**Practice Guideline Update Recommendations**

**Summary: Disorders of Consciousness**

Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology; the American Congress of Rehabilitation Medicine; and the National Institute on Disability, Independent Living, and Rehabilitation Research

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Go to Neurology.org/N for full disclosures. Funding information and disclosures deemed relevant by the authors, if any, are provided at the end of the article.

This research was supported through a memorandum of understanding between the American Academy of Neurology, the American Congress of Rehabilitation Medicine, and the National Institute on Disability and Rehabilitation Research (NIDRR). In 2014, NIDRR was moved from the US Department of Education to the Administration for Community Living of the US Department of Health and Human Services. This article does not reflect the official policy or opinions of NIDILRR or HHS and does not constitute an endorsement by NIDILRR, HHS, or other components of the federal government.

Approved by the AAN Guideline Development, Dissemination, and Implementation Subcommittee on October 21, 2017; by the AAN Practice Committee on April 9, 2018; by the American Congress of Rehabilitation Medicine Board of Governors on April 30, 2018; by the National Institute on Disability, Independent Living, and Rehabilitation Research Review Committee on April 5, 2018; and by the AAN Institute Board of Directors on May 2, 2018.

This practice guideline was endorsed by the American Academy of Physical Medicine and Rehabilitation on April 4, 2018; by the American College of Surgeons Committee on Trauma on July 3, 2018; and by the Child Neurology Society on April 17, 2018.

This special article is published simultaneously in Neurology® and the Archives of Physical Medicine and Rehabilitation. Neurology was responsible for peer review of this article.

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Abstract

Objective: To update the 1995 American Academy of Neurology (AAN) practice parameter on persistent vegetative state and the 2002 case definition on minimally conscious state (MCS) and provide care recommendations for patients with prolonged disorders of consciousness (DoC).

Methods: Recommendations were based on systematic review evidence, related evidence, care principles, and inferences using a modified Delphi consensus process according to the AAN 2011 process manual, as amended.

Recommendations: Clinicians should identify and treat confounding conditions, optimize arousal, and perform serial standardized assessments to improve diagnostic accuracy in adults and children with prolonged DoC (Level B). Clinicians should counsel families that for adults, MCS (vs vegetative state [VS]/unresponsive wakefulness syndrome [UWS]) and traumatic (vs nontraumatic) etiology are associated with more favorable outcomes (Level B). When prognosis is poor, long-term care must be discussed (Level A), acknowledging that prognosis is not universally poor (Level B). Structural MRI, SPECT, and the Coma Recovery Scale—Revised can assist prognostication in adults (Level B); no tests are shown to improve prognostic accuracy in children. Pain always should be assessed and treated (Level B) and evidence supporting treatment approaches discussed (Level B). Clinicians should prescribe amantadine (100–200 mg bid) for adults with traumatic VS/UWS or MCS (4–16 weeks post injury) to hasten functional recovery and reduce disability early in recovery (Level B). Family counseling concerning children should acknowledge that natural history of recovery, prognosis, and treatment are not established (Level B). Recent evidence indicates that the term chronic VS/UWS should replace permanent VS, with duration specified (Level B). Additional recommendations are included.

Recommendation 1 rationale

Our systematic review highlights the complexities of caring for patients with prolonged DoC (i.e., ≥28 days) at every stage. Such patients may be misdiagnosed due to confounding neurologic deficits or inexperience in examining patients for subtle signs of consciousness. Accurate diagnosis is important to educate families about patients’ level of consciousness and function, inform prognostic counseling, and guide treatment decisions. Knowledge gaps often lead to overestimation or underestimation of prognosis by nonspecialists. In addition, patients with prolonged DoC frequently experience significant medical complications that can slow recovery and interfere with treatment interventions. In view of this risk, patients are likely to have a better chance for recovery if care is provided in a specialized setting managed by clinicians who are knowledgeable about the risks associated with DoC and are capable of initiating timely treatment. This is supported by findings from a large retrospective trauma registry, which found that cumulative mortality at 3 years postdischarge is significantly lower for patients discharged to home or inpatient rehabilitation facilities than those discharged to skilled nursing facilities, even after adjusting for covariates. Care for patients with prolonged DoC may benefit from a team of multidisciplinary rehabilitation specialists, including neurologists, psychologists, neuropsychologists, physiatrists, physical therapists, occupational therapists, speech pathologists, nurses, nutritionists, internists, and social workers. A companion article summarizes systematic review conclusions.

List of abbreviations:
- AAN American Academy of Neurology
- ACRM American Congress of Rehabilitation Medicine
- CI confidence interval
- CRS-R Coma Recovery Scale—Revised
- DoC disorders of consciousness
- DRS Disability Rating Scale
- FDG fluorodeoxyglucose
- MCS minimally conscious state
- TBI traumatic brain injury
- UWS unresponsive wakefulness syndrome
- VS vegetative state
such as individualized quantitative behavioral assessment have been useful in distinguishing specific purposeful responses from generalized, nonpurposeful, or reflexive responses. On the basis of these findings, diagnostic accuracy may be enhanced by using standardized neurobehavioral assessment measures over qualitative bedside examination alone. If standardized assessments are used, those with the highest quality of evidence should be employed. A systematic review performed by ACRM recommended the Coma Recovery Scale—Revised (CRS-R), Wessex Head Injury Matrix, Sensory Modality Assessment and Rehabilitation Technique, Western NeuroSensorial Stimulation Protocol, Disorders of Consciousness Scale, and Sensory Stimulation Assessment Measure for use in clinical practice.

**Recommendation 2b rationale**

While there is insufficient high-quality evidence to recommend the use of serial evaluations to improve diagnostic sensitivity and specificity, because of the inconsistency and variability of behavioral responses that is characteristic of individuals with prolonged DoC, reliance on a single examination may contribute to greater risk of misdiagnosis. Multiple behavioral evaluations over time may improve diagnostic reliability and accuracy as compared with a single evaluation. Serial evaluations conducted by trained clinicians using a standardized, validated neurobehavioral assessment instrument have the potential to improve the reliability/validity of diagnosis. There are insufficient data to recommend a minimum duration of time for an assessment session or how often serial examinations should be performed. The frequency of serial standardized neurobehavioral examinations should be based on clinical judgment with consideration given to reported changes in arousal and responsiveness, the removal or cessation of diagnostic confounders, and the length of time since the last assessment.

**Recommendation 2c/2d rationale**

Patients with prolonged DoC may exhibit inconsistent or reduced behavioral responsiveness because of fluctuations in the level of arousal, systemic medical problems, secondary neurologic complications, and other adverse events (e.g., medication side effects). Level of consciousness cannot be assessed accurately during periods of low arousal. In patients who demonstrate fluctuations in wakefulness, efforts should be made to increase arousal level...
This is the one recommendation in this guideline pertaining to individuals in a DoC for less than 28 days. While patients with an acute DoC are not routine EEG or evoked response studies as clinically useful important degree. There is insufficient evidence to support or distinguishing MCS from VS/UWS, generally to an only mildly functioning may also improve arousal and level of consciousness. Prognostic counseling recommendations

Clinical care for patients with prolonged DoC should perform serial standardized behavioral evaluations to identify trends in the trajectory of recovery that are important for establishing prognosis (Level B).

3. When discussing prognosis with caregivers of patients with a DoC during the first 28 days postinjury, clinicians must avoid statements that suggest these patients have a universally poor prognosis (Level A).

4. Clinicians caring for patients with prolonged DoC should perform serial standardized behavioral evaluations to identify trends in the trajectory of recovery that are important for establishing prognosis (Level B).

5. Posttraumatic VS/UWS: Clinicians should perform the DRS at 2–3 months postinjury (Level B) and may assess for the presence of P300 at 2–3 months postinjury (Level C based on feasibility) or assess EEG reactivity at 2–3 months postinjury (Level C based on feasibility) to assist in prognostication regarding 12-month recovery of consciousness for patients in traumatic VS/UWS. Clinicians should perform MRI 6–8 weeks postinjury to assess for corpus callosal lesions, dorsolateral upper brainstem injury, or corona radiata injury in order to assist in prognostication regarding remaining in PVS at 12 months for patients in traumatic VS/UWS (Level B). Clinicians should perform a SPECT scan 1–2 months postinjury to assist in prognostication regarding 12-month recovery of consciousness and degree of disability/recovery for patients in traumatic VS/UWS (Level B). Clinicians may assess for the presence of higher level activation of the auditory association cortex using BOLD fMRI in response to a familiar voice speaking the patient’s name to assist in prognostication regarding 12-month (postsan) recovery of consciousness for patients in traumatic VS/UWS 1–60 months postinjury (Level C based on feasibility, cost).

6. Nontraumatic, postanoxic VS/UWS: Clinicians should perform the CRS-R (Level B) and may assess SEPs (Level C based on feasibility) to assist in prognostication regarding recovery of consciousness at 24 months for patients in nontraumatic postanoxic VS/UWS.

7. Given the frequency of recovery of consciousness after 3 months in patients in nontraumatic VS/UWS, and after 12 months in patients with traumatic VS/UWS (including some cases emerging from MCS), use of the term permanent VS should be discontinued. After these time points, the term chronic VS (UWS) should be applied, accompanied by the duration of the VS/UWS (Level B).

Abbreviations: BOLD, blood oxygen level—dependent; CRS-R, Coma Recovery Scale—Revised; DRS, Disability Rating Scale; MCS, minimally conscious state; MOLST, medical orders for life-sustaining treatment; PVS, persistent vegetative state; SEP, somatosensory evoked potential; TBI, traumatic brain injury; UWS, unresponsive wakefulness syndrome; VS, vegetative state.

This is the one recommendation in this guideline pertaining to individuals in a DoC for less than 28 days. While patients with an acute DoC are not the primary population covered by this guideline, the results of the systematic review and review of related evidence showing the potential for long-term recovery in individuals with DoC lasting longer than 28 days apply when counseling the families of patients who are <28 days from injury.

Using protocols designed for this purpose (e.g., the CRS-R Arousal Facilitation Protocol) before assessing the level of consciousness. Identifying and treating conditions that impair neurologic functioning may also improve arousal and level of consciousness.

Our systematic review identified that some electrophysiologic procedures (EMG thresholds for detecting response to motor commands, EEG reactivity, laser-evoked potential responses, and the Perturbational Complexity Index) possibly have value for distinguishing MCS from VS/UWS, generally to an only mildly important degree. There is insufficient evidence to support or refute the routine clinical use of functional neuroimaging or routine EEG or evoked response studies as clinically useful adjuncts to behavioral evaluations to detect conscious awareness in patients diagnosed with VS/UWS. In addition, functional imaging is not widely available and may not be clinically feasible in large numbers of patients. However, 2 reviewed studies identified fMRI changes in response to a word-counting task and an incorrect-minus-correct activation protocol in patients diagnosed with VS/UWS by the CRS-R (38%, 95% confidence interval [CI] 14%–69%, and 38%, 95% CI 23%–56%, respectively). Research studying DoC populations overlapping with those in this guideline (i.e., cohorts including patients with a DoC for longer than 28 days but not confined exclusively to patients with prolonged DoC) suggests that some individuals without signs of awareness on behavior-based evaluations may have positive findings using other modalities, such as functional MRI, PET scans, or electrophysiologic studies. In 1 study of patients with VS/ UWS based on standardized neurobehavioral assessment,
functional neuroimaging studies (18F-fluorodeoxyglucose [FDG] PET, fMRI) performed at various times postinjury demonstrated evidence of brain activity compatible with at least minimal conscious awareness in approximately 32% of patients scanned using 18F-FDG PET or mental imagery fMRI or both (13/41; 95% CI 20%–47%), with 18F-FDG PET showing results consistent with MCS in 33% of patients diagnosed with VS/UWS by the CRS-R (12/36; 95% CI 20%–50%) and mental imagery fMRI showing results consistent with MCS in 11% (3/28; 95% CI 4%–27%). When using high-density EEG recordings assessing a combination of low-frequency power, EEG complexity, and information exchange in a population overlapping with that in this guideline, 25 of 75 recordings in patients in VS/UWS (33%, 95% CI 24%–45%) were classified as suggestive of MCS, with a greater recovery of consciousness in those categorized as MCS than VS/UWS on the EEG (11/50 VS vs 11/23 MCS, with 2 lost to follow-up; risk difference 26%, 95% CI 3%–47%).27

Although multimodal evaluations show promise in increasing sensitivity for detection of conscious awareness, these studies return negative findings in the majority of patients diagnosed with VS/UWS on behavioral assessment, and the exact link between these findings and consciousness remains unclear. Widespread use of multimodal imaging is unlikely to change the diagnosis in most patients diagnosed with VS/UWS. At the same time, injury sequelae (such as severe hypertonus) may confound behavioral assessment and compromise diagnostic accuracy. In addition, diagnostic findings may remain ambiguous despite serial assessment due to the inconsistency or subtlety of the behavioral evidence. The largest functional neuroimaging study conducted to date in patients with DoC reported that ambiguous or erroneous findings clouded clinical diagnosis in 33 of 126 (27%) cases.26

**Recommendation 3 rationale**

In patients with severe traumatic brain injury (TBI), many of whom have a DoC, one study found that hospital mortality was 32%, with 70% of those deaths associated with the withdrawal of life-sustaining therapy.2 Withdrawal of lifesustaining therapy was more closely associated with the facility where care was provided than with baseline characteristics, including age, sex, pupillary

<table>
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<tr>
<th>Table 3</th>
<th>Recommendation statements for care and treatment for adults with a prolonged disorder of consciousness (DoC)</th>
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<tr>
<td>Recommendation Number</td>
<td>Recommendation Statement and Level</td>
</tr>
<tr>
<td>11</td>
<td>Clinicians must identify patient and family preferences early and throughout provision of care to help guide the decision-making process for persons with prolonged DoC (Level A).</td>
</tr>
<tr>
<td>12</td>
<td>Clinicians should be vigilant to the medical complications that commonly occur during the first few months after injury among patients with DoC and, thus, should utilize a systematic assessment approach to facilitate prevention, early identification, and treatment (Level B).</td>
</tr>
<tr>
<td>13</td>
<td>Clinicians should assess individuals with a DoC for evidence of pain or suffering and should treat when there is reasonable cause to suspect that the patient is experiencing pain (Level B), regardless of level of consciousness. Clinicians should counsel families that there is uncertainty regarding the degree of pain and suffering that may be experienced by patients with a DoC (Level B).</td>
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<tr>
<td>14</td>
<td>Clinicians caring for patients with traumatic VS/UWS or MCS who are between 4 and 16 weeks postinjury should prescribe amantadine 100–200 mg twice daily to hasten functional recovery and reduce degree of disability in the early stages of recovery after determining there are no medical contraindications or other case-specific risks for use (Level B).</td>
</tr>
<tr>
<td>15</td>
<td>Clinicians should counsel families about the limitations of existing evidence concerning treatment effectiveness and the potential risks and harms associated with interventions that lack evidentiary support (Level B). When discussing nonvalidated treatments, clinicians should provide evidence-based information regarding the projected benefits and risks of a particular treatment and the level of uncertainty associated with the proposed intervention, keeping in mind that families and caregivers are often in distress and vulnerable (Level B). Clinicians should counsel families that, in many cases, it is impossible to discern whether improvements observed early in the course of recovery were caused by a specific intervention or spontaneous recovery (Level B).</td>
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**Abbreviations:** MCS, minimally conscious state; UWS, unresponsive wakefulness syndrome; VS, vegetative state.

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<th>Table 4</th>
<th>Recommendation statements for care for children with a prolonged disorder of consciousness (DoC)</th>
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<tr>
<td>Recommendation Number</td>
<td>Recommendation Statement and Level</td>
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<tr>
<td>16</td>
<td>Clinicians should treat confounding conditions, increase arousal prior to diagnostic assessments, use valid and reliable standardized behavioral assessments (particularly those targeting pediatric populations), and conduct serial assessments to improve diagnostic accuracy in children with prolonged DoC (Level B).</td>
</tr>
<tr>
<td>17</td>
<td>Clinicians should counsel families that the natural history and prognosis of children with prolonged DoC is not well-defined and that there are no current evaluations established to improve prognostic accuracy in this population (Level B).</td>
</tr>
<tr>
<td>18</td>
<td>Clinicians should counsel families that there are no established therapies for children with a prolonged DoC (Level B).</td>
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</table>
Recommendation 4 rationale

The natural history of DoC is not well-defined, particularly for populations with nontraumatic brain injury, and diagnosis and prognosis can be challenging. Individuals with DoC can fluctuate between different diagnostic categories such as VS and MCS. Fluctuation is particularly common early in the course of recovery, and one study suggests a 30% probability of observing behaviors suggestive of MCS in patients diagnosed with VS/UWS when assessments are conducted in the morning. Patients with VS may also emerge to MCS over time. MCS is probably associated with a better prognosis than VS. Serial examinations, already suggested to improve diagnostic accuracy, may also aid prognosis in view of the relationship between diagnosis and prognosis.

Recommendation 5 rationale

In patients diagnosed with prolonged traumatic VS/UWS, Disability Rating Scale (DRS) scores <26 at 2–3 months postinjury, a detectable P300 at 2–3 months postinjury, a reactive EEG at 2–3 months postinjury, and higher activation of the auditory association cortex using blood oxygen level–dependent fMRI in response to a familiar voice speaking the patient’s name probably have prognostic utility, suggesting an increased chance of recovering consciousness within 12 months. A normal SPECT scan at 1–2 months postinjury, lower DRS scores in general 2–3 months postinjury, and a detectable P300 2–3 months postinjury after controlling for DRS and EEG reactivity are possibly associated with either an increased likelihood of recovery of consciousness or a more favorable outcome, while MRI performed 6–8 weeks postinjury showing corpus callosal lesions, dorsolateral upper brainstem injury, or corona radiata injury are possibly associated with a worse prognosis at 12 months.

Recommendation 6 rationale

In patients diagnosed with nontraumatic postanoxic VS/UWS, it is highly probable that CRS-R scores of ≥6 obtained more than 1 month after onset and the presence of somatosensory evoked potentials from bilateral median nerve stimulation each have prognostic utility as independent predictors of recovery, suggesting an increased likelihood of recovery of responsiveness by 24 months postinjury.

Recommendation 7 rationale

The 1994 AAN Multi-Society Task Force defined VS as permanent 3 months after a nontraumatic injury leading to VS and 12 months following a traumatic injury, acknowledging that unexpected recoveries will occur after these times but that these cases will be rare and typically associated with severe disability. A reanalysis of the Task Force data concluded that the estimated rates of late recovery for traumatic and nontraumatic VS were unreliable due to inconsistent follow-up (only 27 cases were available with follow-up after 12 months), unreliable reporting (in some cases, follow-up was obtained through “personal communications”), and questionable diagnostic accuracy. Relying only on the portion of the Task Force dataset that was extracted from the Traumatic Coma Data Bank (which appropriately defined VS and reported findings on 25 cases followed after 12 months), 6 patients (14%) recovered consciousness between 1 and 3 years postinjury. This recovery rate is substantially higher than the 1.6% reported in the Task Force Report and raised questions about the appropriateness of the term permanent VS.

In the current systematic review, no study evaluated the prognosis of patients with traumatic VS/UWS after 12 months of injury. One Class II study mixing patients with traumatic and nontraumatic VS/UWS found that none of these patients in VS/UWS 12 months after onset improved when assessed at 2, 3, 4, and 5 years postinjury (1 lost to follow-up, 9 died, and 2 remained in VS/UWS), but due to the small sample size, CIs for the possibility of improving were wide (0%, 95% CI 0%–14%).

Recent studies suggest that some patients with prolonged nontraumatic VS/UWS may experience ongoing recovery after 3 months. Meta-analyses performed in this systematic review found it is possible that 17% (95% CI 5%–30%) will recover consciousness (emerge from VS/UWS) at 6 months. After 6 months, it is possible that an estimated 7.5% (95% CI 0%–24%) may recover consciousness. In one study of prolonged anoxic vegetative state included in the systematic review, of the 9 of 43 recovering responsiveness, 2 recovered between 3 and 6 months, 3 recovered at 6–12 months, and 4 recovered at 12–24 months. Of the 2 individuals emerging from MCS, 1 patient recovered consciousness at 16 months and emerged from MCS at 18 months and the other recovered consciousness at 22 months and emerged from MCS at 25 months; both remained severely disabled. Of 41 patients who remained in VS/UWS at 6 months, 7 additional patients recovered consciousness before 24 months (17%, 95% CI 9%–31%). The natural history of nontraumatic VS/UWS is likely tied to the underlying etiology, with nontraumatic VS/UWS related to a specific insult (e.g., anoxic injury, ischemia) different from that relating to ongoing neurodegeneration.

Additional evidence suggests that late transition to MCS from VS/UWS may occur in as many as 20% of patients who meet permanence criteria. One study followed 50 patients who remained unconscious for a mean of 11.1 (±4.8) months after traumatic or nontraumatic brain injury and reported that 10 patients (7 traumatic, 3 nontraumatic) recovered consciousness between 14 and 28 months postonset. A second study followed 108 patients with TBI across a 5-year interval, all of whom failed to recover command-following during the course of inpatient rehabilitation. Among the 17 patients who were still unable to follow commands at 12 months postonset, 8 (47.0%) regained this ability between 1 and 5 years postinjury.
Although the majority of patients who remain in VS/UWS across the first 3 (after nontraumatic) and 12 months (after traumatic) postinjury will remain in this condition permanently, a substantial minority will recover consciousness beyond this time frame. While most of these patients will be left with severe disability, functional outcome ratings indicate that some will regain the ability to communicate reliably, perform self-care activities, and interact socially. In view of these findings, continued use of the term permanent VS is not justified. Use of this term implies irreversibility, which is not supported by the current research and has implications for family counseling, decision-making, and the ethics of the field. The guideline panel suggests that the term permanent VS be replaced by the term chronic VS to indicate the stability of the condition (keeping with other diseases that have a chronic phase). This should be accompanied by a description of the current duration of the VS/UWS, as evidence supports a decreasing likelihood of recovery with longer duration of unresponsiveness. Because most patients with late recovery of consciousness will remain fully or partially dependent upon others for activities of daily living, prognostic counseling should emphasize the need for long-term care and specify the type of supportive care required.

Recommendation 8 rationale
Systematic review evidence showed that in patients with prolonged DoC, those diagnosed with MCS within the first 5 months of injury have a more favorable long-term prognosis for functional recovery than those diagnosed with VS/UWS. Long-term prognosis is also more favorable in patients who have sustained traumatic vs nontraumatic brain injury. The evidence reviewed does not clearly support or refute age and time post-injury as prognostic features. As described in the rationale for recommendation 3 above, evidence from the systematic review identified that individuals with a DoC at 1 month postinjury may still attain functionally significant recovery after 1 year postinjury, with additional longitudinal studies showing that approximately 20% of patients recover to the level where they could return to work or school.

Recommendation 9 rationale
Patients with prolonged DoC may have a prolonged recovery over months to years, and many will remain severely disabled. Employment and personal finances in the short term and the long term will be significantly affected, and these effects will have implications for family members. Patients and families benefit from planning in advance for an expected prolonged recovery.

Recommendation 10 rationale
See rationale for recommendation 7.

Recommendation 11 rationale
Preexpressed wishes of patients with prolonged DoC and values of families of persons with prolonged DoC can be highly variable. Values may also change over the course of illness. Personal values should be identified early and need to be reassessed over time when making decisions regarding care for individuals with prolonged DoC.

Recommendation 12 rationale
Complication rates are high in patients with prolonged DoC and negatively affect morbidity and mortality. It is important that clinicians remain vigilant to medical complications in the short term to facilitate their early identification and to help optimize long-term outcomes. The most common complications in patients with prolonged DoC include agitation/aggression, hypertonia, sleep disturbance, and urinary tract infections. Other, more severe complications, such as hydrocephalus, pneumonia, and paroxysmal sympathetic hyperactivity, can disrupt rehabilitation efforts, as they often require rehospitalization. Strategies for early detection and rapid management of complications include daily physician rounds, 24-hour specialty physician coverage, on-site availability of diagnostic resources, and timely access to specialty consultations.

Recommendation 13 rationale
The potential to experience pain and suffering is an issue frequently raised with respect to treatment, ethical, and legal questions in individuals with DoC. Some studies using functional imaging indicate that brain activation in networks supporting pain perception is lower in patients diagnosed with VS compared with those in MCS and conscious controls, suggesting that patients in VS lack capacity for full pain awareness. Other studies suggest that the relationship between level of consciousness and pain perception is unclear. Accurate assessment of pain and suffering in individuals with DoC is limited by challenges in accurately diagnosing pain due to the level of consciousness and conflicting evidence regarding the potential of patients in VS or MCS to experience pain and suffering. Clinicians should be cautious in making definitive conclusions about pain and suffering in individuals with DoC.

Recommendation 14 rationale
Amantadine (100–200 mg twice daily), when administered over a period of 4 weeks in patients between 16 and 65 years old with traumatic DoC who are between 4 and 16 weeks of injury, probably hastens functional recovery in the early stages. Faster recovery reduces the burden of disability, lessens health care costs, and minimizes psychosocial stressors in patients and caregivers.

Recommendation 15 rationale
Most therapies proposed for treating patients with DoC (e.g., hyperbaric oxygen, nutraceuticals, stem cell therapies, primrose oil) have insufficient evidence to support or refute their use, and many have associated risks. Families may pursue these treatments in the absence of evidence because they are desperate for ways to help their loved one and interventions supported by high-quality evidence are sparse. Counseling families about treatment effectiveness is complicated by the difficulties inherent in determining whether improvements observed early in the course of recovery are related to interventions or due to spontaneous recovery.

Recommendation 16 rationale
No evidence was identified regarding the diagnosis of children with prolonged DoC. In the absence of pediatric-specific evidence, it is reasonable to apply the diagnostic recommendations for adult
populations that address the treatment of confounding conditions to improve diagnosis, the importance of increasing arousal prior to diagnostic assessments, using valid and reliable standardized behavioral assessments, and conducting serial assessments to children with DoC.

**Recommendation 17 rationale**

The natural history of DoC in children is not well-defined. In children with prolonged DoC, traumatic etiology is possibly associated with a better chance of recovery, as is the absence of posttraumatic autonomic dysfunction. Posttraumatic hyperthermia may be associated with a worse outcome. No other evidence was identified.

**Recommendation 18 rationale**

No identified therapeutic studies enrolled pediatric populations. The only therapeutic intervention shown to have efficacy in adults (16–65 years) is amantadine. A retrospective case-controlled study of amantadine use in patients with TBI reported that 9% of children taking this treatment had side effects, but methodologic concerns limit therapeutic conclusions from this study.

**Author contributions**

Dr. Giacino: study concept and design, acquisition, analysis, and interpretation of data, drafting/revising the manuscript, critical revision of the manuscript for important intellectual content, study supervision. Dr. Katz: study concept and design, acquisition, analysis, and interpretation of data, drafting/revising the manuscript, critical revision of the manuscript for important intellectual content. Dr. Schiff: study concept and design, acquisition, analysis, and interpretation of data, drafting/revising the manuscript, critical revision of the manuscript for important intellectual content. Dr. Whyte: study concept and design, acquisition, analysis, and interpretation of data, drafting/revising the manuscript, critical revision of the manuscript for important intellectual content. Dr. Ashman: acquisition, analysis, and interpretation of data, critical revision of the manuscript for important intellectual content. Dr. Ashwal: study concept and design, acquisition, analysis, and interpretation of data, drafting/revising the manuscript, critical revision of the manuscript for important intellectual content. Dr. Barbano: acquisition, analysis, and interpretation of data, drafting/revising the manuscript, critical revision of the manuscript for important intellectual content, study supervision. Dr. Hammond: acquisition, analysis, and interpretation of data, drafting/revising the manuscript, critical revision of the manuscript for important intellectual content. Dr. Laureys: acquisition, analysis, and interpretation of data, drafting/revising the manuscript, critical revision of the manuscript for important intellectual content. Dr. Ling: acquisition, analysis, and interpretation of data, drafting/revising the manuscript, critical revision of the manuscript for important intellectual content. Dr. Nakase-Richardson: acquisition, analysis, and interpretation of data, drafting/revising the manuscript, critical revision of the manuscript for important intellectual content. Dr. Seel: acquisition, analysis, and interpretation of data, drafting/revising the manuscript, critical revision of the manuscript for important intellectual content. Dr. Yablon: acquisition, analysis, and interpretation of data, drafting/revising the manuscript, critical revision of the manuscript for important intellectual content. Dr. Getchius: acquisition, analysis, and interpretation of data. Dr. Gronseth: acquisition, analysis, and interpretation of data, drafting/revising the manuscript, critical revision of the manuscript for important intellectual content. Dr. Armstrong: acquisition, analysis, and interpretation of data, drafting/revising the manuscript, critical revision of the manuscript for important intellectual content, study supervision.

**Funding**

This practice guideline was funded by the American Academy of Neurology (AAN), the American Congress of Rehabilitation Medicine, and the National Institute on Disability, Independent Living, and Rehabilitation Research. Authors who serve or served as AAN subcommittee members (E.J.A., S.A., R.B., G.S.G.) or as methodologists (M.J.A., G.S.G.), or who were AAN staff members (T.S.D.G.), were reimbursed by the AAN for expenses related to travel to subcommittee meetings where drafts of manuscripts were reviewed.

**Disclosures**

J. Giacino has received funding for travel from the US Department of Defense for a meeting related to the TBI Endpoint Development Project; from the National Institute on Neurological Disorders and Stroke (NINDS) of the NIH for a meeting related to the Transforming Research and Clinical Knowledge in Traumatic Brain Injury study; from the National Institute on Disability, Independent Living, and Rehabilitation Research. Authors who serve or served as AAN subcommittee members (E.J.A., S.A., R.B., G.S.G.) or as methodologists (M.J.A., G.S.G.), or who were AAN staff members (T.S.D.G.), received financial support from the NIH NINDS for Central Thalamic Stimulation for Traumatic Brain Injury, US Department of Defense for TBI Endpoint Development Project, the Huperzine A for the Treatment of Cognitive, Mood and Functional Deficits After Moderate and Severe TBI study, the Injury and Traumatic Stress (INTRuST) Consortium Neuroimaging Acquisition and Archival study, the NIDILRR for the Spaulding Harvard–Traumatic Brain Injury Model System and for Multicenter Evaluation of Memory Remediation after Traumatic Brain Injury with Donepezil, the NINDS for Transforming Research and Clinical Knowledge in Traumatic Brain Injury study, James S. McDonnell Foundation for Study of Recovery of Consciousness After Severe
Brain Injury, Barbara Epstein Foundation, and the Spaulding Rehabilitation Hospital Department of Physical Medicine and Rehabilitation; and has acted as a witness with regard to a legal proceeding. D. Katz has received royalties from Demos for Brain Injury Medicine, 2013, and from Lash Publications; has received honoraria for speaking at HealthSouth/Encompass Health Medical Directors’ Conference, various grand rounds on topics related to DoC, including Harvard Longwood Neurology, Providence VA Hospital, Tufts Medical Center, Baystate Medical Center, and University of Massachusetts Medical Center, and for service as Chair, External Scientific Advisory Board, VA Rehabilitation Research and Development TBI Center of Excellence, Boston; has given expert testimony in several legal cases involving patients with DoC after brain injury; has received travel support for talks and conferences on DoC from organizations, including World Federation of Neurorehabilitation, International Brain Injury Association, and Moody Foundation/Galveston Brain Injury Conference; received a stipend as medical director of the Acquired Brain Injury Program at Braintree Rehabilitation Hospital from HealthSouth; received compensation for less than 10% of his clinical effort for consultations with patients with DoC; and received support from efforts on NIDILRR funded projects on DoC. 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His spouse has received an NIH grant unrelated to the content of this guideline. F. Hammond is a member of the ACRM Disorders of Consciousness Task Force; served on the US Department of Defense INTRuST Scientific Advisory Council and Avanir Prism II Study Steering Committee; has received royalties from Demos Publishing and Lash Publishing; has received financial support for research from the NIDILRR; holds stock in AbbVie Inc., Amgen Inc., AstraZeneca Plc, Edwards Lifesciences, GW Pharmaceuticals Plc, Intuitive Surgical Inc., Konink Logistics Inc., Merck & Co. Inc., Pfizer Inc., Sanofi, Thermo Fisher Scientific Inc., UnitedHealth Group, and Zoetis Inc.; and has given legal testimony and acted as legal consultant in legal proceedings on the care needs of individuals with brain injury. S. 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R. Nakase-Richardson has received financial compensation for travel for speaking at the University of Mississippi Medical Center, New York University, Mayo Clinic, and University of Alabama, Birmingham; and has received research support from General Dynamics Health Solutions from the Defense and Veterans Brain Injury Center within the Defense Health Agency, US Department of Veterans Affairs Health Services Research and Development, Department of Veterans Affairs Rehabilitation Research and Development, and Patient-Centered Outcomes Research Institute. R. 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