

Supplemental Online Content

McCrea MA, Giacino JT, Barber J, et al; the TRACK-TBI Investigators. Functional outcomes over the first year after moderate to severe traumatic brain injury in the prospective, longitudinal TRACK-TBI study. *JAMA Neurol*. Published July 6, 2021. doi:10.1001/jamaneurol.2021.2043

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This supplemental material has been provided by the authors to give readers additional information about their work.

eTable 1. TRACK-TBI INCLUSION/EXCLUSION CRITERIA

Criterion	Data Source	Comments
Inclusion Criteria		
1. Age 0-100	Chart	
2. Documented/verified TBI (ACRM Criteria)	Chart, Interview	
3. Injury occurred < 24 hours ago	Chart, Interview	
4. Acute brain CT for clinical care	Chart	Subject must have brain CT scan
5. Visual acuity/hearing adequate for testing	Chart, Interview	
6. Fluency in English or Spanish	Chart, Interview	Based on Test battery or personnel availability
7. Ability to provide informed consent	Interview	<input type="checkbox"/> Patient <input type="checkbox"/> Surrogate <input type="checkbox"/> Waiver
Exclusion Criteria		
1. Significant polytrauma that would interfere with follow-up and outcome assessment	Chart	Significant body trauma may confound TBI outcomes testing.
2. Prisoners or patients in custody	Chart, Interview	
3. Pregnancy in female subjects	Chart, Interview	
4. Patients on psychiatric hold (eg 5150, 5250)	Chart	
5. Major debilitating baseline mental health disorders (eg schizophrenia or bipolar disorder) that would interfere with follow-up and the validity of outcome assessment	Chart, Interview	Debilitating psychiatric disorders can significantly impact the reliability of follow up and/or pose difficulties in attributing to index TBI.
6. Major debilitating neurological disease (eg stroke, CVA, dementia, tumor) impairing baseline awareness, cognition, or validity of follow-up and outcome assessment	Chart, Interview	Documented debilitating baseline cognitive impairment will confound outcome assessment in addition to not being fully consent able.
7. Significant history of pre-existing conditions that would interfere with follow-up and outcome assessment (eg substance abuse, alcoholism, HIV/AIDS, major transmittable diseases that may interfere with consent, end-stage cancers, learning disabilities, developmental disorders)	Chart, Interview	
8. Contraindications to MRI (for CA+MR/CA+MRI-HDFT cohort)	MRI Screening	
9. Low likelihood of follow-up (eg participant or family indicating low interest, residence in another state or country, homelessness or lack of reliable contacts)	Interview	
10. Current participant in an interventional trial (eg drug, device, behavioral)	Chart, Interview	Exception to co-enrollment exclusion is made for sites participating in Resuscitation Outcomes Consortium Prehospital Tranexamic Acid for TBI Study.
11. Penetrating TBI	Chart	
12. Spinal cord injury with ASIA score of C or worse	Chart	

eTable 2. Results of mixed model analysis on Glasgow Outcome Scale Extended (GOSE) score.

Effect ¹	Linear Analysis			Ranked Analysis		
	B ²	95% CI	p	B ³	95% CI	p
GOSE Change			<.001			<.001
3mo - 2wk	0.96	(0.82, 1.11)	<.001	11.5	(10.0, 13.0)	<.001
6mo - 2wk	1.35	(1.21, 1.50)	<.001	15.4	(13.9, 17.0)	<.001
12mo - 2wk	1.55	(1.41, 1.70)	<.001	17.0	(15.5, 18.6)	<.001
6mo - 3mo	0.39	(0.25, 0.53)	<.001	3.9	(2.4, 5.5)	<.001
12mo - 3mo	0.59	(0.44, 0.73)	<.001	5.5	(4.0, 7.1)	<.001
12mo - 6mo	0.20	(0.05, 0.34)	.007	1.6	(0.0, 3.2)	.043
Moderate-Severe	1.11	(0.70, 1.53)	<.001	13.2	(8.2, 18.1)	<.001

To formally examine change over time on the GOSE, we fit linear mixed models on the score, clustering on participant and site and considering time as categorical. No group by time interactions were found (all $p > .15$) so only results from the main effect model are presented. We also fit the models based on ranked GOSE scores for the entire sample, given that the GOSE is not an interval measure.

Mixed-effects regression clustering on subject and site (LRT $p < .001$)

1 Main-effects model only; an interaction model was also fit, but none of the interactions were statistically significant ($p > .15$)

2 B represents the difference in mean GOSE (1-8) from linear regression

3 B represents the difference in mean GOSE percentile (0-100) from rank regression

eTable 3. Glasgow Outcome Scale Extended (GOSE) frequencies at 3, 6, and 12 months for Severe TBI and Moderate TBI participants in vegetative state at 2 weeks post-injury

	2 Weeks		3 Months		6 Months		12 Months	
	Severe (n=68)	Moderate (n=11)	Severe (n=60)	Moderate (n=9)	Severe (n=57)	Moderate (n=11)	Severe (n=56)	Moderate (n=10)
Vegetative State & Death								
Vegetative state	68 (100%)	11 (100%)	9 (15%)	0 (0%)	3 (5%)	0 (0%)	0 (0%)	0 (0%)
Died			9 (15%)	3 (33%)	11 (19%)	3 (27%)	14 (25%)	3 (30%)
Independence in the home								
No assistance			11 (18%)	1 (11%)	13 (23%)	2 (18%)	17 (30%)	3 (30%)
Infrequent assistance			0 (0%)	0 (0%)	3 (5%)	0 (0%)	1 (2%)	0 (0%)
Frequent assistance			31 (52%)	5 (56%)	27 (47%)	6 (55%)	24 (43%)	4 (40%)
Independence in shopping								
No assistance			8 (13%)	1 (11%)	14 (25%)	2 (18%)	18 (32%)	3 (30%)
Assistance			34 (57%)	5 (56%)	29 (51%)	6 (55%)	24 (43%)	4 (40%)
Independence in travelling								
No assistance			9 (15%)	1 (11%)	13 (23%)	2 (18%)	15 (27%)	3 (30%)
Assistance			33 (55%)	5 (56%)	30 (53%)	6 (55%)	27 (48%)	4 (40%)
Work								
No deficit			1 (2%)	0 (0%)	3 (6%)	2 (18%)	4 (8%)	2 (20%)
Reduced capacity			3 (5%)	1 (11%)	4 (8%)	0 (0%)	4 (8%)	0 (0%)
Limited/unable to work			38 (69%)	5 (56%)	34 (67%)	6 (55%)	32 (64%)	5 (50%)
Social/leisure functioning								
No deficit			3 (5%)	0 (0%)	8 (14%)	2 (18%)	8 (14%)	2 (20%)
A bit less			1 (2%)	0 (0%)	5 (9%)	0 (0%)	2 (4%)	0 (0%)
Much less			9 (15%)	1 (11%)	6 (11%)	0 (0%)	10 (18%)	1 (10%)
Unable			29 (48%)	5 (56%)	24 (42%)	6 (55%)	22 (39%)	4 (40%)

	2 Weeks		3 Months		6 Months		12 Months	
	Severe (n=68)	Moderate (n=11)	Severe (n=60)	Moderate (n=9)	Severe (n=57)	Moderate (n=11)	Severe (n=56)	Moderate (n=10)
Psychological/ interpersonal problems								
No disruption			30 (50%)	3 (33%)	23 (40%)	4 (36%)	24 (43%)	3 (30%)
Occasional			3 (5%)	0 (0%)	5 (9%)	0 (0%)	2 (4%)	1 (10%)
Frequent			4 (7%)	1 (11%)	6 (11%)	0 (0%)	7 (13%)	1 (10%)
Constant			5 (8%)	2 (22%)	9 (16%)	4 (36%)	9 (16%)	2 (20%)
Other disabling symptoms								
No impact			6 (10%)	2 (22%)	12 (21%)	3 (27%)	10 (18%)	1 (10%)
Some impact			36 (60%)	4 (44%)	31 (54%)	5 (45%)	32 (57%)	6 (60%)

Percentages within each domain sum to 100% after adding percent in Vegetative State and Died categories for the group at that time point(column), with the exception of the 'work' domain which excludes pre-injury non-workers.

eTable 4. Disability Rating Scale (DRS) frequencies at 3, 6, and 12 months for Severe TBI and Moderate TBI participants in vegetative state at 2 weeks post-injury.

	2 Weeks		3 Months		6 Months		12 Months	
	Severe (n=68)	Moderate (n=11)	Severe (n=58)	Moderate (n=10)	Severe (n=55)	Moderate (n=11)	Severe (n=56)	Moderate (n=10)
Vegetative State & Death								
Vegetative state	68 (100%)	11 (100%)	9 (16%)	0 (0%)	3 (5%)	0 (0%)	0 (0%)	0 (0%)
Died			9 (16%)	3 (30%)	11 (20%)	3 (27%)	14 (25%)	3 (30%)
DRS #2 Communication								
Oriented			11 (19%)	2 (20%)	11 (20%)	2 (18%)	14 (25%)	3 (30%)
Confused			23 (40%)	5 (50%)	27 (49%)	6 (55%)	23 (41%)	3 (30%)
Inappropriate			6 (10%)	0 (0%)	3 (5%)	0 (0%)	5 (9%)	1 (10%)
DRS #4 Feeding								
Complete			24 (41%)	3 (30%)	26 (47%)	4 (36%)	27 (49%)	5 (50%)
Partial			4 (7%)	1 (10%)	3 (5%)	3 (27%)	2 (4%)	1 (10%)
Minimal			5 (9%)	1 (10%)	5 (9%)	1 (9%)	5 (9%)	1 (10%)
None			7 (12%)	2 (20%)	7 (13%)	0 (0%)	7 (13%)	0 (0%)
DRS #5 Toileting								
Complete			18 (31%)	3 (30%)	25 (45%)	5 (45%)	25 (45%)	5 (50%)
Partial			5 (9%)	1 (10%)	2 (4%)	1 (9%)	2 (4%)	1 (10%)
Minimal			5 (9%)	1 (10%)	3 (5%)	0 (0%)	3 (5%)	1 (10%)
None			12 (21%)	2 (20%)	11 (20%)	2 (18%)	11 (20%)	0 (0%)
DRS #6 Grooming								
Complete			18 (31%)	3 (30%)	22 (40%)	3 (27%)	23 (42%)	5 (50%)
Partial			3 (5%)	1 (10%)	3 (5%)	3 (27%)	4 (7%)	0 (0%)
Minimal			9 (16%)	1 (10%)	7 (13%)	1 (9%)	5 (9%)	2 (20%)
None			10 (17%)	2 (20%)	9 (16%)	1 (9%)	9 (16%)	0 (0%)
DRS #7 Level of Functioning								
Completely independent			4 (7%)	0 (0%)	6 (11%)	2 (18%)	7 (13%)	2 (20%)

	2 Weeks		3 Months		6 Months		12 Months	
	Severe (n=68)	Moderate (n=11)	Severe (n=58)	Moderate (n=10)	Severe (n=55)	Moderate (n=11)	Severe (n=56)	Moderate (n=10)
Independent in special environment			1 (2%)	0 (0%)	0 (0%)	0 (0%)	2 (4%)	0 (0%)
Mildly dependent			10 (17%)	2 (20%)	8 (15%)	0 (0%)	8 (15%)	2 (20%)
Moderately dependent			3 (5%)	0 (0%)	6 (11%)	2 (18%)	4 (7%)	1 (10%)
Markedly dependent			1 (2%)	0 (0%)	2 (4%)	1 (9%)	6 (11%)	1 (10%)
Totally dependent			21 (36%)	5 (50%)	19 (35%)	3 (27%)	14 (25%)	1 (10%)
DRS #8 Employability								
Not restricted			4 (7%)	2 (20%)	8 (15%)	2 (18%)	10 (18%)	2 (20%)
Selected jobs			7 (12%)	1 (10%)	11 (20%)	1 (9%)	6 (11%)	2 (20%)
Sheltered workshop			8 (14%)	0 (0%)	5 (9%)	3 (27%)	8 (15%)	1 (10%)
Unemployable			20 (34%)	4 (40%)	17 (31%)	2 (18%)	17 (31%)	2 (20%)

Percentages within each domain sum to 100% after adding percent in Vegetative State and Died categories for the group at that time point (column).

eTable 5. Cumulative frequencies and risk ratios within each Glasgow Outcome Scale Extended (GOSE) Domain for Severe TBI and Moderate TBI groups at 2 weeks, 3, 6, and 12 months post-injury

GOSE Domain Severity	2 Weeks			3 Months			6 Months			12 Months		
	Severe (n=290)	Moderate (n=93)	Risk Ratio	Severe (n=274)	Moderate (n=84)	Risk Ratio	Severe (n=282)	Moderate (n=75)	Risk Ratio	Severe (n=271)	Moderate (n=72)	Risk Ratio
Vegetative State and Death												
Vegetative state or died	128 (44%) [38, 50]	15 (16%) [10, 24]	2.74 (1.69, 4.43)	83 (30%) [25, 35]	9 (11%) [5, 18]	2.79 (1.46, 5.30)	82 (29%) [24, 35]	9 (12%) [6, 21]	2.42 (1.28, 4.59)	84 (31%) [26, 37]	9 (13%) [6, 21]	2.48 (1.31, 4.69)
Died	60 (21%) [16, 26]	4 (4%) [1, 10]	4.81 (1.80, 12.9)	73 (26%) [21, 32]	9 (11%) [5, 18]	2.45 (1.28, 4.69)	78 (28%) [23, 33]	9 (12%) [6, 21]	2.30 (1.21, 4.38)	83 (31%) [25, 36]	9 (13%) [6, 21]	2.45 (1.30, 4.63)
Independence in the home												
Infrequent assistance (or worse)	259 (89%) [85, 93]	57 (61%) [51, 71]	1.46 (1.23, 1.72)	163 (59%) [53, 64]	29 (35%) [25, 45]	1.70 (1.24, 2.32)	143 (51%) [45, 57]	24 (32%) [22, 43]	1.58 (1.12, 2.25)	134 (49%) [44, 55]	22 (31%) [21, 42]	1.62 (1.12, 2.34)
Frequent assistance (or worse)	254 (88%) [83, 91]	55 (59%) [49, 69]	1.48 (1.24, 1.76)	154 (55%) [50, 61]	26 (31%) [22, 41]	1.79 (1.28, 2.51)	137 (49%) [43, 54]	22 (29%) [20, 40]	1.66 (1.14, 2.40)	129 (48%) [42, 54]	18 (25%) [16, 36]	1.90 (1.25, 2.90)
Independence in shopping												
Assistance (or worse)	256 (89%) [85, 92]	57 (61%) [51, 71]	1.45 (1.22, 1.71)	163 (59%) [53, 64]	30 (36%) [26, 46]	1.64 (1.21, 2.22)	142 (50%) [45, 56]	27 (36%) [26, 47]	1.40 (1.01, 1.93)	136 (50%) [44, 56]	25 (35%) [24, 46]	1.45 (1.03, 2.03)
Independence in travelling												
Assistance (or worse)	256 (89%) [85, 92]	59 (63%) [53, 73]	1.40 (1.19, 1.64)	168 (60%) [55, 66]	30 (36%) [26, 46]	1.69 (1.25, 2.29)	143 (51%) [45, 57]	28 (37%) [27, 49]	1.36 (0.99, 1.86)	138 (51%) [45, 57]	26 (36%) [26, 48]	1.41 (1.02, 1.96)
Work (among pre-injury workers)												
Reduced capacity (or worse)	208 (99%)	71 (90%) [82, 95]	1.10	186 (88%)	51 (71%) [60, 80]	1.24	155 (73%)	39 (63%) [51, 74]	1.16	136 (66%)	31 (51%) [38, 63]	1.30

GOSE Domain Severity	2 Weeks			3 Months			6 Months			12 Months		
	Severe (n=290)	Moderate (n=93)	Risk Ratio	Severe (n=274)	Moderate (n=84)	Risk Ratio	Severe (n=282)	Moderate (n=75)	Risk Ratio	Severe (n=271)	Moderate (n=72)	Risk Ratio
	[97, 100]		(1.02, 1.19)	[83, 92]		(1.06, 1.45)	[67, 79]		(0.94, 1.43)	[59, 72]		(1.00, 1.69)
Limited/unable to work (<i>or worse</i>)	205 (98%) [95, 99]	67 (85%) [76, 92]	1.15 (1.05, 1.27)	161 (76%) [70, 82]	39 (54%) [43, 65]	1.41 (1.12, 1.76)	129 (61%) [54, 67]	27 (44%) [32, 56]	1.40 (1.03, 1.89)	116 (56%) [49, 63]	24 (39%) [28, 52]	1.43 (1.02, 2.00)
Social/leisure functioning												
A bit less (<i>or worse</i>)	278 (96%) [94, 98]	76 (83%) [74, 89]	1.16 (1.06, 1.28)	222 (80%) [75, 84]	50 (60%) [49, 70]	1.34 (1.11, 1.62)	190 (67%) [62, 73]	41 (55%) [43, 66]	1.23 (0.99, 1.54)	173 (64%) [58, 69]	38 (53%) [41, 64]	1.21 (0.96, 1.53)
Much less (<i>or worse</i>)	269 (93%) [90, 96]	69 (75%) [66, 83]	1.24 (1.10, 1.40)	199 (72%) [66, 77]	40 (48%) [37, 58]	1.50 (1.19, 1.90)	166 (59%) [53, 65]	35 (47%) [36, 58]	1.26 (0.97, 1.64)	145 (54%) [48, 59]	29 (40%) [29, 52]	1.33 (0.98, 1.80)
Unable (<i>or worse</i>)	252 (87%) [83, 91]	58 (63%) [53, 72]	1.38 (1.18, 1.63)	148 (53%) [47, 59]	25 (30%) [21, 40]	1.79 (1.26, 2.53)	128 (45%) [40, 51]	20 (27%) [18, 37]	1.70 (1.14, 2.53)	118 (44%) [38, 49]	16 (22%) [14, 33]	1.96 (1.25, 3.08)
Psychological/ interpersonal problems												
Occasional (<i>or worse</i>)	188 (65%) [59, 70]	54 (59%) [48, 68]	1.11 (0.92, 1.34)	156 (56%) [50, 62]	37 (44%) [34, 55]	1.27 (0.98, 1.66)	168 (60%) [54, 65]	41 (55%) [43, 66]	1.09 (0.87, 1.37)	162 (60%) [54, 66]	37 (51%) [40, 63]	1.16 (0.91, 1.49)
Frequent (<i>or worse</i>)	182 (63%) [57, 68]	50 (54%) [44, 64]	1.16 (0.94, 1.43)	140 (50%) [44, 56]	32 (38%) [28, 49]	1.32 (0.98, 1.78)	143 (51%) [45, 57]	35 (47%) [36, 58]	1.09 (0.83, 1.42)	149 (55%) [49, 61]	30 (42%) [31, 53]	1.32 (0.98, 1.77)
Constant (<i>or worse</i>)	166 (57%) [52, 63]	36 (39%) [30, 49]	1.47 (1.12, 1.93)	103 (37%) [32, 43]	19 (23%) [15, 32]	1.64 (1.07, 2.50)	103 (37%) [31, 42]	17 (23%) [14, 33]	1.61 (1.03, 2.52)	106 (39%) [33, 45]	15 (21%) [13, 31]	1.88 (1.17, 3.02)
Other disabling symptoms												
Some impact (<i>or worse</i>)	251 (87%) [83, 90]	81 (87%) [79, 93]	1.00 (0.91, 1.09)	229 (82%) [78, 87]	69 (83%) [74, 90]	0.99 (0.89, 1.11)	230 (82%) [77, 86]	60 (80%) [70, 88]	1.02 (0.90, 1.16)	218 (80%) [75, 85]	54 (75%) [64, 84]	1.07 (0.93, 1.24)

"Severe" and "Moderate" columns report the n and percent of cases with a severity at or worse than the category label. Risk ratios were calculated as the percent with disability of the indicated level or worse in the Severe TBI group divided by the corresponding percent in the Moderate TBI group. For example, for reduced work capacity, the percentage includes those with reduced work capacity, limited/unable to work, vegetative state, or dead. The 95% confidence intervals on risk ratios were estimated based on the near-normal distribution of the log of the risk ratio.³⁶ Statistical significance determined by Fisher's exact tests. Bold cells indicate statistical significance ($p < .05$) following post-hoc adjustment for all 108 multiple comparisons using a false discovery rate of 5%.³

eTable 6. Frequencies within each Disability Rating Scale (DRS) domain for Severe TBI and Moderate TBI groups at 2 weeks and 3, 6, and 12 months post-injury

DRS Domain Severity Unweighted Analyses	2 Weeks		3 Months		6 Months		12 Months	
	Severe (n=326)	Moderate (n=106)	Severe (n=297)	Moderate (n=93)	Severe (n=290)	Moderate (n=77)	Severe (n=273)	Moderate (n=72)
Vegetative State & Death								
Veg. State	72 (22%)	12 (11%)	11 (4%)	0 (0%)	5 (2%)	0 (0%)	1 (0%)	0 (0%)
Died	60 (18%)	4 (4%)	73 (25%)	9 (10%)	78 (27%)	9 (12%)	83 (30%)	9 (13%)
DRS #2 Communication								
Oriented	55 (17%)	41 (39%)	119 (40%)	57 (61%)	118 (41%)	41 (53%)	115 (42%)	48 (67%)
Confused	84 (26%)	36 (34%)	80 (27%)	26 (28%)	83 (29%)	27 (35%)	68 (25%)	14 (19%)
Inappropriate	55 (17%)	13 (12%)	14 (5%)	1 (1%)	6 (2%)	0 (0%)	6 (2%)	1 (1%)
DRS #4 Feeding								
Complete	93 (29%)	61 (58%)	176 (59%)	74 (80%)	180 (62%)	64 (83%)	169 (62%)	61 (85%)
Partial	18 (6%)	8 (8%)	9 (3%)	3 (3%)	9 (3%)	3 (4%)	4 (1%)	1 (1%)
Minimal	14 (4%)	5 (5%)	11 (4%)	3 (3%)	6 (2%)	1 (1%)	6 (2%)	1 (1%)
None	69 (21%)	16 (15%)	17 (6%)	4 (4%)	12 (4%)	0 (0%)	10 (4%)	0 (0%)
DRS #5 Toileting								
Complete	89 (27%)	58 (55%)	166 (56%)	72 (77%)	176 (61%)	63 (82%)	163 (60%)	60 (83%)
Partial	10 (3%)	11 (10%)	8 (3%)	6 (6%)	4 (1%)	1 (1%)	3 (1%)	1 (1%)
Minimal	18 (6%)	2 (2%)	15 (5%)	1 (1%)	7 (2%)	1 (1%)	6 (2%)	2 (3%)
None	78 (24%)	19 (18%)	24 (8%)	5 (5%)	20 (7%)	3 (4%)	17 (6%)	0 (0%)
DRS #6 Grooming								
Complete	85 (26%)	57 (54%)	161 (54%)	74 (80%)	167 (58%)	61 (79%)	160 (59%)	61 (85%)
Partial	8 (2%)	6 (6%)	12 (4%)	3 (3%)	12 (4%)	4 (5%)	9 (3%)	0 (0%)
Minimal	23 (7%)	6 (6%)	16 (5%)	2 (2%)	12 (4%)	1 (1%)	7 (3%)	2 (3%)
None	78 (24%)	21 (20%)	24 (8%)	5 (5%)	16 (6%)	2 (3%)	13 (5%)	0 (0%)
DRS #7 Level of Functioning								
Completely independent	23 (7%)	31 (29%)	83 (28%)	44 (47%)	104 (36%)	43 (56%)	103 (38%)	38 (53%)
Independent in special environment	2 (1%)	1 (1%)	10 (3%)	4 (4%)	9 (3%)	2 (3%)	6 (2%)	1 (1%)

DRS Domain Severity Unweighted Analyses	2 Weeks		3 Months		6 Months		12 Months	
	Severe (n=326)	Moderate (n=106)	Severe (n=297)	Moderate (n=93)	Severe (n=290)	Moderate (n=77)	Severe (n=273)	Moderate (n=72)
Mildly dependent	29 (9%)	9 (8%)	45 (15%)	15 (16%)	30 (10%)	11 (14%)	31 (11%)	11 (15%)
Moderately dependent	16 (5%)	8 (8%)	16 (5%)	6 (6%)	14 (5%)	4 (5%)	11 (4%)	7 (10%)
Markedly dependent	14 (4%)	6 (6%)	11 (4%)	3 (3%)	15 (5%)	3 (4%)	13 (5%)	5 (7%)
Totally dependent	110 (34%)	35 (33%)	48 (16%)	12 (13%)	35 (12%)	5 (6%)	25 (9%)	1 (1%)
DRS #8 Employability								
Not restricted	27 (8%)	20 (19%)	88 (30%)	47 (51%)	95 (33%)	36 (47%)	96 (35%)	35 (49%)
Selected jobs	38 (12%)	24 (23%)	42 (14%)	14 (15%)	49 (17%)	16 (21%)	38 (14%)	15 (21%)
Sheltered workshop	14 (4%)	6 (6%)	20 (7%)	6 (6%)	14 (5%)	7 (9%)	19 (7%)	6 (8%)
Unemployable	111 (34%)	37 (35%)	57 (19%)	17 (18%)	40 (14%)	8 (10%)	33 (12%)	6 (8%)

Percentages within each domain sum to 100% after adding percent in Vegetative State and Died categories for the group at that time point (column).

eTable 7. Cumulative frequencies and risk ratios within each Disability Rating Scale (DRS) domain for Severe TBI and Moderate TBI groups at 2 weeks, 3 months, 6 months and 12 months post-injury

DRS Domain Severity	2 Weeks			3 Months			6 Months			12 Months		
	Severe (n=326)	Moderate (n=106)	Risk Ratio	Severe (n=297)	Moderate (n=93)	Risk Ratio	Severe (n=290)	Moderate (n=77)	Risk Ratio	Severe (n=273)	Moderate (n=72)	Risk Ratio
Vegetative State & Death												
Vegetative state or Died	132 (40%) [35, 46]	16 (15%) [9, 23]	2.68 (1.68, 4.29)	84 (28%) [23, 34]	9 (10%) [5, 17]	2.92 (1.53, 5.58)	83 (29%) [24, 34]	9 (12%) [6, 20]	2.45 (1.29, 4.65)	84 (31%) [25, 36]	9 (13%) [6, 21]	2.46 (1.30, 4.65)
Died	60 (18%) [14, 23]	4 (4%) [1, 9]	4.88 (1.82, 13.1)	73 (25%) [20, 30]	9 (10%) [5, 17]	2.54 (1.32, 4.88)	78 (27%) [22, 32]	9 (12%) [6, 20]	2.30 (1.21, 4.38)	83 (30%) [25, 36]	9 (13%) [6, 21]	2.43 (1.29, 4.60)
DRS #2 Communication												
Confused (<i>or worse</i>)	271 (83%) [79, 87]	65 (61%) [52, 70]	1.36 (1.16, 1.59)	178 (60%) [54, 65]	36 (39%) [29, 49]	1.55 (1.18, 2.03)	172 (59%) [54, 65]	36 (47%) [36, 58]	1.27 (0.98, 1.64)	158 (58%) [52, 64]	24 (33%) [23, 45]	1.74 (1.23, 2.44)
Inappropriate (<i>or worse</i>)	187 (57%) [52, 63]	29 (27%) [19, 36]	2.10 (1.52, 2.90)	98 (33%) [28, 38]	10 (11%) [6, 18]	3.07 (1.67, 5.63)	89 (31%) [26, 36]	9 (12%) [6, 20]	2.63 (1.39, 4.97)	90 (33%) [28, 39]	10 (14%) [7, 23]	2.37 (1.30, 4.32)
DRS #4 Feeding												
Partial (<i>or worse</i>)	233 (71%) [66, 76]	45 (42%) [33, 52]	1.68 (1.33, 2.12)	121 (41%) [35, 46]	19 (20%) [13, 29]	1.99 (1.31, 3.05)	110 (38%) [32, 44]	13 (17%) [10, 26]	2.25 (1.34, 3.77)	104 (38%) [32, 44]	11 (15%) [8, 25]	2.49 (1.42, 4.39)
Minimal (<i>or worse</i>)	215 (66%) [61, 71]	37 (35%) [26, 44]	1.89 (1.44, 2.48)	112 (38%) [32, 43]	16 (17%) [10, 26]	2.19 (1.37, 3.50)	101 (35%) [29, 40]	10 (13%) [7, 22]	2.68 (1.47, 4.88)	100 (37%) [31, 42]	10 (14%) [7, 23]	2.64 (1.45, 4.79)
None (<i>or worse</i>)	201 (62%) [56, 67]	32 (30%) [22, 39]	2.04 (1.51, 2.76)	101 (34%) [29, 40]	13 (14%) [8, 22]	2.43 (1.43, 4.13)	95 (33%) [28, 38]	9 (12%) [6, 20]	2.80 (1.48, 5.29)	94 (34%) [29, 40]	9 (13%) [6, 21]	2.75 (1.46, 5.19)
DRS #5 Toileting												
Partial (<i>or worse</i>)	237 (73%) [68, 77]	48 (45%) [36, 55]	1.61 (1.29, 2.00)	131 (44%) [39, 50]	21 (23%) [15, 32]	1.95 (1.31, 2.91)	114 (39%) [34, 45]	14 (18%) [11, 28]	2.16 (1.32, 3.55)	110 (40%) [35, 46]	12 (17%) [9, 26]	2.42 (1.41, 4.13)

DRS Domain Severity	2 Weeks			3 Months			6 Months			12 Months		
	Severe (n=326)	Moderate (n=106)	Risk Ratio	Severe (n=297)	Moderate (n=93)	Risk Ratio	Severe (n=290)	Moderate (n=77)	Risk Ratio	Severe (n=273)	Moderate (n=72)	Risk Ratio
Minimal (<i>or worse</i>)	227 (70%) [64, 74]	37 (35%) [26, 44]	1.99 (1.52, 2.61)	123 (41%) [36, 47]	15 (16%) [10, 24]	2.57 (1.58, 4.16)	110 (38%) [32, 44]	13 (17%) [10, 26]	2.25 (1.34, 3.77)	107 (39%) [34, 45]	11 (15%) [8, 25]	2.57 (1.46, 4.51)
None (<i>or worse</i>)	209 (64%) [59, 69]	35 (33%) [25, 42]	1.94 (1.46, 2.58)	108 (36%) [31, 42]	14 (15%) [9, 23]	2.42 (1.46, 4.01)	103 (36%) [30, 41]	12 (16%) [9, 25]	2.28 (1.32, 3.92)	101 (37%) [31, 43]	9 (13%) [6, 21]	2.96 (1.58, 5.56)
DRS #6 Grooming												
Partial (<i>or worse</i>)	241 (74%) [69, 78]	49 (46%) [37, 56]	1.60 (1.29, 1.98)	136 (46%) [40, 51]	19 (20%) [13, 29]	2.24 (1.47, 3.41)	123 (42%) [37, 48]	16 (21%) [13, 31]	2.04 (1.29, 3.22)	113 (41%) [36, 47]	11 (15%) [8, 25]	2.71 (1.54, 4.75)
Minimal (<i>or worse</i>)	233 (71%) [66, 76]	43 (41%) [32, 50]	1.76 (1.39, 2.24)	124 (42%) [36, 47]	16 (17%) [10, 26]	2.43 (1.52, 3.87)	111 (38%) [33, 44]	12 (16%) [9, 25]	2.46 (1.43, 4.21)	104 (38%) [32, 44]	11 (15%) [8, 25]	2.49 (1.42, 4.39)
None (<i>or worse</i>)	210 (64%) [59, 69]	37 (35%) [26, 44]	1.85 (1.41, 2.42)	108 (36%) [31, 42]	14 (15%) [9, 23]	2.42 (1.46, 4.01)	99 (34%) [29, 40]	11 (14%) [8, 23]	2.39 (1.35, 4.23)	97 (36%) [30, 41]	9 (13%) [6, 21]	2.84 (1.51, 5.35)
DRS #7 Level of Functioning												
Independent in special environment (<i>or worse</i>)	303 (93%) [90, 95]	75 (71%) [62, 79]	1.31 (1.16, 1.49)	214 (72%) [67, 77]	49 (53%) [43, 63]	1.37 (1.11, 1.68)	186 (64%) [59, 70]	34 (44%) [33, 55]	1.45 (1.11, 1.89)	170 (62%) [56, 68]	34 (47%) [36, 59]	1.32 (1.02, 1.71)
Mildly dependent (<i>or worse</i>)	301 (92%) [89, 95]	74 (70%) [61, 78]	1.32 (1.16, 1.50)	204 (69%) [63, 74]	45 (48%) [38, 58]	1.42 (1.14, 1.78)	177 (61%) [55, 67]	32 (42%) [31, 53]	1.47 (1.11, 1.94)	164 (60%) [54, 66]	33 (46%) [35, 57]	1.31 (1.00, 1.72)
Moderately dependent (<i>or worse</i>)	272 (83%) [79, 87]	65 (61%) [52, 70]	1.36 (1.16, 1.59)	159 (54%) [48, 59]	30 (32%) [23, 42]	1.66 (1.21, 2.27)	147 (51%) [45, 56]	21 (27%) [18, 38]	1.86 (1.27, 2.72)	133 (49%) [43, 55]	22 (31%) [21, 42]	1.59 (1.10, 2.31)
Markedly dependent (<i>or worse</i>)	256 (79%) [74, 83]	57 (54%) [44, 63]	1.46 (1.21, 1.76)	143 (48%) [42, 54]	24 (26%) [18, 35]	1.87 (1.30, 2.69)	133 (46%) [40, 52]	17 (22%) [14, 32]	2.08 (1.34, 3.22)	122 (45%) [39, 51]	15 (21%) [13, 31]	2.15 (1.34, 3.43)
Totally dependent (<i>or worse</i>)	242 (74%) [69, 79]	51 (48%) [39, 58]	1.54 (1.25, 1.90)	132 (44%) [39, 50]	21 (23%) [15, 32]	1.97 (1.32, 2.93)	118 (41%) [35, 46]	14 (18%) [11, 28]	2.24 (1.37, 3.67)	109 (40%) [34, 46]	10 (14%) [7, 23]	2.87 (1.59, 5.20)
DRS #8 Employability												

DRS Domain Severity	2 Weeks			3 Months			6 Months			12 Months		
	Severe (n=326)	Moderate (n=106)	Risk Ratio	Severe (n=297)	Moderate (n=93)	Risk Ratio	Severe (n=290)	Moderate (n=77)	Risk Ratio	Severe (n=273)	Moderate (n=72)	Risk Ratio
Selected jobs (or worse)	295 (92%) [88, 94]	83 (81%) [72, 87]	1.14 (1.03, 1.26)	203 (70%) [64, 75]	46 (49%) [39, 60]	1.41 (1.13, 1.76)	186 (66%) [61, 72]	40 (53%) [41, 64]	1.26 (1.00, 1.58)	174 (64%) [59, 70]	36 (51%) [39, 62]	1.27 (0.99, 1.63)
Sheltered workshop (or worse)	257 (80%) [75, 84]	59 (57%) [48, 67]	1.39 (1.17, 1.66)	161 (55%) [50, 61]	32 (34%) [25, 44]	1.61 (1.19, 2.17)	137 (49%) [43, 55]	24 (32%) [22, 43]	1.54 (1.09, 2.20)	136 (50%) [44, 56]	21 (30%) [20, 41]	1.70 (1.17, 2.49)
Unemployable (or worse)	243 (75%) [71, 80]	53 (51%) [42, 61]	1.47 (1.20, 1.79)	141 (48%) [43, 54]	26 (28%) [20, 38]	1.73 (1.22, 2.45)	123 (44%) [38, 50]	17 (22%) [14, 33]	1.96 (1.26, 3.04)	117 (43%) [38, 49]	15 (21%) [13, 32]	2.05 (1.28, 3.28)

"Severe" and "Moderate" columns report the n and percent of cases with a severity at or worse than the category label. Risk ratios were calculated as the percent with disability of the indicated level or worse in the Severe TBI group divided by the corresponding percent in the Moderate TBI group. For example, for minimal feeding, the percent includes those with minimal feeding, no feeding, vegetative state, or dead. The 95% confidence intervals on risk ratios were estimated based on the near-normal distribution of the log of the risk ratio.³⁶ Statistical significance determined by Fisher's exact tests. Bold cells indicate statistical significance (p<.05) following post-hoc adjustment for all 108 multiple comparisons using a false discovery rate of 5%.³⁷

eTable 8. Group differences on clinical outcome assessment measures at 12 months post-injury

All subjects with at least one neuropsych score	Severe TBI n=108	Moderate TBI n=36	Severe TBI vs. Moderate TBI
Continuous Measures	Mean (95% CI)		Cohen's d Effect Size (95% CI)
Memory			
RAVLT Immediate Memory ¹	43.6 (41.3, 45.8)	44.3 (40.3, 48.2)	-0.07 (-0.44, 0.31)
RAVLT Delayed Recall ¹	8.2 (7.5, 9.0)	8.0 (6.8, 9.2)	0.03 (-0.35, 0.41)
Processing Speed (PS)			
WAIS-IV PS Index ¹	93 (90, 97)	95 (89, 101)	-0.12 (-0.51, 0.26)
Executive Functioning			
Trails A Time ¹	34.3 (30.5, 38.2)	30.8 (25.0, 36.5)	0.26 (-0.12, 0.64)
Trails B Time ¹	95 (81, 109)	84 (66, 102)	0.08 (-0.30, 0.47)
All subjects with at least one neuropsych score, plus those who are missing due to death or TBI-related impairment	Severe TBI n=227	Moderate TBI n=57	Severe TBI vs. Moderate TBI
Continuous Measures	Mean (95% CI)		Cohen's d Effect Size (95% CI)
Memory			
RAVLT Immediate Memory ¹	19.6 (16.5, 22.8)	27.4 (21.1, 33.8)	-0.46 (-0.75, -0.17)
RAVLT Delayed Recall ¹	3.0 (2.2, 3.7)	4.5 (3.1, 5.9)	-0.43 (-0.72, -0.14)
Processing Speed (PS)			
WAIS-IV PS Index ¹	69 (66, 73)	78 (71, 85)	-0.47 (-0.77, -0.18)
Executive Functioning			
Trails A Time ¹	70.1 (65.3, 74.9)	57.3 (47.4, 67.2)	0.53 (0.24, 0.83)
Trails B Time ¹	206 (191, 221)	166 (135, 196)	0.48 (0.19, 0.78)
All subjects with at least one self-report score	Severe TBI n=147	Moderate TBI n=49	Severe TBI vs. Moderate TBI
Patient Reported Outcomes			
Psychological Distress (BSI-18 GSI) T ²	49.7 (47.9, 51.4)	49.9 (46.5, 53.2)	-0.02 (-0.34, 0.31)
Life Satisfaction (SWLS) ²	23.0 (21.6, 24.3)	23.3 (21.2, 25.4)	-0.04 (-0.37, 0.29)
TBI Symptoms (RPQ Score) ²	14.4 (12.3, 16.5)	13.6 (10.0, 17.2)	0.06 (-0.26, 0.39)

Rivermead Symptoms (value≥2)	N (%) Endorsed (95% CI)		Risk Ratio (95% CI)
Headache ³	42 (29%) [22, 36]	12 (24%) [14, 38]	1.17 (0.68, 2.04)
Dizziness ³	41 (28%) [21, 36]	14 (29%) [17, 42]	0.98 (0.59, 1.64)
Nausea ³	10 (7%) [3, 12]	2 (4%) [1, 12]	1.68 (0.38, 7.40)
Noise sensitivity ³	40 (27%) [21, 35]	16 (33%) [21, 46]	0.84 (0.52, 1.36)
Sleep disturbances ³	49 (34%) [26, 41]	16 (33%) [21, 46]	1.03 (0.65, 1.63)
Fatigue ³	67 (46%) [38, 54]	24 (49%) [35, 63]	0.94 (0.67, 1.31)
Irritability/anger ³	69 (47%) [39, 55]	22 (45%) [31, 59]	1.05 (0.74, 1.50)
Depression/tearfulness ³	50 (34%) [27, 42]	18 (37%) [24, 51]	0.93 (0.61, 1.43)
Frustration/impatience ³	70 (48%) [40, 56]	22 (45%) [31, 59]	1.07 (0.75, 1.52)
Forgetfulness/poor memory ³	97 (66%) [59, 74]	26 (53%) [39, 67]	1.25 (0.94, 1.67)
Poor concentration ³	70 (48%) [40, 56]	24 (49%) [35, 63]	0.98 (0.70, 1.36)
Taking longer to think ³	79 (54%) [46, 62]	25 (51%) [37, 65]	1.06 (0.78, 1.45)
Blurred vision ³	32 (22%) [16, 29]	12 (24%) [14, 38]	0.89 (0.50, 1.60)
Light sensitivity ³	24 (16%) [11, 23]	11 (22%) [12, 35]	0.73 (0.39, 1.38)
Double vision ³	17 (12%) [7, 18]	3 (6%) [2, 15]	1.90 (0.58, 6.21)
Restlessness ³	38 (26%) [19, 34]	13 (27%) [16, 40]	0.98 (0.57, 1.68)

Abbreviations: RAVLT, Rey Auditory Verbal Learning Test; WAIS-IV, Wechsler Adult Intelligence Scale, Fourth Edition; PS Index, Processing Speed Index (normative M=100, SD=15); BSI-18, Brief Symptom Inventory, 18 item version; GSI T, Global Severity Index T score (normative M=50, SD=10); SWLS, Satisfaction with Life Scale; RPQ, Rivermead Post Concussion Symptoms Questionnaire.

¹Differences in performance on neuropsychological measures were analyzed after adjusting for age, sex, and education using linear regression on ranked data. Cohen's d effect sizes were calculated from the regression output as the unstandardized coefficient divided by the root mean square error (B/RMSE). Statistical significance was interpreted in the context of multiple comparisons.³⁷ These measures were evaluated both with and without participants who could not be assessed due to death or impairment due to TBI. These latter cases are represented in the analysis by imputing a score 2 points and 1 point, respectively, worse than the worst observed score. Thus, where included, deaths were given the worst rank and those too impaired to take the tests were given ranks just above the deaths.

²Self-report measures analyzed by linear regression.

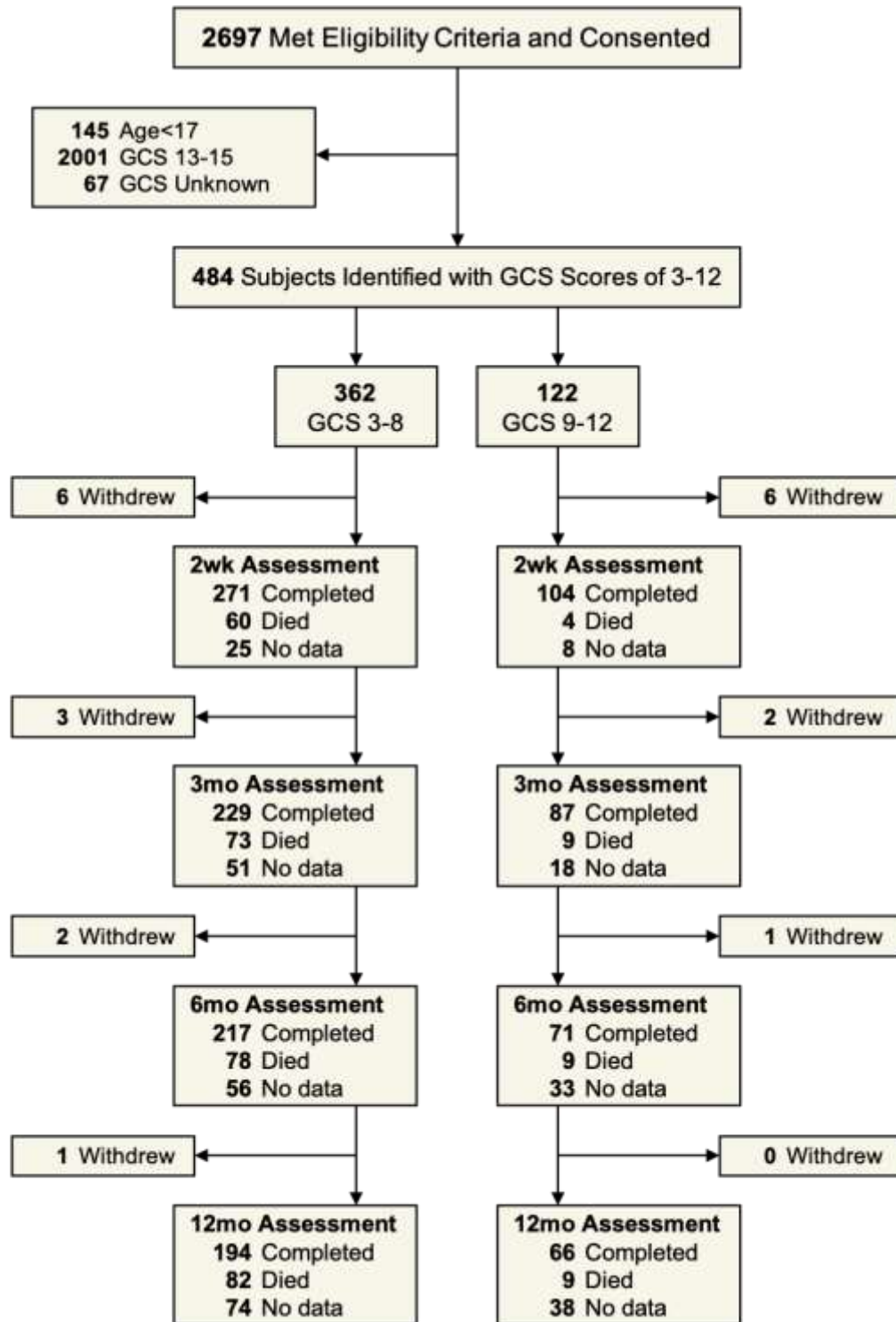
³Differences in individual symptom endorsement were characterized using risk ratios and assessed for significance using Fisher's exact tests with p-values interpreted accounting for multiple comparisons.³⁷

Statistical significance. All p-values are 2-tailed. No comparisons were statistically significant (p<.05) using post-hoc adjustment for all 29 multiple comparisons per Benjamini-Hochberg (1995) using a false discovery rate of 5%.

Missingness. Self-report measures were available for 40% (n=196) of cases at 12 months, with 29% (n=140) dead or too impaired to complete the measures, and 31% (n=148) lost to follow-up. Neuropsychological test scores were available for 30% (n=144) of the participants at 12 months with 29% (n=140) dead or too impaired to complete the measures, 11% (n=52) assessed by telephone, and 31% (n=148) lost to follow-up. To determine if any bias caused by missing outcomes impacted the findings, separate propensity models were constructed at each time point for the presence/absence of neuropsychological (with and without subjects who either died or were too impaired to be tested) and Rivermead outcomes. See the Statistical Analysis section for details on the propensity models. These sensitivity analyses showed that the missing outcomes impacted the results to a negligible degree, thus only the unweighted analyses are reported.

Power. The study had at least 80% power to detect an effect size of .41 between those with moderate and severe TBI on neuropsychological measures when those who died and those who were too impaired to undergo assessment were included. The study had at least 80% power to detect an effect size of .55 when only those who completed the test battery were included), and an effect size of .42 on self-report measures.

eFigure. STROBE diagram of participant enrollment and follow-up for Moderate TBI (GCS 9-12) and Severe TBI (GCS 3-8) groups



"Completed" refers to a follow-up visit with at least one completed functional outcome measure (GOSE or DRS).