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COMMENT & RESPONSE

Traumatic Brain Injury Recovery Trajectories in Patients With Disorders of Consciousness

To the Editor We congratulate Kowalski et al[1] for their longitudinal nested cohort of patients with moderate to severe traumatic brain injury (TBI) using the long-standing, federally supported Traumatic Brain Injury Model Systems (TBIMS) National Database,[2] which has 3 decades of follow-up. Their findings are remarkable in that the majority (82%) of initially comatose patients recovered consciousness after a stay in an inpatient rehabilitation center. More impressive is that 2 of 5 patients with disorders of consciousness (DOC) regained either partial or full independence. However, there are several interesting limitations that we thought were worth highlighting to the *JAMA Neurology* readership.

As the authors note, this represents a cohort of patients who were discharged from an acute care hospital to an inpatient rehabilitation center. Often a condition of acceptance to an inpatient rehabilitation hospital in the United States is insurance status. The parent TBIMS National Database cohort eligibility and selection procedures create a TBI sample that is more privileged, and with higher socioeconomic standing, than the larger TBI population with and without health insurance.[3] This sample and selection bias would limit these results' real-world applicability, as approximately 20% to 40% of trauma patients are classified as uninsured or self-pay, depending on the institution.[4,5]

Notably, at the time of admission to inpatient rehabilitation under the TBIMS umbrella, only 12% had a persistent DOC, improved from 57% on presentation. While only 2% were discharged from inpatient rehabilitation with DOC, it is clear the overall trajectory of this cohort during hospitalization and prior to rehabilitation was already toward an encouraging recovery. That said, we still find these results quite impressive and agree with the message that there should be caution in withdrawing or withholding support after severe TBI based on DOC. Shared and informed decision-making with surrogates and family members is ideal, given the potential for recovery, often only seen posthospitalization. We also fear false hope may be instilled in families at time of injury that more than 80% of comatose patients will recover.

We feel this study provides strong insight into the importance of recovery time and post-acute care rehabilitation in the continuum of management of a specific cohort of patients with TBI that are eligible for postdischarge inpatient rehabilitation. We hope for further work to expand the population receiving rehabilitation to patients of all socioeconomic backgrounds, irrespective of insurance status, to determine more widespread and equitable applicability of these encouraging findings.

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To the Editor We read the article by Kowalski et al[1] on the recovery of consciousness in 17 470 patients with traumatic brain injury (TBI) with interest. Eighty-two percent of patients with disorders of consciousness (DOC) showed recovery of consciousness after clinical rehabilitation, defying the often ill-informed therapeutic nihilism that families of many such patients encounter. Prolonged DOC, such as the unresponsive wakefulness syndrome and minimally conscious state (MCS), are devastating conditions, but with the right treatment, some patients can recover to a meaningful outcome.

The criteria used to identify patients with DOC in this study, however, allow for the inclusion of conscious patients with less severe impairments. In the Kolwalski et al article, DOC is defined by a Glasgow Coma Scale M score of less than 6 and recovery of consciousness as M = 6. However, command following can be impaired by causes much more prevalent than DOC, such as language disorders and posttraumatic confusion. In comparison, Bruno et al[2] used the JFK Coma Recovery Scale-Revised, considered the gold standard for postacute consciousness assessment, in their study of 88 patients with TBI with DOC.[3] They registered recovery of consciousness, defined as emergence from MCS, in only 23% of patients with unresponsive wakefulness syndrome and 48% of patients with MCS after 12 months' follow-up. The definition of MCS– requires visual fixation/pursuit, localization to noxious stimulation, object manipulation, or automatic motor response, whereas MCS+ requires reproducible movement to command, object recognition, intelligible verbalization, or nonfunctional but intentional communication. The definition of emergence from MCS is even more stringent and requires functional object use or functional communication. The rationale behind this stringency is to identify the patients whose consciousness recovers in such a way to allow for meaningful interaction with the outside world.

Patients who only follow commands inconsistently would still qualify as being in an MCS according to the JFK Coma Recovery Scale-Revised, whereas they would qualify for recovery of consciousness within the Kowalski et al study. This difference in approach is crucial while evaluating the relevance of this reported 82% recovery. Indeed, in those who entered rehabilitation with DOC, the median Functional Independence Measure score only reached 71 (still requiring professional assistance) after rehabilitation. For ischemic stroke, such an outcome is considered unacceptable by many health care workers and (older) patients.[4,5] Although we agree with Kowalski et al that a healthy amount of caution is warranted in making decisions regarding withdrawal of care in the acute phase after TBI, we believe too optimistic expectations regarding the long-term outcome should be prevented as well.

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In Reply We thank Arnts et al and Smith et al for their insightful comments on our article[1] showing that almost all survivors of traumatic brain injury with a disorder of consciousness (DOC) early after injury recover consciousness by the end of inpatient rehabilitation, and a substantial proportion regain functional independence.

Our article defined DOC as failure to follow commands, assessed with the motor component of the Glasgow Coma Scale (GCS) (GCS motor score <6) or the Disability Rating Scale (Disability Rating Scale motor score >0). Arnts et al question the specificity of this approach, particularly the motor score's ability to distinguish DOC from other impairments such as language disorders. They suggest the JFK Coma Recovery Scale-Revised (CRS-R)[2] is the gold standard for DOC and a better measure of recovery of consciousness.

We acknowledge these concerns about the definition of DOC. While command following is an imperfect measure of DOC, we believe it is justified in this context for several reasons. First, at present, routine use of the CRS-R in acute care is uncommon. Second, the CRS-R is equally subject to language and attentional confounds. Third, while other measures such as a GCS total score of 8 or less conventionally have denoted "coma" in previous literature,[3] the motor score is increasingly accepted as a more appropriate measure of neurologic status, and outcome prediction, in intubated patients. For replication of our study results, we believe the motor score is arguably a superior definition for coma because of the reduced complexity of this component of the GCS, its ease of administration at the bedside, improved interrater reliability,[4] and the obvious advantage of applicability for intubated patients.

Smith et al suggest potential selection bias favoring better outcomes in the study sample. Although we do not know with certainty the effect of rehabilitation referral bias on outcome, and cannot know this without a randomized clinical trial

in which patients with TBI are either referred or not referred to inpatient rehabilitation, we do not believe current referral practices systematically favor patients with a more favorable prognosis, regardless of socioeconomic status. There are no established, validated clinical criteria that identify a higher probability of recovery of consciousness in patients with traumatic DOC. This is true both for acute care professionals, and for rehabilitation admissions decision makers. Among patients with TBI, several reports found that some social and demographic considerations played a larger role in rehabilitation referral than severity of injury or presence of DOC.[5] Previous reports estimated approximately 13% of patients with moderate and severe TBI receive subsequent rehabilitation.[6] Overall, there is a lack of uniformity in referral patterns for patients with TBI to rehabilitation,[5] suggesting a selection bias favoring patients with better prognosis is unlikely.

The idea of "false hope" is subjective. While we cannot quantify how representative outcomes in our study are, they point to improved recovery with more extensive care. We agree that access to treatment following TBI should not be dictated by insurance/funding considerations but rather patient disease/injury factors. Finding solutions to this dilemma remains a challenge for the neurological trauma community serving these patients.

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CORRECTION

Error in Figure: In the Original Investigation titled "Infection Risks Among Patients With Multiple Sclerosis Treated With Fingolimod, Natalizumab, Rituximab, and Injectable Therapies,"[1] published in the February 2020 issue, the y-axis was incorrect in the Figure. The data should span 87% to 100% rather than 15% to 100%. This article has been corrected online.

1. Luna G, Alping P, Burman J, et al. Infection risks among patients with multiple sclerosis treated with fingolimod, natalizumab, rituximab, and injectable therapies. *JAMA Neurol*. 2020;77(2):184-191. doi:10.1001/jamaneurol.2019.3365