NINDS CDE Project

Working group: NINDS CDE Project Chiari I Malformation Working Group
Completed by:
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The overall NINDS CDE Project Chiari I malformation Working Group first met in April of 2013 to discuss the need for an international patient registry that incorporates both patient-reported data as well as clinician-reported data, as one does not currently exist. When the CDE Project was presented, the group felt that it would be a critical step to ensuring the data housed within the database would be of even better quality.

The initial steering committee of ten members was formed from the CSF SEA Board and CSF staff. The steering committee reached out to national and international medical, scientific and lay people to attend the first physical meeting. To be inclusive, our first working group included representatives from industry, neurosurgery, neuro-radiology, neurology, genetics, internal medicine, veterinary medicine, National Institutes of Health, NINDS and the lay public. The first face to face meeting of 40 working group members was held in San Francisco, CA with NINDS, China, Italy, and UK participating via Web-Ex and speakerphone. The working group was subsequently assigned to subgroups to focus on: Demographics, Presentation, Co-Morbidities, Spine, Imaging, Treatment and Outcomes. Each group presented their work at the meeting and it was decided that we would meet weekly on conference calls to review the progress of each subgroup. This was followed by face to face meetings in September of 2014, April of 2015, September 2015 and April of 2016.

At every in-person meeting, each subgroup held round-table discussions on what to include or recommend. Following extensive break-out sessions, the subgroups would come together and propose their conclusions to the group as a whole. Comments, questions and critiques would be weighed and, if appropriate, incorporated into the CDEs as edits, additions or deletions. International members who were not able to physically be in attendance were conferenced in via Web-Ex to ensure a comprehensive understanding of the elements and instruments used in many clinical practices around the world.

Between these larger-scale meetings, the subgroups continued to refine, add and delete CDEs as necessary, using electronic resources. Additionally, a Working Group steering committee made up of leadership within each subgroup met via teleconference every Tuesday evening to provide updates and to report new developments.

CDEs were defined by the steering committee as either being Core, Supplemental – Highly Recommended, Supplemental or Exploratory. During the large in-person meetings, these classifications were presented to each group and consensus was drawn as to whether or not these classifications were apt. If not, adjustments were made as necessary.

As a part of the development of the CDEs, a select group of about 15 neurosurgeons and neuro-radiologists were tasked with making the same measurement of tonsillar herniation on the same MRI. Even amongst the most experienced Chiari and syringomyelia clinicians, there was an average of 9 mm difference between the measurements. The Spine subgroup and Imaging subgroup were found to have substantial overlap and were therefore condensed into one group, retaining the name of the latter.

To begin the process of development, the group first ranked high-priority research topics that have thus far gone unaddressed or insufficiently addressed in the literature. Higher priority topics informed the development of appropriate CDEs meant to answer those questions. Notably, issues of radiological measurement in diagnosis and patient-report quality-of-life outcomes were given the highest priority.

The working group decided to focus the CDEs on Chiari I malformation and its related disorders, specifically. Because the different types of Chiari malformation (II, III and IV) are unrelated to one another in many ways other than name, the Working Group felt it would have been inappropriate to group CDEs for Chiari II, III or IV together with each other or with CDEs for Chiari I.

Because Chiari I malformation is not well understood there is extremely high variability in technical clinical approaches to diagnosis and treatment. Therefore, in selecting elements to be recommended as CDEs, the group attempted to be as thorough as possible in providing any or all the elements or instruments that may be used by clinicians to diagnose or treat Chiari I malformation and any of its related disorders.

There is a high degree of variability in methodology for taking measurements amongst even the most experienced Chiari clinicians. As a part of the development of the CDEs, a select group of about 15 neurosurgeons and/or neuro-radiologists were tasked with making the same measurement of tonsillar herniation on the same MRI and there was an average of 9mm difference between the measurements. This amount of variation is likely clinically significant to patient care. The development of the CDEs further through public comment and further edits should bear this in mind.

Prior to this project, databases housing health and outcomes data concerning Chiari I malformation, SM and related disorder patients were either exclusively clinician-reported, or exclusively patient-reported. The Working Group seeks to develop a database that includes both clinician- and patient-reported data. The development of a database such as this would help improve the quality and relevance of health and outcomes data and improve epidemiological and clinical research conclusions for these populations. Therefore, the group sought out elements and instruments that would be relevant to both clinicians and patients or caregivers, alike.

So little is known about the natural history, cause and appropriate treatment of Chiari I malformation and syringomyelia that the following are questions that still warrant further investigation:

- What is the incidence and natural history of Chiari I malformation with and without syringomyelia?

- What are the causes and associated comorbidities (genetic, developmental and acquired) of the anatomical abnormalities observed?
- What are the key anatomical findings which define Chiari I malformation and which generate symptoms and neurological deficit? What is the level of clinical relevance of key anatomical findings?
- What are the symptoms of Chiari I malformation, their cause and response to treatment? How can they be differentiated from those resulting from other diseases?
- How is Chiari I malformation currently diagnosed and treated around the country and the world? What is the effectiveness of these treatments in relieving patient suffering and morbidity? How do we define successful surgical treatment?
- What is the current level of healthcare utilization and public health cost of Chiari and syringomyelia treatment? What potential utilization, cost and quality improvements exist in diagnosis and treatment methods?