Common Data Elements for Research on Traumatic Brain Injury: Pediatric Considerations

A. Cate Miller,¹ Joanne Odenkirchen,² Ann-Christine Duhaime,³ and Ramona Hicks²

Abstract

Traumatic brain injury (TBI) is a significant global health problem, with a notably high incidence in children and adolescents. Despite the prevalence of TBI and the disabilities that often follow, research on which to base effective treatment is limited by several challenges, including but not limited to the complexity and heterogeneity of TBI. Even when rigorous methods are employed, the utility of the research may be limited by difficulties in comparing findings across studies resulting from the use of different measures to assess similar TBI study variables. Standardization of definitions and data elements is an important step toward accelerating the process of data sharing that will ultimately lead to a stronger evidence base for treatment advances. To address this need, recommendations for common data elements (CDEs) for research on TBI were developed through a 2009 national initiative. To ensure that the TBI CDE recommendations are relevant to pediatric populations, the National Institute on Disability and Rehabilitation Research (NIDRR) and the National Institute of Neurological Disorders and Stroke (NINDS) called for a review of the original recommendations. Following the process used for the original initiative, multidisciplinary work groups composed of pediatric TBI experts were formed (Demographics and Clinical Assessment; Biomarkers; Neuroimaging; and Outcomes Assessment). Recommendations for modifications and additions to the original CDEs were developed by the work groups, vetted at a 2010 workshop and further refined in preparation for publication. The pediatric considerations for TBI CDEs are described in a series of articles in this journal. This article describes the efforts leading to this pediatric CDE initiative and the CDE review and development process. It concludes with general recommendations for future iterations of the CDE initiative.

Key words: assessment tools; bioinformatics; CDE; clinical trials; database; meta-analysis; pediatrics; rehabilitation; research; TBI

Introduction

TRAUMATIC BRAIN INJURY (TBI) is a worldwide health problem affecting adults and children alike. Each year 1.7 million people in the United States die, are hospitalized, or are seen in an emergency department with a TBI (Centers for Disease Control and Prevention [CDC], 2010; Faul et al., 2010). This number is known to be an underestimate of prevalence of TBI, as it does not include people treated in physicians' offices or military or veteran health care facilities. Children aged 0–4 years and adolescents aged 15–19 years comprise two of the largest demographic groups affected by TBI (CDC, 2010; Faul et al., 2010). Approximately half a million children per year (<15 years of age) are seen in emergency departments in the United States because of trauma to the head (CDC, 2010), and TBI is a leading cause of death and disability in children and

young adults around the world (Keenan and Bratton, 2006; World Health Organization, 2006).

Despite the prevalence of TBI and the disabilities that often follow, research on which to base effective treatment is limited by several challenges. Currently, <20% of the management guidelines for TBI are supported by either Class I or Class II evidence (Maas et al., 2010b). Even when rigorous methods are employed, the utility of the research may be limited by difficulties in comparing findings across studies, resulting from the use of different measures to assess similar TBI study variables. TBI clinical data can be challenging, if not impossible, to combine and/or compare in meaningful ways because of the variability of terms and tools used to describe the patients, the interventions, and the outcomes. Standardization of definitions and data elements, therefore, is an important step toward accelerating the process of data

¹National Institute on Disability and Rehabilitation Research, United States Department of Education, Washington, DC.

²National Institute of Neurological Disorders and Stroke, National Institutes of Health, Bethesda, Maryland.

³Massachusetts General Hospital, Boston, Massachusetts.

sharing that will ultimately lead to a stronger evidence base for treatment advances. Despite the advantages of standardization, there have been only limited efforts by the scientific community to arrive at consensus on the conceptual domains that hold the greatest relevance for TBI research and on which measurement tools are most useful in quantifying those domains.

This need to identify common data elements (CDEs, i.e., “consensus-based content domains of importance and recommended ways to measure them” [Whyte et al., 2010, p.1692]) for TBI research was at the heart of a multi-agency initiative aimed at facilitating data sharing and meta-analysis of clinical studies on TBI (Saatman et al., 2008; Thurmond et al., 2010). The National Institute of Neurological Disorders and Stroke (NINDS), the Department of Veterans Affairs, the National Institute on Disability and Rehabilitation Research (NIDRR), the Defense Centers of Excellence for Psychological Health and Traumatic Brain Injury, and the Defense and Veterans Brain Injury Center sponsored an initiative in 2009 to standardize definitions, data collection methods, and data elements for TBI clinical research. The TBI CDE recommendations from the working groups were published in a series of manuscripts (Duhaime et al., 2010; Maas et al., 2010 a; Manley et al., 2010; Thurmond et al., 2010; Whyte et al., 2010; Wilde et al., 2010), and are also available online (NINDS, 2010). The CDEs are currently undergoing beta testing in multiple centers, with the expectation that they will be refined and modified with input from a community of users.

A key recommendation from the 2009 initiative was to further evaluate the CDE recommendations for their relevance to pediatric populations. In recognition of the significant public health impact that TBI has on children and the importance of facilitating research in this area, the federal agencies funding pediatric TBI research, NIDRR and NINDS, invited researchers with expertise across a range of pediatric TBI clinical disciplines to consider the need for age-specific modifications to the CDE recommendations. The goal was to recommend modifications that would make the data elements and tools relevant to pediatric TBI, while also maintaining the integrity of the original set of recommendations to the greatest extent possible, to enable data sharing across the life span. The methods used were similar to those used for the 2009 initiative, with scientific experts participating in working groups, preparing white papers for discussion at the workshop *Common Data Elements for Traumatic Brain Injury: Pediatric Considerations* held March 20–21, 2010 in Houston, Texas, and subsequently refining the recommendations for publication. The methods are described in greater detail in this article, and CDE recommendations are presented in separate reports in this issue.

Background

The federal agencies that cosponsored the pediatric CDE initiative, NINDS of the National Institutes of Health and NIDRR of the United States Department of Education, share a strong commitment to pediatric and adult TBI research. Together with other federal agencies, they co-sponsored the 2009 TBI CDE initiative referenced previously. Selected agency activities that laid the groundwork for the 2009 initiative and, therefore, for the 2010 pediatric modifications, were discussed in a publication regarding the original

TBI CDE initiative (Thurmond et al., 2010), and are summarized here.

In October 2007, NINDS sponsored a TBI Classification workshop (Saatman et al., 2008) during which scientists recommended that a pathoanatomic-based classification system be developed for TBI. However, the lack of standardization in terminology and data elements was a major obstacle to developing a new pathoanatomic classification system. The 2009 CDE effort and this pediatric-specific CDE initiative also built on the NINDS CDE Project, which aims to decrease study start-up time and accelerate data sharing in neurology. To this end, the NINDS has developed core data elements that are commonly collected in clinical studies regardless of type of study or therapeutic area, such as demographic information. Core common data elements can be found on the NINDS CDE Web site www.commondataelements.ninds.nih.gov.

Similarly, two NIDRR initiatives provided a foundation for the current work. NIDRR was a partner in early efforts to create CDEs for spinal cord injury, an initiative that conceptually parallels that of the current CDE effort for TBI (Alexander et al., 2009). A second NIDRR initiative provides evidence of the utility of TBI CDEs and their potential for advancing the field. The NIDRR-funded TBI Model Systems Centers Program funds centers of excellence throughout the country to provide comprehensive systems of brain injury care, conduct clinical research, and contribute to a centralized prospective longitudinal database. The database includes CDEs for diagnostic and functional information about persons with TBI from inpatient admission through 20 years post-injury (<https://www.tbindsc.org/>). The published results from >100 studies of this database attest to the utility and significance of such a CDE resource. Beginning in 2008, NIDRR and its grantee, the TBI Model Systems National Data and Statistical Center at Craig Hospital, Englewood, Colorado, partnered with the Department of Veterans Affairs and the Defense and Veterans Brain Injury Center to create the VA Polytrauma Rehabilitation Centers longitudinal database. This database includes the same (common) data elements already being collected with civilians for the TBI Model Systems National Database, and holds promise for future comparative studies.

Methods

The methods used closely followed those for the 2009 CDE initiative (see Thurmond et al., 2010). The CDE topic areas addressed by the four TBI working groups in the 2009 initiative were adopted for this initiative as well: 1) Demographics and Clinical Assessment; 2) Biomarkers; 3) Neuroimaging; and 4) Outcomes Assessment. Participants with experience working with pediatric populations were recruited by NINDS and NIDRR from a range of clinical disciplines including neurology, neuropsychology, neurosurgery, pediatrics, physical radiology, and rehabilitation (see Appendix for a list of work group members).

The working groups met regularly via teleconference for several months to review the recommendations from the 2009 CDE initiative and to prepare white papers with their initial recommendations for pediatric modifications. A consensus process was used, with discussions continuing until agreement was reached regarding recommendations. Preliminary

recommendations in the form of white papers were presented by each work group at the workshop entitled Common Data Elements for Traumatic Brain Injury: Pediatric Considerations held March 20–21, 2010 in Houston, Texas. Workshop participants included members of all four work groups, and of the planning committee for the pediatric CDE initiative. Feedback from all attendees was used to refine the CDE recommendations. After the workshop, working groups finalized their recommendations in a series of manuscripts. The TBI Common Data Elements Interagency Steering Committee composed of work group chairs and one internal editor from the 2009 CDE initiative, and of representatives and stakeholders from the cosponsoring federal agencies, were informed of the process and provided an opportunity to comment on it. The authors of this article edited the manuscripts before journal submission to ensure consistency and reduce redundancies or overlap across the manuscript series. After editorial review, working groups revised their manuscripts before submission to the *Journal of Neurotrauma* for independent review. The recommendations are also available online (NINDS, 2010).

As in the 2009 initiative, CDE recommendations from all working groups were formulated using three general descriptive levels: core, supplemental, and emerging. Data elements described as *core* are intended to encompass the minimal set of measures to characterize a broad spectrum of subjects in the domain. A *supplemental* element is intended for greater depth/breadth of exploration and/or more specialized subpopulations. Data elements described as *emerging* may require further validation, but may fill gaps in currently validated measures and/or substitute for recommended measures when validation is complete.

The recommendations of the three work groups resulted in five manuscripts, three of which provide the primary CDE recommendations from each work group. Of these, the manuscript from the neuroimaging work group includes core and supplemental CDE recommendations only, leaving the discussion of emerging neuroimaging measures to an additional manuscript that identifies the emerging measures and the current considerations and unresolved challenges of using them. Finally, a fifth manuscript discusses an important set of predictor variables that is otherwise missing in the recommendations of the three work groups: psychosocial risk and protective factors. This category of variables does not fit neatly with the domains of the three workgroups (Demographics, Clinical Assessment and Biomarkers; Neuroimaging; and Outcomes Assessment), hence the variables were not included in the CDE recommendations from these groups. Recognizing the importance of these variables, a manuscript is included that identifies characteristics of the individual child and his or her social environment that are known to be important determinants of recovery, above and beyond the effects of injury severity. The authors provide a compelling, evidence-based rationale for including psychosocial variables in addition to demographic variables such as socioeconomic status, age, and sex in the study design and analyses of pediatric TBI research.

Discussion

One limitation of the current initiative is the work group structure. In a commentary on the initial CDE effort, Whyte

and colleagues (2010) discussed the limitations of using a mix of conceptual frameworks for the different working groups, for example, including work groups that were defined by a broad measurement domain such as clinical assessment or outcomes, and groups defined by a particular tool set such as biomarkers or neuroimaging. "The heterogeneity of conceptual frameworks increased the challenge of arriving at uniform and consistent recommendations." Because the pediatric CDE initiative is conceptually consistent with its predecessor and uses the same methodology and similar work group structure, the limitation of the earlier initiative is likely applicable to the pediatric CDE initiative as well.

To address this limitation, Whyte and colleagues recommended that future CDE efforts use a different strategy that involves a matrix that crosses clinical problems (TBI, post-traumatic stress disorder [PTSD], and/or others) with three broad measurement domains (patient-specific factors, treatment factors, and outcomes). Using this strategy, measurement tools such as biomarkers and imaging would be included as subclasses of patient-specific variables. We can see the applicability of this recommendation in the case of the "misfit" between psychosocial risk and protective factors and the existing workgroup structure (discussed earlier in this article). Although psychosocial risk and protective factors do not "fit" in the domains of the current workgroups, they would fit nicely in the broad measurement domain of "patient-specific factors" proposed by Whyte and colleagues.

Conclusion

The CDE TBI initiative, begun in 2009 with resulting recommendations applicable to research related to adults with TBI and/or psychological health issues, has been extended to now include recommendations relevant to pediatric TBI research. This initiative addresses the need for a common battery of measures and methods that will promote multi-site research and facilitate the comparison of research results across studies. In addition to the specific pediatric CDE recommendations reported in concurrent publications in this issue, several general recommendations resulted from the workshop proceedings. These include:

- Pediatric TBI CDEs should be integrated into a single larger set of TBI CDEs that includes elements applicable to all age groups.
- Data elements should encompass all phases of timing after injury, from acute to chronic.
- CDEs for pediatric TBI should parallel those for other neurological conditions, including epilepsy and stroke, to facilitate comparisons and accelerate research relevant to the immature brain.
- Further work in pediatric CDE development may require innovative matrix and work group organization to encompass the complexity and overlap of approaches in this heterogeneous but common disorder.

In order to enhance consensus among researchers with similar interests without stifling the innovation, scientific rigor, or relevance of the research, the CDE initiative must be a dynamic effort that allows for reexamination and updates as new tools, technologies, and knowledge become available.

Acknowledgments

We gratefully acknowledge the working group members and chairpersons for their dedication of time and expertise to this initiative. Support for the workshop came from the National Institute for Disability and Rehabilitation Research of the United States Department of Education (NIDRR/DoE) and the National Institute of Neurological Disorders and Stroke of the National Institutes of Health (NINDS/NIH)

Author Disclosure Statement

The views expressed are those of the authors and do not necessarily reflect those of the agencies or institutions with which they are affiliated, including the United States Department of Health and Human Services or the United States Department of Education. This work is not an official document, guidance, or policy of the United States government, nor should any official endorsement be inferred.

No competing financial interests exist.

References

- Alexander, M.S., Anderson, K.D., Biering-Sorensen, F., Blight, A.R., Brannon, R., Bryce, T.N., Creasey, G., Catz, A., Curt, A., Donovan, W., Ditunno, J., Ellaway, P., Finnerup, N.B., Graves, D.E., Haynes, B.A., Heinemann, A.W., Jackson, A.B., Johnston, M.V., Kalpakjian, C.Z., Kleitman, N., Krassioukov, A., Krogh, K., Lammertse, D., Magasi, S., Mulcahey, M.J., Schurch, B., Sherwood, A., Steeves, J.D., Stiens, S., Tulskey, D.S., van Hedel, H.J.A., and Whiteneck, G. (2009). Outcome measures in spinal cord injury: recent assessments and recommendations for future directions. *Spinal Cord*, 47, 582–591.
- Centers for Disease Control and Prevention (2010). Injury prevention & control: traumatic brain injury. Available at <http://www.cdc.gov/traumaticbraininjury/statistics.html> (Last accessed November 9, 2011).
- Duhaime, A. C., Gean, A. D., Haacke, E. M., Hicks, R., Wintermark, M., Mukherjee, P., Brody, D., Latour, L., and Riedy, G. (2010). Common data elements in radiologic imaging of traumatic brain injury. *Arch. Phys. Med. Rehabil.* 91, 1661–1666.
- Faul, M., Xu, L., Wald, M.M., and Coronado, V.G. (2010). *Traumatic Brain Injury in The United States: Emergency Department Visits, Hospitalizations, and Deaths*. Centers for Disease Control and Prevention, National Center for Injury Prevention and Control: Atlanta.
- Keenan, H. T. and Bratton, S. L. (2006). Epidemiology and outcomes of pediatric traumatic brain injury. *Dev. Neurosci.* 28, 256–263.
- Maas, A.I., Harrison-Felix, C.L., Menon, D., Adelson, P.D., Balkin, T., Bullock, R., Engel, D.C., Gordon, W., Langlois Orman, J., Lew, H.L., Robertson, C., Temkin, N., Valadka, A., Verfaellie, M., Wainwright, M., Wright, D.W., and Schwab, K. (2010a). Common data elements for traumatic brain injury: recommendations from the interagency working group on demographics and clinical assessment. *Arch. Phys. Med. Rehabil.* 91, 1641–1649.
- Maas, A.I.R., Roozenbeek, R., and Manley, G.T. (2010b). Clinical trials in traumatic brain injury: past experience and current developments. *Neurotherapeutics* 7, 115–126.
- Manley, G.T., Diaz-Arrastia, R., Brophy, M., Engel, D., Goodman, C., Gwinn, K., Veenstra, T.D., Ling, G., Ottens, A.K., Tortella, F., and Hayes, R.L. (2010). Common data elements for traumatic brain injury: recommendations from the biospecimens and biomarkers working group. *Arch. Phys. Med. Rehabil.* 91, 1667–1672.
- National Institute of Neurological Disorders and Stroke (2010). NINDS common data elements: traumatic brain injury CDE standards. <http://www.commondataelements.ninds.nih.gov/TBI.aspx> (Last accessed November 9, 2011).
- Saatman, K.E., Duhaime, A.C., Bullock, R., Maas, A.I.R., Valadka, A., and Manley, G.T. (2008). Classification of traumatic brain injury for targeted therapies. *J. Neurotrauma* 25, 719–738.
- Thurmond, V.A., Hicks, R., Gleason, T., Miller, A.C., Szufita, N., Orman, J., and Schwab, K. (2010). Advancing integrated research in psychological health and traumatic brain injury: common data elements (CDE). *Arch. Phys. Med. Rehabil.* 91, 1633–1636.
- World Health Organization (2006). Neurological disorders: A public health approach, 3.10 traumatic brain injuries, in: *Neurological Disorders: Public Health Challenges*. Available at: http://whqlibdoc.who.int/publications/2006/9241563362_eng.pdf (Last accessed November 9, 2011).
- Whyte, J., Vasterling, J., and Manley, G. T. (2010). Common data elements for research on traumatic brain injury and psychological health: current status and future development. *Arch. Phys. Med. Rehabil.* 91, 1692–1696.
- Wilde, E.A., Whiteneck, G.G., Bogner, J., Bushnik, T., Cifu, D.X., Dikmen, S., French, L., Giacino, J.T., Hart, T., Malec, J.F., Millis, S.R., Novack, T.A., Sherer, M., Tulskey, D.S., Vanderploeg, R.D., and von Steinbuechel, N. (2010). Recommendations for the use of common outcome measures in traumatic brain injury research. *Arch. Phys. Med. Rehabil.* 91, 1650–1660.

Address correspondence to:

A. Cate Miller, Ph.D.

National Institute on Disability and Rehabilitation Research

U.S. Department of Education

400 Maryland Avenue SW

Washington, DC 20202

E-mail: cate.miller@ed.gov

APPENDIX: WORKING GROUP MEMBERS

Demographics and Clinical Assessment Working Group:

Mark S. Wainwright¹ (co-chair), P. David Adelson² (co-chair), Nicholas Abend,³ Michael J. Bell,⁴ Rachel P. Berger,⁴ Christopher Giza,⁵ Ramona Hicks,⁶ Gillian Hotz,⁷ Jose Pineda⁸

Biomarkers Working Group:

Rachel P. Berger⁴ (chair), Sue R. Beers,⁴ Michael J. Bell,⁴ Linda Papa⁹

Neuroimaging Working Group:

Ann-Christine Duhaime¹⁰ (chair), Barbara Holshouser,¹¹ Jill Hunter,¹² Karen Tong¹¹

Outcomes Assessment Working Group:

Elizabeth A. Wilde¹² (chair), Vicki A. Anderson,¹³ Gary Bedell,¹⁴ Sue R. Beers,⁴ Thomas F. Campbell,¹⁵ Sandra B. Chapman,¹⁵ Linda Ewings-Cobbs,¹⁶ Joan P. Gerring,¹⁷ Gerard A. Gioia,¹⁸ Ramona Hicks,⁶ Harvey S. Levin,¹² Stephen R. McCauley,¹² Linda J. Michaud,¹⁹ A. Cate Miller,²⁰ Mary R. Prasad,¹⁶ Bonnie R. Swaine,²¹ Lyn S. Turkstra,²² Shari L. Wade,¹⁹ Keith Owen Yeates²³

Planning Committee Members:

Ramona Hicks,⁶ A. Cate Miller,²⁰ Joanne Odenkirchen⁶

Additional Invitees:

Joan Austin,²⁴ Charles Cox¹⁶

¹Northwestern University, Chicago, Illinois

²Phoenix Children's Hospital, Phoenix, Arizona

³Children's Hospital of Philadelphia, Philadelphia, Pennsylvania

⁴University of Pittsburgh, Pittsburgh, Pennsylvania

⁵University of California, Los Angeles, California

⁶National Institute of Neurological Disorders and Stroke, National Institutes of Health, Bethesda, Maryland

⁷University of Miami, Miami, Florida

⁸Washington University, St. Louis, Missouri

⁹Orlando Regional Medical Center, Orlando, Florida

¹⁰Massachusetts General Hospital, Boston, Massachusetts

¹¹Loma Linda University, Loma Linda, California

¹²Baylor College of Medicine, Houston, Texas

¹³Murdoch Childrens Research Institute, Melbourne, Australia

¹⁴Tufts University, Medford, Massachusetts

¹⁵University of Texas at Dallas, Dallas, Texas

¹⁶University of Texas Health Science Center-Houston, Houston, Texas

¹⁷Johns Hopkins University, Baltimore, Maryland

¹⁸George Washington University, Washington, D.C.

¹⁹Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio

²⁰National Institute on Disability and Rehabilitation Research, United States Department of Education, Washington, DC

²¹Université de Montréal, Montréal, Canada

²²University of Wisconsin-Madison, Madison, Wisconsin

²³Nationwide Children's Hospital, Columbus, Ohio

²⁴Indiana University, Bloomington, Indiana