1,554), had no target codes, and were classified as ‘no dementia’.

Statistical Procedure:

Given the small number of participants with dementia ascertained by ICD codes, hypothesis testing was not conducted. Instead, we report descriptive data on the characteristics of each dementia case. To provide context, we also calculated group summary data on the same characteristics for those without any dementia ICD codes, with means for continuous data and percentages for categorical variables.

RESULTS

The detailed characteristics of the five dementia cases and the group summary data for the ‘no dementia’ group (n=1,554) are displayed in Table 1.

DISCUSSION

Established in 2013, the LIMBIC-CENC PLS is currently an 11-center, longitudinal, observational study of the long-term, including remote, effects of single and repetitive,

blast and non-blast, combat-related and non-combat-related mTBIs in US SMs and Veterans from all US military conflicts. A major driving force behind this nationwide research consortium was concern about the potential role of combat-related mTBI in the development of neurodegenerative disease, and an association with early cognitive decline and dementia in particular. In the PLS' current cohort of predominantly middle-aged, combat-exposed individuals, we have identified 5 individuals (0.03% of the cohort) with VA medical records that reflect an ICD-10 diagnosis of dementia. Their ages at the time of ICD diagnosis ranged from 37 to 60 years, suggesting these individuals may have early-onset dementia (i.e., onset of dementia diagnosis occurs before the age of 65 years).

A goal of this case series study was to determine how dementia presents in the clinic after mTBI and whether it differs from other neurodegenerative disorders, such as Alzheimer's disease (AD), which typically presents with a predominantly amnestic syndrome.[45] Some have reported that TBI-associated dementia may have unique neurobehavioral presentations that are less frequently amnestic at onset and differs from that of AD.[46], [47] Because of the heterogeneity of mTBI, one might expect a heterogeneity of TBI-associated dementia. In this study, cognitive performance within the dementia group reflected variability in the magnitude and pattern of impairment, but poor performance was noted most consistently in measures of visual memory (n = 4) and on verbal learning and memory (n = 3). Performance on measures of processing speed or executive function (working memory, verbal fluency, inhibitory control) was less consistently abnormal in individuals with an ICD diagnosis of dementia. Interestingly, the oldest individual (age 60 years) in the dementia group demonstrated the most consistent and severe impairment across cognitive domains, with scores that fell far below expectation given age and severity of remote mTBI. The youngest participant (age 37 years), and the one subclassified with possible psychoactive substance use cognitive dysfunction, demonstrated more variable performance. Performance validity testing was administered to all participants at baseline and 10.5% participants produced scores in the invalid range overall; all five participants coded with dementia were in the valid range on the standalone validity test in our battery. Future serially-collected neurocognitive data of the entire cohort will permit further investigation of the longer-term impacts of mTBI and its interaction with aging as well as the characteristics of cognitive dysfunction, including incident dementia, as it emerges.

Another study aim was to assess whether ICD dementia coding commonly used in VA population-based studies of dementia in older Veterans is valid for dementia diagnoses among middle-aged Veterans as represented in our cohort. Our analysis of a limited number of participants with ICD coding for dementia suggests a potential false positive rate of 40%. By routine clinical guidelines, two of the five would not have received a diagnosis of dementia based on the PLS study neurocognitive battery administered to all participants at baseline and selected *a priori* to detect incident dementia as it occurred. For example, even though case #2 scored below the 1st percentile on a delayed visual memory test, the participant otherwise had normal standardized scores on tests of verbal learning and memory. Overall participant #2's verbal learning was average at the 46th percentile (CVLT-II Total T=49) and long delay free verbal recall was also average at the 69th percentile (CVLT-II Long Delay Free Recall Z=0.5). Case #2 also scored higher than the larger non-dementia group on self-reported cognitive functional status. Although this may reflect

a self-awareness deficit, it more likely reflects a false positive diagnosis. Case #2's overall cognitive functional status combined with the normal verbal learning and memory scores argue against memory impairment due to dementia. As another example, case # 5 had a verbal delayed recall score at the 93rd percentile on the CVLT, and a verbal total learning score at the 95th percentile. Visual delayed recall was also in the average range at the 31st percentile. Four of the dementia-diagnosed cases were subclassified with non-specific dementia, either with (cases #2 and #4) or without (cases #1 and #3) behavioral disturbance. Of note, case #5 was also the only one of the five who was subclassified as psychoactive substance induced, suggesting that TBI or blast exposure was unlikely to be the causative factor. In fact, for this participant, a review of his or her medications revealed polypharmacy of psychoactive agents. The extent of medication classes in use raises the possibility of an iatrogenic contribution to their dementia diagnosis. While the misclassification rate is lower than what has been identified in other manual examinations of administrative data [18], [20], the number of potential false positives calls into question the accuracy of relying solely on ICD codes to identify dementia, especially in middle-age Veterans.

The small size of our dementia cases precluded formal hypothesis testing, but the group summary data for the dementia-code negative participants provides some context for comparison. Within our non-dementia group, Good Recovery as assessed by Glasgow Outcome Scale - Extended (GOS-E) was by far the most functional level, but this highest GOSE level was not reported by any of the five dementia cases. The ICD dementia cases all scored at either Moderate or Severe Disability, suggesting daily life functioning problems which may have contributed to receiving their ICD dementia codes. It further suggests that ICD dementia diagnosis from clinical records may be a useful parameter to monitor within our mTBI cohort. Given the challenges, complexity and variable reliability of clinical dementia diagnosis in established healthcare settings, it is even more difficult to determine a definitive diagnosis in a research setting. Many research studies may not have the resources, staff expertise, informant availability and/or participant burden bandwidth to accurately determine criteria for dementia using rigorous methods such as the Clinical Dementia Rating scale [48], [49]. This is particularly true for population-based studies that rely on administrative claims data or retrospective health records.

Of particular importance in the SM and Veteran population is the potential relationship between PTSD and the development of dementia after mTBI. Four of our five ICD dementia cases had PTSD symptom severity in the clinical disorder range. Prior research in military populations shows that PTSD tends to correlate with cognitive symptoms and complaints more than concussion does.[50], [51] These subjective complaints may have influenced the clinicians who entered the ICD dementia codes. Regardless, additional research is needed to determine the relationship between PTSD and remote mTBI. Of additional note, all five of the dementia-diagnosis cases fulfilled criteria for blast-related mTBI. Although too small of a number to make any firm conclusions, our findings warrant further investigation as our cohort ages. SMs in warzones are uniquely susceptible to blast exposures, including blast-related mTBI. SMs in certain occupational specialties, such as breachers and heavy weapons operators, are also uniquely susceptible to repetitive low-level blast exposures which may perturbate brain function.[13]–[15] This may parallel the risk level or pathophysiologic

pathway of early neurodegeneration proposed by repetitive low-level blunt head impacts as in contact sports [8], [11], [12].

Regarding medication usage, two of the dementia cases were prescribed cholinesterase inhibitors, of whom one was also prescribed a NMDA receptor antagonists. Both of these medications typically prescribed for dementia-related memory impairment, but also increasingly for TBI-related cognitive symptoms that do not fulfill criteria for AD or other dementias. The participant receiving both of these medication classes also was prescribed an antidepressant plus seven other psychoactive medications (broadly defined). We do not have data on the indication for these prescriptions, but this does raise a concern for polypharmacy in this case. These medication classes can be used to mitigate symptoms common with dementia, but they can also have significant cognitive side effects that might induce signs of delirium or other reversible causes of cognitive impairment which may be worsening or even mimicking dementia. Hence, screening for psychoactive medication use in a population of individuals with mTBI and a dementia-diagnosis ICD-10 code population may be warranted to consider medication review and elimination of any that could negatively impact cognitive and overall function.

Limitations:

The small number (five) of ICD-10 dementia diagnosis coded participants in this case series report limits generalizability of the findings. Additionally, these ICD-code diagnoses were limited to those provided in the context of VA inpatient and outpatient care and some private sector inpatient care reimbursed by VA. It is possible there could have been additional dementia diagnosis in the private sector that was not reimbursed by VA (i.e., care reimbursed by a non-VA payor which would not be captured in the VINCI databases). Nevertheless, finding this small sub-group provides a unique opportunity to comprehensively describe prospectively collected clinical research data of individuals with mild TBI who have been diagnosed independently with dementia during their routine clinical care and compare them to the overwhelming majority of individuals without dementia with mild TBI in our cohort. Further LIMBIC-CENC PLS analyses, including an assessment of initial and longitudinal neuroimaging and fluid biomarkers will be performed as additional annual virtual and 5-year in-person data are collected and as the number of dementia cases grows over time with aging.

Conclusion:

ICD codes for early dementia in the VA system have specificity concerns, but appear to have some utility in tracking cognitive functioning. Further research is needed to better determine links to blast exposure, blast-related mTBI, and PTSD to early dementia in the military population.

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Table 1.

Dementia code positive case descriptions alongside summary data from dementia code negative participants

	Case 1	**Case 2**	**Case 3**	**Case 4**	**Case 5**	**Dementia Code Negative (N=1554) Mean(SD) or N(%)**
Dementia Code Descriptions	Dementia, unspecified	Dementia in other diseases	Dementia, unspecified	Dementia in other diseases	Psychoactive substance-induced	N/A
Age at Baseline (years):	44	56	60	47	37	40.0(9.7)
Gender:	Female	Male	Male	Male	Male	1353(87.1%) Male
Race	White	Asian	Black	White	White	1126(72.5%) White
Ethnicity:	non-Hispanic	non-Hispanic	non-Hispanic	non-Hispanic	non-Hispanic	284(18.3%) Hispanic
ApoE e4 status (0, 1, 2)	0	1	0	0	UNK	835(53.7%) zero
PTSD status	Yes	Yes	No	Yes	Yes	567(36.5%) Yes
# mTBIs	3+	1–2	1–2	3+	3+	288(18.5%) none
Blast mTBI positive	Yes	Yes	Yes	Yes	Yes	589(37.9%) Yes
Controlled blast exposures	Medium	None	Medium	Heavy	Heavy	186(12%) Heavy
Neurocognitive Test Effort Validity (MSVT)	Pass	Pass	Pass	Pass	Pass	1390(89.4%) Pass
NIHTB-CB Fluid Intelligence Composite Standardized	missing	92	65	122	77	96.6(18.7)
CVLT-II: Total Recall T-Score	24	49	36	31	66	49.0(12.4)
CVLTII: Long Delay Free Recall Z-score	−3	0.5	−3	−1.5	1.5	−0.2(1.1)
BVMT Item 8: Total Recall T-Score:	20	23	20	23	45	42.7(12.4)
DKEFS VF: Letter Fluency Total Correct Scaled Score	7	8	5	14	15	10.4(3.4)
DKEFS VF: Category Fluency Total Correct Scaled Score:	3	7	8	12	13	10.9(3.5)
WAIS-IV Processing Speed Index Scaled Score	8	5.5	6.5	15	10.5	10.1(2.5)
WAIS-IV Working Memory Index Scaled Score	6	4.5	7	8.5	11	9.6(2.3)
TBIQOL Cognition: Total Score	missing	33	26	12	24	32.4(10.1)
TBIQOL Exec Fxn: Total Score	missing	33	33	27	28	36.9(8.2)
TBIQOL Social: Total Score	missing	21	30	21	24	32.9(9.8)
GOS Category:	Severe Disability	Moderate Disability	Moderate Disability	Moderate Disability	Moderate Disability	741(47.7%) Good

	Case 1	Case 2	Case 3	Case 4	Case 5	Dementia Code Negative (N=1554) Mean(SD) or N(%)
Classes of Current Medications						
Cholinesterase Inhibitor Y/N	Y	0	0	Y	0	0(0.0%) Y
NMDA Receptor Antagonist Y/N	Y	0	0	0	0	0(0.0%) Y
Stimulant Y/N	0	0	0	Y	0	8(0.7%) Y
Antipsychotic Y/N	0	Y	0	0	0	19(1.6%) Y
Antidepressant Y/N	Y	Y	Y	0	0	235(19.6%) Y
# Other Psychoactive or potential cognitive effects	7	1	0	0	1	930(77.8%) None

Notes:

Stimulant = Central Nervous System (CNS) Stimulant, Sympathomimetic-like agent (Modafinil or Armodafinil only), NOREPINEPHRINE REUPTAKE INHIBITOR (atomoxetine)

Antidepressant = SELECTIVE SEROTONIN REUPTAKE INHIBITOR (SSRI), SEROTONIN-NOREPINEPHRINE REUPTAKE INHIBITOR (SNRI), Tricyclic Antidepressant, Tetracyclic Antidepressant (e.g. mirtazapine) / Aminoketone (e.g. Bupropion)

Antipsychotic = Atypical Antipsychotic, Typical Antipsychotic

Other psychoactive or potential cognitive effect = Alpha Adrenergic Agonist, Anti-Epileptic Agent, Anticholinergic, Antihistamine, Barbiturate, Benzodiazepine, Lithium, Beta-Adrenergic Blocker, Cannabinoid, Central Alpha 2 Adrenergic Agonist, Nonbenzodiazepine Anxiolytic (e.g. buspirone), Nonbenzodiazepine Hypnotic, Opioid Agonist, Muscle Relaxant (also include if prefixed by Skeletal or Central Acting).