Supplemental Materials

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eTable 1. Standards for the Reporting of Diagnostic Accuracy Studies (STARD) checklist

Section & Topic	No	Item	Reported on page #
TITLE OR ABSTRACT			
	1	Identification as a study of diagnostic accuracy using at least one measure of accuracy (such as sensitivity, specificity, predictive values, or AUC)	4
ABSTRACT			
	2	Structured summary of study design, methods, results, and conclusions (for specific guidance, see STARD for Abstracts)	4
INTRODUCTION			
	3	Scientific and clinical background, including the intended use and clinical role of the index test	6-7
	4	Study objectives and hypotheses	7
METHODS			
Study design	**5**	Whether data collection was planned before the index test and reference standard were performed (prospective study) or after (retrospective study)	7
Participants	**6**	Eligibility criteria	7-8
	7	On what basis potentially eligible participants were identified (such as symptoms, results from previous tests, inclusion in registry)	7-8
	8	Where and when potentially eligible participants were identified (setting, location and dates)	7-8
	9	Whether participants formed a consecutive, random or convenience series	7
Test methods	**10a**	Index test, in sufficient detail to allow replication	9-11
	10b	Reference standard, in sufficient detail to allow replication	8
	11	Rationale for choosing the reference standard (if alternatives exist)	No alternative
	12a	Definition of and rationale for test positivity cut-offs or result categories of the index test, distinguishing pre-specified from exploratory	9-11
	12b	Definition of and rationale for test positivity cut-offs or result categories of the reference standard, distinguishing pre-specified from exploratory	8
	13a	Whether clinical information and reference standard results were available to the performers/readers of the index test	9
	13b	Whether clinical information and index test results were available to the assessors of the reference standard	8
Analysis	**14**	Methods for estimating or comparing measures of diagnostic accuracy	11-13
	15	How indeterminate index test or reference standard results were handled	N/A; methods did not allow for indeterminate results
	16	How missing data on the index test and reference standard were handled	8-9
	17	Any analyses of variability in diagnostic accuracy, distinguishing pre-specified from exploratory	11-13
	18	Intended sample size and how it was determined	7
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Participants	**19**	Flow of participants, using a diagram	e17
	20	Baseline demographic and clinical characteristics of participants	28-29, e4, e9-10
	21a	Distribution of severity of disease in those with the target condition	14, e9-10
	21b	Distribution of alternative diagnoses in those without the target condition	29, 31-32, e10
	22	Time interval and any clinical interventions between index test and reference standard	N/A; both performed post-mortem
Test results	**23**	Cross tabulation of the index test results (or their distribution) by the results of the reference standard	30

	24	Estimates of diagnostic accuracy and their precision (such as 95% confidence intervals)	14, 30
	25	Any adverse events from performing the index test or the reference standard	N/A; non-living participants
DISCUSSION			
	26	Study limitations, including sources of potential bias, statistical uncertainty, and generalisability	19-20
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OTHER INFORMATION			
	28	Registration number and name of registry	N/A; non-living participants
	29	Where the full study protocol can be accessed	7
	30	Sources of funding and other support; role of funders	21-22

eTable 2. Demographic, head trauma-related, and neuropathology characteristics by TES-CTE consensus diagnosis.

	TES-CTE absent (27)	TES-CTE present (309)	Total (336)
Demographics			
Mean age (SD)	48.2 (24.5)	60.9 (20.0)	59.8 (20.7)
Black race (%)	6 (22.2)	40 (12.9)	46 (13.7)
Hispanic ethnicity (%)	1 (3.7)	7 (2.3)	8 (2.4)
Women (%)	0 (0)	3 (1)	3 (0.9)
Mean education in years (SD)	15.1 (2.5)	15.9 (2.1)	15.8 (2.2)
Head trauma-related exposure			
Contact sports (%)[a]	18 (66.7)	294 (95.1)	312 (92.9)
Football (%)	17 (63)	262 (84.8)	279 (83)
Professional highest level (%)	1 (3.7)	109 (35.3)	110 (32.7)
College/semi-professional highest level (%)	6 (22.2)	121 (39.2)	127 (37.8)
High school/youth highest level (%)	10 (37)	34 (11)	44 (13.1)
Boxing (%)	4 (14.8)	20 (6.5)	24 (7.1)
Professional highest level (%)	0 (0)	3 (1)	3 (0.9)
Amateur highest level (%)	4 (14.8)	17 (5.5)	20 (6)
Mixed martial arts (%)	1 (3.7)	2 (0.6)	3 (0.9)
Hockey (%)	0 (0)	27 (8.7)	27 (8)
Professional highest level (%)	0 (0)	9 (2.9)	9 (2.7)
Semi-professional highest level (%)	0 (0)	6 (1.9)	6 (1.8)
College/juniors highest level (%)	0 (0)	1 (0.3)	1 (0.3)
High school/youth highest level (%)	0 (0)	10 (3.2)	10 (3)
Rugby (%)	0 (0)	16 (5.2)	16 (4.8)
Amateur wrestling (%)	4 (15.8)	26 (8.4)	30 (8.9)
Soccer (%)	2 (7.4)	26 (8.4)	28 (8.3)
Professional highest level (%)	0 (0)	0 (0)	0 (0)
College/ semi-professional highest level (%)	0 (0)	4 (1.3)	4 (1.2)
High school/youth highest level (%)	1 (3.7)	20 (6.5)	21 (6.3)
Lacrosse (%)	0 (0)	10 (3.2)	10 (3)
Other (%)	0 (0)	4 (1.3)	4 (1.2)
Military service (%)[b]	6 (22.2)	83 (26.9)	89 (26.5)
With combat (%)	0 (0)	12 (3.9)	12 (3.6)
Physical violence (%)[c]	1 (3.7)	12 (3.9)	13 (3.9)
4 or more concussions (%)	16 (59.3)	257 (83.2)	273 (81.3)
Median concussion count (IQR)	4.5 (14)	30 (91)	25 (92)
Moderate to Severe traumatic brain injuries (TBI) (%)	2 (7.4)	19 (6.1)	21 (6.3)
2 or more moderate to severe TBIs (%)	0 (0)	3 (1)	3 (0.9)
Pathologies			
Chronic traumatic encephalopathy (%)	8 (29.6)	236 (76.4)	244 (72.6)
Alzheimer's disease pathology (%)	1 (3.7)	55 (17.8)	56 (16.7)
Mean CERAD neuritic plaque score (SD)	0.2 (0.5)	0.6 (0.9)	0.6 (0.9)
Mean Braak neurofibrillary tangle stage (SD)	1.1 (2.0)	3.0 (4.0)	2.4 (2.0)
Lewy body disease pathology (%)	3 (11.1)	58 (18.8)	61 (18.2)
Brainstem predominant (%)	2 (7.4)	25 (8.1)	27 (8)
Limbic/ neocortical (%)	1 (3.7)	33 (10.7)	34 (10.1)
Frontotemporal lobar degeneration pathology (%)	2 (7.4)	40 (12.9)	42 (12.5)
Tau pathology (%)	2 (7.4)	20 (6.5)	22 (6.5)
TDP-43 pathology (%)	1 (3.7)	20 (6.5)	21 (6.3)
Cerebrovascular pathology (%)	8 (29.6)	190 (61.5)	198 (58.9)

[a]89 (28.5%) donors played more than 1 contact sport
[b]77 (86.5%) donors served in the military and played contact sports
[c]either in the form of intimate partner violence or child abuse

eTable 3. TES-CTE diagnoses by CTE pathology status: frequencies, validity and reliability; stratified by age 60.

eTable 3A. TES-CTE consensus diagnosis by CTE pathology frequencies in donors age < 60

	CTE Pathological Diagnosis			
TES-CTE Clinical Consensus Diagnosis		Yes	No	Total
	Yes	74 (56.1%)	41 (31.1%)	115 (87.1%)
	No	7 (5.3%)	10 (7.6%)	17 (12.9%)
	Total	81 (61.4%)	51 (38.6%)	132

eTable 3B. Validity and reliability (95% CI) of TES-CTE diagnoses in donors age < 60

	Pre-Consensus	Consensus
Sensitivity	0.86 (0.79, 0.94)	0.91 (0.85, 0.97)
Specificity	0.19 (0.07, 0.31)	0.20 (0.09, 0.31)
Positive likelihood ratio	1.06 (0.56, 2.01)	1.14 (0.98, 1.32)
Negative likelihood ratio	0.73 (0.41, 1.30)	0.44 (0.18, 1.08)
Inter-rater reliability	0.60 (0.47-0.76)	0.97 (0.93-1.00)

eTable 3C. TES-CTE consensus diagnoses by CTE pathology frequencies in donors age ≥ 60.

	CTE Pathological Diagnosis			
TES-CTE Clinical Consensus Diagnosis		Yes	No	Total
	Yes	162 (79.4%)	32 (15.7%)	194 (95.1%)
	No	1 (0.5%)	9 (4.4%)	10 (4.9%)
	Total	163 (79.9%)	42 (20.6%)	204

eTable 3D. Validity and reliability (95% CI) of TES-CTE diagnoses in donors age ≥ 60.

	Pre-Consensus	Consensus
Sensitivity	0.98 (0.95, 1.00)	0.99 (0.98, 1.00)
Specificity	0.23 (0.09, 0.36)	0.22 (0.09, 0.35)
Positive likelihood ratio	1.26 (0.70, 2.29)	1.27 (1.08, 1.50)
Negative likelihood ratio	0.11 (0.04, 0.29)	0.03 (0.00, 0.21)
Inter-rater reliability	0.89 (0.79-0.97)	0.99 (0.96-0.99)

Pre-consensus refers to individual diagnoses made by consensus panel members prior to discussion.
Consensus refers to the group consensus diagnoses after discussion, except for inter-rater reliability for which consensus refers to individual diagnoses made after discussion.
Sensitivity: Among donors *with* a CTE neuropathological diagnosis, the frequency with which a TES-CTE clinical diagnosis *was* made.
Specificity: Among donors *without* a CTE neuropathological diagnosis, the frequency with which a TES-CTE clinical diagnosis *was not* made.
Positive likelihood ratio: Ratio of the frequency with which a TES-CTE clinical diagnosis was made among donors with a CTE neuropathological diagnosis to the frequency with which a TES-CTE clinical diagnosis was made among donors without a CTE neuropathological diagnosis.
Negative likelihood ratio: Ratio of the frequency with which a TES-CTE clinical diagnosis was not made among donors with a CTE neuropathological

diagnosis to the frequency with which a TES-CTE clinical diagnosis was not made among donors without a CTE neuropathological diagnosis.
Inter-rater reliability: A measure of agreement (range: 0-1) among consensus panel members that accounts for varying identity and number of raters

eTable 4. TES-CTE diagnoses by CTE pathology status: different levels of pathology

eTable 4A. TES-CTE consensus diagnosis by CTE stage ≥II frequencies

	CTE stage ≥ II			
TES-CTE Clinical Consensus Diagnosis		Yes	No	Total
	Yes	195 (58.0%)	114 (33.9%)	309 (92.0%)
	No	3 (0.9%)	24 (7.1%)	27 (8.0%)
	Total	197 (58.6%)	138 (41.1%)	336

eTable 4B. Validity (95% CI) of TES-CTE diagnoses for CTE stage ≥II

	Pre-Consensus	Consensus
Sensitivity	0.96 (0.94, 0.99)	0.98 (0.97, 1.00)
Specificity	0.19 (0.12, 0.26)	0.17 (0.11, 0.24)
Positive likelihood ratio	1.20 (0.83, 1.72)	1.19 (0.83, 1.72)
Negative likelihood ratio	0.18 (0.09, 0.38)	0.09 (0.03, 0.27)

eTable 4C. TES-CTE consensus diagnosis by CTE stage ≥III frequencies

	CTE stage ≥ III			
TES-CTE Clinical Consensus Diagnosis		Yes	No	Total
	Yes	152 (45.2%)	157 (46.7%)	309 (92.0%)
	No	0	27 (8.0%)	27 (8.0%)
	Total	152 (45.2%)	184 (54.8%)	336

eTable 4D. Validity (95% CI) of TES-CTE diagnoses for CTE stage ≥III

	Pre-Consensus	Consensus
Sensitivity	0.98 (0.96, 1.00)	1.00 (1.00, 1.00)
Specificity	0.16 (0.11, 0.22)	0.15 (0.10, 0.20)
Positive likelihood ratio	1.17 (0.83, 1.65)	1.17 (0.83, 1.66)
Negative likelihood ratio	0.12 (0.04, 0.38)	0

eTable 4E. TES-CTE consensus diagnosis by CTE stage IV frequencies

	CTE Stage IV Pathological Diagnosis			
TES-CTE Clinical Consensus Diagnosis		Yes	No	Total
	Yes	69 (20.5%)	240 (71.4%)	309 (92.0%)
	No	0	27 (8.0%)	27 (8.0%)
	Total	69 (20.5%)	167 (49.7%)	336

eTable 4F. Validity (95% CI) of TES-CTE diagnoses for CTE stage IV

	Pre-Consensus	Consensus
Sensitivity	0.99 (0.97, 1.01)	1.00 (1.00, 1.00)
Specificity	0.12 (0.08, 0.16)	0.10 (0.06, 0.14)
Positive likelihood ratio	1.13 (0.81, 1.58)	1.11 (0.78, 1.59)
Negative likelihood ratio	0.06 (0.00, 1.01)	0

Pre-consensus refers to individual diagnoses made by consensus panel members prior to discussion.
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Sensitivity: Among donors *with* a CTE neuropathological diagnosis, the frequency with which a TES-CTE clinical diagnosis *was* made.
Specificity: Among donors *without* a CTE neuropathological diagnosis, the frequency with which a TES-CTE clinical diagnosis *was not* made.
Positive likelihood ratio: Ratio of the frequency with which a TES-CTE clinical diagnosis was made among donors with a CTE neuropathological diagnosis to the frequency with which a TES-CTE clinical diagnosis was made among donors without a CTE neuropathological diagnosis.
Negative likelihood ratio: Ratio of the frequency with which a TES-CTE clinical diagnosis was not made among donors with a CTE neuropathological diagnosis to the frequency with which a TES-CTE clinical diagnosis was not made among donors without a CTE neuropathological diagnosis.

eTable 5. Consensus TES subtypes, symptom timeline, individual clinical symptoms, other consensus diagnoses and objective clinical data stratified by CTE pathological status.

	CTE pathology absent (92)	CTE pathology present (244)	Total (336)
TES Diagnoses			
TES (%)	78 (84.8)	239 (98)	317 (94.3)
TES-CTE (%)	73 (79.3)	236 (96.7)	309 (92)
TES-CTE probable (%)	9 (9.8)	37 (15.2)	46 (13.7)
TES-CTE possible (%)	64 (69.6)	199 (81.6)	263 (78.3)
TES-mood/behavior only (%)	25 (27.2)	23 (9.4)	48 (14.3)
TES-cognition only (%)	0	3 (1.2)	3 (0.9)
TES-mixed (%)	19 (20.7)	48 (19.7)	67 (19.9)
TES-dementia (%)	34 (37)	165 (67.6)	199 (59.2)
TES-progressive course (%)	69 (75)	229 (93.9)	298 (88.7)
TES-motor (%)	20 (21.7)	94 (38.5)	114 (33.9)
Symptom timeline			
Behavior/mood only (%)	22 (23.9)	13 (5.3)	35 (10.4)
Behavior/mood preceding cognition (%)	36 (39.1)	97 (39.8)	133 (39.6)
Behavior/mood concurrent with cognition (%)	9 (9.8)	39 (16)	48 (14.3)
Cognition preceding behavior/mood (%)	8 (8.7)	78 (32)	86 (25.6)
Cognition only (%)	2 (2.2)	13 (5.3)	15 (4.5)
Delay in symptom onset after head trauma (%)	36 (39.1)	169 (69.3)	205 (61)
Mood/behavior symptoms (%)	89 (96.7)	239 (98.0)	328 (97.6)
Depressive symptoms (%)	65 (70.7)	163 (66.8)	228 (67.9)
Apathy (%)	50 (54.3)	130 (53.3)	180 (53.6)
Anxiety (%)	53 (57.6)	136 (55.7)	189 (56.3)
Irritability (%)	78 (84.8)	190 (77.9)	268 (79.8)
Mania (%)	7 (7.6)	14 (5.7)	21 (6.3)
Explosivity (%)	56 (60.9)	124 (50.8)	180 (53.6)
Social inappropriateness (%)	32 (34.8)	86 (35.2)	118 (35.1)
Psychosis (%)	32 (34.8)	63 (25.8)	95 (28.3)
Impulsivity (%)	75 (81.5)	192 (78.7)	267 (79.5)
Hopelessness (%)	45 (48.9)	124 (50.8)	169 (50.3)
Paranoia (%)	32 (34.8)	86 (35.2)	118 (35.1)
Suicidality (ideation, attempts or completions) (%)	31 (33.7)	72 (29.5)	103 (30.7)
Visual hallucinations (%)	19 (20.7)	55 (22.5)	74 (22)
Physical violence (%)	59 (64.1)	143 (58.6)	202 (60.1)
Verbal violence (%)	62 (67.4)	157 (64.3)	219 (65.2)
Cognitive symptoms (%)	67 (72.8)	220 (90.2)	287 (85.4)
Memory (%)	58 (63)	206 (84.4)	264 (78.6)
Judgment and problem-solving (%)	53 (57.6)	181 (74.2)	234 (69.6)
Language (%)	33 (35.9)	127 (52)	160 (47.6)
Visuospatial function (%)	27 (29.3)	104 (42.6)	131 (39)
Attention/concentration (%)	58 (63.0)	185 (75.8)	243 (72.3)
Fluctuating cognition (%)	10 (10.9)	40 (16.4)	50 (14.9)
Motor symptoms (%)	88 (95.7)	236 (96.7)	324 (96.4)
Gait instability (%)	41 (44.6)	130 (53.3)	171 (50.9)
Slowness (%)	31 (33.7)	113 (46.3)	144 (42.9)
Coordination difficulties (%)	26 (28.3)	98 (40.2)	124 (36.9)
Falls (%)	31 (33.7)	31 (12.7)	132 (39.3)
Tremor (%)	26 (28.3)	81 (33.2)	107 (31.8)
Dysphagia (%)	17 (18.5)	50 (20.5)	67 (19.9)
Dysarthria (%)	26 (28.3)	43 (17.6)	69 (20.5)

	CTE pathology absent (92)	CTE pathology present (244)	Total (336)
Sleep disturbance (%)	23 (25.0)	63 (25.8)	86 (25.6)
Obstructive sleep apnea (diagnosis in life) (%)	23 (25)	61 (25)	84 (25)
REM sleep behavior disorder (diagnosis in life) (%)	1 (1.1)	6 (2.5)	7 (2.1)
Substance use disorder (%)	45 (48.9)	94 (38.5)	139 (41.4)
Alcohol (%)	14 (15.2)	39 (16)	53 (15.8)
Marijuana (%)	30 (32.6)	53 (21.7)	83 (24.7)
Other (%)	41 (44.6)	77 (31.6)	50 (14.9)
Other			
Headache (%)	56 (60.9)	121 (49.6)	177 (52.7)
Other diagnoses at consensus meeting			
Post-concussive syndrome (%)	25 (27.2)	25 (10.2)	50 (14.9)
Behavioral variant frontotemporal dementia (%)	5 (5.4)	3 (1.2)	8 (2.4)
Primary progressive aphasia (%)	2 (2.2)	0 (0)	2 (0.6)
Alzheimer's disease (%)	17 (18.5)	72 (29.5)	89 (26.5)
Amyotrophic lateral sclerosis (%)	3 (3.3)	8 (3.3)	11 (3.3)
Dementia with Lewy bodies (%)	3 (3.3)	21 (8.6)	24 (7.1)
Parkinson's disease dementia[a] (%)	2 (2.2)	1 (0.4)	3 (0.9)
Other neurodegenerative disorder (%)	2 (2.2)	1 (0.4)	3 (0.9)
Cerebrovascular disease (stroke, vascular dementia, moderate to severe microvascular burden; note imaging confirmation was needed for these diagnoses) (%)	12 (13)	44 (18)	56 (16.7)
Depression (did not need to meet DSM major depressive disorder criteria) (%)	25 (27.2)	52 (21.3)	77 (22.9)
Anxiety (did not need to meet DSM criteria) (%)	6 (6.5)	9 (3.7)	15 (4.5)
Bipolar disorder (%)	9 (9.8)	10 (4.1)	19 (5.7)
Post-traumatic stress disorder (%)	10 (10.9)	13 (5.3)	23 (6.8)
Intermittent explosive disorder (%)	4 (4.3)	1 (0.4)	5 (1.5)
Other major psychiatric disorder (%)	8 (8.7)	5 (2)	13 (3.9)
Substance use disorder (%)	37 (40.2)	105 (43)	142 (42.3)
Epilepsy (%)	1 (1.1)	7 (2.9)	8 (2.4)
CNS neoplasm (%)	3 (3.3)	6 (2.5)	9 (2.7)
Other medical illness (%)	35 (38)	72 (29.5)	107 (31.8)
Iatrogenic impairment (%)	11 (12)	30 (12.3)	41 (12.2)
Objective clinical data available			
Neuropsychological evaluation (scores or report) (%)	18 (19.6)	45 (18.4)	63 (18.8)
Structural brain imaging (report or actual image) (%)	40 (43.5)	111 (45.5)	151 (44.9)
Amyloid and/or tau biomarkers (PET or CSF) (%)	2 (2.2)	5 (2)	7 (2.1)

[a]All donors diagnosed with Parkinson's disease at the consensus conference were also diagnosed with Parkinson's disease dementia.

eTable 6. Association of TES criteria clinical components with presence of CTE neuropathology

Clinical component	Odds Ratio (95% CI)	P-value
Cognitive symptoms	3.6 (1.77, 7.34)	< 0.001
Mood/ behavior symptoms	0.7 (0.32, 1.50)	0.40
Motor symptoms	1.4 (0.84, 2.30)	0.28
Features present ≥ 12 months	3.5 (1.70, 7.21)	0.03

Separate logistic regression models were run for each symptom due to multicollinearity. The outcome for all models was the presence of CTE neuropathology. Models were adjusted for age≥ 60 and race.

eTable 7. TES-CTE diagnoses by CTE pathology status after re-categorization requiring cognitive symptoms to be present to meet TES-CTE criteria

Table S7A. TES-CTE consensus diagnosis by CTE pathology frequencies after recategorization

	CTE Pathological Diagnosis			
TES-CTE Clinical Consensus Diagnosis		Yes	No	Total
	Yes	220 (65.5%)	48 (14.3%)	268 (79.8%)
	No	24 (7.1%)	44 (13.1%)	68 (20.2%)
	Total	244 (72.6%)	92 (27.4%)	336

Table S7B. Validity (95% CI) of TES-CTE diagnoses in donors after recategorization

	Pre-Consensus	Consensus
Sensitivity	0.88 (0.84, 0.92)	0.90 (0.86, 0.94)
Specificity	0.42 (0.31, 0.53)	0.48 (0.38, 0.58)
Positive likelihood ratio	1.52 (1.17, 1.98)	1.73 (1.41, 2.11)
Negative likelihood ratio	0.29 (0.19, 0.41)	0.21 (0.13, 0.32)

Pre-consensus refers to individual diagnoses made by consensus panel members prior to discussion.
Consensus refers to the group consensus diagnoses after discussion.
Sensitivity: Among donors *with* a CTE neuropathological diagnosis, the frequency with which a TES-CTE clinical diagnosis *was* made.
Specificity: Among donors *without* a CTE neuropathological diagnosis, the frequency with which a TES-CTE clinical diagnosis *was not* made.
Positive likelihood ratio: Ratio of the frequency with which a TES-CTE clinical diagnosis was made among donors with a CTE neuropathological diagnosis to the frequency with which a TES-CTE clinical diagnosis was made among donors without a CTE neuropathological diagnosis.
Negative likelihood ratio: Ratio of the frequency with which a TES-CTE clinical diagnosis was not made among donors with a CTE neuropathological diagnosis to the frequency with which a TES-CTE clinical diagnosis was not made among donors without a CTE neuropathological diagnosis.

eTable 8. Validity (95% CI) of consensus clinical Alzheimer's dementia and Parkinson's disease dementia/ dementia with Lewy bodies consensus diagnoses using neuropathology as the gold standard.

	Alzheimer's disease (AD)	Parkinson's disease dementia (PDD)/ dementia with Lewy bodies (DLB)
Sensitivity	0.70 (0.58, 0.82)	0.41 (0.25, 0.58)
Specificity	0.82 (0.78, 0.87)	0.95 (0.93, 0.97)
Positive likelihood ratio	3.89 (2.87, 5.29)	8.29 (4.39, 15.66)
Negative likelihood ratio	0.37 (0.25, 0.55)	0.62 (0.47, 0.82)

AD dementia diagnoses were made using modified 2011 NIA-AA Criteria[1]. DLB diagnoses were made using modified 2005 McKeith Criteria[2]. PDD diagnoses were made using modified 2005 MDS recommendations[3]. For AD and DLB, if formal neuropsychological testing was not conducted in life or was not performed close to death, the presence of cognitive symptoms together with clinician judgement was considered sufficient. For DLB and PDD, if a formal neurological exam had not been conducted in life or was not performed close to death, informant reported parkinsonian symptoms together with clinician judgement was considered sufficient. PDD and DLB were combined due to small sample size alone.
Accuracy: Among all donors, the frequency with which the TES-CTE clinical diagnosis matched the CTE neuropathological diagnosis.
Sensitivity: Among donors *with* a CTE neuropathological diagnosis, the frequency with which a TES-CTE clinical diagnosis *was* made.
Specificity: Among donors *without* a CTE neuropathological diagnosis, the frequency with which a TES-CTE clinical diagnosis *was not* made.
Positive likelihood ratio: Ratio of the frequency with which a TES-CTE clinical diagnosis was made among donors with a CTE neuropathological diagnosis to the frequency with which a TES-CTE clinical diagnosis was made among donors without a CTE neuropathological diagnosis.
Negative likelihood ratio: Ratio of the frequency with which a TES-CTE clinical diagnosis was not made among donors with a CTE neuropathological diagnosis to the frequency with which a TES-CTE clinical diagnosis was not made among donors without a CTE neuropathological diagnosis.

eTable 9. Association of comorbid neuropathology with accuracy of TES-CTE consensus diagnosis stratified by age 60

eTable 9A. Age ≥60 years

Comorbid Neuropathology	Odds Ratio (95% CI)	P-value
Alzheimer's disease	0.27 (0.12, 0.59)	0.002
Frontotemporal lobar degeneration	0.56 (0.23, 1.38)	0.24
Lewy body disease (limbic or neocortical)	0.89 (0.35, 2.28)	0.82
Cerebrovascular disease	0.98 (0.32, 3.00)	0.97

eTable 9B. Age <60 years

Comorbid Neuropathology	Odds Ratio (95% CI)	P-value
Alzheimer's disease	1.37 (0.12, 0.59)	0.81
Frontotemporal lobar degeneration	0.76 (0.23, 1.38)	0.79
Lewy body disease (limbic or neocortical)	0.67 (0.35, 2.28)	0.78
Cerebrovascular disease	2.04 (0.32, 3.00)	0.18

A diagnosis was considered accurate if the TES-CTE clinical diagnosis matched the CTE neuropathological diagnosis. A single binary logistic regression model was run that included all four comorbid pathologies as predictors and accuracy as the outcome. The model was also adjusted for race.

eTable 10. TES-CTE diagnoses by CTE pathology status after re-categorization to exclude donors with AD pathology from a TES-CTE diagnosis

Table S10A. TES-CTE consensus diagnosis by CTE pathology frequencies after recategorization

		CTE Pathological Diagnosis		
TES-CTE Clinical Consensus Diagnosis		Yes	No	Total
	Yes	199 (59.2%)	55 (16.4%)	254 (75.6%)
	No	45 (13.4%)	37 (11.0%)	82 (24.4%)
	Total	244 (72.6%)	92 (27.4%)	336

Table S10B. Validity (95% CI) of TES-CTE diagnoses in donors after recategorization

	Pre-Consensus	Consensus
Sensitivity	0.78 (0.73, 0.84)	0.82 (0.77, 0.86)
Specificity	0.39 (0.28, 0.50)	0.40 (0.30, 0.50)
Positive likelihood ratio	1.29 (0.97, 1.71)	1.36 (1.06, 1.76)
Negative likelihood ratio	0.55 (0.41, 0.75)	0.46 (0.34, 0.63)

Pre-consensus refers to individual diagnoses made by consensus panel members prior to discussion.
Consensus refers to the group consensus diagnoses after discussion.
Sensitivity: Among donors *with* a CTE neuropathological diagnosis, the frequency with which a TES-CTE clinical diagnosis *was* made.
Specificity: Among donors *without* a CTE neuropathological diagnosis, the frequency with which a TES-CTE clinical diagnosis *was not* made.
Positive likelihood ratio: Ratio of the frequency with which a TES-CTE clinical diagnosis was made among donors with a CTE neuropathological diagnosis to the frequency with which a TES-CTE clinical diagnosis was made among donors without a CTE neuropathological diagnosis.
Negative likelihood ratio: Ratio of the frequency with which a TES-CTE clinical diagnosis was not made among donors with a CTE neuropathological diagnosis to the frequency with which a TES-CTE clinical diagnosis was not made among donors without a CTE neuropathological diagnosis.

eTable 11. TES-CTE diagnoses by CTE pathology status after re-categorization requiring cognitive symptoms and excluding AD pathology from a TES-CTE diagnosis

Table S11A. TES-CTE consensus diagnosis by CTE pathology frequencies after recategorization

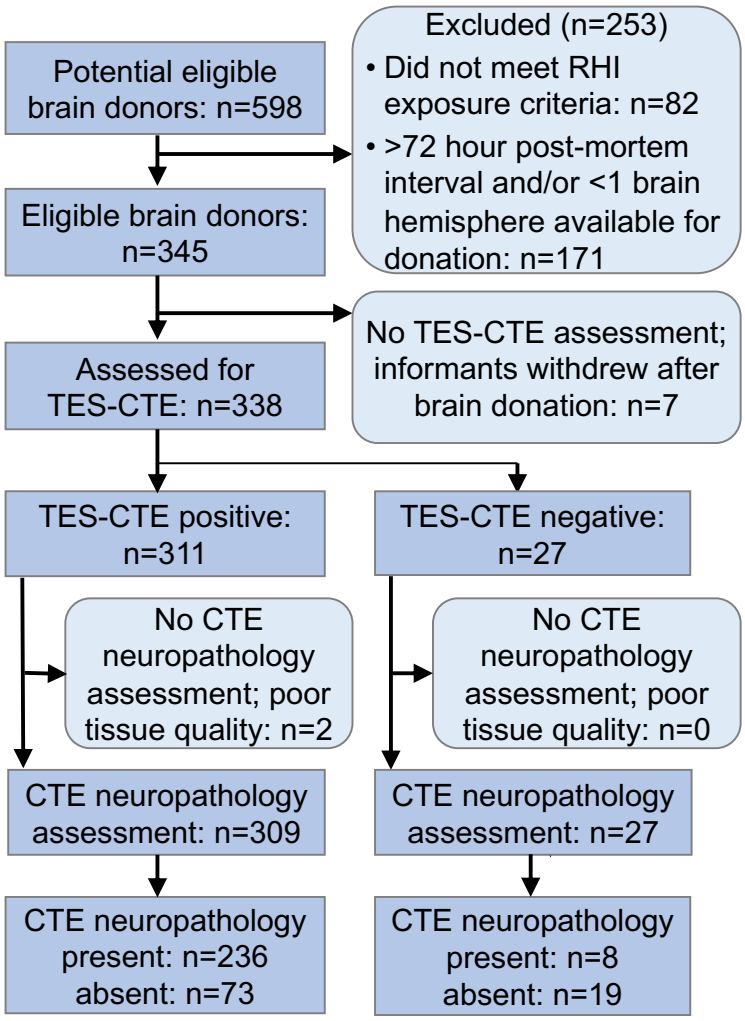
	CTE Pathological Diagnosis			
TES-CTE Clinical Consensus Diagnosis		Yes	No	Total
	Yes	183 (54.5%)	36 (10.7%)	219 (65.2%)
	No	61 (18.2%)	56 (16.7%)	117 (34.8%)
	Total	244 (72.6%)	92 (27.4%)	336

Table S11B. Validity (95% CI) of TES-CTE diagnoses in donors after recategorization

	Pre-Consensus	Consensus
Sensitivity	0.73 (0.67, 0.79)	0.75 (0.70, 0.80)
Specificity	0.56 (0.45, 0.67)	0.61 (0.51, 0.71)
Positive likelihood ratio	1.66 (1.35, 2.05)	1.92 (1.60, 2.29)
Negative likelihood ratio	0.48 (0.35, 0.67)	0.41 (0.29, 0.57)

Pre-consensus refers to individual diagnoses made by consensus panel members prior to discussion.
Consensus refers to the group consensus diagnoses after discussion.
Sensitivity: Among donors *with* a CTE neuropathological diagnosis, the frequency with which a TES-CTE clinical diagnosis *was* made.
Specificity: Among donors *without* a CTE neuropathological diagnosis, the frequency with which a TES-CTE clinical diagnosis *was not* made.
Positive likelihood ratio: Ratio of the frequency with which a TES-CTE clinical diagnosis was made among donors with a CTE neuropathological diagnosis to the frequency with which a TES-CTE clinical diagnosis was made among donors without a CTE neuropathological diagnosis.
Negative likelihood ratio: Ratio of the frequency with which a TES-CTE clinical diagnosis was not made among donors with a CTE neuropathological diagnosis to the frequency with which a TES-CTE clinical diagnosis was not made among donors without a CTE neuropathological diagnosis.

eFigure 1. Standards for the Reporting of Diagnostic Accuracy Studies (STARD) flow diagram



Abbreviations: RHI: repetitive head impact; TES-CTE: Traumatic Encephalopathy Syndrome with possible or probable chronic traumatic encephalopathy;

Supplemental References

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