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# Validation of the GCS–Pupil Scale in Traumatic Brain Injury: Incremental Prognostic Value of Pupillary Reactivity with GCS in the Prospective Observational Cohorts CENTER-TBI and TRACK-TBI

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**Abstract**

To compare the incremental prognostic value of pupillary reactivity captured as part of the Glasgow Coma Scale–Pupils (GCS–P) score or added as separate variable to the GCS+P, in traumatic brain injury (TBI). We analyzed patients enrolled between 2014 and 2018 in the Collaborative European NeuroTrauma Effectiveness Research in Traumatic Brain Injury (CENTER-TBI, $n$ = 3521) and the Transforming Research and Clinical Knowledge in Traumatic Brain Injury (TRACK-TBI, $n$ = 1439) cohorts. Logistic regression was utilized to quantify the prognostic performances of GCS–P (GCS minus number of unreactive pupils) and GCS+P versus GCS alone according to Nagelkerke's $R^2$. End-points were mortality and unfavorable outcome (Glasgow Outcome Scale–Extended score 1–4) at 6 month post-injury. We estimated 95% confidence intervals (CIs) with bootstrap resampling to summarize the improvement in prognostic capability. In a meta-analysis of CENTER-TBI and TRACK-TBI, GCS as a linear score had a $R^2$ of 25% (95% CI 19–31%) for mortality and 33% (4–41%) for unfavorable outcome. Pupillary reactivity as a separate variable improved the $R^2$ by an absolute value of 6% (4.0–7.7%) and 2% (1.2–3.0%) for mortality and unfavorable

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outcome, respectively, while comparatively half of this improvement was captured by the GCS–P score (3% [2.1–3.3%], 1% [1–1.7%], respectively). GCS–P showed a stronger association with 6-month outcome after TBI than GCS alone and provides a single integrated score. However, this comes at a loss of clinical and prognostic information compared with GCS+P. For prognostic models, inclusion of GCS and pupillary reactivity as separate factors may be preferable to using a GCS–P summary score.

**Keywords:** GCS–P; GCS–Pupil; Glasgow Coma Scale; prognostication; pupillary reactivity; TBI



## Background

Traumatic brain injury (TBI) is a pressing, multifaceted health concern affecting millions of people worldwide annually.[1–3] The initial clinical severity of TBI is commonly reported using the total Glasgow Coma Scale (GCS) score of 3–15, which is often grouped into three classes of severity: mild (GCS 13–15), moderate (GCS 9–12), and severe (GCS ≤8). This tripartite division is embedded in clinical practice and research; however, it does not fully capture the heterogeneity within the divisions such as the detailed neurological exam and clinical information. Consequently, therapeutic nihilism may result in patients with presumed "severe" injuries while disabling complaints and symptoms may be disregarded in patients with presumed "mild" injuries.[4–6] Under the direction of the National Institute of Neurological Disorders and Stroke (NINDS), the TBI Classification and Nomenclature Workshop in Bethesda, USA, in January 2024 was convened as part of the international initiative to develop and implement more precise approaches to TBI classification.[7]

In preparation of this workshop, the working group on clinical assessment considered the relative value of using the total GCS score (3–15) or the GCS–Pupils (GCS–P) score for classifying the clinical severity of TBI. The GCS–P was proposed in 2018, in which one point is deducted from the total GCS score for each unreactive pupil, resulting in a score from 1 to 15.[8,9] Both the total GCS and pupillary reactivity are important factors to guide clinical decision-making, as lower scores corroborate greater injury severity and consequently are associated with poorer outcome. Moreover, the GCS (or its motor component) and pupillary reactivity are key components of well-validated TBI prognostic models using large multi-institutional datasets, such as the International Mission for Prognosis and Analysis of Clinical Trials in Traumatic Brain Injury (IMPACT) and Corticosteroid Randomization after Significant Head Injury (CRASH) models.[10–12]

Studies in patients with moderate to severe TBI from the IMPACT and CRASH datasets showed that merging the GCS and pupillary reactivity into the GCS–P may yield comparable prognostic information compared with using these two factors separately.[8,9] It is, however, uncertain if this remains consistent across all severities. The current study aimed to analyze the performance of the GCS–P and the GCS and pupillary reactivity as separate features (GCS+P) for outcome prediction across the spectrum of TBI severity (GCS 3–15) from two large, recently completed multi-institutional datasets encompassing patients with acute TBI from Europe, Israel, and the United States.

## Methods

### Study population

We analyzed data from two prospectively enrolling observational cohorts: the Collaborative European NeuroTrauma Effectiveness Research in Traumatic Brain Injury (CENTER-TBI) and the Transforming Research and Clinical Knowledge in Traumatic Brain Injury (TRACK-TBI) studies.[13,14] CENTER-TBI enrolled patients presenting to one of 65 participating centers across Europe and Israel between 2014 and 2017. TRACK-TBI enrolled patients presenting to one of 18 U.S. Level 1 trauma centers between 2014 and 2019 through convenience sampling. CENTER-TBI and TRACK-TBI are registered on ClinicalTrials.gov (number NCT02210221 and NCT02119182, respectively). Inclusion and exclusion criteria for these two studies are publicly available.[13–16]

All adults (≥18 years) with a TBI recruited to these two studies were included in the current analysis. Exclusion criteria were missing the motor component of the initial GCS score or pupillary reactivity upon emergency department (ED) admission or missing the 6-month Glasgow Outcome Scale–Extended (GOS-E) scores.

### GCS–P and pupillary reactivity

In CENTER-TBI, initial GCS and pupillary reactivity were defined using IMPACT methodology as the most recent non-missing value between ED discharge (post-stabilization) and pre-hospital assessment. Untestable eye (swelling) and verbal (intubation) components of the GCS were imputed with the number "1."[17] In TRACK-TBI, initial GCS and pupillary reactivity were defined as the assessment at ED presentation. Missing GCS eye and verbal components were imputed as follows:

In case only verbal score is untestable: Total GCS = 0.55 + 1.45*[eye]+1.44*[mot].

In case both eye and verbal score are untestable: Total GCS = 0.6 + 2.4*[mot].

Extensive information and reasoning regarding imputation strategies are publicly available for both cohorts.[13,15,17]

The total GCS was analyzed as an ordinal scale between 3 (lowest score) and 15 (highest score). Pupillary reactivity was expressed using the Pupil Reactivity Score (PRS), which was scored as both reactive, one reactive, and none reactive, resulting in a score of 0, −1, or −2, respectively. The GCS and PRS were combined into an integrated GCS–P score in accordance with the predefined methodology from the source study using the GCS–P, which subtracted the PRS from the GCS, yielding scores from 1 to 15.[8]

### Outcomes

Patient functional outcome was expressed using the GOS-E scale at 6 months post-injury. GOS-E consists of an 8-point scale ranging from 1 (death) to 8 (upper good recovery, i.e., back to baseline functional status).[18] GOS-E of 2 (vegetative state) and 3 (lower severe disability) were merged as these could not be differentiated on assessments performed by postal questionnaire. Primary outcomes were death and unfavorable outcome at 6 months. Unfavorable outcome was defined as GOS-E of 1–4 (death, vegetative state, or severe disability). In CENTER-TBI, missing outcomes at 6 months postinjury were imputed using a multinomial model if assessments at one or more other time points were available.[13] In TRACK-TBI, only patients with available GOS-E scores at 6 months were included.

### Statistical analysis

Logistic regression modeling was used to analyze the relationships between GCS, PRS, GCS–P, and patient outcome (GOS-E and mortality). Nagelkerke's pseudo $R^2$ was used as primary measure to quantify the prognostic capability of the included parameters.[19] Nagelkerke's $R^2$ is calculated at the log-likelihood scale. It is a measure of how much better the model fits the data compared with a model with no predictors. Nagelkerke's $R^2$ can be interpreted as a measure of the proportion of variation explained in the dependent variable (the 6-month outcome) that is explained by the independent variables (predictors) in a logistic regression model.[20,21] The uncertainty of the $R^2$ estimate was quantified by bootstrap resampling (5000 repetitions). We estimated the increase in $R^2$, the $\Delta R^2$, for GCS–P versus GCS models and GCS plus PRS (GCS+P) versus GCS–P models within each bootstrap sample. The distribution of bootstrapped $R^2$ estimates was used to estimate 95% confidence intervals (CIs) for $R^2$ and differences between $R^2$ estimates. A pooled estimate across the CENTER-TBI and TRACK-TBI studies was estimated with inverse variance weighting. The regression analyses estimated odds ratios (OR) and 95% CI. The OR indicates the ratio of the odds of a less favorable outcome (over more favorable outcome) per 1-point increase in the GCS, PRS, GCS–P, and GCS+P scales.

A subgroup analysis was performed to assess the prognostic capabilities (mortality and unfavorable outcome) of GCS+P and GCS–P versus GCS alone in patients with moderate to severe TBI (GCS 3–12). Moreover, an additional age-stratified subgroup analysis was performed on three different age-groups based on the age distribution in the cohorts, namely age <45, age 45–64, and age ≥65 years.

Statistical analysis was performed using R version 4.1.2.[22] Rather than *p*-values for statistical tests, 95% CIs were provided throughout.

## Results

### Demographics and baseline characteristics

Overall, the CENTER-TBI and TRACK-TBI cohorts enrolled 4509 and 2552 patients, respectively; 3521 from CENTER-TBI and 1439 from TRACK-TBI subjects were eligible for the current study (Fig. 1).

The included patients from both studies were similar in sex, median GCS, PRS, and computed tomography imaging variables such as the presence of epidural hematoma, acute subdural hematoma, traumatic subarachnoid hemorrhage, and diffuse axonal injury (DAI; Table 1). TRACK-TBI patients were generally younger than CENTER-TBI patients (median age: 39 years vs 51 years, respectively). Furthermore, mild TBI was more frequent in TRACK-TBI (78%) patients compared with CENTER-TBI (67%). Moreover, cerebral contusions (36% and 25%, respectively) and midline shift (16% and 11%, respectively) were more prevalent in CENTER-TBI compared with TRACK-TBI, respectively.

### Distribution of outcomes

Mortality and unfavorable outcome occurred more in CENTER-TBI (12% and 25%) versus TRACK-TBI (7% and 14%). However, there were no large differences in the distribution of unfavorable outcome and mortality per GCS and PRS and within GCS–P scores (Supplementary Table S1 and S2). In CENTER-TBI, a small decrease in mortality at both GCS and GCS–P = 7 and 8 was observed while mortality increased again at GCS and GCS–P = 9 (Fig. 2). Moreover, low GCS–P (1–2) displayed higher percentages of mortality and unfavorable outcome compared with low GCS (3–4). Mild and moderate TBI displayed similar distributions (Fig. 2). In TRACK-TBI, low GCS–P (1–2) displayed lower mortality percentages at 6 months compared with CENTER-TBI (Fig. 2 and Supplementary Table S3).

### Associations of GCS–P and PRS with outcome

The explained variance was higher for the regression model containing GCS+P ($R^2$ 30% and 35%; Table 2) as

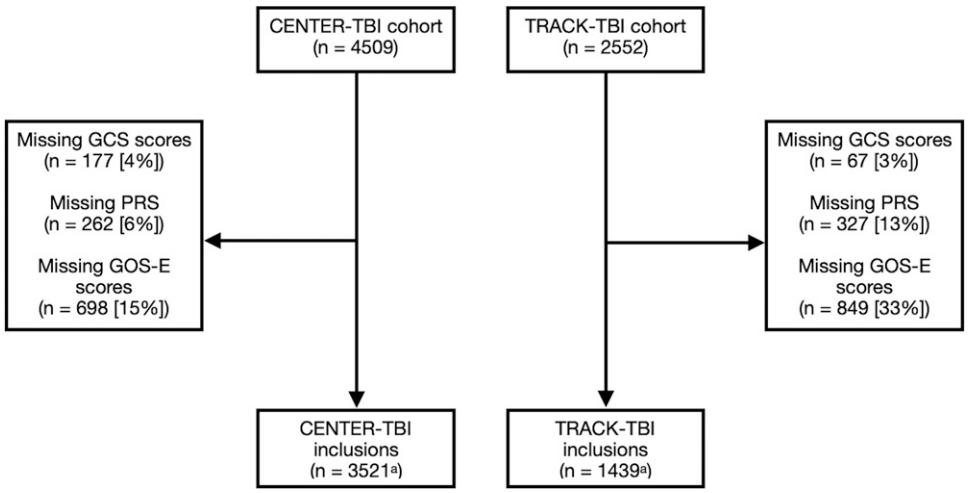


**FIG. 1.** Flowchart of inclusions. CENTER-TBI, Collaborative European NeuroTrauma Effectiveness Research in Traumatic Brain Injury; GCS, Glasgow Coma Scale; GOS-E, Glasgow Outcome Scale Extended; n, number; PRS, Pupil Reactivity Score; TRACK-TBI, Transforming Research and Clinical Knowledge in Traumatic Brain Injury. [a]Total number of patients without any GCS, PRS, or GOS-E missing. Certain patients had both GCS and PRS or GOS-E scores missing and are therefore counted twice in the exclusion.

separate predictors compared with the model containing GCS–P ($R^2$ 27% and 33%) for mortality in both CENTER-TBI and TRACK-TBI, respectively (Fig. 3).

A model containing only GCS had the lowest model performance in CENTER-TBI and TRACK-TBI ($R^2$ 24% and 30%, respectively). GCS had a lower range of predicted risks compared with GCS–P and GCS+P (Supplementary Fig. S1). Regarding unfavorable outcome, explained variance was highest in the model containing GCS+P as separate predictors compared with GCS–P in both CENTER-TBI and TRACK-TBI (GCS+P: $R^2$ 32% and 40% and GCS–P: $R^2$ 31% and 39%, respectively; Table 2). Moreover, a model containing only GCS had the lowest model performance in both cohorts ($R^2$ 29% and 38% for CENTER-TBI and TRACK-TBI, respectively). In a meta-analysis, pupils as a separate variable improved the $R^2$ by an absolute value of 6% and 2% for mortality and unfavorable outcome, with half the improvement captured in the GCS–P score (3% and 1%, respectively; Table 2, Figs. 3 and 4).

For both cohorts, in a logistic regression model containing GCS, an incremental 1-point increase in GCS significantly decreased the odds for mortality within 6 months after injury (OR 0.79, 95% CI 0.77–0.81 and OR 0.75, 95% CI 0.72–0.79 for CENTER-TBI and TRACK-TBI, respectively; Table 3). Similarly, more favorable GCS–P showed comparable odds ratios in both CENTER-TBI and TRACK-TBI (OR 0.79, 95% CI 0.77–0.81 and OR 0.76, 95% CI 0.73–0.79, respectively). In a model with GCS+P, incremental 1-point decreases in PRS decreased the odds of mortality more strongly (OR 0.40, 95% CI 0.33–0.45 and OR 0.43, 95% CI 0.32–0.58 for CENTER-TBI and TRACK-TBI, respectively) than the odds for GCS (OR 0.84, 95% CI 0.82–0.86 and 0.80, 95% CI 0.76–0.85).

**Table 1. Baseline Patient Characteristics**

| | *CENTER-TBI* | *TRACK-TBI* |
|---|---|---|
| No of patients | 3521 | 1439 |
| Age (median [IQR]) | 51 [30, 67] | 39 [26, 56] |
| Male sex (%) | 2341 (67) | 982 (68) |
| GCS scores (median [IQR]) | 15 [9, 15] | 15 [13, 15] |
| TBI severity | | |
| Mild (GCS 13–15) | 2360 (67) | 1122 (78) |
| Moderate (GCS 9–12) | 316 (9) | 70 (5) |
| Severe (GCS <9) | 845 (24) | 247 (17) |
| Pupils (%) | | |
| Both reacting | 3141 (89) | 1333 (93) |
| One reacting | 137 (4) | 31 (2) |
| None reacting | 243 (7) | 76 (5) |
| Epidural hematoma (%) | 382 (11) | 122 (9) |
| Subdural hematoma, acute (%) | 1107 (33) | 431 (31) |
| Cerebral contusion (%) | 1219 (36) | 341 (25) |
| Traumatic subarachnoid haemorrhage (%) | 1092 (35) | 536 (39) |
| Midline shift[a] (%) | 540 (16) | 154 (11) |
| DAI (%) | 341 (11) | 132 (10) |
| 6-month unfavorable outcome (GOS-E < 5) | 878 (25) | 200 (14) |
| 6-month mortality (GOS-E = 1) | 418 (12) | 98 (7) |

[a]Defined as midline shift more than 5 mm.
CENTER-TBI, Collaborative European NeuroTrauma Effectiveness Research in Traumatic Brain Injury; DAI, diffuse axonal injury; GCS, Glasgow Coma Scale; GOS-E, Glasgow Outcome Scale Extended; IQR, interquartile range; No, number; TRACK-TBI, Transforming Research and Clinical Knowledge in Traumatic Brain Injury.

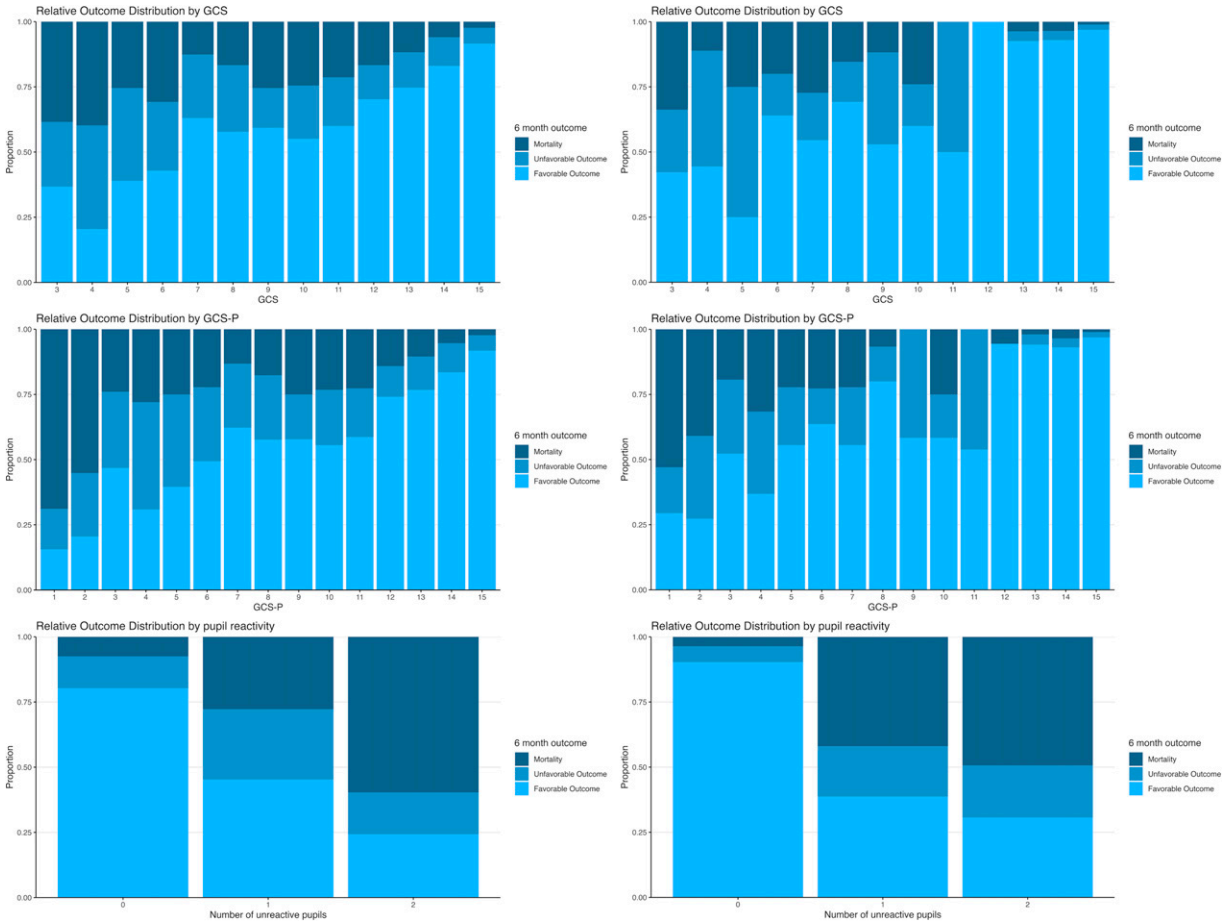


**FIG. 2.** Distribution of mortality versus GCS and GCS-P in CENTER-TBI (left) and TRACK-TBI (right). GCS, Glasgow Coma Scale; GCS–P, Glasgow Coma Scale–Pupils.

When predicting unfavorable outcome (GOS-E 1–4) using comparable models, similar associations were found (Table 3). Again, in a model with GCS+P, a poorer PRS was more strongly associated with a lower odds of unfavorable outcome in both CENTER-TBI and TRACK-TBI patients (OR 0.50, 95% CI 0.42–0.59 and OR 0.56, 95%

**Table 2. Overall Prognostic Performance of Different Regression Models**

| *Model specifications* | *Nagelkerke's $R^2$ (%) for mortality*[a] | *Absolute $\Delta R^2$ for mortality*[a,b] | *Nagelkerke's $R^2$ (%) for unfavorable outcome*[a] | *Absolute $\Delta R^2$ for unfavorable outcome*[a,b] |
|---|---|---|---|---|
| CENTER-TBI | | | | |
| GCS | 24 [17–30] | | 29 [25–34] | |
| GCS–P | 27 [20–33] | 2.7 [2.1–3.4] | 31 [26–35] | 1.4 [1–1.8] |
| GCS+P | 30 [24–37] | 6.3 [4.4–8.7] | 32 [27–36] | 2.4 [1.4–3.7] |
| TRACK-TBI | | | | |
| GCS | 30 [17–43] | | 38 [29–47] | |
| GCS–P | 33 [20–45] | 2.5 [1.4–3.9] | 39 [31–48] | 1.1 [0.3–2.0] |
| GCS+P | 35 [21–47] | 4.6 [1.8–8.9] | 40 [31–48] | 1.5 [0.2–3.5] |
| Meta analysis | | | | |
| GCS | 25 [19–31] | | 33 [24–42] | |
| GCS–P | 28 [22–34] | 2.7 [2.1–3.3] | 34 [26–42] | 1.3 [1–1.7] |
| GCS+P | 31 [25–37] | 5.8 [4–7.7] | 35 [27–42] | 2.1 [1.2–3] |

[a]Estimates and bracketed 95% CI are bootstrapped unless mentioned otherwise.
[b]$\Delta R^2$ values are based on the model containing only GCS.
CENTER-TBI, Collaborative European NeuroTrauma Effectiveness Research in Traumatic Brain Injury; CI, confidence interval; GCS, Glasgow Coma Scale; GCS–P, Glasgow Coma Scale–Pupils; Mo, month; No, number; PRS, Pupil Reactivity Score; TRACK-TBI, Transforming Research and Clinical Knowledge in Traumatic Brain Injury.

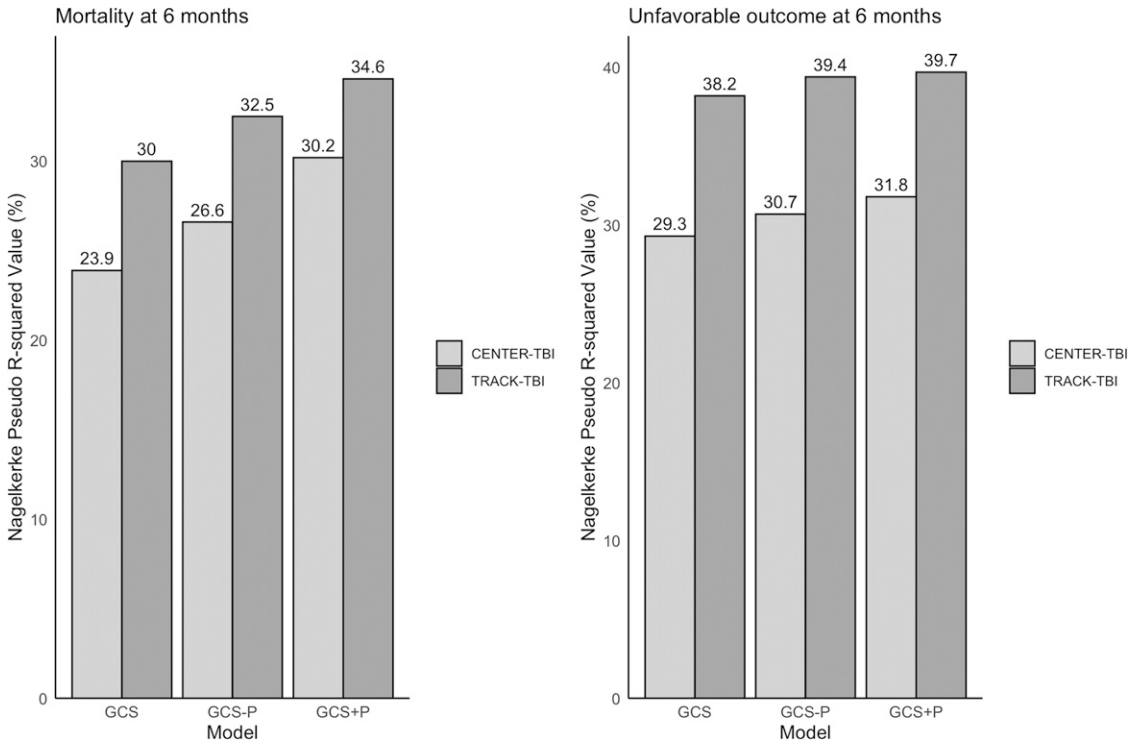


**FIG. 3.** Overall prognostic model performance. GCS, Glasgow Coma Scale; GCS–P, Glasgow Coma Scale–Pupils.

CI 0.42–0.76, respectively) than a lower GCS score (OR 0.81, 95% CI 0.79–0.83 and OR 0.77, 95% CI 0.74–0.8, respectively).

### Subgroup analysis

In the subgroup of 1161 patients in CENTER-TBI and 317 patients in TRACK-TBI with moderate and severe TBI (GCS 3–12), strong correlations were confirmed for GCS–P, GCS, and GCS+P with similar differences in explained variability (Supplementary Table S4, Supplementary Fig. S2). In the age-stratified subgroups, similar differences in explained variability between GCS–P, GCS, and GCS+P were found, with greater explained variance in younger patients in CENTER-TBI and older patients in TRACK-TBI (Supplementary Table S4).

## Discussion

This study confirmed that across all prognostic models explored, pupillary reactivity adds important prognostic information over the GCS. Including PRS above GCS separately had the greatest increment in prognostic performance for mortality and unfavorable outcome ($\Delta R^2$ 6% and 2%), with half of this increase captured by GCS–P ($\Delta R^2$ 3% and 1%).

These results are consistent with findings reported by the original GCS–P paper using the IMPACT and CRASH cohorts.[8] In these studies, the addition of PRS to GCS as separate predictors (i.e., the GCS+P) in a regression model had a $\Delta R^2$ of 4.0% and 3.2% with a $\Delta R^2$ of 3.4% and 2.2% between GCS and GCS–P for mortality and unfavorable outcome, respectively.[8,9] The authors of the original article suggested that the GCS–P is a valuable summary score over the GCS alone. Our study confirms that the GCS+P provides an incremental advantage in prognostic information across the full spectrum of TBI severity (GCS 3–15). The replication of these results in our main analysis and subgroup analyses is remarkable in the presence of disparities between cohorts. A major difference is the fraction of patients with mild and moderate TBI (GCS >8): 78% in CENTER-TBI and 67% in TRACK-TBI compared with 21% in the combined IMPACT and CRASH cohorts.[11] Patients in the original IMPACT and CRASH cohorts were considerably younger compared with CENTER-TBI and TRACK-TBI, with the median age in CENTER-TBI over 20 years higher than the median age in IMPACT.[11] Pupillary abnormalities were also more common in the IMPACT cohort.

### Subgroup analyses

Comparable with the primary analysis, we observed similar trends in the prognostic information from GCS+P and GCS–P in the subgroup analysis on patients with

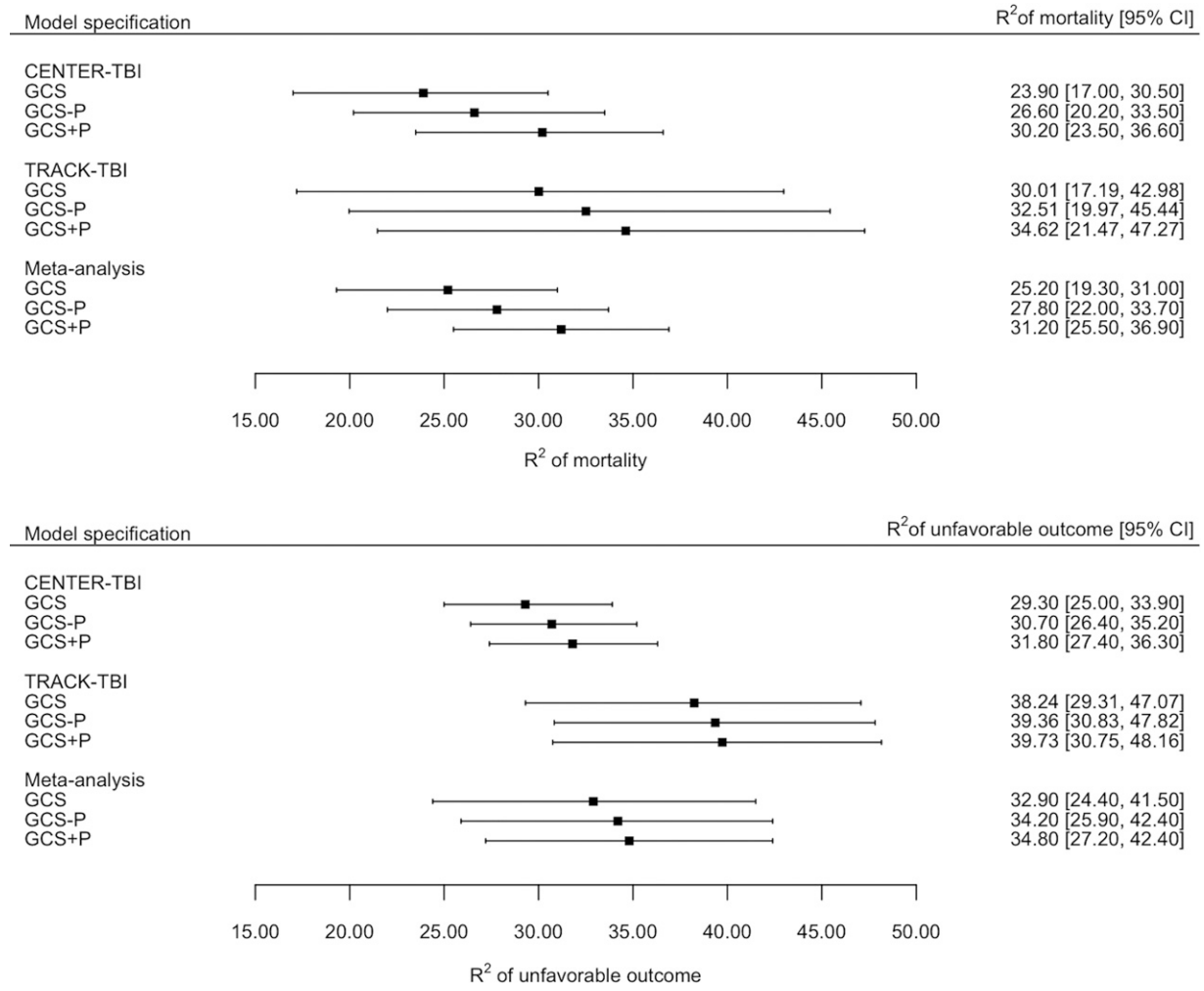


**FIG. 4.** Forest plot of $R^2$ values between cohort studies. CENTER-TBI, Collaborative European NeuroTrauma Effectiveness Research in Traumatic Brain Injury; GCS, Glasgow Coma Scale; GCS–P, Glasgow Coma Scale—Pupils; PRS, Pupil Reactivity Score; TRACK-TBI, Transforming Research and Clinical Knowledge in Traumatic Brain Injury.



moderate and severe TBI (GCS 3–12). Differences in explained variance between groups were more pronounced in moderate and severe TBI and among younger patients (Supplementary Table S4).

### Pros and cons of a summary score

Simplifications of the GCS inevitably convey less information and therefore loss of clinical value. Such considerations hold, for example, for the trichotomy of the GCS into mild, moderate, and severe categories versus use of the full ordinal GCS sum score, but also to the GCS sum score compared with use of the underpinning eye, motor, and verbal components, as their cumulative prognostic value is higher than that of the sum score alone.[23]

The integration of multiple clinical characteristics into a single score attempts to provide a single integrated articulation of TBI severity and status, without substantial loss of information. A balance should be sought between loss of information and practical utility. A strength of the GCS–P is that it combines two of the most relevant clinical predictors for TBI into a summary score and yet maintains the simplicity and ease of use of the GCS. Relative disadvantages include some loss of information compared with the use of PRS as a separate predictor. Its utility as an overall parameter of injury severity is influenced by its additional value in patients with moderate to severe TBI. However, the subtraction of PRS from the GCS across the entire GCS range potentially reduces efficacy when nonreactive pupils occur at higher GCS scores. We also recognize implementation barriers, which may be substantial

**Table 3. Odds Ratios and Logistic Regression Coefficients of Baseline Variables Predicting Outcome**

| *Model specifications* | *Odds ratio for mortality (95% CI)* | *Model coefficient for mortality* | *Odds ratio for unfavorable outcome (95% CI)* | *Model coefficient for unfavorable outcome* |
|---|---|---|---|---|
| CENTER-TBI | | | | |
| GCS | 0.79 (0.77–0.81) | –0.24 | 0.78 (0.77–0.8) | –0.24 |
| GCS–P | 0.79 (0.77–0.81) | –0.23 | 0.79 (0.78–0.8) | –0.24 |
| GCS+P[a] | 0.84 (0.82–0.86) and 0.4 (0.33–0.45), respectively | –0.18 and –0.92, respectively | 0.81 (0.79–0.83) and 0.5 (0.42–0.59), respectively | –0.21 and –0.68, respectively |
| TRACK-TBI | | | | |
| GCS | 0.75 (0.72–0.79) | –0.28 | 0.74 (0.71–0.77) | –0.3 |
| GCS–P | 0.76 (0.73–0.79) | –0.28 | 0.75 (0.73–0.78) | –0.29 |
| GCS+P[a] | 0.8 (0.76–0.85) and 0.43 (0.32–0.58), respectively | –0.22 and –0.84 | 0.77 (0.74–0.8) and 0.56 (0.42–0.76), respectively | –0.27 and –0.58 |

[a]Odds ratios are expressed using decreases in PRS score, for example, lower number of unreactive equally lower odds of mortality and unfavorable outcome.

CENTER-TBI, Collaborative European NeuroTrauma Effectiveness Research in Traumatic Brain Injury; CI, confidence interval; GCS, Glasgow Coma Scale; GCS–P, Glasgow Coma Scale–Pupils; IQR, interquartile range; Mo, month; No, number; PRS, Pupil Reactivity Score.



when introducing a modification of the GCS, which is deeply embedded in clinical practice.

Importantly, different contributions from unreactive pupils and motor responses may add up to identical GCS–P scores but may have widely different clinical import and outcome. For example, a patient with a GCS of 3 and two reactive pupils (GCS–P = 3) may indeed have a very severe brain injury but could also have relatively less severe injury with examination confounded by alcohol, residual sedative drugs or a post-ictal state. However, a patient who has extensor motor responses and one unreactive pupil (E1 V1 M2 P-1) would be more uniformly likely to have a severe brain injury. Indeed, despite a small sample size and missing combinations, a comparison of outcomes of categories equaling a GCS–P score of 3 confirmed the variability in outcome in the first category, and a more dominant poor outcome in the second (Supplementary Table S2). Similarly, differences in type of severe brain injuries and lesions might also result in different prognosis with identical GCS–P scores, such as DAIs without brain herniation versus with brain herniation and brainstem compression.

On balance, we consider the superiority of the GCS–P over the GCS modest, and from a prognostic perspective, scoring of GCS and pupillary reactivity should be preferred. We further emphasize on a more general note that we would not recommend use of summary scores as replacements for the separate assessment of neurological status using GCS and PRS in individual patients.[8]

### Study strengths and weaknesses

The major strength of this study is the thorough analysis of prospectively collected contemporary data from two large multicenter observational studies across all severities in different continents with standardized data collection. The broad inclusion criteria improve generalizability but potentially result in significant disparities between the CENTER-TBI and TRACK-TBI cohorts.[24–26] CENTER-TBI patients were generally older and suffered more severe TBI compared with TRACK-TBI patients. These factors potentially delineate the apparent differences in mortality and unfavorable outcome between both cohorts. Care should be taken comparing the model performance between the CENTER-TBI and TRACK-TBI models. Discrepancies in case-mix, however, do not preclude comparative analysis of GCS versus GCS–P or GCS+P separately and may even increase generalizability.

Limitations of our study include the restriction of data collection to North America and Europe, while the majority of TBI worldwide occurs in low- and middle-income countries. Further limitations stem from its observational design with pragmatic data collection. We cannot exclude the possibility that some bias may have occurred by missing values. In CENTER-TBI, a derived baseline GCS score was used with imputation of missing GCS scores according to IMPACT methodology. In TRACK-TBI the GCS scores were always calculated using the GCS ED admission scores and only imputed if the motor score was available.[14]

In conclusion, the GCS–P has a stronger association with outcome after TBI than the GCS alone, and provides a single integrated score. However, this comes at a loss of clinical and prognostic information compared with the GCS+P. For prognostic models, inclusion of GCS and pupillary reactivity as separate factors may be preferable to the use of a GCS–P summary score.

### Transparency, Rigor, and Reproducibility Summary

CENTER-TBI and TRACK-TBI are pre-registered at clinicaltrials.gov (number NCT02210221 and NCT02119182, respectively).[1] The analysis plan for the current study was

presented in a protocol available on: https://www.center-tbi.eu/data/approved-proposals.2 The sample size was the available one from both cohort studies, namely, 4509 subjects in CENTER-TBI and 2552 subjects in TRACK-TBI. After excluding patients with missing data in crucial predictor and outcome variables, 3521 and 1439 subjects were included from CENTER-TBI and TRACK-TBI, respectively.[3,4] Data were labeled using Global Unique Patient Identifier codes.[5] CENTER-TBI included patients between 2014 and 2017, and TRACK-TBI enrolled patients between 2014 and 2019.[6] Data were analyzed using R version 4.1.2. All equipment and software used to perform analysis are publicly available from: https://www.R-project.org.[7] The key prognostic factors used in the current study are established standards in the neurosurgical field.[8] Statistical analysis was supervised by well-known statistical expert in the field of TBI research and prognostic modeling.[9] Missing data have been handled in CENTER-TBI using imputation according to IMPACT methodology and using motor score-based imputation in TRACK-TBI, as reported in the methods. Extensive methodology statements of both CENTER-TBI and TRACK-TBI are publicly available, as stated and referenced to in the methods.[9] This report serves as an external validation of an earlier study on the GCS–P score in the IMPACT and CRASH cohorts.[11] Data and analytic code from this study are available upon reasonable request to the study authors, after approval by the management teams of CENTER-TBI and TRACK-TBI. Packages used for coding are publicly available on GITHUB. Common Data Elements used are based on the NIH Common Data Elements for TBI (https://www.commondataelements.ninds.nih.gov/Traumatic%20Brain%20Injury).[12,13] The authors agree to provide the full content of the article on request by contacting the corresponding author.



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## Author Disclosure Statement

The authors declare no competing interests.

## Supplementary Material

Supplementary Table S1
Supplementary Table S2
Supplementary Table S3
Supplementary Table S4
Supplementary Figure S1
Supplementary Figure S2

## References

1. Brazinova A, Rehorcikova V, Taylor MS, et al. Epidemiology of traumatic brain injury in Europe: A living systematic review. J Neurotrauma 2021; 38(10):1411–1440; doi: 10.1089/neu.2015.4126
2. Guan B, Anderson DB, Chen L, et al. Global, regional and national burden of traumatic brain injury and spinal cord injury, 1990–2019: A systematic analysis for the Global Burden of Disease Study 2019. BMJ Open 2023;13(10):e075049; doi: 10.1136/bmjopen-2023-075049
3. James SL, Theadom A, Ellenbogen RG, et al. Global, regional, and national burden of traumatic brain injury and spinal cord injury, 1990–2016: A systematic analysis for the Global Burden of Disease Study 2016. The Lancet Neurology 2019;18(1):56–87; doi: 10.1016/S1474-4422(18)30415-0
4. Tenovuo O, Diaz-Arrastia R, Goldstein LE, et al. Assessing the severity of traumatic brain injury-time for a change? J Clin Med 2021;10(1); doi: 10.3390/jcm10010148
5. Silverberg ND, Iverson GL, Cogan A, et al. ACRM Mild TBI Diagnostic Criteria Expert Consensus Group. The American Congress of Rehabilitation Medicine diagnostic criteria for mild traumatic brain injury. Arch Phys Med Rehabil 2023;104(8):1343–1355; doi: 10.1016/j.apmr.2023.03.036
6. Stroke NIoNDa. Focus on traumatic brain injury research; NINDS TBI classification and nomenclature workshop. 2024. Available from: https://www.ninds.nih.gov/current-research/focus-disorders/focus-traumatic-brain-injury-research [Last accessed: 09 April, 2024].
7. NIH-NINDS. NINDS TBI Classification and Nomenclature Workshop. 2024. Available from: https://www.ninds.nih.gov/news-events/events/ninds-tbi-classification-and-nomenclature-workshop [Last accessed: 09 April, 2024].
8. Brennan PM, Murray GD, Teasdale GM. Simplifying the use of prognostic information in traumatic brain injury. Part 1: The GCS-Pupils score: An extended index of clinical severity. J Neurosurg 2018;128(6):1612–1620; doi: 10.3171/2017.12.Jns172780
9. Murray G, Brennan P, Teasdale G. Simplifying the use of prognostic information in traumatic brain injury. Part 2: Graphical presentation of probabilities. J Neurosurg 2018;128(6):1621–1634; doi: 10.3171/2017.12.JNS172782
10. Roozenbeek B, Lingsma HF, Lecky FE, et al. Trauma Audit and Research Network (TARN). Prediction of outcome after moderate and severe traumatic brain injury: External validation of the International Mission on Prognosis and Analysis of Clinical Trials (IMPACT) and Corticoid Randomisation After Significant Head injury (CRASH) prognostic models. Crit Care Med 2012;40(5):1609–1617; doi: 10.1097/CCM.0b013e31824519ce
11. Steyerberg EW, Mushkudiani N, Perel P, et al. Predicting outcome after traumatic brain injury: Development and international validation of prognostic scores based on admission characteristics. PLoS Med 2008; 5(8):e165; discussion e165; doi: 10.1371/journal.pmed.0050165
12. Collaborators MCT. Predicting outcome after traumatic brain injury: Practical prognostic models based on large cohort of international patients. Bmj 2008;336(7641):425–429; doi: 10.1136/bmj.39461.643438.25
13. Maas AI, Menon DK, Steyerberg EW, et al. CENTER-TBI Participants and Investigators. Collaborative European NeuroTrauma Effectiveness Research in Traumatic Brain Injury (CENTER-TBI): A prospective longitudinal observational study. Neurosurgery 2015;76(1):67–80; doi: 10.1227/neu.0000000000000575
14. Transforming Research and Clinical Knowledge in Traumatic Brain Injury Pilot: Multicenter Implementation of the Common Data Elements for Traumatic Brain Injury. Journal of Neurotrauma 2013;30(22):1831–1844; doi: 10.1089/neu.2013.2970
15. TRACK-TBI. TRACK-TBI; resources for researchers. TRACKTBI U01 Clinical Protocol V18-January_18_2019. 2014. Available from: https://tracktbi.ucsf.edu/researchers [Last accessed: 09 July, 2024].
16. Collaborative European NeuroTrauma Effectiveness Research in TBI (CENTER-TBI). 2014.
17. Ercole A, Dixit A, Nelson DW, et al. CENTER-TBI Investigators and Participants. Imputation strategies for missing baseline neurological assessment covariates after traumatic brain injury: A CENTER-TBI study. PLoS One 2021;16(8):e0253425; doi: 10.1371/journal.pone.0253425
18. Wilson JT, Pettigrew LE, Teasdale GM. Structured interviews for the Glasgow Outcome Scale and the extended Glasgow Outcome Scale: Guidelines for their use. J Neurotrauma 1998;15(8):573–585; doi: 10.1089/neu.1998.15.573
19. Nagelkerke N, Smits J, Le Cessie S, et al. Testing goodness-of-fit of the logistic regression model in case-control studies using sample reweighting. Stat Med 2005;24(1):121–130; doi: 10.1002/sim.1997
20. Ew S. Clinical Prediction Models a Practical Approach to Development, Validation, and Updating. Springer International Publishing: 2019.
21. Harrell F. Regression Modeling Strategies: With Applications to Linear Models, Logistic and Ordinal Regression, and Survival Analysis. SPRINGER: 2016.
22. Team RC. R. A Language and Environment for Statistical Computing. R Foundation for Statistical Computing: 2021.
23. Reith FCM, Lingsma HF, Gabbe BJ, et al. Differential effects of the glasgow coma scale score and its components: An analysis of 54,069 patients with traumatic brain injury. Injury 2017;48(9):1932–1943; doi: 10.1016/j.injury.2017.05.038
24. van Essen TA, Lingsma HF, Pisică D, et al. CENTER-TBI Collaboration Group. Surgery versus conservative treatment for traumatic acute subdural haematoma: A prospective, multicentre, observational, comparative effectiveness study. Lancet Neurol 2022;21(7):620–631; doi: 10.1016/s1474-4422(22)00166-1
25. van Essen TA, Menon DK, Lingsma HF. Unmeasured confounding in observational studies of management of cerebellar intracranial hemorrhage. JAMA 2020;323(7):665–666; doi: 10.1001/jama.2019.20851
26. van Essen TA, den Boogert HF, Cnossen MC, et al. CENTER-TBI Investigators and Participants. Variation in neurosurgical management of traumatic brain injury: A survey in 68 centers participating in the CENTER-TBI study. Acta Neurochir (Wien) 2019;161(3):435–449; doi: 10.1007/s00701-018-3761-z