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Global disability trajectories over the first decade following Combat Concussion.

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Abstract

Objective: To examine global disability trajectories in US military with and without traumatic brain injury(TBI) over the first decade following deployment to identify risk profiles for better intervention stratification, hopefully reducing long-term cost.

Setting: Patients and participants were enrolled in combat or directly following medical evacuation at the time of injury and followed every 6 months for 10 years.

Participants: There are four main groups(n=475); two primary, two exploratory: (1) combat-deployed controls without history of blast exposure 'non-blast-control' (n=143), (2) concussive blast TBI 'blast-TBI' (n=236) (primary), and (3) combat-deployed controls with history of blast exposure 'blast-control' (n=54), (4) patients sustaining a combat concussion not from blast 'non-blast-TBI' (n=42) (exploratory).

Design: Prospective, observational, longitudinal study.

Main Measures: Combat concussion, blast exposure and subsequent head injury exposure over the first decade post-deployment. Global disability measured by the Glasgow Outcome Scale Extended (GOSE).

Results: Latent class growth analysis identified four main trajectories of global outcome, with service members sustaining combat concussion 37–49 times more likely to be in the higher disability trajectories than non-blast-controls (blast-TBI OR 49.33, CI 19.77–123.11 $p<0.001$, non-blast-TBI OR 37.50, CI 10.01–140.50, $p<0.001$). Even blast-exposed-controls were 5 times more likely to be in these lower disability categories compared to non-blast-controls (OR 5.00, CI 1.59–15.99, $p=0.007$). Adjustment for demographic factors and subsequent head injury exposure did not substantially alter these odds ratios.

Conclusions: Very high odds of poor long-term outcome trajectory was identified for those who sustained a concussion in combat, were younger at the time of injury, had lower education, and enlisted in the Army above the risk of deployment alone. These findings help identify a risk profile that could be used to target early intervention and screen for poor long-term outcome to aid in

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reducing the high public health cost and enhance the long-term quality of life for these service members following deployment.

Keywords

concussion; global disability; military; veteran; long-term outcome; trajectory analysis

INTRODUCTION

Annual costs for US combat-related traumatic brain injury (TBI) have been previously estimated to be between $591–910 million[1]; however, this is now thought to be grossly underestimated. Additionally, it has been reported that peak disability payout for veterans of world conflicts is incurred decades after the conflict is over[2]. World War 1 (1917–1918) disability cost reportedly peaked in 1969, World War II (1941–1945) disability cost reportedly peaked in 1980, and Vietnam (1959–1975) disability cost was still on the rise in 2011 when reported[3]. With the conflicts in the middle east (2001-Present) as defined by US policy already exceeding cost projections, the true impact is likely not to be felt for decades[4]. Recent efforts have demonstrated that annual health care costs for veterans with mild TBI, the majority of TBIs in combat, were 2–3 times higher than those without mild TBI with greatest cost utilization in the behavioral health domain[5]. This has, and remains, a major public health burden, as this population ages, motivating efforts to understand these global disability trajectories in our service men and women.

To our knowledge, global disability trajectories over the first decade following TBI have primarily been studied in more moderate to severe civilian cases using the Glasgow Outcome Scale Extended[6,7] (GOSE)[8,9]. In the study by Dr. Dams-O'Connor and colleagues, GOSE trajectories were explored in the US-based TBI-Model Systems study to understand the difference between TBI patients who survived and those who died within the first decade post-injury[8]. In a Finnish population-based cohort, Dr. Forslund and colleagues reported on GOSE trajectories over the first decade post-TBI finding that key demographic and injury metrics such as duration of post-traumatic amnesia were predictive of decline in later years[9].

Additionally, there have been a small number of studies that have reported incremental GOSE disability over this time period in largely moderate to severe civilian brain injury. An example is the study by Dr. Ponsford and colleagues, where GOSE disability scores were reported 2, 5, and 10-years post-injury across the TBI severity spectrum[10]. While this sheds light on the longer-term impact of these moderate to severe civilian brain injuries, questions remain regarding similar trajectories in milder forms of brain injury, particularly in the service member and veteran populations.

Through the "Evaluation Of Longitudinal outcomes in mild TBI Active-Duty Military and Veterans" (EVOLVE) study, we have been provided the unique opportunity to examine GWoT service members with combat-related concussion, at the point of injury in combat, or after medical evacuation to Landstuhl Regional Medical Center in Germany, and follow them out to 1-year[11,12], 5-year[13,14], and now 10-year outcome. In parallel, we have followed non-brain-injured combat-deployed services members for comparison. Through this, the GOSE has been collected every 6 months on these patients and participants. The objective

of the current study was to use latent class growth analysis to determine global disability outcome trajectories and characterize the profile of the patients in those trajectories. The hope was to understand who is most at risk of a poor long-term outcome to help focus earlier targeted intervention with the ultimate goal of reducing the extremely high public health cost documented following prior conflicts.

METHODS

Participants

This study was approved by the University of Washington Institutional Review Board with additional approval from the US Army Medical Research and Materiel Command Institutional Review Board and carried out in accordance with the approved protocol. Consent and subsequent reconsent for each follow-up evaluation were provided by all participants according to the Declaration of Helsinki; no surrogate consent was allowed.

Design and Procedure

Participants were originally enrolled into one of four previous cohorts from 2008–2013[11–13,15,16] (See Table 1 for Demographics). This is a prospective, observational, longitudinal study that has followed these very same patients for 10 years. There are four main groups (n=475), two primary and two exploratory: (1) combat-deployed controls without history of blast exposure ‘non-blast-control’ (n=143), (2) concussive blast TBI ‘blast-TBI’ (n=236) (primary), and (3) combat-deployed controls with history of blast exposure ‘blast-control’ (n=54) (4) patients sustaining a combat concussion not arising from blast ‘non-blast-TBI’ (n=42) (exploratory). Inclusion criteria have been reported elsewhere[11,12,16]. Briefly, inclusion criteria were defined as service members, deployed to the combat theatre, in which original enrollment was completed either directly in Afghanistan[11] or following medical evacuation to Landstuhl Regional Medical Center in Germany[12,16]. For the TBI groups, TBI diagnosis was determined by trained medical personnel working in the TBI clinics in Afghanistan or Germany using the same protocol. First the Military Acute Concussion Evaluation (MACE) was administered by clinic staff followed by examination for diagnosis corroboration by a TBI Neurologist. For the concussive blast TBI group, all available clinical histories indicated blast exposure plus another mechanism of head injury such as a fall, motor vehicle crash, or being struck by a blunt object. None suffered an isolated blast injury. All concussive-blast and non-blast TBI patients met the Department of Defense definition for mild, uncomplicated traumatic brain injury[17] defined as GCS 13–15, LOC 0–30 minutes, AOC less than 24 hours, PTA less than 24 hours, and unremarkable CT or MRI at the time of evaluation. For the control groups, all combat-deployed controls were clinically evaluated to be free of signs and symptoms of head injury for both the ‘non-blast’ and ‘blast’ control groups and additionally no history of blast exposure for the ‘non-blast-control’ group. Prior psychiatric and TBI diagnoses were exclusions for all groups and were ascertained both by clinician evaluation as noted above, patient-reported history, as well as medical records review at the time of screening.

Measurement of Disability

Through these efforts 475 participants have been prospectively enrolled and assessed over the phone with the Glasgow Outcome Scale Extended (GOSE)[6] at a six-month frequency. These data were leveraged to understand trajectories of global disability outcome in the first decade following enrollment during deployment. The GOSE is scored from 1–8: 1=dead, 2=vegetative, 3–4=severe disability, 5–6=moderate disability, 7–8=good recovery. Moderate disability (GOSE = 5–6) is defined as one or more of the following: 1) inability to work to previous capacity, 2) inability to resume much of regular social and leisure activities outside the home, 3) psychological problems which have frequently resulted in ongoing family disruption or disruption of friendships. Severe disability (GOSE = 3–4) is defined as one or more of the following: 1) inability to drive and/or travel locally without assistance, 2) inability to shop or run errands without assistance, 3) support required for activities of daily living. Standardized, structured interviews were performed per published guidelines[6,7]. Participants were instructed to consider deployment and for those with concussion, the brain injury, as the reference point for this interview and to compare current functional level to that pre-deployment. As the GOSE can be administered multiple ways, the decision was made to focus on disability from the brain injury in contrast to disability from all bodily injuries of which there were minimal across groups (enrollment ISS mean ± stdev, non-blast control 0.15±1, blast control 0.26±0.96, blast TBI 1.43±2.91, non-blast TBI 1.64±3.87). Also utilized was the consideration of subsequent head injury exposure which was revisited at each study wave (1-year, 5-year, 10-year) and inquired about with each GOSE evaluation. This included a TBI history intake interview modified from the Brain Injury Screening Questionnaire (BISQ)[18] to include more military-specific and combat-specific scenarios, to confirm life history of head injury exposure and identify any subsequent head injuries sustained since last evaluation.

Statistical Analysis

Analysis was completed January to April 2021. GOSE data were analyzed using latent class growth analysis, in which subjects are hypothesized to be clustered into unobserved longitudinal trajectory classes[19] based on individual response patterns. We chose this method over mixed effects regression because it does not assume that all members of an injury or control group have a similar outcome. Rather it looks for participants with similar levels and patterns of outcome, called trajectory groups, and then examines these trajectory groups to identify the characteristics of the participants belonging to them. As is suggested, multiple candidate trajectory models were estimated, varying both the number (4–5 based on BIC, Bayesian Information Criteria) and shape of the trajectory curves (linear, quadratic, cubic although cubic was ruled out due to lack of significance) and a single model was selected based on fit indices criteria including BIC, posterior probability, minimum class-size, interpretability, and parsimony[20]. All of the models reviewed classified the observed deaths into their own trajectory. The decision was made to narrow the search to just the 4-class models, as this was the maximum number that consistently yielded class-sizes between 10–50% (excluding the deaths) and posterior probabilities all above 80%. Among the 4-class models, consideration was given to various combinations of cubic effects among the individual trajectories, evaluating each on significance, fit indices, and resulting class-size. In the end, the model containing only linear and quadratic effects was

selected for the analysis, as it minimized BIC among those with sufficient class sizes and had the added feature of parsimony.

Differences in demographic characteristics among the four trajectory groups were assessed for statistical significance using Kruskal-Wallis tests for continuous/ordinal variables and Fisher's exact tests for categorical variables. Group-membership in each trajectory (excluding the worst due to low membership) was modelled using nominal logistic regression. Univariable significance was used initially to identify potential predictors, and a multivariable model was constructed controlling for sex and other demographic variables found to be significant in the univariable analysis. A sensitivity analysis was also carried out on the subset of patients with known status of subsequent head-injury exposure (SHIE) since the time of enrollment to investigate whether additional head injury exposures impacted global outcome and subsequently this modelling. All reported p-values are reported prior to adjustment for multiple comparisons. A Benjamini-Hochberg false discovery rate of 5% was then applied across the entire set of p-values for each table, with those that did not remain statistically significant explicitly noted[21].

The trajectory analyses were carried out in SAS[22] statistical software version 9.4 using the 'proc traj' application available for free download at https://www.andrew.cmu.edu/user/bjones[23]. Additional statistical analyses were carried out in SPSS version 26. P-values of .05 or lower were considered significant.

RESULTS:

Figure 1 shows the latent class growth trajectories identified by model fitting. Dotted lines indicate the model trajectory and black vertical lines show the confidence intervals at each time point while solid lines indicate the group means for each trajectory. Four primary trajectories were identified with corresponding mean GOSE values over the first 10 years following deployment displayed for comparison. As the study sought to collect GOSE evaluations from every service member, patient or control, every 6 months, the general frequency of the GOSE scores as shown is biannual. The primary GOSE disability range corresponding to each trajectory included: good recovery (Trajectory 1), upper moderate disability (Trajectory 2), lower moderate disability (Trajectory 3), and death (Trajectory 4). There were no appreciable differences in follow-up rates at each time point among the trajectories and so for this outcome analysis, the missingness was assumed to be random. As we previously reported, all of the known deaths to date were in blast exposed service members and were primarily death by suicide[14]. It is worth noting that even Trajectory 1, the good recovery trajectory, was found to have a downward trend beginning around year 8.

As we enrolled both combat concussion and combat-deployed controls, this provided the opportunity to examine whether concussion exposure may impact the service member's long-term outcome separate from deployment exposure. By group, 143 non-blast-controls, 54 blast-controls, 236 blast-TBI, and 42 non-blast-TBI were followed (Table 1). While there was no significant difference in sex or race across the trajectories, there were significant differences by trajectory group in the proportion of each study group, age, education, military rank, branch of service, and where captured, SHIE. Evaluation of the missingness

of SHIE by patient group did not reveal any significant differences across trajectories (p=0.47, N.S.). As military rank is a surrogate for education and there were a few missing entries for education but complete reporting on military rank, all subsequent analyses were interrogated and adjusted for military rank along with patient group, age, and branch of service. Given the interest in sex as a biological variable possibly impacting outcomes, we included sex in all further analyses as well even though there were no significant differences across trajectories. As SHIE since enrollment in combat was captured in a proportion of the sample, further analysis focusing just on this subsample was also examined.

Univariable analysis of patient group, age, sex, military rank, and branch of service from the entire cohort were compared among trajectories (Table 2). Overall, each parameter other than sex was found to be significantly related to the GOSE trajectories. As the death trajectory (Trajectory 4) had very few members, comparative analysis focused on the top three trajectories using multinomial logistic regression modeling. Comparing the lower moderate disability trajectory (Trajectory 3) to the good recovery disability trajectory (Trajectory 1) we found that participants were much more likely to have sustained a concussion in combat (OR 49.33 blast-TBI, OR 37.50 non-blast-TBI, $p<0.001$ for both compared to non-blast control) and more likely to have been enlisted (OR 24.90, p=0.002). Blast-controls still had five times the odds of being in the lower-moderate disability category than non-blast-controls (OR 5.00 blast control, p=0.007). They also had four times the odds of having served in the Army (OR 4.58, $p<0.001$) and were more likely to be younger (OR 1.45, p=0.03 per 10-year decrease), though the latter did not remain significant after adjustment for multiple comparisons. Comparing the upper moderate disability trajectory (Trajectory 2) to the good recovery disability trajectory (Trajectory 1) again revealed a similar profile with odds ratios of smaller magnitude although with similar significance. Those who fell into Trajectory 2, were more likely to have sustained a concussion in combat (OR 13.67 blast-TBI, OR 8.36 non-blast-TBI, $p<0.001$ for both compared to non-blast-control) or have sustained blast exposure (OR 3.32 blast-control, p=0.001), and more likely to have been enlisted (OR 3.80, $p<0.001$). They were also more likely to be younger (OR 1.93, $p<0.001$ per 10-year decrease). Comparing the two middle trajectories of lower moderate disability group to the upper moderate disability group, we found the lower moderate disability group was significantly more likely to have sustained a concussion in combat (OR 3.61 blast-TBI, p=0.002, OR 4.48 non-blast-TBI, p=0.003) and have been in the Army (OR 2.95, p=0.003) compared to the upper moderate disability group.

Univariable analysis was followed by multivariable analysis of the entire sample adjusting for patient group, age, sex, military rank, and branch of service (Table 3). Comparing the lower moderate disability trajectory (Trajectory 3) to the good recovery disability trajectory (Trajectory 1) by multivariable regression further confirmed the higher odds of combat concussion to the worse disability trajectories. Patients in Trajectory 3 had over 40 times the odds of having sustained a blast-related concussion and over 30 times the odds of having sustained a non-blast concussion compared to non-blast-controls (OR 43.31 blast-TBI, OR 31.06 non-blast-TBI, $p<0.001$ for both) and still more likely to have been enlisted (OR 14.93, p=0.01). Among those not sustaining a concussion in combat, they had four times the odds of having experienced blast exposure (OR 4.09 blast-controls, p=0.02). Comparing the upper moderate disability trajectory (Trajectory 2) to the good recovery disability trajectory

(Trajectory 1) by multivariable regression again revealed a similar profile with odds ratios of smaller magnitude although with similar significance. Interestingly, comparing the two middle trajectories of lower moderate disability group to the upper moderate disability group by multivariable regression still found a greater odds of those in the worse disability trajectory for combat concussion (OR 3.70 blast-TBI, p=0.002; OR 4.08 non-blast-TBI, p=0.01).

To account for the possible relationship of subsequent head injury exposure to these outcome trajectories, we performed a sensitivity analysis using multivariable regression on the subset where SHIE was captured (Table 4). In this subset analysis, SHIE was not found to add predictive power to the model compared to the other measures examined (overall p=0.17). Given that the general significance stayed roughly the same for the other factors, we interpret this non-significant contribution to also mean that it is not likely confounding the effect of other measures in our models that include the entire cohort (Table 2 and Table 3).

DISCUSSION:

In summary we found very high odds of being in a trajectory of worse long-term outcome for those who sustained a concussion in combat and were younger at the time of exposure well above the risk of deployment alone. Furthermore, the risk profile included those with lower education and those who had enlisted in the Army. Also worth noting, was the downward trend even in the highest functioning group which included the majority of combat-deployed controls starting around the 8-year mark post-deployment. Taken together, we believe these findings help inform targeting of more aggressive treatment strategies in service members meeting this profile of greatest risk following deployment to aide in reducing the extremely high public health burden identified with prior conflicts. Additionally, this trajectory analysis brings to light the long-term effects of these seemingly more mild brain injuries which we have also seen substantiated by continued evolution of both clinical outcome measures[14] and neuroimaging[13] changes in these very same patients. This study adds to the literature on global disability trajectories previously focused on moderate to severe civilian TBI[8–10], by extending the findings to the service member population with milder brain injuries.

Strengths of the study include the prospective, observational, longitudinal study design with initial evaluation at the point of injury reducing the likelihood of recall bias which often plagues chronic injury studies, the repeated collection of the primary outcome measure (GOSE) every 6 months over the 10-years of follow up evaluation to date providing granularity to the trajectory data, the relatively robust sample size in our two primary groups of non-blast-controls and blast-TBI, utilization of two different control groups and TBI groups to be able to directly examine impact of combat exposure plus head injury via blast or non-blast mechanism relative to combat exposure alone, as well as impact of sub-concussive blast injuries in our blast-control patients, and consideration of additional head injury exposures that may have ensued since original enrollment in the study.

Limitations of this study include the inability to control for the heterogeneity of treatment centers in the United States in which our patients and participants sought care and the impact this may have on global disability outcome, lack of pre-deployment information that could have yielded insight into baseline global disability, the relative paucity of female service members at the time of enrollment to more adequately examine sex as a biological variable, and unmeasured covariates that may have influenced the outcome trajectories.

Overall, the United States is facing a rapidly expanding public health burden from these conflicts as mortality rates have notably decreased but morbidity rates have substantially risen. Survival does not come without financial and psychological costs to the service members, their families, and the community. There are over 23 million US veterans of all previous conflicts alive today with TBI diagnosis from prior conflicts[24] and mild TBI in particular from recent conflicts[25,26] impacting 20%[25,27]–40%[24] of this population; even a small increase in life quality could have significant impact on reducing the public health burden. We believe by being informed from longitudinal studies such as this one, the medical community can be proactive in mitigating the potentially negative and extremely costly impact of these combat-related injuries.

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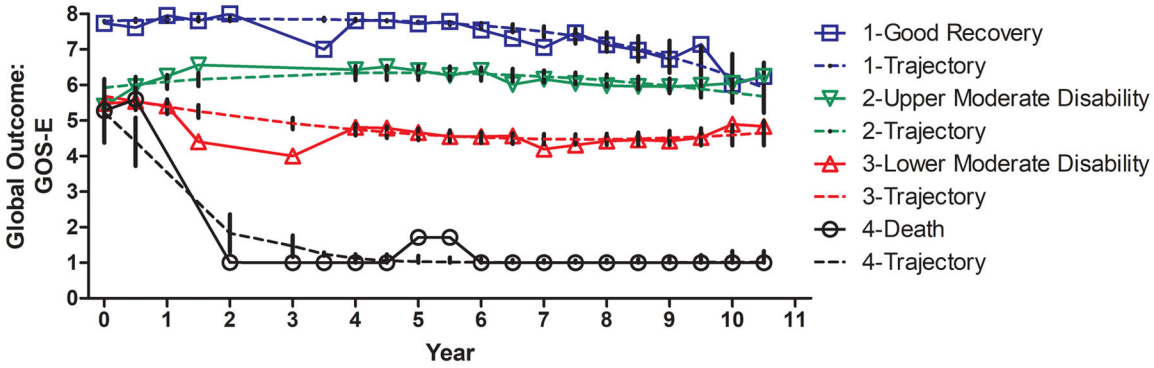

Figure 1.

Latent Growth Class Trajectories of Global Disabilty in the first Decade following Combat Concussion

Table 1.

Patient Demographics by GOSE Latent Class Growth Trajectory

	Overall	Trajectory 1 n (%)	Trajectory 2 n (%)	Trajectory 3 n (%)	Trajectory 4 n (%)	P-Value
Main GOSE Disability Level of Trajectory		**Good Recovery**	**Upper Moderate**	**Lower Moderate**	**Death**	
Total Number of Patients	475	113	251	104	7	
Patient Group						
Non-blast-Controls	143	80 (71%)	55 (22%)	8 (8%)	0 (0%)	<0.001
Blast-Controls	54	14 (12%)	32 (13%)	7 (7%)	1 (14%)	
Blast-TBI	236	15 (13%)	141 (56%)	74 (71%)	6 (86%)	
Non-blast-TBI	42	4 (4%)	23 (9%)	15 (14%)	0 (0%)	
Age						
Mean (St Dev)	29.5 (7.9)	32.3 (8.5)	28.1 (7.1)	29.7 (8.1)	29.6 (9.5)	<0.001
Sex						
Male	439 (92%)	100 (88%)	233 (93%)	99 (95%)	7 (100%)	0.29
Female	36 (8%)	13 (12%)	18 (7%)	5 (5%)	0 (0%)	
Education (Years)						
Mean (St Dev)	13.7 (2.3)	15.2 (3.1)	13.4 (1.8)	13.1 (1.7)	12.3 (1.0)	<0.001
Military Rank						
Enlisted	437 (92%)	91 (81%)	236 (94%)	103 (99%)	7 (100%)	<0.001
Officer	38 (8%)	22 (19%)	15 (6%)	1 (1%)	0 (0%)	
Race						
Caucasian	347 (73%)	86 (76%)	186 (74%)	70 (67%)	5 (71%)	0.36
African-American	64 (13%)	15 (13%)	37 (15%)	12 (12%)	0 (0%)	
Hispanic/Latinx	53 (11%)	9 (8%)	23 (9%)	19 (18%)	2 (29%)	
Asian / Pacific Islander	7 (2%)	2 (2%)	3 (1%)	2 (2%)	0 (0%)	
Other	4 (1%)	1 (1%)	2 (1%)	1 (1%)	0 (0%)	
Branch of Service						
Army	368 (77%)	76 (68%)	191 (76%)	94 (90%)	7 (100%)	<0.001
Marines	50 (11%)	7 (6%)	35 (14%)	8 (8%)	0 (0%)	
Navy	30 (6%)	14 (12%)	15 (6%)	1 (1%)	0 (0%)	
Air Force	27 (6%)	16 (14%)	10 (4%)	1 (1%)	0 (0%)	
Subsequent Head Injury Exposure						
0	222 (47%)	70 (62%)	104 (41%)	48 (46%)	0 (0%)	<0.001
1	73 (15%)	10 (9%)	39 (16%)	24 (23%)	0 (0%)	
2+	47 (10%)	4 (4%)	20 (8%)	22 (21%)	1 (14%)	
Not Captured	133 (28%)	29 (25%)	88 (35%)	10 (10%)	6 (86%)	

Statistical significance by Kruskal-Wallis and Fisher's Exact as appropriate.

Table 2.

Univariable Analysis of GOSE Trajectories

	Overall P-Value	Lower Moderate vs. Good Recovery			Upper Moderate vs. Good Recovery			Lower Moderate vs. Upper Moderate		
		OR	95% CI	P-Value	OR	95% CI	P-Value	OR	95% CI	P-Value
Patient Group	<0.001									
Blast-Control vs Non-blast-Control		5.00	(1.56,15.99)	0.007	3.32	(1.63,6.80)	0.001	1.50	(0.50,4.54)	0.47
Blast-TBI vs Non-Blast-Control		49.33	(19.77,123.11)	<0.001	13.67	(7.26, 25.76)	<0.001	3.61	(1.63, 7.98)	0.002
Non-blast-TBI vs Non-blast-Control		37.50	(10.01,140.50)	<0.001	8.36	(2.74, 25.53)	<0.001	4.48	(1.67,12.02)	0.003
Blast-TBI vs Non-Blast-TBI		1.32	(0.38, 4.52)	0.66	1.63	(0.50,5.36)	0.42	0.80	(0.40,1.63)	0.55
Age										
(per 10yr decrease)	<0.001	1.45	(1.05,2.01)	0.03	1.93	(1.46,2.56)	<0.001	0.75	(0.55,1.02)	0.07
Sex										
(Male vs. Female)	0.17	2.57	(0.88,7.49)	0.08	1.68	(0.79,3.57)	0.17	1.53	(0.55,4.23)	0.41
Military Rank										
(Enlisted vs Officer)	<0.001	24.90	(3.29,188.42)	0.002	3.80	(1.89,7.66)	<0.001	6.55	(0.85,50.22)	0.07
Branch of Service										
(Army vs. Other)	<0.001	4.58	(2.14,9.80)	<0.001	1.55	(0.95,2.53)	0.08	2.95	(1.45,6.03)	0.003

Estimates based on multinomial logistic regression modeling, with the death trajectory excluded due to low cell counts.

OR – Odds Ratio, CI – Confidence Interval

All significant p-values ($p<.05$) remained so after applying a Benjamini-Hochberg 5% false discovery rate (m=29)

Table 3.

Multivariable Analysis of GOSE Trajectories

	Overall P-Value	Lower Moderate vs. Good Recovery			Upper Moderate vs. Good Recovery			Lower Moderate vs. Upper Moderate		
		OR	95% CI	P-Value	OR	95% CI	P-Value	OR	95% CI	P-Value
Patient Group										
Blast-Control vs Non-blast-Control	<0.001	4.09	(1.25,13.41)	0.02	3.51	(1.67,7.39)	0.001	1.16	(0.38,3.58)	0.79
Blast-TBI vs Non-Blast-Control		43.31	(16.64,112.72)	<0.001	11.70	(5.99,22.87)	<0.001	3.70	(1.62,8.47)	0.002
Non-blast-TBI vs Non-blast-Control		31.06	(8.10,119.10)	<0.001	7.62	(2.46,23.58)	<0.001	4.08	(1.48,11.25)	0.01
Blast-TBI vs Non-Blast-TBI		1.39	(0.39,4.94)	0.61	1.54	(0.46,5.09)	0.48	0.91	(0.43,1.92)	0.80
Age										
(per 10yr decrease)	0.02	0.85	(0.56,1.30)	0.46	1.34	(0.95,1.90)	0.10	0.64	(0.46,0.89)	0.01
Sex										
(Male vs. Female)	0.65	1.01	(0.27,3.84)	0.99	0.70	(0.28,1.76)	0.45	1.44	(0.48,4.32)	0.52
Military Rank										
(Enlisted vs Officer)	0.005	14.93	(1.74, 128.02)	0.01	2.42	(1.01,5.76)	*0.05	6.18	(0.77,49.55)	0.09
Branch of Service										
(Army vs. Other)	0.07	2.16	(0.90,5.21)	0.09	0.96	(0.53,1.73)	0.89	2.26	(1.08,4.72)	*0.03

Estimates based on multinomial logistic regression modeling, with the death trajectory excluded due to low cell counts.

OR – Odds Ratio, CI – Confidence Interval

*Unless noted, all significant p-values (p<.05) remained so after applying a Benjamini-Hochberg 5% false discovery rate (m=29)

Table 4.

Multivariable Analysis of GOSE Trajectories in the subset with known Subsequent Head Injury Exposure

	Overall P-Value	Lower Moderate vs. Good Recovery			Upper Moderate vs. Good Recovery			Lower Moderate vs. Upper Moderate		
		OR	95% CI	P-Value	OR	95% CI	P-Value	OR	95% CI	P-Value
Patient Group										
Blast-Control vs Non-blast-Control	<0.001	3.26	(0.82,12.99)	0.09	2.75	(1.13,6.89)	*0.03	1.19	(0.33,4.33)	0.79
Blast-TBI vs Non-Blast-Control		80.84	(23.88,273.67)	<0.001	17.28	(6.90,43.29)	<0.001	4.68	(1.76,12.41)	0.002
Non-blast-TBI vs Non-blast-Control		95.85	(10.26,895.25)	<0.001	17.10	(2.10,139.33)	0.01	5.61	(1.72,18.26)	0.004
Blast-TBI vs Non-Blast-TBI		0.84	(0.09,7.58)	0.88	1.01	(0.11,8.94)	0.99	0.83	(0.35,1.98)	0.68
Age										
(per 10yr decrease)	0.07	0.58	(0.33,1.00)	*0.05	0.87	(0.55,1.37)	0.55	0.67	(0.45,0.98)	*0.04
Sex										
(Male vs. Female)	0.13	0.36	(0.07,1.81)	0.22	0.30	(0.09,0.99)	*0.05	1.20	(0.37,3.93)	0.76
Military Rank										
(Enlisted vs Officer)	0.22	33.83	(3.40,336.38)	0.003	4.51	(1.60,12.74)	0.004	7.50	(0.85,65.85)	0.07
Branch of Service										
(Army vs. Other)	<0.001	1.89	(0.68,5.26)	0.23	0.93	(0.45,1.91)	0.84	2.04	(0.89,4.66)	0.09
Subsequent Head Injury Exposure										
1 vs. 0	0.17	2.19	(0.80,6.04)	0.13	1.68	(0.69,4.10)	0.26	1.31	(0.68,2.51)	0.42
2+ vs. 0		3.36	(0.89:12.71)	0.07	1.62	(0.47:5.65)	0.45	2.07	(0.99:4.32)	*0.05

Estimates based on multinomial logistic regression modelling, with the death trajectory excluded due to low cell counts.

OR – Odds Ratio, CI – Confidence Interval

*Unless noted, all significant p-values (p<.05) remained so after applying a Benjamini-Hochberg 5% false discovery rate (m=36)