NEUROCRITICAL CARE SOCIETY GUIDELINES · 2024

Neuroprognostication in Moderate–Severe TBI

Scope: Critically ill adults (GCS 3-12) after standard-of-care treatment · GRADE methodology · 8,125 abstracts screened → 41 studies included

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- I report no financial relationships with ineligible companies (as defined by the Accreditation Council for Continuing Medical Education).
- No conflicts of interest exist related to the content of this presentation.

WHY PROGNOSTICATION MATTERS

~80%

of msTBI deaths occur in the ICU after withdrawal of life-sustaining treatment (WLST)

>50%

of msTBI deaths occur within 72 hours of injury

45–96%

Variability in WLST rates across North American and European trauma centers

The stakes of WLST decisions:

Premature WLST → death of a patient who might have recovered with a good outcome
Prolonged treatment → severe disability the patient would not have chosen

WLST is the single most important predictor of outcomes after msTBI, regardless of injury severity (Izzy et al., 2013).

RELIABILITY FRAMEWORK: HOW TO USE THESE GUIDELINES

RELIABLE	**Counseling language:** *"Very likely"* · **Uncertainty:** Present but low **Criteria:** High/moderate QoE · AUC >0.8 · No miscalibration in external validation · Low false-positive rate **Usage:** Use alone if appropriate clinical context and no confounders
MODERATELY RELIABLE	**Counseling language:** *"Likely"* · **Uncertainty:** Substantial **Criteria:** Any QoE level · AUC >0.7 · Some miscalibration allowed · Must acknowledge significant uncertainty **Usage:** Individual predictors: require ≥1 additional reliable/mod-reliable predictor. Prediction models: may use alone.
NOT RELIABLE	**Counseling language:** *Do not use alone* · **Uncertainty:** N/A **Criteria:** Does not meet above criteria — regardless of statistical significance in multivariate analysis **Usage:** Cannot be formally recommended. May be component of a reliable model.

INDIVIDUAL CLINICAL PREDICTORS: RELIABILITY SUMMARY

Predictor	Mortality	6-mo Functional Outcome
Age	Not reliable	Not reliable
Bilateral pupillary nonreactivity*	Not reliable	**MODERATELY RELIABLE**
Unilateral pupillary nonreactivity	Not reliable	Not reliable
GCS / Motor GCS (admission)	Not reliable	Not reliable
Hypotension (SBP <90 pre/on admission)	Not reliable	Not reliable
Hypoxia (O_2 sat <90% / PaO_2 <110)	Not reliable	Not reliable
Elevated ICP (>20 mmHg)	Not reliable	Not reliable
Major extracranial injury	Not reliable	No data
Acute kidney injury (ICU)	Not reliable	Not reliable
Alcohol intoxication (admission)	Not reliable	No data
Hypernatremia (ICU course)	Not reliable	No data
Posttraumatic cerebral infarction	No data	Not reliable

** Conditional on accurate assessment — exclude confounders (medications, orbital trauma, diffuse axonal injury, prior surgery, CN III compression)*

Bilateral Pupillary Nonreactivity on Admission

Moderately reliable for: 6-month unfavorable functional outcome · In-hospital mortality

Requirements for use

- Accurate bedside assessment required
- Exclude confounding medications (sedation, paralytics)
- Exclude orbital trauma or external injury to eye
- Exclude diffuse axonal injury at mesencephalon level
- Exclude TBI-related seizures
- Exclude CN III compression from elevated ICP (must treat first)

Limitations & caveats

- Weak recommendation, low-quality evidence
- Only 1 predictor reaching mod-reliable for mortality — and threshold for 'reliable' not met
- Self-fulfilling prophecy risk: bilat fixed pupils may trigger early WLST
- Must be used alongside other clinical context
- Cannot be used in isolation for counseling — requires acknowledgment of substantial uncertainty

CLINICAL PREDICTION MODELS: RECOMMENDED

5 models rated MODERATELY RELIABLE for both mortality and 6-month functional outcome

CRASH-basic	**Inputs:** Age · GCS · Pupillary reactivity · Major extracranial injury **Mortality:** 14-day AUC 0.80–0.82 · **Funct. outcome:** 6-mo AUC 0.80–0.86 · *Derived incl. mild TBI (GCS 13–14); validated in large multicenter cohorts*
CRASH-CT	**Inputs:** CRASH-basic + CT: petechial hemorrhages, basal cisterns, SAH, midline shift, mass lesion **Mortality:** 14-day AUC 0.83 · **Funct. outcome:** 6-mo AUC 0.86–0.89 · *Derived incl. mild TBI; best calibration among CRASH models*
IMPACT-core	**Inputs:** Age · GCS motor subscore · Pupillary reactivity **Mortality:** 6-mo AUC 0.66–0.90 · **Funct. outcome:** 6-mo AUC 0.71–0.87 · *Most widely validated msTBI model; derived from 8,509 patients in 11 pooled studies*
IMPACT-extended	**Inputs:** Core + CT (Marshall class, SAH, EDH) + Hypotension + Hypoxia **Mortality:** 6-mo AUC 0.71–0.85 · **Funct. outcome:** 6-mo AUC 0.73–0.88 · *Adds imaging and secondary insults; broader discrimination range*
IMPACT-lab	**Inputs:** Extended + Glucose + Hemoglobin (admission) **Mortality:** 6-mo AUC 0.72–0.80 · **Funct. outcome:** 6-mo AUC 0.75–0.87 · *Smaller derivation cohort (n=3,554); requires lab values*

CT SCORING MODELS: NOT RELIABLE FOR ISOLATED COUNSELING

All four CT grading scales rated NOT RELIABLE for mortality and functional outcome when used alone:

Marshall CT

No calibration in most studies; includes up to 25–33% mild TBI patients in validation cohorts; original paper did not report discrimination.

Rotterdam CT

Low quality evidence; AUC inconsistent (0.682–0.875); calibration rarely reported; significant indirectness from mild TBI inclusion.

Helsinki CT

Moderate QoE for mortality only; limited external validation; calibration not consistently reported.

Stockholm CT

Single paper basis for mortality; calibration never reported; large mild TBI inclusion; inconsistency across studies.

Note: Variables deemed 'not reliable' alone may still serve as components within the CRASH or IMPACT models.

GOOD PRACTICE STATEMENTS (GRADE STRONG RECOMMENDATIONS)

01

Consider the whole picture

Prognostication must be based on the complete clinical condition — never on a single variable in isolation. Multimodal assessment is required.

02

Avoid ultra-early prognostication

Do not base WLST decisions solely on characteristics within the first 3 days. TBI involves primary injury plus secondary injuries (growing hemorrhage, cerebral edema, microcellular processes). Minimum 3 days of full critical care support is recommended; 1–2 weeks is preferred. Prognosis may remain uncertain even after 2 weeks in patients who remain unconscious.

03

Acknowledge uncertainty — avoid nihilism

Prognostication must be delivered carefully and must explicitly convey inherent uncertainty. Do not base prognosis on personal anecdotal experience alone. Premature pessimism is a patient safety risk.

PRACTICAL CLINICAL SUMMARY

✓ What you CAN use

CRASH-basic / CRASH-CT
crash2.lshtm.ac.uk · 14-day mortality + 6-mo outcome

IMPACT-core / IMPACT-extended / IMPACT-lab
tbi-impact.org · 6-month mortality + outcome

Bilateral pupillary nonreactivity*
6-mo functional outcome · mod-reliable only

All require: explicit uncertainty language + clinical context

✗ What you CANNOT use alone

Age alone
GCS or motor GCS alone
Hypotension / Hypoxia alone
Elevated ICP alone
Unilateral pupillary nonreactivity
Hypernatremia · AKI · Alcohol · Extracranial injury
Marshall / Rotterdam / Helsinki / Stockholm CT scores

These are associated with outcome but do not meet reliability thresholds for surrogate counseling in the context of WLST decisions.

** Requires confounders excluded. Use with substantial uncertainty language.*

KEY TAKEAWAYS

1. No single clinical variable meets 'reliable' threshold for surrogate counseling — isolated predictors cannot be used to justify WLST
2. Bilateral fixed pupils is the only clinical sign reaching 'moderately reliable' — for functional outcome only, and only when confounders are excluded
3. CRASH and IMPACT models are moderately reliable and should be used routinely with online calculators — express results as probabilities with explicit uncertainty
4. CT scoring systems (Marshall, Rotterdam, Helsinki, Stockholm) are not recommended for standalone counseling
5. Always wait ≥3 days, ideally 1–2 weeks — do not prognosticate based on ultra-early characteristics
6. Always counsel with uncertainty language: 'likely' not 'certain' — prognostic nihilism is a patient safety concern

Muehlschlegel S et al. Neurocrit Care 2024;40:448–476 · doi:10.1007/s12028-023-01902-2

OUTCOME DEFINITIONS & MEASUREMENT VARIABILITY

A critical limitation across all 41 included studies: 'poor outcome' was defined inconsistently

Outcome scales used across studies

Glasgow Outcome Scale (GOS)
5-point ordinal (1=death → 5=good recovery) · Most common

GOS-Extended (GOSE)
8-point scale; finer gradation of upper GOS bands

Functional Independence Measure (FIM)
18-item; rates functional ability across domains

Ranchos Los Amigos Scale
10-level cognitive functioning scale; used in rehab

Disability-free outcome
Binary; definition of 'disability' varies by study

Why this matters clinically

Dichotomization varies widely
GOS ≤2, ≤3, or ≤4 all used as 'unfavorable' — incomparable effect sizes across studies

Time point inconsistency
Outcomes assessed at discharge, 3mo, 6mo, 12mo — or combined

Recovery beyond 6 months is underestimated
Recent trials show continued recovery past 6mo; 6-mo endpoint may overestimate 'poor' outcomes

No QoL or cognitive outcome data
Zero eligible studies reported QoL or cognitive outcomes — a critical evidence gap for counseling

Guideline convention: 'poor' = 'unfavorable' throughout. AUC and OR comparisons should be interpreted with awareness of outcome definition heterogeneity.

COMMUNICATING UNCERTAINTY TO FAMILIES: LANGUAGE GUIDE

How you say it matters as much as what you say — these guidelines specify counseling language by reliability tier

Moderately reliable predictor	**Context:** Bilateral fixed pupils (confounders excluded) + 1 other mod-reliable predictor **Say:** *"Based on our assessment, a poor outcome is likely. However, there is substantial uncertainty — we cannot predict individual outcomes with certainty."* **Avoid:** "She will not survive" or "There is no hope"
Moderately reliable model	**Context:** CRASH or IMPACT model used alone **Say:** *"The IMPACT model estimates a [X]% probability of death at 6 months. This is an objective estimate only, subject to considerable uncertainty — it reflects population-level data, not a certainty for this individual."* **Avoid:** Presenting the probability as a definitive forecast
Not reliable predictors only	**Context:** Only age, GCS, or CT scoring scale available **Say:** *"At this stage, we do not have enough reliable information to make a confident prognosis. We recommend continuing full support and reassessing in [X] days."* **Avoid:** Using these variables alone to justify early WLST

Always: name uncertainty explicitly · centre patient values · avoid nihilism · do not prognosticate within first 3 days

CLINICAL CASE A: WHEN PREDICTORS CONFLICT

52-year-old male · MVC · GCS 6 post-resuscitation · Bilateral fixed pupils at ED · BAL 280 mg/dL · No major extracranial injury

Clinical picture

- CT: bifrontal contusions, thin bilateral SDH, no MLS, basal cisterns patent
- No hypotension, no hypoxia
- Blood alcohol 280 mg/dL on arrival
- At 6h post-admission: LEFT pupil now reactive after osmotherapy
- No sedation or paralytics at exam

Model outputs

- IMPACT-core: ~65% predicted 6-mo mortality
- CRASH-basic: ~58% predicted 14-day mortality
- Alcohol NOT a reliable predictor — may have falsely lowered GCS
- Unilateral → bilateral → unilateral pupils: dynamic; reassessment essential
- Both models: moderate reliability only

Counseling approach

- Day 1: Do NOT prognosticate — alcohol confounds GCS; pupils changed; cisterns open
- Tell family: 'Too early — we will reassess over 72 hours'
- Day 3–7: Repeat full exam, re-run models with updated variables
- If bilateral nonreactivity confirmed (no confounders): mod-reliable predictor then applicable
- Avoid: using day-1 GCS 6 + arrival bilat pupils to justify same-day WLST

Teaching point: Dynamic reassessment is essential. Alcohol, osmotherapy, and sedation are common confounders. A single time-point snapshot is never sufficient.

CLINICAL CASE B: USING PREDICTION MODELS IN PRACTICE

78-year-old female · Ground-level fall · GCS 7 (M4, V1, E2) · Bilateral fixed pupils at admission · No alcohol · No sedation · No orbital trauma

Clinical data & model inputs

CT: large right SDH, 12mm MLS, compressed basal cisterns, bilateral contusions, traumatic SAH

IMPACT-core inputs: Age 78 · Motor GCS 4 · Bilateral pupils non-reactive
IMPACT-extended adds: No hypotension · No hypoxia · Marshall IV · SAH present · No EDH

Confounders excluded: No medications · No orbital trauma · No prior surgery · CT consistent with bilateral CN III compression — treat ICP first, then reassess pupils

Age alone: NOT a reliable predictor — no cutoff above which death is certain

Model outputs & counseling

IMPACT-core: ~82% 6-mo mortality
IMPACT-extended: ~88% 6-mo mortality

Bilateral fixed pupils: Moderately reliable once ICP treated and pupils reassessed

Suggested language:
"The IMPACT model estimates ~85% probability of death within 6 months. The pupil findings also suggest a likely poor outcome. Both carry substantial uncertainty — this reflects patterns across many patients, not a certainty for your mother."

Next steps: Neurosurgery consult · Treat ICP · Reassess pupils · Explore patient's known wishes · Formal goals-of-care meeting at 72h

Teaching point: Converging mod-reliable evidence (model + pupil finding) strengthens prognosis — but uncertainty language remains mandatory. Always treat ICP before using pupils as predictor

FUTURE DIRECTIONS IN NEUROPROGNOSTICATION

Four priorities identified by the guideline panel

01

Mitigate self-fulfilling prophecy in study design

Future studies must blind clinicians to prognostic variables not integral to clinical care, and where feasible restrict early WLST. Every included study was at risk from this bias. Multivariate analysis must include at minimum age and GCS score.

02

Evaluate new predictors as add-ons to validated models

Biomarkers, advanced imaging, and EEG should be assessed as additions to CRASH/IMPACT — not standalone predictors. The question is whether they improve discrimination and calibration beyond existing models with acceptable risk of bias.

03

Model time-varying clinical course, not just admission data

ICU complications, evolving radiographic features, and secondary injuries unfold over days. Survival analysis and Bayesian models incorporating time-to-event data are needed to improve accuracy and help define the optimal timing of prognostication.

04

Extend outcome follow-up beyond 6 months

Multiple recent trials (TRACK-TBI, RESCUEicp) document neurological recovery continuing past 6 months. A 6-month endpoint likely overestimates poor outcomes. Future studies should assess functional status, QoL, and cognitive outcomes at 12+ months.

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Reference

Susanne Muehlschlegel, Venkatakrishna Rajajee, Katja E. Wartenberg, Thomas Westermaier, et al. **Guidelines for Neuroprognostication in Critically Ill Adults with Moderate–Severe Traumatic Brain Injury.**
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