

# Disorders of Consciousness due to Traumatic Brain Injury: Functional Status Ten Years Post-Injury

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## Abstract

Few studies have assessed the long-term functional outcomes of patients with a disorder of consciousness due to traumatic brain injury (TBI). This study examined functional status during the first 10 years after TBI among a cohort with disorders of consciousness (i.e., coma, vegetative state, minimally conscious state). The study sample included 110 individuals with TBI who were unable to follow commands prior to inpatient rehabilitation and for whom follow-up data were available at 1, 2, 5, and 10 years post-injury. The sample was subdivided into those who demonstrated command-following early (before 28 days post-injury) versus late ( $\geq 28$  days post-injury or never). Functional Independence Measure (FIM) at 1, 2, 5, and 10 years following TBI was used to measure functional outcomes. Measureable functional recovery occurred throughout the 10-year period, with more than two thirds of the sample achieving independence in mobility and self-care, and about one quarter achieving independent cognitive function by 10 years. Following commands prior to 28 days was associated with greater functional independence at all outcome time-points. Multi-trajectory modeling of recovery of three FIM subscales (self-care, mobility, cognition) revealed four distinct prognostic groups with different temporal patterns of change on these subscales. More than half the sample achieved near-maximal recovery by 1 year post-injury, while the later command-following subgroups recovered over longer periods of time. Significant late functional decline was not observed in this cohort. Among a cohort of patients unable to follow commands at the time of inpatient rehabilitation, a substantial proportion achieved functional independence in self-care, mobility, and cognition. The proportion of participants achieving functional independence increased between 5 and 10 years post-injury. These findings suggest that individuals with disorders of consciousness may benefit from ongoing functional monitoring and updated care plans for at least the first decade after TBI.

**Keywords:** brain injuries; cognition; consciousness disorders; minimally conscious state; prognosis; rehabilitation outcome; vegetative state

## Introduction

**F**EW STUDIES HAVE ASSESSED the long-term functional outcomes of patients with disorders of consciousness (DOC) due to traumatic brain injury (TBI). In addition, many utilized broad,

non-specific outcome measures with variable samples at follow-up intervals. There is consequently a lack of data to guide families, providers, and payers in trying to plan for future needs, compare outcomes, and assess quality of interventions. Given the lack of knowledge regarding meaningful long-term outcomes, it is not

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surprising that healthcare providers tend to provide pessimistic prognostic information.<sup>1,2</sup> It is possible such low prognostic expectations influence care and outcomes. In fact, in the United States, individuals on mechanical ventilation with a Glasgow Coma Scale (GCS) score of 5 or less are referred for organ procurement.<sup>3</sup> Many providers and payers deem patients with DOC who lack command-following as inappropriate for acute inpatient rehabilitation.<sup>4,5</sup> Thus, there is great need for data on specific long-term functional outcomes to inform post-acute treatment recommendations.

In contrast to these poor outcome expectations, recent literature has supported a more favorable outcome trajectory for those admitted to inpatient rehabilitation. Several studies have shown recovery of consciousness and functional independence during the first year following TBI for many individuals with DOC.<sup>6</sup> Greater recovery is generally observed for those who are in the minimally conscious state as compared with the vegetative state at rehabilitation admission.<sup>6–12</sup>

Studies of the Traumatic Brain Injury Model Systems (TBIMS) cohort have shown that of 396 TBIMS participants who were admitted to inpatient rehabilitation unable to follow commands, 268 (68%) regained command-following and, of these, 91 (23%) emerged from post-traumatic amnesia prior to rehabilitation discharge.<sup>10</sup> Of those who had failed to recover command-following by rehabilitation discharge, the majority of those with follow-up were able to follow commands by post-injury Years 1 (59%;  $n = 46/78$ ), 2 (66%;  $n = 31/47$ ), and 5 (74%;  $n = 25/34$ ). Of 337, 20% were living without in-house supervision, and 19% were competitively employable. This study found significant improvements in FIM Motor and Cognition subscale scores from rehabilitation discharge to Year 1, Year 1 to 2, and Year 2 to 5 ( $N = 108$ ). To better understand these improvements, Whyte and colleagues<sup>13</sup> studied the changes in individual FIM items over the first 5 years post-injury. Among those who recovered command-following during inpatient rehabilitation, 56 to 85% (depending on the FIM item) were functionally independent by 5 years. The proportion with independent function across FIM items increased from each assessment interval to the next. For those without command-following by rehabilitation discharge, 19 to 36% were functioning independently by 5 years. In summary, those without return of command-following during inpatient rehabilitation showed less functional progress than with command-following recovery during rehabilitation, though clinically meaningful change after rehabilitation discharge was observed.

These studies highlight important prognostic information in the first 5 years following TBI resulting in DOC. This issue has taken on great significance in the context of recent conceptualization of TBI as a chronic disease<sup>14</sup> and preliminary evidence that some persons with TBI show functional decline by 5 years post-injury.<sup>15</sup> However, outcomes of well-characterized samples with traumatic DOC beyond 5 years post-injury have not been described in the literature. The present study uses the same TBIMS cohort as Nakase-Richardson and colleagues<sup>10</sup> and Whyte and colleagues<sup>13</sup> to assess the level of independence achieved over the first 10 years post-injury. Additionally, this study examined whether there were distinct subgroups of DOC patients with characteristic patterns of recovery or decline. As in the study by Whyte and colleagues,<sup>13</sup> the sample was subdivided into those who regained command-following earlier versus later. However, many other studies define prolonged DOC as lasting more than 28 days. Thus, to study patterns of functional recovery over the first 10 years post-injury, the cohort was by subdivided by timing of following command post-

injury: those who first followed commands prior to 28 days post-injury and those that did not. We hypothesized that function would change from 5 to 10 years post-injury with distinct recovery groups identified.

## Methods

### Study participants

Participants are consecutive inpatient rehabilitation admissions who were prospectively enrolled in the National Institute on Disability, Independent Living, and Rehabilitation Research (NI-DILRR) funded TBIMS multi-site longitudinal registry with no evidence of command-following prior to rehabilitation admission (verified across two TBIMS variables as defined below) and completed 1-, 2-, 5-, and 10-year follow-ups. TBIMS database participants for this study were discharged from acute inpatient rehabilitation from January 1, 1989, through December 31, 2015. TBI is defined by at least one of the following: GCS score <13 on emergency department admission, loss of consciousness >30 min, post-traumatic amnesia >24 h, or trauma-related intracranial abnormality on neuroimaging. Additional TBIMS inclusion criteria are: age 16 years or older at the time of injury, received medical care in a TBIMS-affiliated trauma center within 72 h of injury, transferred directly to a TBIMS affiliated inpatient TBI rehabilitation program, and informed consent provided by legal proxy or participant. Excluded from the sample were participants who had incomplete follow-up at 1, 2, 5, or 10 years post-injury, were missing functional outcome (FIM) data, or were dead. Those with FIM data at all four intervals but missing individual FIM items were included. All TBIMS sites have approval by their local institutional review board.

### Measures

**Disorders of consciousness.** Participants were coded as having DOC based on command-following status across two TBIMS variables at the time of rehabilitation admission.<sup>10,13</sup> The first variable was the date a participant exhibited command-following on two consecutive examinations within a 24-h period following TBI. Acute rehabilitation medical records including nursing flow sheets and progress notes were exhaustively reviewed to determine if command-following was demonstrated prior to rehabilitation hospital admission. Such documentation might include mention of command-following or a GCS Motor score of 6 (indicating command-following). The second is the GCS Motor score coded as part of the Disability Rating Scale collected at rehabilitation admission. Participants were coded as having DOC if both variables indicated that no command-following ability prior to or at the time of inpatient rehabilitation admission.

**FIM.** The FIM<sup>16</sup> measures functional independence or burden of care with 18 items that assess Self-care (six items), Mobility (seven items), and Cognition (five items). The bath to shower transfer item was not used in the present study given other transfer types being represented. Items are scored 1 through 7 with a score of 1 representing complete dependence and a score of 7 indicating complete independence.

### Procedures

Trained TBIMS research assistants collected information regarding injury severity (GCS, time to follow commands [TFC]), and medical course from hospital and emergency medical service records consistent with the protocol for the TBIMS database. TFC is the interval in days from the date of injury until the first of two consecutive reports of command-following within a 24-h period. Demographic information such as date of birth, education, and pre-

morbid functioning were collected in interview with the subjects or family/significant others. The Disability Rating Scale (including the GCS motor score) was administered at the time of rehabilitation admission. Follow up data were collected at 1, 2, 5, and 10 years post-injury using a standardized telephone follow-up assessment protocol.<sup>17</sup> If the patient was not able to provide accurate information, data were collected from family members or care providers who were familiar with the participant.

### Statistical analysis

Data were analyzed using statistical software R (R Foundation for Statistical Computing, Vienna, Austria) for data manipulation and descriptive statistics, and SAS (SAS Institute Inc., Cary, NC; <https://www.andrew.cmu.edu/user/bjones/download.htm>) macro for group-based multi-trajectory models.<sup>18</sup> Descriptive statistics were expressed as quartiles (1st/median/3rd) for continuous variables and count (percent) for categorical variables. The proportion of the sample that was Independent (FIM=6-7), required Some Assistance (FIM=2-5), or was Totally Dependent (FIM=1), was determined for each FIM item. For ambulation, independence level was determined using primary mobility mode (walking vs. wheelchair). The total Self-care, Mobility and Cognition indices were calculated as the sums of the respective item scores. To calculate summary scores for Self-care, Mobility, and Cognition, mean scores >5.5 indicated Independent, mean scores >1.5 to 5.5 indicated Some Assistance needed, and mean scores from 1 to 1.5 indicated Total Dependence. In cases of missing FIM scores, the data were omitted for that individual.

Group-based multi-trajectory modeling was carried out to identify latent clusters of individuals who followed similar trajectories of function over time with regard to Self-care, Mobility, and Cognition. Censored normal distributions were used for modeling the scores as both Self-care and Mobility scores ranged from 6 to 42, and the cognition score ranged from 5 to 35. Because it is challenging to

identify trajectory patterns over time on multiple scores, we fitted trajectory models for each FIM subscale separately to clarify the types of distinctive trajectories represented in our study sample. Trajectories were assumed to follow a quadratic function of follow-up years except for participants who were at floor or ceiling (i.e., Total Dependence or Independent) at 1-year follow-up and stayed the same across years. Models for up to five groups were explored. While the five-group multi-trajectory model had a slightly better Bayesian Information Criterion (BIC) score than the four-group model, the five-group model did not include a group that was substantively distinct from those in the four-group model. The performance of the four-group multi-trajectory model was assessed. The average posterior probability for those assigned to a group based on the maximum posterior probability rule was 99.2%, which is far beyond the 70% threshold of acceptability. The proportion assigned to each group closely matched the estimated probability of group assignment.

## Results

### Patient characteristics

Figure 1 summarizes the number excluded from analyses by reason and the number lost-to-follow up with a final sample of 110 who met study criteria. Among the TBIMS national database participants, 664 met the case definition for a disorder of consciousness, as defined above. Of those, 530 were excluded due to: missing at least one follow up at Year 1, 2, 5, or 10 ( $n=325$ ), dead at Year 1, 2, 5, or 10 ( $n=91$ ), center no longer funded to follow the participant ( $n=23$ ), or missing 10-year FIM data ( $n=4$ ). Overall sample and subgroup characteristics (based on recovery trajectory group) are summarized in Table 1. Comparison of the sample that had consistent follow-up 10 years to those excluded due to inconsistent follow-up revealed similarities, except the study sample had more TBI due to motor vehicle crash and more chemically paralyzed.

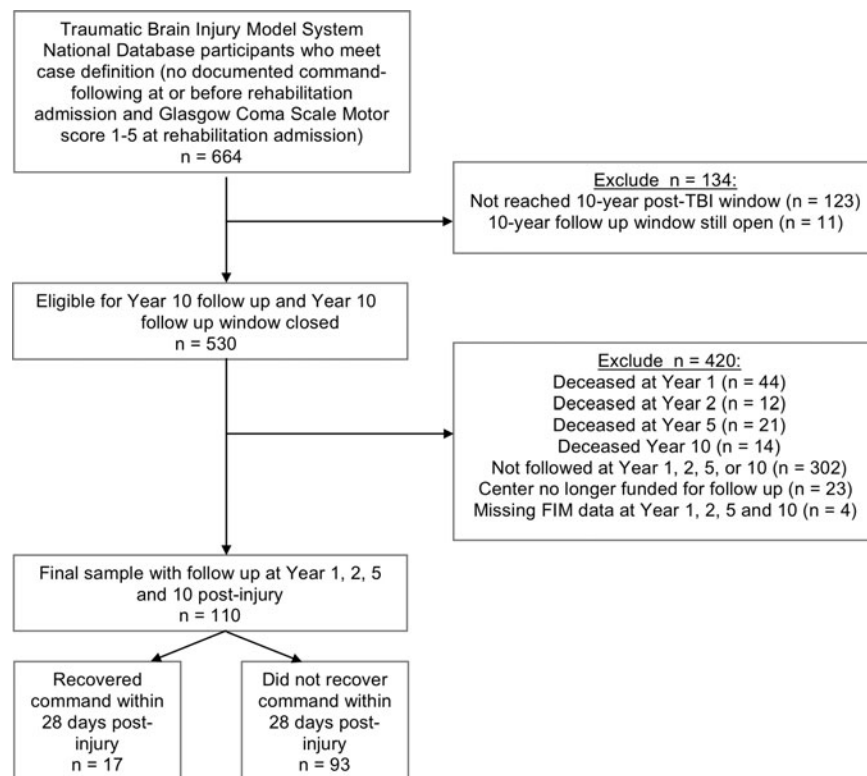


FIG. 1. Participant flow diagram.

TABLE 1. CHARACTERISTICS OF THE STUDY SAMPLE AND THE FOUR DISTINCT RECOVERY PATTERN GROUPS IN THE MULTI-TRAJECTORY MODEL

Parameter	Excluded due to missed visit Year 1, 2, or 5	n	Total sample	Group 1	Group 2	Group 3	Group 4
				(n=16; 15%) 19/22/33	(n=16; 15%) 18.75/21.00/30.00	(n=20; 18%) 20/23/36	(n=58; 53%) 21/28/39
Age at injury (years)	(N=110) 23.0/33.5/52.0	110	(N=110) 19/25/37				
Gender		110					
Female	24.9% (93)		28.2% (31)	18.8% (3)	18.8% (3)	35.0% (7)	31.0% (18)
Male	75.1% (281)		71.8% (79)	81.2% (13)	81.2% (13)	65.0% (13)	69.0% (40)
Race		110					
White	58.9% (219)		80.0% (88)	93.8% (15)	81.2% (13)	70.0% (14)	79.3% (46)
Black	17.2% (64)		15.5% (17)	0.0% (0)	12.5% (2)	25.0% (5)	17.2% (10)
Hispanic	18.5% (69)		1.8% (2)	0.0% (0)	0.0% (0)	0.0% (0)	3.4% (2)
Other	5.4% (20)		2.7% (3)	6.2% (1)	6.2% (1)	5.0% (1)	0.0% (0)
Education		83					
≤ High school diploma	65.5% (203)		61.4% (51)	83.3% (10)	57.1% (8)	66.7% (10)	54.8% (23)
> High school diploma	34.5% (107)		38.6% (32)	16.7% (2)	42.9% (6)	33.3% (5)	45.2% (19)
Cause of Injury		110					
Motor vehicle	40.8% (152)		68.2% (75)	62.5% (10)	81.2% (13)	65.0% (13)	67.2% (39)
Other	59.2% (221)		31.8% (35)	37.5% (6)	18.8% (3)	35.0% (7)	32.8% (19)
Paralyzed or chemically induced coma		109					
No	41.3% (152)		27.5% (30)	43.8% (7)	12.5% (2)	10.0% (2)	33.3% (19)
Yes	58.7% (216)		72.5% (79)	56.2% (9)	87.5% (14)	90.0% (18)	66.7% (38)
GCS among those not paralyzed or chemically-induced coma		152					
Acute LOS (days)	3/6/10	30	3.00/4.00/6.75	3.5/5.0/9.0	3/3/3	3.25/3.50/3.75	4.0/5.0/7.5
Rehabilitation LOS (days)	20/28/38	110	21/29/40	39/52/63	27/39/47	28/32/42	18/23/31
Recovery of command-following	28/42/73	110	28/46/65	23/37/58	38/60/109	34/56/86	27/43/57
During rehabilitation		110					
After rehabilitation or never	64.2% (240)		70.0% (77)	12.5% (2)	56.2% (9)	75.0% (15)	87.9% (51)
TFC days (excluding those never able to follow commands)	35.8% (134)		30.0% (33)	87.5% (14)	43.8% (7)	25.0% (5)	12.1% (7)
TFC ≥28 days	28/38/51	77	29/40/54	80/80/81	62/68/88	35/40/52	27/37/48
No	15.5% (58)	110	15.5% (17)	0.0% (0)	6.2% (1)	5.0% (1)	25.9% (15)
Yes	84.5% (316)		84.5% (93)	100.0% (16)	93.8% (15)	95.0% (19)	74.1% (43)

GCS, Glasgow Coma Scale score; LOS, length of stay; TFC, time to follow commands.

### *Proportion of individuals who were functionally independent*

Table 2 shows the proportion and number of individuals who were Independent, required Some Assistance, and Total Dependence at each of the summary areas of function and each FIM item at the follow-up periods subdivided into those with TFC before versus after 28 days post-injury. In general, both subsamples demonstrated functional gains across the three FIM domains from Year 1 to 2, Year 2 to 5, and Year 5 to 10. Although the percentage of individuals improving to full independence between Years 5 and 10 was relatively small, increased proportions were noted across all but three FIM items. For both subsamples, all three FIM domains showed increases in the proportion of independent individuals between 5 and 10 years and decreases in the proportion of Totally Dependent individuals. Among the group who regained command-following before 28 days, 88–100% were independent across the three FIM subscores by 10 years, compared with 50–75% for those who did not. Supplementary Figures 1 through 3 summarize the proportion independent at each epoch for the entire sample and by TFC timing subsample using a more visually friendly format (see online supplementary material at <http://www.liebertpub.com>).

For direct comparison to Whyte and colleagues<sup>13</sup> Supplementary Table 1, Supplementary Figure 4, and Supplementary Figure 5 present the results by dividing the cohort based on those who recovered command-following during versus after rehabilitation (see online supplementary material at <http://www.liebertpub.com>).

### *Patterns of functional recovery*

Multi-trajectory modeling identified four distinctive recovery patterns between Years 1 and 10, with respect to the three FIM subscales, as depicted in Figure 2. The characteristics of the four groups in the final multi-trajectory model are summarized in Table 1. Group 1 demonstrated poor recovery in all three functional domains at all time-points, with slightly greater mobility and cognitive improvement. Group 1 ( $n = 16$ ; 15%) had the most severe injuries, as indicated by the latest onset of command-following and the longest acute care length of stay (LOS) among the four groups. Further, this group had the highest proportion of individuals with  $\leq 12$  years of education compared with other trajectory subgroups. Group 2 showed disproportionate mobility impairment at 1 year, but robust recovery in this and the other domains over time from Years 2 to 5 and 5 to 10. This group ( $n = 16$ ; 15%) appeared to have the second most severe injuries in terms of time until commands were followed and may have had a high proportion of patients with diffuse axonal injury given the prevalence of motor vehicle collisions as the mechanism. A large proportion of participants in this group had an initial GCS of 3. Group 3 showed particular impairment in self-care at 1 year, but showed greater recovery in self-care and mobility than cognitive function for later follow-ups. This group ( $n = 20$ ; 18%) had less severe injuries in terms of time to follow commands and acute care LOS. Group 4 was high functioning at 1 year for all three domains and continued to be so up until year 10. This was the largest subgroup ( $n = 58$ ; 53%) with more than half of the sample. While the characteristic injury for this group was very severe, this group was less severely injured than other groups with a median interval from injury to command-following of 37 days and a median initial GCS of 5. Of note, there was no evidence of a pattern of deterioration up to 10 years in any functional domain or subgroup.

### **Discussion**

In this prospective longitudinal cohort study, we monitored the trajectory of recovery over the course of 10 years in patients with severe TBI and disturbance in consciousness persisting up to the time of admission to inpatient rehabilitation. We conducted follow-up assessments at 1, 2, 5, and 10 years post-injury and were particularly interested in comparing outcomes in patients who regained command-following ability before 28 days post-injury and those who recovered later. We also sought to identify distinct patterns of functional recovery during the 10-year time frame. Despite an inability to follow commands at the time of inpatient rehabilitation admission, the majority of the sample achieved independence in daily functional activities across self-care, mobility, and cognitive domains. Improvement was observed at each assessment epoch, with recovery of functional independence continuing between 5 and 10 years post-injury.

We identified four distinct recovery patterns associated with varied demographic and injury severity (i.e., time to command-following) characteristics: globally poor functional recovery (15%); robust recovery of functional cognitive status and self-care ability with delayed recovery of mobility (15%); recovery of mobility and self-care ability with residual functional cognitive limitations (18%); and globally good functional recovery (53%). Rate of recovery is known to be an important prognostic variable,<sup>19,20</sup> and thus it is not surprising that those who regained command-following prior to 28 days had more favorable recovery trajectories and outcomes at all time-points than those who did not. These findings extend the findings of prior longitudinal studies that report improvement across rehabilitation outcomes at 5-years post-injury.<sup>10,13</sup> Although the sample patients from racial and ethnic minorities was small, especially when further divided into recovery pattern groups, it is notable that there were no blacks or Hispanics participants in the least recovered group (Group 1). Given the small subsample of these participants, this could simply be due to chance; however, future research should assess whether there might be bias in admitting more severely affected minority patients to rehabilitation at the outset or in survival from severe TBI during acute care. The minority patients enrolled in this study were comparable in severity to the whites, at least as defined by not following commands at rehabilitation admission.

There has been a concern about decline in function over time in the years following TBI.<sup>14,21</sup> In a study of persons with moderate and severe TBI that was not restricted to participants without command following at the time of rehabilitation admission, Corrigan and colleague<sup>15</sup> found 30% declined in function and 20% expired between Year 1 or 2 and the 5-year post-injury mark. The present study did not find evidence of a pattern of deterioration up to 10 years in any functional domain or subgroup. Inspection of individual level data revealed only a few isolated instances of decline. There were four instances of decline from independence in Year 5 to needing some assistance in Year 10 spread evenly across the two TFC subsamples. Areas of decline involved problem solving, memory comprehension and wheelchair mobility/walking. The cause for decline in independence for these few instances is not known, nor is it known if the decrease in independence reflects a permanent or progressive decline versus temporary change, such as might occur due to temporary illness or as a function of measurement variability. The instances of decline do not necessarily represent the same people at each epoch. For example, one individual may have declined in Year 5 and 10 while another improved over the same interval, giving the appearance of no change in

TABLE 2. NUMBER AND PERCENT OF COHORT PARTICIPANTS AT EACH FIM ITEM INDEPENDENCE LEVEL (INDEPENDENT, SOME ASSISTANCE, AND TOTAL DEPENDENCE) AT YEARS 1, 2, 5, AND 10 POST-INJURY BY COMMAND-FOLLOWING BEFORE 28 DAYS OR MORE DAYS

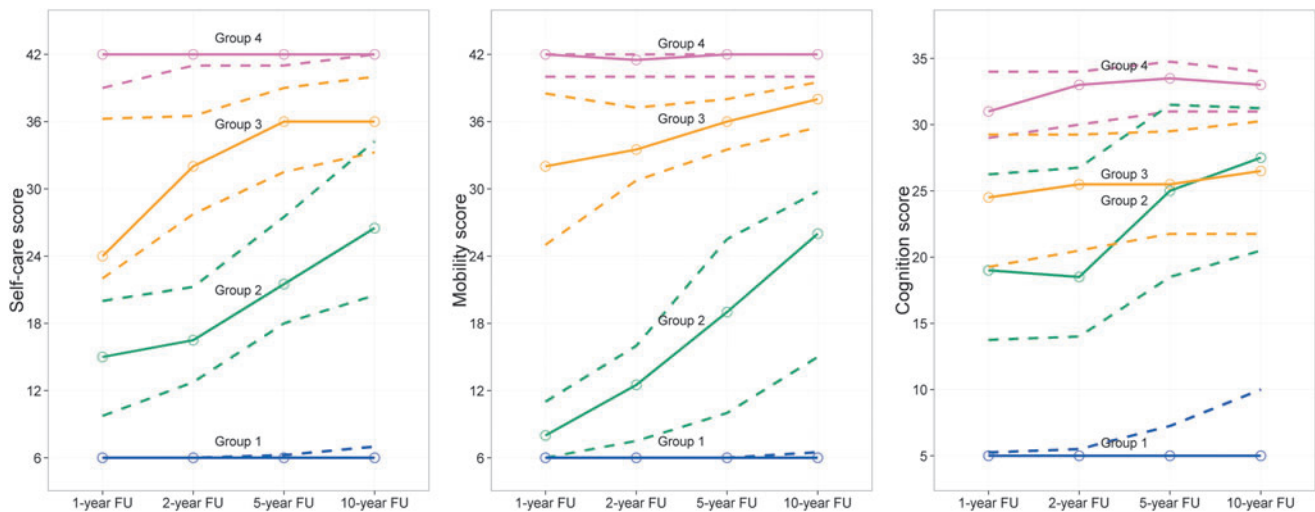
Time	Year 1			Year 2			Year 5			Year 10					
	TFC <28 days (n=17)	TFC ≥28 days (n=93)	Walk=16 W/C=1	TFC <28 days (n=17)	TFC ≥28 days (n=93)	Walk=17 W/C=0	TFC <28 days (n=17)	TFC ≥28 days (n=93)	Walk=16 W/C=1	TFC <28 days (n=17)	TFC ≥28 days (n=93)	Walk=63 W/C=29	Entire sample (N=110)		
Command-following group															
Mode: Walk vs. W/C															
Independence Level	I	SA	TD	I	SA	TD	I	SA	TD	I	SA	TD	I	SA	TD
Self-Care	16	1	0	53	24	16	17	0	0	65	16	12	82	16	12
Eating	94%	6%	0%	57%	26%	17%	100%	0%	0%	60%	23%	17%	13%	75%	15%
Grooming	16	1	0	47	25	21	15	2	0	63	13	17	82	15	13
Bathing	94%	6%	0%	51%	27%	23%	88%	12%	0%	68%	14%	18%	75%	14%	12%
	15	2	0	43	27	23	15	2	0	59	16	18	72	17	14
	88%	12%	0%	46%	29%	25%	88%	12%	0%	63%	17%	19%	72%	15%	13%
UB-Dressing	15	2	0	47	24	22	16	1	0	56	18	19	76	21	13
	88%	12%	0%	51%	26%	24%	94%	6%	0%	60%	19%	20%	63%	23%	14%
LB-Dressing	15	2	0	44	24	25	16	1	0	55	15	23	72	20	18
	88%	12%	0%	47%	26%	27%	94%	6%	0%	59%	16%	25%	60%	20%	19%
Toileting	15	2	0	50	17	26	16	1	0	62	12	19	72	18	16
	88%	12%	0%	54%	18%	28%	94%	6%	0%	67%	13%	20%	71%	10%	19%
Total	15	2	0	47	26	20	16	1	0	49	25	19	79	18	13
	88%	12%	0%	51%	28%	22%	94%	6%	0%	61%	20%	18%	67%	19%	14%
Mobility	16	1	0	54	10	27	16	1	0	60	9	22	72	18	12%
Bladder management	94%	6%	0%	59%	11%	30%	94%	6%	0%	67%	9%	24%	74%	7%	20%
Bowel management	15	2	0	57	7	27	16	1	0	61	8	22	75	5	17%
	88%	12%	0%	63%	8%	30%	94%	6%	0%	67%	10%	23%	75%	5%	17%
BCW- transfer	16	1	0	51	18	24	16	1	0	59	14	20	74	13	16
	94%	6%	0%	55%	19%	26%	94%	6%	0%	63%	15%	22%	69%	14%	17%
Toilet transfer	16	1	0	51	15	27	16	1	0	61	12	20	73	10	17
	94%	6%	0%	55%	16%	29%	94%	6%	0%	66%	13%	22%	71%	11%	18%
W/W	14	3	0	50	15	28	16	0	1	64	13	16	79	16	15
	82%	18%	0%	54%	16%	30%	94%	0%	0%	69%	14%	17%	72%	15%	14%
Stairs	14	1	1	43	12	36	14	1	1	49	11	31	72	8	29
	88%	6%	6%	47%	13%	40%	88%	6%	6%	54%	12%	34%	62%	9%	30%
Total	14	2	0	11	64	18	15	1	0	57	14	18	73	17	15
	88%	12%	0%	12%	69%	19%	94%	6%	0%	64%	16%	20%	70%	16%	14%

(continued)

TABLE 2. (CONTINUED)

Time	Year 1		Year 2		Year 5		Year 10				
	TFC <28 days (n=17)	TFC ≥28 days (n=93)	TFC <28 days (n=17)	TFC ≥28 days (n=93)	TFC <28 days (n=17)	TFC ≥28 days (n=93)	TFC <28 days (n=17)	TFC ≥28 days (n=93)			
Command-following group											
Mode: Walk vs. W/C	Walk=16 W/C=1	Walk=62 W/C=30	Walk=17 W/C=0	Walk=63 W/C=29	Walk=16 W/C=1	Walk=60 W/C=32	Walk=16 W/C=1	Walk=63 W/C=29	Walk=79 W/C=30		
Cognition	15 88%	2 0%	0 60%	56 24%	13 14%	13 14%	3 18%	0 0%	60 65%	20 22%	11 10%
Expression	14 82%	3 18%	0 55%	26 17%	16 76%	15 24%	4 24%	0 0%	57 94%	26 28%	10 9%
Social Interact	15 88%	2 12%	0 0%	48 33%	31 15%	14 23%	3 18%	0 0%	51 29%	27 16%	15 9%
Problem solving	13 76%	4 24%	0 41%	38 37%	21 23%	14 30%	3 18%	0 0%	44 30%	28 35%	15 14%
Memory	11 65%	6 35%	0 0%	35 45%	42 17%	16 23%	4 24%	0 0%	40 39%	36 18%	17 13%
Total	7 41%	10 59%	0 0%	11 12%	64 69%	18 19%	7 41%	10 59%	17 18%	60 65%	13 11%

FIM, Functional Independence Measure; TFC, time to follow commands; W/C, wheelchair; I, independent; SA, some assistance; TD, total dependence; UB-Dressing, upper body dressing; LB-Dressing, lower body dressing; BCW, transfer, bed to chair transfer; W/W, walk/wheelchair.



**FIG. 2.** Multi-trajectory modeling of recovery patterns. Modeling revealed four distinct recovery patterns. Group 1 demonstrated poor recovery in all three functional domains at all time-points, with slightly greater cognitive and mobility improvement. Group 2 showed disproportionate mobility impairment at 1 year, but robust recovery in this and the other domains over time. Group 3 showed particular impairment in self-care at 1 year, but showed greater recovery in self-care and mobility than cognitive function for later follow-ups. Group 4 was high functioning at 1 year for all three domains, which continued through Year 10.

independence for the group. It is important to note that this study did not include the 91 individuals who expired before the 10-year mark, including 14 deaths between Years 5 and 10. This current study focuses solely on function (FIM) across years, requiring functional data at each of the intervals. Those who died during the 10-year follow up period could not be included in the study as they did not have FIM data at each of the four required follow up intervals. Data on death among individuals in the TBIMS cohort who are unable to follow commands at the time of rehabilitation admission have been previously studied using the TBIMS cohort.<sup>22</sup>

Prognostic formulations developed by clinicians and payers in relation to persons with TBI of the severities included in this study sample, particularly in the early post-injury period, need to incorporate the present study findings—and to avoid the tendency towards prognostic and therapeutic nihilism that has become too common in this area of medicine in recent decades. Table 1 and Figure 2 serve as useful tools for providers when considering the potential for recovery. Supplementary Figures 1–5 visually illustrate the proportion who are independent at each epoch using easy to understand daily activities. These figures may also aid in family education or counseling.

These data expand knowledge of long-term outcome after severe TBI and have direct implications for clinical care. Similar multicenter studies are needed to inform clinical decision-making in patients with non-traumatic brain injuries, as even less is known about long-term outcome in this population.<sup>23</sup>

### Study Limitations

Several limitations should be considered in interpreting and applying the study findings. The first consideration is statistical power, particularly for the analyses of the smaller subgroups. This limited the ability to test the significance of observed FIM changes in individual items. Another consideration is the effect of possible selection bias. This study only included individuals treated at an acute care hospital and transferred directly to acute inpatient rehabilitation for specialized brain injury care. Admission to acute inpatient rehabilitation may not be offered or payment authorized

for many who are not following commands. Consequently, it is unclear whether patients who are admitted to rehabilitation despite not following commands may differ from those who are not, or the degree to which intensive rehabilitation influenced the observed recovery trajectories. Further selection bias is possible through missed visits by requiring participant data across all follow up intervals, and survival bias due to exclusion of deaths. While improvement appears to continue over a decade of time among those who survive, this is counter balanced by a reasonably high mortality rate and loss to follow up raising the possibility of survivorship and ascertainment bias.

The subsample categorized as TFC 28 days or longer includes those who did command-following recover at some time-point and those who never regained command-following. As a consequence, the findings do not indicate how later recovery of command-following may alter subsequent functional achievements.

Some change may be due to measurement artifact. The FIM is an observational rating scale and follow-up FIM scores were based on self or proxy report. A change in rating from independent to need for some level of assistance may reflect differences in opinion across persons interviewed from one epoch to the next, or changes in perception by the same person.

Health policies, available technologies, research evidence, practice guidelines, and clinical care practices certainly have changed over the time, both during the 10-year follow up period for each individual and during the enrollment period for this study. Such factors may have influenced the outcomes and outcome trajectories of the study participants.

Finally, there may be unknown/unmeasured treatment differences between the TFC recovery groups. In general, the later TFC recovery groups had longer acute care length of stay, and the earlier TFC recovery groups had longer rehabilitation length of stay. It is unknown if the groups differed on receipt of therapy services and specialized medical follow up in the years that followed rehabilitation discharge. It is possible that those with earlier TFC recovery were perceived to have greater rehabilitation potential and therefore received more rehabilitation services over the years post-injury. What outcomes might have been observed with different



amounts and types of services is unknown. It is also possible that the longer rehabilitation stay permitted for those with earlier TFC recovery allowed for a better chance and/or longer time to recover command-following.

### Next Steps

The findings reported here represent a complex interplay between the natural history of severe brain injury, the effects of attitudes about prognosis, and healthcare and rehabilitation access. Negative functional trajectories coupled with negative caregiver and professional attitudes may contribute to service denials or the decision to withdraw care, either of which may contribute to further functional decline or mortality. Conversely, positive functional trajectories may drive more positive attitudes and greater service access, contributing to further functional improvement. Thus, future longitudinal research with larger samples should attempt to study the interplay over time between care transitions and functional change, to isolate the role that aggressive rehabilitation care can play in shaping long-term outcome.

### Conclusion

A substantial proportion of patients who are unable to follow commands upon inpatient rehabilitation admission achieve independence in cognitive, mobility, and self-care functions with improvements evident up to 10 years post-injury. A greater proportion of those who recovered command-following early (i.e., <28 days) achieved independence. While most functional recovery occurs by 1-year post-injury, improvements may occur over a more prolonged interval, particularly in those who regain command-following after 28 days post-injury. Late functional decline appears to be infrequent in this population that survived to Year 10. These findings suggest individuals with DOC may benefit from ongoing functional monitoring and updated care plans during the post-acute phase. Our findings can inform clinical decision-making, prognosis, and treatment planning.

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