Guidelines for the Management of Pediatric Severe Traumatic Brain Injury, Third Edition: Update of the Brain Trauma Foundation Guidelines, Executive Summary

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Objectives: The purpose of this work is to identify and synthesize research produced since the second edition of these Guidelines was published and incorporate new results into revised evidence-based recommendations for the treatment of severe traumatic brain injury in pediatric patients.

Methods and Main Results: This document provides an overview of our process, lists the new research added, and includes the revised recommendations. Recommendations are only provided when there is supporting evidence. This update includes 22 recommendations, nine are new or revised from previous editions. New recommendations on neuroimaging, hyperosmolar therapy, analgesics and sedatives, seizure prophylaxis, temperature control/hypothermia, and nutrition are provided. None are level I, three are level II, and 19 are level III. The Clinical Investigators responsible for these Guidelines also created a companion algorithm that supplements the recommendations with expert consensus where evidence is not available and organizes possible interventions into first and second tier utilization. The purpose of publishing the algorithm as a separate document is to provide guidance for clinicians while maintaining a clear distinction between what is evidence based and what is consensus based. This approach allows, and is intended to encourage, continued creativity in treatment and research where evidence is lacking. Additionally, it allows for the use of the evidence-based recommendations as the foundation for other pathways, protocols, or algorithms specific to different organizations or environments. The complete guideline document and supplemental appendices are available electronically from this journal. These documents contain summaries and evaluations of all the studies considered, including those from prior editions, and more detailed information on our methodology.

Conclusions: New level II and level III evidence-based recommendations and an algorithm provide additional guidance for the development of local protocols to treat pediatric patients with severe traumatic brain injury. Our intention is to identify and institute a sustainable process to update these Guidelines as new evidence becomes available. (*Pediatr Crit Care Med* 2019; 20:280–289)

Key Words: critical care; evidence-based medicine; guidelines; pediatrics; systematic review; traumatic brain injury

The Third Edition of the Brain Trauma Foundation's Guidelines for the Management of Pediatric Severe Traumatic Brain Injury (TBI) (1) updates the Second Edition published in 2012 (2). This new publication is part of an effort to update a suite of three Brain Trauma Foundation Guidelines, including similar acute care guidelines for adults (published in January 2017) (3) and guidelines for prehospital management of all ages (forthcoming). It represents a substantial effort by a multidisciplinary group of individuals assembled to reflect the team approach to the treatment of these complex, critically ill patients that is essential to optimizing critical care and improving outcomes.

A total of 48 new studies were included in this Third Edition. Although some progress has been made and should be celebrated, overall the level of evidence informing these Guidelines remains low. High-quality randomized studies that could support level I recommendations remain absent; the available evidence produced only three level II recommendations, whereas most recommendations are level III, supported by lower quality evidence.

In addition to the Guidelines, we have authored a companion article that presents a "Critical Pathway" algorithm of care for both first tier and second tier (refractory intracranial hypertension) approaches (4). The algorithm reflects both the evidence-based recommendations from these Guidelines as well as consensus-based expert opinion, vetted by the full committee, where evidence was not available. The algorithm also addresses a number of issues that are important but were not previously covered in the Guidelines, given the lack of research. Specifically, the algorithm addresses issues such as a step-wise approach to elevated intracranial pressure (ICP), differences in tempo of therapy in different types of patients, scenarios with a rapidly escalating need for ICP-directed therapy in the setting of impending herniation, integration of multiple monitoring targets, and other complex issues such as minimal versus optimal therapeutic targets and approaches to weaning therapies.

It is important to acknowledge that these Guidelines were written as the Approaches and Decisions in Acute Pediatric TBI Trial (ADAPT) (5–7), one of the most important in the field of pediatric TBI, was coming to a close. The ADAPT completed enrollment of 1,000 cases of severe pediatric TBI and is one example of the recent, heightened general interest in TBI as a disease. This new interest in the importance of TBI has emerged in part from the recognition of the high prevalence of TBI across the injury severity spectrum, particularly concussion, and from the need for new classification systems and new trial design for TBI in both children and adults (8, 9). We expect that the results of ADAPT, along with those of other ongoing trials and recently completed research in the field, will help provide new insight and clarity into the acute medical management of infants, children, and adolescents with severe TBI and support further refinement of the recommendations in these documents.

THE SCOPE OF THE GUIDELINES

The Guidelines address monitoring, thresholds for ICP and cerebral perfusion pressure (CPP), and 10 categories of treatments specific to TBI in infants, children, or adolescents. The Guidelines are not intended to cover all topics relevant to the care of patients with severe TBI. Specifically, topics related to general good care for all patients, or all trauma patients, are not included.

Developing protocols that integrate TBI-specific, evidence-based recommendations with general best practices for trauma patients, and that provide guidance, suggestions, or options in areas of TBI management where the evidence is insufficient, is outside the scope of these Guidelines. These recommendations are intended to provide the foundation on which protocols can be developed that are appropriate to different treatment environments. The algorithm developed by the clinical investigators is one example of such a protocol, but not the only possible protocol that could be developed based on these Guidelines.

METHODS

The methods for developing these Guidelines were organized in two phases—the systematic review, including the identification, assessment, and synthesis of the literature; and the use of that foundation for evidence-based recommendations.

Systematic Evidence Review and Synthesis

Literature Search and Review. Our literature search protocol is described in detail, and the search strategies are in Appendix D of the full online guideline document (1). Please note that all appendices mentioned in this executive summary refer to appendices to the full guidelines document (1).

The key criteria for including studies in the review were as follows: the population included pediatric patients (age ≤ 18 yr) with severe TBI (defined as Glasgow Coma Scale score of 3–8), and the study assessed an included outcome (mortality, neurologic function, or appropriate intermediate outcomes for the topic). Two reviewers independently identified studies to include, and differences were resolved via consensus or by a third reviewer. Detailed inclusion criteria and a list of studies excluded after full-text review are in the online document in Appendices B and E (1). This edition adds studies published from 2010 to June 2017.

Quality Assessment and Data Abstraction of Individual Studies. All included studies were assessed for potential for bias, which is a systematic approach to assessing the internal validity or quality of studies. The quality criteria used in the second edition were maintained and applied to the newly identified studies of monitoring and treatments. The criteria for threshold studies were revised to be specific to the quality of threshold studies. (See appendix F in the online document [1] for a complete list of the quality criteria used for individual studies.) Key data elements were then extracted from each study and placed into tables. The tables were provided to the clinical investigators and summarized by topic in the guideline document (see summaries by topic in the full report online [1]). Class 1 is the highest class and is limited to good-quality randomized trials. Class 2 includes moderate-quality randomized controlled trials (RCTs) and good-quality cohort or case-control studies. Class 3 is the lowest class and is given to low-quality RCTs, moderate- to low-quality cohort or case-control studies, and treatment series and other noncomparative designs.

Synthesis. The final phase of the evidence review is the synthesis of individual studies into information that the clinical investigators and the methods team use to develop recommendations. This synthesis is described for each topic in the online document in the sections titled Evaluation of the Evidence, following the Recommendations and preceding the Evidence Summary.

Quality of the Body of Evidence. Assessing the quality of the body of evidence involves four domains: the aggregate quality of the studies, the consistency of the results, whether the evidence provided is direct or indirect, and the precision of the effect estimates. The criteria and ratings are outlined in the *Methods* section of the online document and more detailed definitions are in Appendix G (1). In addition, the number of studies and number of included subjects are considered. Based on these, an overall assessment is made as to whether the quality of the body of evidence is high, moderate, low, or insufficient. The assessment of the body of evidence for each subtopic is included in a table in each topic section in the full guideline document.

Applicability. Applicability is the extent to which research findings are useful for informing recommendations for a broader population (usually the population that is the target of the recommendations). In this edition, we considered the applicability of individual studies in the *Quality of the Body of Evidence and Applicability* section immediately following the recommendations in the full guideline document.

Recommendations

Development of Recommendations. Classes 1, 2, and 3 studies constitute the evidence on which the recommendations are based. Once evidence was identified, whether or not it could be used to inform recommendations was based on the quality of the body of evidence and consideration of applicability. Under our current methods, identification of evidence is necessary but not sufficient for the development of evidence-based recommendations. If no evidence was identified, no recommendations were made. If the identified evidence was extremely limited (e.g., inconsistent results, imprecise), it could be considered insufficient to support a recommendation.

Given this approach, there were cases in which evidence was identified, but the quality was low and applicability concerns restricted the ability to translate the evidence into recommendations. Even if a recommendation was not made, the studies contributing evidence were included in the full Guideline to acknowledge their place in the body of evidence and make the evidence accessible for future consideration. As new studies are generated and added to the evidence base, we expect to see changes in the assessment of the quality of the body of evidence.

Level of Recommendations. Recommendations in this edition are designated as level I, level II, or level III. The level of recommendation is determined by the assessment of the quality of the body of evidence, which includes, but is not limited to, the class of the included studies.

The levels were primarily based on the quality of the body of evidence as follows:

1) Level I recommendations were based on a high-quality body of evidence.

2) Level II recommendations were based on a moderate-quality body of evidence.
3) Level III recommendations were based on a low-quality body of evidence.

In addition to the quality of evidence, we also considered applicability. Currently, there is a lack of standards and developed methods to assess applicability. For this reason, applicability alone was not used to downgrade a recommendation; however, we did include and document in the full guideline any applicability issues that were identified and discussed by the authors.

"Insufficient" was used in cases where the body of evidence was insufficient to support a recommendation either because there were no studies identified or because the body of evidence had major quality limitations. If the evidence was rated insufficient, no recommendation was made.

REVISED RECOMMENDATIONS

Summary of Changes to Recommendations

This update includes 22 evidence-based recommendations; nine are new or revised significantly from the previous edition. There are no level I recommendations, three recommendations are level II, and the remaining 19 are level III.

Tables 1, **2**, and **3** provide the recommendations for monitoring, thresholds, and treatments, respectively. Each recommendation is numbered with a roman numeral for the level followed by a period and a number counting the recommendations in each topic (So III.1 is the first Level III recommendation and III.2 is the second level III recommendation). In these tables, the recommendations in italics are new or have been significantly revised, whereas those in regular text have not changed or only have changes in wording. The online guideline document includes a section on each topic consisting of an Introduction, Recommendations, Evaluation of the Evidence, and Summary of the Evidence (including evidence tables and a narrative overview).

Monitoring Recommendations

Monitoring does not affect outcomes directly; rather the information from monitoring can be used to direct treatment decisions. Treatment informed by data from monitoring may result in better outcomes than treatment informed solely by data from clinical assessment. Monitoring recommendations are related to the influence on patient outcomes of three types of monitoring: ICP monitoring, advanced cerebral monitoring (ACM), and neuroimaging. The recommendations for ICP and ACM did not change; however, two notes were added to the ACM recommendation. For neuroimaging, one new recommendation suggesting that CT examinations not be used to rule out the possibility of elevated ICP was added to the existing recommendation.

Threshold Recommendations

These recommendations are related to threshold values for variables that are monitored during the in-hospital management

TABLE 1. Updated Recommendations: Monitoring

Topics	Recommendations
Intracranial pressure monitoring	**Level III** **To Improve Overall Outcomes** III.1. Use of ICP monitoring is suggested.
Advanced neuromonitoring	**Level III** **To Improve Overall Outcomes** III.1. If $Pbro_2$ monitoring is used, maintaining a level > 10 mm Hg is suggested. *Note 1: There was insufficient evidence to support a recommendation for the use of a monitor of Po_2 in brain interstitium ($Pbro_2$) to improve outcomes.* *Note 2: Use of advanced neuromonitoring (brain oxygenation) should only be for patients with no contraindications to invasive neuromonitoring, such as coagulopathy, and for patients who do not have a diagnosis of brain death.*
Neuroimaging	**Level III** **To Improve Overall Outcomes** *III.1. Excluding the possibility of elevated ICP on the basis of a normal initial (0–6 hr after injury) CT examination of the brain is not suggested in comatose pediatric patients.* III.2. Routinely obtaining a repeat CT scan > 24 hr after the admission, and initial follow-up is not suggested for decisions about neurosurgical intervention, unless there is either evidence of neurologic deterioration or increasing ICP.

ICP = intracranial pressure, $Pbro_2$ = brain tissue oxygen.
Italics indicate new or revised recommendations.

TABLE 2. Updated Recommendations: Thresholds

Topics	Recommendations
Threshold for treatment of intracranial hypertension	**Level III** **To Improve Overall Outcomes** III.1. Treatment of intracranial pressure targeting a threshold of < 20 mm Hg is suggested.
Thresholds for cerebral perfusion pressure	**Level III** **To Improve Overall Outcomes** III.1. Treatment to maintain a CPP at a minimum of 40 mm Hg is suggested. III.2. A CPP target between 40 and 50 mm Hg is suggested to ensure that the minimum value of 40 mm Hg is not breached. There may be age-specific thresholds with infants at the lower end and adolescents at or above the upper end of this range.

CPP = cerebral perfusion pressure.

TABLE 3. Updated Recommendations: Treatments

Topics	Recommendations
Hyperosmolar therapy	**Level II** **For ICP Control** *II.1. Bolus hypertonic saline (3%) is recommended in patients with intracranial hypertension. Recommended effective doses for acute use range between 2 and 5 mL/kg over 10–20 min.* **Level III** **For ICP Control** III.1. Continuous infusion hypertonic saline is suggested in patients with intracranial hypertension. Suggested effective doses as a continuous infusion of 3% saline range from between 0.1 and 1.0 mL/kg of body weight per hour, administered on a sliding scale. The minimum dose needed to maintain ICP < 20 mm Hg is suggested. *III.2. Bolus of 23.4% hypertonic saline is suggested for refractory ICP. The suggested dose is 0.5 mL/kg with a maximum of 30 mL.* *Safety recommendation (applies to all recommendations for this topic): In the context of multiple ICP-related therapies, avoiding sustained (> 72 hr) serum sodium > 170 mEq/L is suggested to avoid complications of thrombocytopenia and anemia, whereas avoiding a sustained serum sodium > 160 mEq/L is suggested to avoid the complication of deep vein thrombosis.* Note: Although mannitol is commonly used in the management of raised ICP in pediatric traumatic brain injury, no studies meeting inclusion criteria were identified for use as evidence for this topic.
Analgesics, sedatives, and neuromuscular blockade	**Level III** **For ICP Control** *III.1. With use of multiple ICP-related therapies, as well as appropriate use of analgesia and sedation in routine ICU care, avoiding bolus administration of midazolam and/or fentanyl during ICP crises is suggested due to risks of cerebral hypoperfusion.* Note 1: In the absence of outcome data, the specific indications, choice, and dosing of analgesics, sedatives, and neuromuscular blocking agents should be left to the treating physician. Note 2: Based on guidance from the U.S. Food and Drug Administration, prolonged continuous infusion of propofol for either sedation or the management of refractory intracranial hypertension is not recommended.

(*Continued*)

TABLE 3. (*Continued*). Updated Recommendations: Treatments

Topics	Recommendations
Cerebrospinal fluid drainage	**Level III** **For ICP Control** III.1. Cerebrospinal fluid drainage through an external ventricular drain is suggested to manage increased ICP.
Seizure prophylaxis	**Level III** **For Seizure Prevention (Clinical and Subclinical)** *III.1. Prophylactic treatment is suggested to reduce the occurrence rate of early (within 7 d) PTS.* *Note: At the present time, there is insufficient evidence to recommend levetiracetam over phenytoin based on either efficacy in preventing early PTS or toxicity.*
Ventilation therapies	**Level III** **To Improve Overall Outcomes** III.1. Prophylactic severe hyperventilation to a $Paco_2 < 30$ mm Hg in the initial 48 hr after injury is not suggested. III.2. If hyperventilation is used in the management of refractory intracranial hypertension, advanced neuromonitoring for evaluation of cerebral ischemia is suggested.
Temperature control/ hypothermia[a]	**Level II** **To Improve Overall Outcomes** *II.1. Prophylactic moderate (32–33°C) hypothermia is not recommended over normothermia to improve overall outcomes.* **Level III** **For ICP Control** *III.1. Moderate (32–33°C) hypothermia is suggested for ICP control.* *Safety recommendation 1: If hypothermia is used and rewarming is initiated, it should be carried out at a rate of 0.5–1.0°C every 12–24 hr or slower to avoid complications.* *Safety recommendation 2: If phenytoin is used during hypothermia, monitoring and dosing adjusted to minimize toxicity, especially during the rewarming period, is suggested.*
Barbiturates	**Level III** **For ICP Control** III.1. High-dose barbiturate therapy is suggested in hemodynamically stable patients with refractory intracranial hypertension despite maximal medical and surgical management. Safety recommendation: When high-dose barbiturate therapy is used to treat refractory intracranial hypertension, continuous arterial blood pressure monitoring and cardiovascular support to maintain adequate cerebral perfusion pressure are required because cardiorespiratory instability is common among patients treated with barbiturate coma.
Decompressive craniectomy	**Level III** **For ICP Control** III.1. Decompressive craniectomy is suggested to treat neurologic deterioration, herniation, or intracranial hypertension refractory to medical management.

(*Continued*)

of patients with severe TBI. This includes thresholds for ICP and CPP. There are no changes to the recommendations from the prior edition. Additional studies that supported the existing recommendations were added to the evidence tables in the full guideline document and are listed in **Table 4**.

Treatment Recommendations

Table 3 contains the recommendations for 10 treatments included in the Guidelines. These topics are included because they are specific to the in-hospital management of TBI or are related to risks experienced by pediatric TBI patients.

TABLE 3. (*Continued*). Updated Recommendations: Treatments

Topics	Recommendations
Nutrition	**Level II** **To Improve Overall Outcomes** II.1. Use of an immune-modulating diet is not recommended. **Level III** **To Improve Overall Outcomes** *III.1. Initiation of early enteral nutritional support (within 72 hr from injury) is suggested to decrease mortality and improve outcomes.*
Corticosteroids	**Level III** **To Improve Overall Outcomes** *III.1. The use of corticosteroids is not suggested to improve outcome or reduce ICP.* *Note: Recommendation III.1 is not intended to circumvent use of replacement corticosteroids for patients needing chronic steroid replacement therapy, those with adrenal suppression, and those with injury to the hypothalamic-pituitary steroid axis.*

ICP = intracranial pressure, PTS = posttraumatic seizures.

[a]The first recommendation indicates that prophylactic hypothermia does not improve overall outcomes for pediatric patients with severe traumatic brain injury. The second recommendation indicates that hypothermia is effective in control of ICP. Although this may appear to be somewhat antithetical, the two endpoints of overall outcomes and ICP control are clearly distinct. Please see the full Guideline for additional detail.

Italics indicate new or revised recommendations.

The topics that are included reflect current practice but are expected to change as new treatments are developed that may replace or complement existing treatments. These topics include 15 recommendations; of these seven are new or revised. These seven include two recommendations in hyperosmolar therapy; one in analgesics, sedatives, and neuromuscular blockade; one in seizure prophylaxis; two in temperature control; and one in nutrition.

DISCUSSION

New Evidence

Table 4 lists the 35 new studies (10–46) added to the evidence base that was used to support new or existing recommendations. This table presents the studies by topic, provides the citation, and includes the studies design, the number of patients included (*n*), and data class. An additional 13 new studies were added to the guideline document that addressed topics without sufficient evidence to support a recommendation (47–59). More details, such as the outcomes and results for all new studies, are included in the evidence tables and narrative in the full online guideline.

Ongoing and Future Research

Evidence-based guidelines rarely (if ever) contain enough data to fully populate a clinical protocol. This is certainly the case with the treatment of severe pediatric TBI. Rather the goal is to contribute to a transparent, ongoing process that leads to better research and more evidence in the future. These Guidelines provide recommendations based on the available evidence and at the same time identify gaps that can inform the future research agenda. These gaps can be filled by creating clinical protocols using consensus where evidence is lacking. Together the gaps and protocols provide structure and identify patient samples for the generation of new research. The new research populates the evidence base which can then be used to further develop the Guidelines, creating a recursive cycle designed to grow the evidence base and increase the number of evidence-based recommendations in the future.

Although the number of studies has increased in this update of the Guidelines, most recommendations are based on a small number of studies that are mostly class 3. We hope this will change as the impact of evidence-based practice is documented and new studies undertaken. We are optimistic that the next update will have a stronger evidence base because an important study of pediatric TBI, designed and executed by a guidelines clinical investigator and coauthor, is concluding. This study, ADAPT, was designed to address 12 a priori hypotheses across five Guidelines topics (advanced neuromonitoring, hyperosmolar therapy, cerebrospinal fluid drainage, ventilation, and nutrition) and is likely to also provide information on other topics and questions from post hoc analyses (5). ADAPT is an important example of the value of a guideline in highlighting what cannot be said due to lack of evidence; those gaps provide opportunities for innovation and direction for research.

In addition to ADAPT, the pediatric TBI community needs to promote and support innovate ways to generate higher quality class 1 and class 2 studies that can inform stronger (i.e., level I and level II) recommendations. These other needs include the following:

1) Research that examines the integration of individual treatments in the context of goal-directed therapy. No treatment

TABLE 4. New Studies Added Since Last Edition to Evidence Supporting Revisions to Recommendations

Topics	References	Study Design and Sample Size (*n*)	Data Class
Monitoring			
Intracranial pressure monitoring	Bennett et al (10)	Retrospective, *n* = 3,084	3
	Alkhoury et al (11)	Retrospective, *n* = 3,107	3
	Bennett et al (12)	Retrospective, *n* = 4,667	3
Advanced neuromonitoring	Stippler et al (13)	Treatment series, *n* = 46	3
	Figaji et al (14)	Treatment series, *n* = 28	3
Neuroimaging	Bailey et al (15)	Treatment series, *n* = 9	3
	Bata et al (16)	Retrospective, *n* = 71	3
Thresholds			
Thresholds for treatment of intracranial hypertension	Miller Ferguson et al (17)	Retrospective, *n* = 85	3
	Mehta et al (18)	Retrospective, *n* = 22	3
Thresholds for cerebral perfusion pressure	Allen et al (19)	Retrospective, *n* = 317	2
	Miller Ferguson et al (17)	Retrospective, *n* = 85	3
	Vavilala et al (20)	Retrospective, *n* = 236	3
Treatments			
Hyperosmolar therapy	Shein et al (21)	Prospective, *n* = 16	2
	Piper et al (22)	Treatment series, *n* = 32	3
	Webster et al (23)	Retrospective, *n* = 58	3
	Gonda et al (24)	Retrospective, *n* = 48 traumatic brain injury	3
Analgesics, sedatives, and neuromuscular blockade	Welch et al (25)	Treatment series, *n* = 31	3
	Shein et al (21)	Prospective, *n* = 16	3
Cerebrospinal fluid drainage	Andrade et al (26)	Treatment series, *n* = 58, *n* = 11 (younger than 17)	3
Seizure prophylaxis	Liesemer et al (27)	Retrospective, *n* = 54 moderate, *n* = 221 severe	3
Ventilation therapies	No new studies		
Temperature control/ hypothermia	Tasker et al (28, 30)	Meta-analysis, *n* = 470	Fair quality
	Crompton et al (29, 31)	Meta-analysis, *n* = 454	Poor quality
	Adelson et al (32)	RCT, *n* = 77	1
	Beca et al (33)	RCT, *n* = 50	2
	Hutchinson et al (34)	Retrospective (secondary analysis of 2008 RCT), *n* = 225	2
	Empey et al (35)	RCT, *n* = 19	3
Barbiturates	Vavilala et al (20)	Retrospective, *n* = 236	3
	Mellion et al (36)	Treatment series, *n* = 36	3
Decompressive craniectomy	Pechmann et al (37)	Treatment series, *n* = 12	3
	Prasad et al (38)	Treatment series, *n* = 71	3
	Desgranges et al (39)	Treatment series, *n* = 12	3
	Khan et al (40)	Treatment series, *n* = 25, 21 severe	3
	Csokay et al (41)	Treatment series, *n* = 8	3
	Suarez et al (42)	Treatment series, *n* = 14	3
	Adamo et al (43)	Treatment series, *n* = 7	3
	Figaji et al (44)	Treatment series, *n* = 12	3
	Messing-Junger et al (45)	Treatment series, *n* = 7	3
Nutrition	Taha et al (46)	Retrospective, *n* = 90	3
Corticosteroids	No new studies		

RCT = randomized controlled trial.

or management approach exists independent of other treatments and approaches or independent of the ecology of the treatment setting. The design of meaningful and effective future research must be consistent with this clinical reality.

2) Ongoing identification of new topics for investigation. As our understanding of TBI and trauma improves, it is likely new topics will need to be added to the Guidelines. The literature and ongoing trials need to be scanned regularly. It is important that the Guidelines reliably include what evidence is available for new, emerging topics and treatments.
3) Consistency in data collection across studies. Future research should emphasize consistency in data collection across research projects, such as utilization of the Common Data Elements of the National Institutes of Health (60–63).

It is important that the pediatric TBI research community systematically address these questions by creating a prioritized research agenda and advocating for additional high-quality research that can populate the evidence base for future guidelines.

CONCLUSIONS

The increase in the number of studies as well as the number of class 2 studies and level II recommendations is encouraging. The growth in the evidence base strengthens the utility of the evidence-based recommendations as a basis for local protocols, which can incorporate consensus where evidence is still not available. However, this update also underscores that much work remains to be done if our goal is evidence-based treatment designed to improve outcomes for children who sustain severe TBI.

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