

SPECIAL ARTICLE



# Common Data Elements for Unruptured Intracranial Aneurysms and Aneurysmal Subarachnoid Hemorrhage: Recommendations from the Working Group on Hospital Course and Acute Therapies—Proposal of a Multidisciplinary Research Group

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## Abstract

**Introduction:** The Common Data Elements (CDEs) initiative is a National Institute of Health/National Institute of Neurological Disorders and Stroke (NINDS) effort to standardize naming, definitions, data coding, and data collection for observational studies and clinical trials in major neurological disorders. A working group of experts was established to provide recommendations for Unruptured Aneurysms and Aneurysmal Subarachnoid Hemorrhage (SAH) CDEs.

**Methods:** This paper summarizes the recommendations of the Hospital Course and Acute Therapies after SAH working group. Consensus recommendations were developed by assessment of previously published CDEs for traumatic brain injury, stroke, and epilepsy. Unruptured aneurysm- and SAH-specific CDEs were also developed. CDEs were categorized into “core”, “supplemental—highly recommended”, “supplemental” and “exploratory”.

**Results:** We identified and developed CDEs for Hospital Course and Acute Therapies after SAH, which included: surgical and procedure interventions; rescue therapy for delayed cerebral ischemia (DCI); neurological complications (i.e. DCI; hydrocephalus; rebleeding; seizures); intensive care unit therapies; prior and concomitant medications; electroencephalography; invasive brain monitoring; medical complications (cardiac dysfunction; pulmonary edema); palliative

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Unruptured Aneurysms and SAH – CDE Project Investigators Members are listed in “Appendix”.

comfort care and end of life issues; discharge status. The CDEs can be found at the NINDS Web site that provides standardized naming, and definitions for each element, and also case report form templates, based on the CDEs.

**Conclusion:** Most of the recommended Hospital Course and Acute Therapies CDEs have been newly developed. Adherence to these recommendations should facilitate data collection and data sharing in SAH research, which could improve the comparison of results across observational studies, clinical trials, and meta-analyses of individual patient data.

**Keywords:** Clinical studies, Common Data Elements, Data coding, Data collection, Standardization, Subarachnoid hemorrhage, Aneurysm

## Introduction

Aneurysmal subarachnoid hemorrhage (SAH) carries high levels of disability and mortality. Although functional outcome has initially improved, a plateau has been observed since 1990s [1]. A large number of randomized clinical trials have been published; however, the use of oral nimodipine and endovascular treatment of the culprit aneurysm remain the sole interventions which have broadly impacted management of SAH patients [2, 3].

The conduct of large randomized clinical trials is laborious, difficult, and costly. One alternative is the use of large databases to tackle knowledge gaps in the field of aneurysmal SAH. An example includes the use of comparative effectiveness research exploiting variations in hospital practices to define best practices [4]. However, data are usually difficult to compare or pool, due to lack of uniformity in data coding, definitions, and procedures for sample collection, because researchers tend to use their own data element definitions for new research projects. The variability of definitions may also hamper other uses of combining large prospective databases, such as the development and validation of prognostic models.

Therefore, in an effort to standardize definitions of data among clinical trials in the field of SAH, the National Institute of Health (NIH)/National Institute of Neurological Disorders and Stroke (NINDS) Common Data Elements (CDE) Project [5] instituted the “Unruptured Aneurysm and Aneurysmal Subarachnoid Hemorrhage – Common Data Elements Project” aimed to help investigators conduct clinical research through the development of standardized naming, definitions, and data structure for clinical research variables. The CDEs will facilitate systematic clinical data collection, analysis, and sharing across the research community. Central to the project is the identification of common definitions and the standardization of case report forms and other instruments. This article summarizes the

recommendations of the working group (WG) on “Hospital Course and Acute Therapies” within this project.

## Common Data Elements Overview

### Summary

The CDEs project is a joint effort between the NIH and the NINDS to develop standardized naming, definitions, and data structure for clinical research variables, with the main goal of facilitating the comparison of clinical studies results in major neurological diseases (e.g., traumatic brain injury, ischemic stroke, multiple sclerosis, epilepsy, SAH).

Therefore, recommendations for CDEs for research on Unruptured Intracranial Aneurysms and aneurysmal SAH were established through an interdisciplinary, worldwide initiative, supported by NINDS and the National Library of Medicine CDE teams.

The Hospital Course and Acute Therapies is a WG of the Unruptured Aneurysm and Aneurysmal SAH – CDE Project aimed to construct CDEs regarding hospital-based acute interventions (surgical, endovascular or medical, either considered standard or rescue therapy), course (including systemic and neurological complications) and monitoring, either within or outside the intensive care unit (ICU). The CDE categories included: prior or concomitant medications; electroencephalography (EEG); invasive brain monitoring; medical complications (i.e., pulmonary and cardiac complications); palliative comfort care and end of life issues; discharge status; surgical procedures and other interventions; rescue therapy; neurological complications [i.e., delayed cerebral ischemia (DCI), hydrocephalus, rebleeding, seizures]; and ICU therapies.

### Process for Selecting CDEs

The Hospital Course and Acute Therapies WG consisted of an international and interdisciplinary (neurology, neurosurgery, intensive care, and pharmacology) ad hoc panel of experts in the field of aneurysmal SAH. The

subcommittee was further divided into two subgroups, and two members were assigned as superusers, being responsible for CDEs administration and data entering into the NINDS website (<http://www.commondataelements.ninds.nih.gov/default.aspx>.) [5].

All WG members were trained by the NIH/NINDS staff by means of a webinar to use the CDE Web site and online tools. Previously published CDEs from other neurological diseases such as traumatic brain injury [6], epilepsy [7], and ischemic stroke [8] were assessed for potential inclusion in the SAH-CDE set. SAH-specific CDEs, not described by other CDE projects, were developed by the subgroup committee based on their expertise, by the review of observational studies, and by the review of Clinical Research Forms from specific clinical trials on SAH [2, 9–11]. The Hospital Course and Acute therapies CDEs were selected and prioritized through a consensus-building process. The concept CDEs were discussed and refined during several Skype meetings, telephone conferences, and e-mail interaction. The complete CDEs list was presented and discussed with the entire Unruptured Aneurysm and SAH – CDE Project Group at the Cerebral Aneurysm and Subarachnoid Hemorrhage CDE meeting (May 13–15, 2016 in Houston, TX). All the queries and criticism raised by the group were thoroughly assessed, and adjustments were made accordingly. The final list of CDEs by the Hospital Course and Acute Therapies WG were submitted to the NINDS by the end of June 2016, and went through an internal review along with the combined reports of all WGs. The CDEs were internally reviewed through December 2016, followed by a public review on the NINDS CDE website from January to March 2017. NINDS subsequently translated the concept CDEs into Case Report Form documents to further facilitate application and use of the CDEs in future

SAH studies, and which underwent further scrutiny by the WG members for usability.

### CDE Terminology

*The Hospital Course and Acute Therapies* CDEs were classified according to NINDS into Core, Supplemental—Highly Recommended, Supplemental, and Exploratory (Table 1). An online-voting process was performed, and the co-chairs assembled the final classification after the Houston Neurocritical Care meeting. Only a minority of CDEs was classified as “Core”. The remainder of the Hospital Course and Acute Therapies CDEs was classified as Supplemental—Highly Recommended, Supplemental, and Exploratory.

### Description of CDEs

The construction of the CDEs was performed according to the process described above among two subgroups of experts within the *Hospital Course and Acute Therapies* WG (Subgroup—1: Surgical Procedures and Interventions, Rescue Therapies, Neurological Complications, ICU Therapies. Subgroup—2: Prior and Concomitant Medications, EEG, Invasive Brain Monitoring, Medical Complications, Palliative Comfort Care and End of Life Issues, Discharge Status). All CDEs are stratified into Core, Supplemental—Highly Recommended, Supplemental, and Exploratory. A general description of the CDE categories is given below followed by a brief explanation for the individual CDEs as appropriate. The full set of CDEs is given in online supplemental file 1.

### Core Data Elements

#### *Surgical Procedure and Interventions* [12, 13]

This category contains CDEs regarding the treatment (surgical or endovascular) of target intracranial aneurysms (either ruptured or unruptured) and details

**Table 1 Classification of Common Data Elements according to the level of recommendation (Source: <http://www.commondataelements.ninds.nih.gov>)**

Class	Meaning
Core	A data element that collects essential information applicable to any study, including either those which span across all disease and therapeutic areas or those that are specific to one disease area. The NINDS and their appointed working groups assign the “Core” classification based on the current clinical research best practices. This term applies to both the General CDEs and the Disease-specific CDEs. In each case, the Core CDEs are a small subset of the available CDEs, where it is anticipated that investigators will need to collect the Core CDEs on any type of study
Supplemental—Highly Recommended	A data element, which is essential, based on certain conditions or study types in clinical research studies. In most cases, these have been used and validated in the disease area. These data elements are strongly recommended for the specified disease condition, study type or design
Supplemental	A data element, which is commonly collected in clinical research studies, but whose relevance depends upon the study design (i.e., clinical trial, cohort study, etc.) or type of research involved
Exploratory	A data element that requires further validation, but may fill current gaps in the CDEs and/or substitute for an existing CDE once validation is complete. Such data elements show great promise, but require further validation before they are ready for prime-time use in clinical research studies. They are reasonable to use, but limited study has been done in the target group

regarding the procedure. Within this category, only “type of aneurysm occlusion procedure” (surgery or endovascular) was classified as “core”.

*Type of Intervention: Surgery/Type of Intervention—Endovascular* The nature of the intervention for treatment of SAH source is recommended as a core element. Surgical and endovascular treatment are each defined separately as yes, no or attempted/failed given that an individual aneurysm may ultimately be exposed to both modalities of treatment if one is not successful in securing the rupture source.

### Supplemental-Highly Recommended Data Elements

#### ***Surgical Procedures and Interventions***

*SAH: Day of Intervention* The timing of intervention is an important data element in SAH since it captures timely aneurysm occlusion and thus can have a significant impact on outcomes by prevention of rebleeding. The WG suggests it to be documented relative to the day of rupture (ictus; day 0). “SAH time of intervention” measured in hours after ictus, is also included as a CDE and is therefore more detailed than “Date of intervention”, but is included as a “supplemental” CDE.

*Vessel Repaired* This CDE indicates the location of the artery harboring the target aneurysm (the ruptured aneurysm in case of SAH or target aneurysm for occlusion when it is unruptured and there is no SAH).

#### ***Neurological Complications***

CDEs in this category include global cerebral edema, herniation syndromes, rebleeding, hydrocephalus, DCI, seizures and meningitis/ventriculitis. These CDEs are mostly “supplemental”, but a few were classified “supplemental-highly recommended” as follows.

*Rebleeding* Whether there is a documented rebleed is deemed essential information for almost any type of study, given its strong adverse prognostic impact. We suggest therefore that it is documented, or strongly considered for documentation in SAH studies.

*Clinical Deterioration/Cerebral Infarction (or Both) Due to Delayed Cerebral Ischemia* The WG suggests two CDEs related to DCI as “Supplemental-highly recommended”, and thus to be strongly considered for documentation within any type of study given the strong prognostic impact of DCI. It is expected that future intervention studies are likely to focus on mitigating the consequences of DCI, which renders these CDEs an important study outcome, increasing the need for uniformity in their definition. The DCI CDEs are based on the definition

previously published in a consensus document [14], one focused on an imaging-based definition (i.e., infarction on computed tomography or magnetic resonance imaging), and another defined as clinical signs and/or imaging evidence of infarction.

### Supplemental Data Elements

#### ***Surgical Procedure and Interventions***

*Ventriculostomy Placement/Lumbar Drain Placement* Depending on the type of study, these CDEs may be useful for reporting.

*Type of Surgery or Endovascular Repair/Success of Surgical or Endovascular Intervention/Treatment of Multiple Aneurysms/Number of Aneurysms Treated* These CDEs pertain to general information about surgical or endovascular aneurysm occlusion. “Type of surgery” details whether simple clipping was performed or a more complicated procedure. “Type of endovascular repair” similarly describes whether uncomplicated coiling was done or a more complex procedure, e.g., utilizing stenting or intended vessel occlusion. We suggest that success of aneurysm occlusion be categorized as complete, partial with neck remnant, partial with residual fundus or unsecured based on follow-up radiological assessment for surgically treated aneurysms and with Raymond-Roy grade for endovascular-treated aneurysms [13, 15]. For multiple aneurysms, a CDE to indicate presence or absence and a CDE to indicate the number of aneurysms is included.

*Surgery: Craniotomy Type/Craniectomy/Hematoma Evacuation/Temporary Vessel Occlusion/Temporary Occlusion Time Max/Temporary Occlusion Time Total/Intraoperative Rupture/Intraoperative Assessment of Vessel Patency and/or Aneurysm Occlusion/Intraoperative Complication/Postoperative Complication/Operative Time/Blood Transfusion/Estimated Blood Loss/Intraoperative Neurophysiological Monitoring* These CDEs relate to the surgical procedure details. The CDEs are deemed appropriate and suggested for studies focused on surgical management of ruptured, and some for unruptured, intracranial aneurysms. The CDEs specifically pertain to the details of the aneurysm surgery and those surgical aspects that may contribute to cerebral ischemia or (ultimately) infarction. Neurophysiological monitoring details may be included in studies when deemed appropriate.

*Endovascular: Intraprocedural or Postprocedural Complication/Antithrombotic Medication/Fluoroscopy Dose/Procedure Time* CDEs relate to endovascular aneurysm occlusion and procedural complications and can be used for studies where details of the endovascular procedures are important, including new device assessments.

### **Rescue Therapy**

This category pertains to rescue therapies for vasospasm either by intra-arterial chemical agent or mechanical balloon angioplasty, including potential complications of these procedures. Classification was “supplemental” for all CDEs in this category.

*Intra-arterial Chemical Therapy/Mechanical Angioplasty/Type of Intra-arterial Vasodilator/Adverse Clinical Exam Changes Related to Therapy/Procedural Adverse Events* The use of intra-arterial chemical or mechanical therapies for vasospasm is included in this category of CDEs, including the day of administration and potential neurological complications. The complications of medical and mechanical therapies are each defined individually as a clinically defined CDE (pertaining to neurological deterioration) and additionally as a CDE defined by adverse local or systemic effects such as those related to hyperperfusion or systemic toxicity of vasodilators (e.g., hypotension) or related to mechanical/technical complications (e.g., perforation or embolic events).

### **Neurological Complications**

Apart from rebleeding and DCI-related CDEs classified as supplemental highly recommended, all other CDEs in this category are supplemental and pertain to specific complications which, depending on the type of study, may be considered for reporting.

*Global Cerebral Edema/Brain Stem Herniation/Hydrocephalus/Seizures and Meningitis/Ventriculitis* The most common and relevant neurological complications encountered in patients with SAH were considered by the subgroup experts and CDEs related to those have been selected and defined [14, 16–19].

### **ICU Therapies**

This category contains CDEs for interventions that routinely occur in the ICU setting because SAH patients are typically admitted to an ICU and are cared for by an interdisciplinary team [20, 21]. CDEs pertain to systemic therapies and include hemodynamic management, temperature management, glucose control, (invasive) mechanical ventilation and the use of osmotherapy [9, 20–24]. All ICU therapies CDEs were classified as “supplemental”.

*Blood Pressure Management Goal: Upper, Lower/Blood Pressure Augmentation—Specific* The upper and lower blood pressure management goal CDE assesses the range of mean arterial blood pressure that is aimed for as a goal in the routine setting. When blood pressure

augmentation (or induced hypertension) is studied as a treatment modality for DCI/vasospasm, we suggest defining the target blood pressure by either mean arterial pressure or systolic blood pressure [20, 25].

*Hemodynamic Therapy: General/Hemodynamic Augmentation—General/Hypovolemic Therapy or Volume Augmentation—General or Specific* These CDEs are focused on hemodynamic interventions in the ICU and provide suggested terminologies to enhance uniformity in future reporting. Hemodynamic intervention-related CDEs are defined as being directed at cardiac output, volume status (however defined) and/or blood pressure or any combination of these. Hemodynamic augmentation and hypovolemic therapy/volume augmentation are terms that we suggest are only used in conjunction with targeting supraphysiological values of cardiac output, volume status or blood pressure. Of note, with regard to volume status specifically, recent guidelines and some pertinent studies have generally recommended to stay away from such supraphysiological targets [21, 26]. However, in spite of the lack of evidence, application of induced hypertension is still suggested as a viable option in selected cases [27].

*Target for Fever Management/Glucose Control: Upper and Lower Limit* Temperature and serum glucose represent important systemic targets whose mitigation may impact on patients with SAH. We suggest that studies reporting on fever management mention the cutoff temperature that prompts treatment and similarly glucose upper and lower limits for normality should be reported when appropriate.

*Mechanical Ventilation (Invasive, Noninvasive, Total Duration)* We suggest that for appropriate studies or settings, the application of mechanical ventilation, mode (invasive or noninvasive) and its duration should be considered for reporting since it often represents systemic critical illness next to a comatose state and prognosis is worse in these patients. For this CDE, we suggest a dichotomous reporting, i.e., yes/no, and duration in days.

*Osmotherapy for Intracranial Hypertension or Cerebral Edema* We suggest the reporting of application of any osmotherapy as a dichotomous variable (i.e., yes/no) for appropriate studies.

### **Prior or Concomitant Medications**

We suggest the reporting of prior and concomitant medications, which include but are not limited to: anti-epileptic drugs, anticoagulants, antiplatelets, antithrombotic therapy, and diabetes treatment type. The use of imaging

contrast agent, vasopressors, fluid replacement (i.e., type of fluid), intra-arterial vasodilator, pain medications, neuromuscular blockers, and sedatives are also described in these CDEs. Along with prior and concomitant medications, we suggest also reporting medication allergies, drug dose and frequency, stroke discharge medications, and drug or illicit substance use.

#### **Electroencephalography (EEG)**

Intermittent or continuous EEG monitoring is frequently used to assess brain function, and monitor SAH patients in the ICU. These CDEs are focused on EEG and provide suggested terminologies to enhance uniformity in future reporting. We suggest that for appropriate studies or settings, the application of EEG should be reported (yes/no), along with the date and time the study was started and ended, and the duration of monitoring. The EEG indication (e.g., seizure detection, ischemia detection, prognosis) should be also recorded. Recording and technical specifications, behavioral states recorded, EEG background, ictal and ischemia findings, recording circumstances, and artifacts may be recorded [28–30].

#### **Invasive Brain Monitoring**

These CDEs are focused on intracranial pressure (ICP) [31, 32], brain tissue oxygenation [33], and cerebral microdialysis [34] monitoring. Regarding ICP we suggest the following variables to be recorded: start date/time, stop reason, stop date/time, monitoring problem type, catheter revised indicator, catheter anatomic site, device type, ICP (mmHg), ICP maximum daily measurement (mmHg), mean ICP daily measurement (mmHg), number of ICP episodes >20 mmHg longer than 5 min, number of ICP episode >20 mmHg, cerebral perfusion pressure value (cerebral perfusion pressure [CPP] mmHg = mean arterial pressure measured at tragus level – ICP), number of CPP episodes lower than 60 mmHg. For brain tissue oxygenation [33], we suggest the recording of: start date/time, stop date/time, stop reason, problem type, probe revised (yes/no), anatomic site, values (minimum value over a 24-h period, mean value over a 24-h period), number of episodes below threshold lasting longer than 5 min, time of decreased tissue oxygenation below threshold in hours over a 24-h period. For cerebral microdialysis [34], we suggest the recording of: start date/time, stop date/time, stop reason, problem type, probe revised (yes/no), anatomic site, mean lactate level over a 24-h period, mean pyruvate level over a 24-h period, calculated lactate/pyruvate (L/P) ratio, mean L/P ratio over a 24-h period, maximum L/P ratio over a 24-h period, burden of metabolic crisis (time of increased L/P ratio above threshold in hours over a 24-h period).

#### **Medical Complications (Cardiac Dysfunction; Pulmonary Edema)**

Cardiac and pulmonary complications are very common after SAH. These CDEs are focused on the assessment of cardiac and pulmonary function, which includes the assessment and use of vital signs, laboratory tests, electrocardiogram, echocardiogram, holter, and cardiac magnetic resonance imaging.

#### **Palliative Comfort Care and End of Life Issues**

These CDEs indicates if patients' care were limited to "Comfort Measures Only". These CDEs includes: comfort care earliest documentation timepoint type, comfort care measure type, do not resuscitate or intubate (DNR or DNI) indicator, and DNR or DNI earliest documentation timepoint type.

#### **Discharge Status**

The WG suggests the reporting of discharge status of SAH patients, which includes: diagnosis principal discharge stroke related ICD-10-CM code, hospital discharge data/time, ICU discharge destination type, hospital discharge destination type, location post-acute stroke discharge type, discharge destination type, stroke discharge medication category, stroke service accredited discharge destination type, total ICH and hospital length of stay. The CDEs focused on case fatality/survival, disability (e.g., modified Rankin Scale, Glasgow outcome scale), cognitive impairment (e.g., Montreal Cognitive Assessment, Mini-Mental State Examination), and other cognitive domains assessment is described separately in the *Outcomes and Endpoints Subcommittee*.

#### **Limitations**

Construction of the subcommittee CDEs was complex, because data to be collected about hospital course and acute therapies are often dictated by specific study questions and the type of study and is therefore ill-defined in advance. Therefore, it is quite ambitious to try and develop a sufficient number of CDEs that would cover all possible topics and variables. These subgroup CDEs will need to be updated and re-assessed over time as new treatments for aneurysmal SAH may be introduced in the future. Many CDEs had to be newly constructed because SAH-specific CDEs were largely unavailable, but this also supports the need for the conception of these CDEs through the SAH-CDE project.

#### **Next Steps and Future Work**

The Hospital Course and Acute Therapies CDEs should now be tested on their feasibility for practical use in future SAH studies. A first step is to communicate the CDEs to the broader scientific community to facilitate

wider application. A second step is that studies using them record the use of the SAH-CDE set as made available by NINDS, so that it may become a new standard. Finally, the SAH-CDEs should be viewed as a starting point for standardized reporting of future SAH studies, including trials and systematic reviews, and when new insights or shortcomings of the CDEs become clear, adaptations should be encouraged.

## Conclusions

The Hospital Course and Acute Therapies WG recognized and defined CDEs to be used in future studies pertaining to the aneurysmal SAH field of research. A substantial number of CDEs were incorporated from previously developed CDEs from traumatic brain injury, stroke, and epilepsy, but rearranged for the SAH-CDEs for practical purposes. Additionally, elements specific for the SAH field were developed. The recommendations cover the following areas: surgical and procedure interventions, rescue therapy for delayed cerebral ischemia, neurological complications, intensive care unit therapies, prior and concomitant medications, electroencephalography, invasive brain monitoring, medical complications, palliative comfort care and end of life issues, and discharge status. The implementation of and adherence to these recommendations will facilitate data collection and data sharing in SAH research, which could improve the comparison of results across observational studies and clinical trials and facilitate meta-analyses of individual patient data or updating of prognostic models for SAH.

### Electronic supplementary material

The online version of this article (<https://doi.org/10.1007/s12028-019-00726-3>) contains supplementary material, which is available to authorized users.

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### Author Contributions

ALdOM, MvdJ, SAH, NCB, GMB, KB, JC, ESC, SAH, BLH, RGH, AGK, SAM, PN, AAR, PV, MDIV, HW, GJZ, JIS contributed to manuscript writing/editing. The corresponding author confirms that authorship requirements have been met, the final manuscript was approved by ALL authors, and that this manuscript has not been published elsewhere and is not under consideration by another journal. The UIA and SAH-CDEs project adhered to ethical guidelines.

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### Conflicts of interest

Dr Suarez reports being President of the Neurocritical Care Society, a member of the Editorial Board of Stroke Journal, and Chair of the DSMB for the INTREPID Study sponsored by BARD, outside of the submitted work. Dr Mayer reports having received personal consulting fees from Edge Therapeutics and Idorsia Pharmaceuticals outside of the submitted work. Dr Amin-Hanjani, has nothing to disclose. Dr Vergouwen has nothing to disclose. Dr de Oliveira Manoel has nothing to disclose. Dr van der Jagt has nothing to disclose. Dr Bambakidis has nothing to disclose. Dr Brophy has nothing to disclose. Dr Bulsara has nothing to disclose. Dr Claassen reports grants from Charles A Dana Foundation, grants from James S McDonnell Foundation, from NIH: The Stroke Hyperglycemia Insulin Network Effort (SHINE) Trial, grants from NIH: I-SPOT, grants from NIH: Established Status Epilepticus Treatment Trial (ESETT), grants from BARD: Intrepid, grants from NIH: Futility Study of Deferoxamine Mesylate in Intracerebral Hemorrhage (I-DEF), grants from NIH/NLM: BIGDATA: Causal Inference in Large-Scale Time Series with Rare and Latent Events, grants from NIH: Rhapsody (ZZ-3K3A-201), other from iCE Neurosystems, outside the submitted work. Dr Connolly has nothing to disclose. Dr Hoffer has nothing to disclose. Dr Hoh has nothing to disclose. Dr Holloway has nothing to disclose. Dr Kelly has nothing to disclose. Dr Nakaji has nothing to disclose. Dr Rabinstein has nothing to disclose. Dr Vajkoczy has nothing to disclose. Dr Woo has nothing to disclose. Dr Zipfel has nothing to disclose.

### Ethical approval/informed consent

This article does not contain any studies with human participants or animals performed by any of the authors.

## Appendix: SAH Working Group Members

### Steering Committee

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**References**

- de Oliveira Manoel AL, Mansur A, Silva GS, Germans MR, Jaja BNR, Kouzmina E, et al. Functional outcome after poor-grade subarachnoid hemorrhage: a single-center study and systematic literature review. *Neurocrit Care*. 2016;25:338–50.
- Molyneux AA, Kerr RR, Stratton II, Sandercock PP, Clarke MM, Shrimpton JJ, et al. International Subarachnoid Aneurysm Trial (ISAT) of neurosurgical clipping versus endovascular coiling in 2143 patients with ruptured intracranial aneurysms: a randomised trial. *Lancet*. 2002;360:1267–74.
- Dorhout Mees SM, Rinkel GJE, Feigin VL, Algra A, van den Bergh WM, Vermeulen M, et al. Calcium antagonists for aneurysmal subarachnoid haemorrhage. *Cochrane Database Syst Rev*. 2007;18(3):CD000277.
- Maas AIR, Menon DK, Steyerberg EW, Citerio G, Lecky F, Manley GT, et al. Collaborative European NeuroTrauma Effectiveness Research in Traumatic Brain Injury (CENTER-TBI). *Neurosurgery*. 2015;76:67–80.
- Goto Y, Yamagata S. [Differences in outcome in patients with poor grade subarachnoid hemorrhage (WFNS grade IV and V): according to the perioperative management against vasospasm]. *No Shinkei Geka*. 2004;32:579–84.
- Maas AIR, Harrison-Felix CL, Menon D, Adelson PD, Balkin T, Bullock R, et al. Standardizing data collection in traumatic brain injury. *J Neurotrauma*. 2011;28:177–87.
- Loring DW, Lowenstein DH, Barbaro NM, Fureman BE, Odenkirchen J, Jacobs MP, et al. Common data elements in epilepsy research: development and implementation of the NINDS epilepsy CDE project. *Epilepsia*. 2011;52:1186–91.
- Saver JL, Warach S, Janis S, Odenkirchen J, Becker K, Benavente O, et al. Standardizing the structure of stroke clinical and epidemiologic research data: the National Institute of Neurological Disorders and Stroke (NINDS) Stroke Common Data Element (CDE) project. *Stroke*. 2012;43:967–73.
- Suarez JJ, Martin RH, Calvillo E, Dillon C, Bershad EM. The Albumin in Subarachnoid Hemorrhage (ALISAH) multicenter pilot clinical trial safety and neurologic outcomes. *Stroke*. 2012;43(3):683–90.
- Todd MM, Hindman BJ, Clarke WR, Torner JC. Mild intraoperative hypothermia during surgery for intracranial aneurysm. *N Engl J Med*. 2005;352:135–45.
- McDougall CG, Spetzler RF, Zabramski JM, Partovi S, Hills NK, Nakaji P, et al. The barrow ruptured aneurysm trial. *J Neurosurg*. 2012;116:135–44.
- Sheth SA, Hausrath D, Numis AL, Lawton MT, Josephson SA. Intraoperative rerupture during surgical treatment of aneurysmal subarachnoid hemorrhage is not associated with an increased risk of vasospasm. *J Neurosurg*. 2014;120:409–14.
- Darflinger R, Thompson LA, Zhang Z, Chao K. Recurrence, retreatment, and rebleed rates of coiled aneurysms with respect to the Raymond-Roy scale: a meta-analysis. *J NeuroInterv Surg*. 2016;8:507–11.
- Vergouwen MDI, Vermeulen M, van Gijn J, Rinkel GJE, Wijdicks EF, Muzelaar JP, et al. Definition of delayed cerebral ischemia after aneurysmal subarachnoid hemorrhage as an outcome event in clinical trials and observational studies: proposal of a multidisciplinary research group. *Stroke*. 2010;41:2391–5.
- Roy D, Milot G, Raymond J. Endovascular treatment of unruptured aneurysms. *Stroke*. 2001;32:1998–2004.
- van Gijn J, Hijdra A, Wijdicks EF, Vermeulen M, van Crevel H. Acute hydrocephalus after aneurysmal subarachnoid hemorrhage. *J Neurosurg*. 1985;63:355–62.
- Claassen J, Carhuapoma JR, Kreiter KT, Du EY, Connolly ES, Mayer SA. Global cerebral edema after subarachnoid hemorrhage: frequency, predictors, and impact on outcome. *Stroke*. 2002;33:1225–32.
- Frontera JAJ, Fernandez AA, Schmidt JMJ, Claassen JJ, Wartenberg KEK, Badjatia NN, et al. Defining vasospasm after subarachnoid hemorrhage: what is the most clinically relevant definition? *Stroke*. 2009;40:1963–8.
- Horan TC, Andrus M, Dudeck MA. CDC/NHSN surveillance definition of health care-associated infection and criteria for specific types of infections in the acute care setting. *Am J Infect Control*. 2008;36:309–32.
- Diringer MN, Bleck TP, Claude Hemphill J, Menon D, Shutter L, Vespa P, et al. Critical care management of patients following aneurysmal subarachnoid hemorrhage: recommendations from the Neurocritical Care Society's Multidisciplinary Consensus Conference. *Neurocrit Care*. 2011;15:211–40.
- de Oliveira Manoel AL, Turkel-Parrella D, Duggal A, Murphy A, McCredie V, Marotta TR. Managing aneurysmal subarachnoid hemorrhage: it takes a team. *Cleve Clin J Med*. 2015;82:177–92.
- van der Jagt M. Fluid management of the neurological patient: a concise review. *Crit Care*. 2016;20:1–11.
- Jagt M, Haitsma I. An injured brain needs cooling down: no. *Intensive Care Med*. 2015;41:1129–31.
- de Oliveira Manoel AL, Goffi A, Marotta TR, Schweizer TA, Abrahamson S, Macdonald RL. The critical care management of poor-grade subarachnoid haemorrhage. *Crit Care*. 2016;20:21.
- Suarez JJ, Martin RH. Treatment of subarachnoid hemorrhage with human albumin: ALISAH Study. Rationale and design. *Neurocrit Care*. 2010;13:263–77.
- Oddo M, Poole D, Helbok R, Meyfroidt G, Stocchetti N, Bouzat P, et al. Fluid therapy in neurointensive care patients: ESICM consensus and clinical practice recommendations. *Intensive Care Med*. 2018;44:1–15.
- Participants in the International Multi-disciplinary Consensus Conference on the Critical Care Management of Subarachnoid Hemorrhage, Treggiari

- 
- MM. Hemodynamic management of subarachnoid hemorrhage. *Neurocritical Care*. 2011;15:329–35.
28. The Participants in the International Multi-disciplinary Consensus Conference on Multimodality Monitoring, Claassen J, Vespa P. Electrophysiologic monitoring in acute brain injury. *Neurocritical Care*. 2014;21:129–47.
29. Hirsch LJ, LaRoche SM, Gaspard N. American Clinical Neurophysiology Society's standardized critical care EEG terminology: 2012 version. *J Clin Neurophysiol*. 2013;30:1–27.
30. Claassen J, Taccone FS, Horn P, Holtkamp M, Stocchetti N, Oddo M. Recommendations on the use of EEG monitoring in critically ill patients: consensus statement from the neurointensive care section of the ESICM. *Intensive Care Med*. 2013;39:1337–51.
31. The Participants in the International Multidisciplinary Consensus Conference on Multimodality Monitoring, Helbok R, Olson DM, Le Roux PD, Vespa P. Intracranial pressure and cerebral perfusion pressure monitoring in non-TBI patients: special considerations. *Neurocritical Care*. 2014;21:85–94.
32. The Participants in the International Multidisciplinary Consensus Conference on Multimodality Monitoring, Chesnut R, Videtta W, Vespa P, Le Roux P. Intracranial pressure monitoring: fundamental considerations and rationale for monitoring. *Neurocritical Care*. 2014;21:S64–84.
33. The Participants in the International Multidisciplinary Consensus Conference on Multimodality Monitoring, Oddo M, Bösel J. Monitoring of brain and systemic oxygenation in neurocritical care patients. *Neurocritical Care*. 2014;21:S103–20.
34. The Participants in the International Multidisciplinary Consensus Conference on Multimodality Monitoring, Hutchinson P, O'Phelan K. International multidisciplinary consensus conference on multimodality monitoring: cerebral metabolism. *Neurocritical Care*. 2014;21:S148–58.