NINDS/NICHD-NCMRR NeuroRehab CDE Project
Treatment/Intervention Data: Therapies Subgroup Summary

The NeuroRehab v1.0 CDE project focused on recommendations from existing NINDS and other NIH supported CDEs within the Core and Supplemental – Highly Recommended classifications. New CDEs or those within the Supplemental and Exploratory classification were not reviewed in this initial process. Identified gap areas will be an important part of informing future NeuroRehab CDE efforts.

The subgroup reviewed existing NINDS CDE case report form (CRF) modules from the Treatment/Intervention Data Domain, Therapies Subdomain. CRFs that overlapped with the Treatment/Intervention Data: Devices subgroup were reassigned to that subgroup for consideration. A rubric based on the NeuroRehab project guidance for selection of instruments and classification definitions was developed by the Chairs to facilitate and standardize subgroup member reviews.

The subgroup determined that it was important to develop their purview and definitions for the subgroup before considering CDEs/CRFs, instruments and gap items. Members first considered the value and utility of the CDEs, specifically, how the CDEs could be used by the NeuroRehab clinical and research community. Therapy-related CDEs could be used in a variety of study types, including experimental studies (e.g., randomized clinical trials) and quasi-experimental studies (e.g., observational studies and health services research). Depending on the study focus, therapy data might be used as descriptive data, treatment data or could be a study outcome (e.g., a study focused on access to therapy). Regarding experimental treatment studies, it was assumed that all or most trials would require individualized measures of the treatment under study. However, a potential function of a CDE in this case might be to provide background or 'usual care' data for comparison to an experimental treatment.

The subgroup divided the CRF list for review. The reviewer feedback can be categorized into 4 categories:
1) Some of the existing NINDS CDEs were limited to specific treatments addressing a particular deficit within one neurological condition and had limited universal NeuroRehab application (e.g., treatment specific to Spinal Cord Injury (SCI)) or were condition-specific and not within the expertise of the group (e.g., surgery for Chiari malformation).
2) Other NINDS CDEs were not rehabilitation focused. These documents may be useful to a limited number of rehabilitation researchers, but do not warrant NeuroRehab CDE classification.
3) Many of the existing CDEs measure the number and/or duration of therapy sessions within a given discipline; however, as discussed below, these data are inadequate for specifying active treatment ingredient(s) within the therapy.
4) For some existing CDEs the response options (permissible values) do not align with standardized data elements used in the US, such as standard insurance billing, or would not be internationally applicable.

The subgroup also considered reviewing CDEs within the context of their own framework focusing on the domains of study type and use case. Study type includes the parameters: clinical trial, intervention application, survey, and observational study. Use case includes: selection variable (inclusion/exclusion criteria), covariate (control), independent variable (predictor), and outcome variable.

Ultimately, the subgroup determined that no existing NINDS or NIH supported CDEs were appropriate to recommend at this time based on the needs for treatment measurement to advance treatment research in neurorehabilitation. Directions for future work were identified within the gap areas.

In reviewing existing CDEs, the subgroup considered different types of studies that might use therapy data, including observational studies, both prospective and retrospective.

For clinical trials that are intended to understand the aspects/features of a treatment that result in better patient outcomes, the CDEs we reviewed were not specified at a level that is needed (i.e., specific ingredients, either active or inactive, are not measured). We have a measure at a higher level with lots of noise and an unknown amount of signal for what we would really want to measure. Unlike the other subgroups that were primarily measuring latent traits/constructs and are measuring these constructs indirectly based on observation or self-report data, therapy can be measured directly. For example, the number of minutes of therapy can be counted in a reliable and valid way. However, those data are poor surrogates for the dose of active treatment ingredients for this type of research.

The subgroup was asked to identify CDEs for the adult population. A separate Infant Pediatrics subgroup was responsible for making recommendations for the pediatric population. The subgroup's list of gaps and recommendations for future CDE work are specific to the adult population.

After thorough review by the Therapies subgroup, it was ultimately decided that no current NINDS CDEs would be recommended for the Treatment/Intervention Data: Therapy domain. It is the subgroup's stance that the existing CDEs for NeuroRehab Therapy are not broadly applicable to neurorehabilitation studies, do not provide the means to measure specific treatment ingredients that are needed for clinical trials and other types of research on intervention effects, and are not aligned with data that would exist in medical records for use in observational studies.

The subgroup found that the breadth of relevance of a variable to be a CDE was undefined. The subgroup grappled with whether a treatment that is used in a very specific disorder warrants having a CDE or whether volume or frequency of use is part of what defines the need for a CDE. Alternatively, there are clear performance criteria for CDEs reflecting latent constructs (e.g., not only reliability and feasibility but validity), and there were no established validity criteria for treatment CDEs. (e.g., Does there need to be any evidence that the treatment, measured in the recommended way, accounts for variance in one or more outcomes?) The current NINDS CDEs can measure minutes of treatment, dosage, or report that someone did or did not get a treatment, but we lack the aspects (details) of the treatment that are what we need for a research study if we want to know how the effectiveness of the treatment.

Currently there is no standard method of specifying and measuring the ingredients of rehabilitation—active or not. Further, rehabilitation treatments are intended to change as newer treatments emerge. The variable nature of new treatments makes it difficult to set CDEs and predict how previously developed CDEs will be used. Investigators in the field will be the best resource for determining when therapy CDEs can be effectively developed and utilized.

There are no established domains in the therapy/interventions area and currently there is no standard method of collecting data on the ingredients of rehabilitation treatments. However, there are recommendations for reporting rehabilitation treatment research in the literature, and these could provide a transparent and standard framework for describing treatments until specific CDEs can be developed. Recent recommendations based on the Template for Intervention Description and Replication (TIDieR) and Rehabilitation Treatment Specification System (RTSS) have been published in the American Journal of Physical Medicine and Rehabilitation.

In their current form, the existing CDEs that may be useful for NeuroRehab Therapy have limitations. For example, a location CDE may not have permissible values that align with standardized medical data. Another potential issue is that the CDEs are US centric rather than internationally applicable.

CDEs need to be globally applicable so it will be important to consider internationally used terminologies in future development and may require older CDEs to be altered to include inclusive language.

After concluding that the group would not recommend any existing CDES to move forward, the Therapies subgroup members held meetings with NINDS/NICHD project leaders to discuss how to develop a framework for future CDE development efforts.

The committee considered an alternative approach, which would begin with a set of guidelines for how investigators should report, in standard and transparent form, the known or hypothesized active ingredients of the study treatment and any comparison treatment(s), as well as background treatments being received that might have confounding effects on study outcomes. Such a system could be modeled on the treatment reporting recommendations discussed above and being further developed by Cochrane Rehab.

As research in focused treatment domains develops and matures, content experts in this domain could be convened to develop more specific CDEs for future studies of treatments in that domain. This leaves the question of when a treatment domain is sufficiently mature to warrant CDE development and who should be involved in that development. One possibility would be a mechanism of NIH-funded consensus conferences with a standardized CDE-development structure. Applicants from a given treatment domain would need to make the case that that domain is significant, that it is ready for CDE development, and that they have assembled the key stakeholders in research in that domain.

Adoption of concepts existing in research frameworks like the Rehabilitation Treatment Specification System (RTSS) and the Template for Intervention Description and Replication (TIDieR) checklist were considered to develop criteria for selecting existing CDEs. However, the subgroup noted limitations with this approach. RTSS suggests that the field needs to do the prework to specify the treatments in use so that they can be in selected menus. The implementation phase is long term as analysis depends on mapping EMR data to the RTSS. Clinicians may not be familiar with the RTSS.

To achieve granularity of the data, treatment intervention could be divided further into subgroups with specific expertise. Granularity is important for both experimental treatment and covariate information. The project design for the next phase can vary for each subgroup. To ensure desired granularity and specificity of CDEs, the subgroup recommends a RTSS-style framework as it identifies target domains such as organ functions; skills and habits learned through practice, and the cognitive and affective representations underlying knowledge, attitudes, and voluntary action.

Several subgroup members noted classifications used by the Centers for Medicare & Medicaid Services are collected in a standardized manner in skilled nursing facilities and inpatient rehabilitation facilities. They include minutes of individual therapy, group therapy, or co-treatment by OT, PT and SLP and these data are interoperable. However, just like the CDEs reviewed, these data lack specificity regarding treatment ingredients, and use would be likely limited to descriptive data in circumscribed observational studies.

Subgroup members discussed whether development of therapy CDEs should be an organic process or a centrally controlled process, and if the NIH should facilitate this process. Subgroup members agree that investigators in the field will be the best resource for determining when therapy CDEs can be effectively developed and utilized. Prior to the next phase of the NeuroRehab CDE Project, NIH needs to consider these multi-faceted issues before moving forward with reconvening a subgroup to develop NeuroRehab Therapy CDEs.

The following references are recommended by the Therapies subgroup to guide future NeuroRehab Therapy CDE development:

Centers for Medicare & Medicaid Services. Data Element Library. https://del.cms.gov/DELWeb/pubHome

The Office of the National Coordinator for Health Information Technology. (ONC). United States Core Data for Interoperability. https://www.healthit.gov/isa/united-states-core-data-interoperability-uscdi#uscdi-v2

Dijkers MP, Ferraro MK, Hart T, Packel A, Whyte J, Zanca JM. Toward a rehabilitation treatment taxonomy: summary of work in progress. Phys Ther. 2014 Mar;94(3):319-21.

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Van Stan JH, Dijkers MP, Whyte J, Hart T, Turkstra LS, Zanca JM, Chen C. The Rehabilitation Treatment Specification System: Implications for Improvements in Research Design, Reporting, Replication, and Synthesis. Arch Phys Med Rehabil. 2019 Jan;100(1):146-155.

Whyte J, Dijkers MP, Fasoli SE, Ferraro M, Katz LW, Norton S, Parent E, Pinto SM, Sisto SA, Van Stan JH, Wengerd L. Recommendations for Reporting on Rehabilitation Interventions. Am J Phys Med Rehabil. 2021 Jan 1;100(1):5-16.