

ICECAP

Influence of Cooling Duration on Efficacy in Cardiac Arrest Patients

Outcomes Manual

Version 1

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Table of Abbreviations

CCC	Clinical Coordinating Center
COA	Central Outcomes Assessor
COWAT	Controlled Oral Word Association Test
COT	Central Outcomes Team
CFT	Category Fluency Test
CRF	Case Report Form
DCC	Data Coordinating Center
DCR	Data Clarification Request
DCU	Data Coordination Unit
LAR	Legally Authorized Representative
MoP	Manual of Procedures
mRS	Modified Rankin Scale
NOA	Neuropsychological Outcomes Assessor
NTB	Neuropsychological Test Battery
OA	Outcomes Assessor
QA	Quality Assurance
RAVLT	Rey Auditory Verbal Learning Test
SIREN	Strategies to Innovate Emergency Care Clinical Trials Network

1.0 SIREN Organization for ICECAP Outcomes

The SIREN Clinical Coordinating Center (CCC) at the University of Michigan will serve as the Clinical Coordinating Center for the ICECAP trial. The CCC is responsible for communication with sites, training and certification of Hubs, assurance of Hub regulatory compliance, monitoring of Hub performance and the provision of feedback to ensure improvement of performance. The Site Manager, Study Monitors, and Training Coordinators perform these tasks. Daily management of the ICECAP trial will be facilitated by weekly meetings of an Operations Working Group and as a standing scheduled agenda item in weekly meetings of the SIREN Operations Committee.

The Clinical Outcomes Team (COT) is housed within the CCC and oversees all aspects of outcomes management. This includes, but is not limited to, outcomes training, certification, retraining and quality assurance. The Central Outcomes Assessor (COA) is the member of the Central Outcomes Team responsible for remotely administering the modified Rankin Scale (mRS) at 90 days.

The SIREN Data Coordinating Center (DCC) at the Medical University of South Carolina will serve as the Data Coordinating Center for the ICECAP trial. More than 50 clinical sites are expected to participate in ICECAP, enrolling an average of 9 participants per year each.

Contact Information
ICECAP CCC: ICECAP-Contact@umich.edu
Central Outcomes Team: ICECAP-Outcomes@umich.edu
Central Outcomes Assessor: ICECAP-QAOutcomes@umich.edu

For additional contact information, please consult the list of contacts maintained on the ICECAP website.

2.0 Study Design and Objectives

A synopsis of the Study Design and Objectives can be found in the study protocol.

3.0 Overview of and Rationale for Study Outcomes

3.1 Primary Efficacy Outcome

The primary outcome will be the modified Rankin Scale (mRS) score at 90 days after return of spontaneous circulation. The mRS score will be determined primarily by the Central Outcomes Assessor at the CCC by telephone or telepresence, and secondarily by site personnel trained to administer the mRS. This individual must be blinded to the treatment group assignment for the participant.

3.2 Secondary Efficacy Outcomes

Secondary efficacy measures will be administered at 90 days following randomization. All secondary measures will be administered by a trained and certified Neuropsychological Outcomes Assessor (NOA). The NOA must be blinded to the treatment group assignment for the participant.

3.2.1 Participant-Reported Outcomes

The Neuro-QOL is a set of self-report measures (developed into item banks). The item banks that will be used in the ICECAP study include: Physical Health (i.e., Mobility, Fine Motor/ADL, Fatigue, Sleep Disturbance),

Social Health (i.e., Ability to Participate in Social Roles & Activities, Satisfaction with Social Roles & Activities), Emotional Health (i.e., Depression, Anxiety, Stigma, Positive Affect & Well-Being, Emotional-Behavioral Dyscontrol) and Cognitive Health (i.e., Cognitive Function, Communication). Item banks will be administered as computer adaptive tests when available.

3.2.2 Neuropsychological Outcomes

Neuropsychological testing provides an opportunity to examine, with great sensitivity, potentially subtle but meaningful differences in outcomes between treatment groups. The traditional measures chosen for the ICECAP trial include those that have proven reliability and validity for use in trials of patients with cardiac arrest (Becker, 2011), as well as measures that comprise the cognitive domain of the NIH Toolbox (Gershon, 2013). This particular combination of tests is designed to capitalize on both the advantages of using traditional paper and pencil tests, as well as those unique to computerized tests (i.e., the NIH Toolbox).

Domain	Neuropsychological Outcome Measure	AdminTime (Mins)
NIH Toolbox Tests		
Language - Vocabulary Comprehension	Picture Vocabulary Test	4
Executive – Inhibition	Flanker Inhibitory Control and Attention Test	3
Working Memory	List Sorting Working Memory Test	7
Executive – Flexibility	Dimensional Change Card Sort Test	4
Processing Speed	Pattern Comparison Processing Speed Test	3
Memory – Episodic	Picture Sequence Memory Test	7
Language - Reading Decoding	Oral Reading Recognition Test	3
Processing Speed - Working Memory	Oral Symbol Digit Test	3
Traditional Neuropsychological Tests		
Memory – Verbal	Rey Auditory Verbal Learning Test	10
Attention (A). Executive – Flexibility (B)	Trail Making Test	7
Executive – Inhibition	Stroop Test	5
Language – Verbal Fluency	Controlled Oral Word Association Test & Category Fluency Test	4

4.0 Study Team Roles and Training

All study team members conducting any outcome assessment for the ICECAP trial must be trained in that assessment. Where so indicated, current certification of such training must be posted in WebDCU along with other required regulatory documents for that study team member such as a CV, HIPAA Training Certificate and Human Subjects Certificate.

ICECAP Training Links

General ICECAP Education and Training

Outcomes Training

- mRS Training
- NTB Training
- NIH Toolbox Training

4.1 Central Outcomes Assessor (COA)

The COA is not part of the site study team. The COA is a centralized assessor associated with the ICECAP CCC who is responsible for remote telephone or videoconference administration and scoring of the 90 Day mRS.

4.2 Outcomes Assessor (OA)

The OA is a role whose responsibilities are limited to administration of the mRS. Any OAs administering the mRS must first undergo the SIREN mRS training and be blinded to the participant's treatment group assignment. The OA will administer the mRS during the 30 day phone visit and may administer the mRS at 90 days if absolutely necessary.

4.3 Neuropsychological Outcomes Assessor (NOA)

NOAs are responsible for administering all of the secondary efficacy measures (collectively known as the ICECAP Neuropsychological Test Battery or ICECAP NTB) at 90 days. They must be blinded to the participant's treatment group assignment. If the NOA at a site will also be administering the mRS, then they also need to be listed as having the OA role in the site's Delegation of Authority log, and be trained on the mRS.

NOAs will be trained and certified by members of the Central Outcomes Team at the Clinical Coordinating Center. After completion of training, the Central Outcomes Team will issue an outcomes training certification. Once awarded, this certificate must be uploaded to WebDCU™. The Instructions for uploading the certifications can be found in the 'WebDCU Regulatory Management' video located on this ICECAP Education and Training Page. Once a NOA's outcomes certification is approved in WebDCU™, s/he may begin performing outcomes assessments.

NOAs are advised to wait to begin the training and certification process until approximately 30 days after the site's first surviving participant is enrolled.

Please see Appendix A for detailed ICECAP NTB training procedures. To facilitate the above training process, previously certified NOAs are strongly encouraged to assist with training of new/additional NOAs at their sites. Additional NOAs at each site will be required to adhere to the same process as initial NOAs; however, it is

expected that subsequent NOAs at each site will require less remedial review of assessments to achieve certification.

The COT will hold regular office hours to answer questions and review and discuss pertinent outcome evaluation topics. NOAs are strongly encouraged to take advantage of these resources to stay up-to-date with the ICECAP trial and continue to fine tune and calibrate their skill in administering the ICECAP NTB.

4.4 Site Investigator and Study Coordinators

Although the Central Outcomes Assessor will be primarily responsible for the administration and scoring of 90 Day mRS, local Site Investigators or Study Coordinators may be asked to administer the mRS at 30 days and/or at 90 days if opportunities to contact the participant are fleeting or unreliable, or the OA or COA is not available. Any study team member administering the mRS must first undergo the SIREN mRS training and be blinded to the participant's treatment group assignment.

5.0 Expiration, Recertification and Retraining

As with initial training, retraining will be completed on a "just in time" basis. That is, the timing of retraining should be strategically planned (e.g., after enrollment of a new study participant) to minimize the likelihood that the certification will expire.

5.1 Modified Rankin Scale

Although study team members collecting an mRS are expected to be trained in the assessment, certifications of mRS training are not being collected. Sites and study personnel should retrain as needed, at least every two years.

5.2 ICECAP NTB

Neuropsychological Outcomes Assessors can maintain certification on the ICECAP NTB by either performing the battery on a study subject at least once every 6 months, or by a COT-supervised retraining process.

NOAs automatically maintain their ICECAP NTB certification by performing the battery on at least one study participant every 6 months. Those who have done this will be certified for an additional 6-month period. The ICECAP NTB certification will be extended by the Site Manager in WebDCU™.

NOAs whose ICECAP NTB certification is scheduled to expire will be notified by the Site Manager approximately one month prior to this expiration. NOAs who are unable to administer the ICECAP NTB for a period of more than 6 months will extend their certifications via the following procedure:

1) Review ICECAP key documents
    a) Outcomes Manual of Procedures (This document)
    b) ICECAP specific NIH Toolbox Administrator's Manual
2) Practice ICECAP NTB testing on at least one non-study participant
3) Video record the next 90 Day ICECAP-NTB outcome assessment conducted.
4) Submit the video, source documents and CRFs to the COT via the appropriate folders in MDropbox (a secure, HIPAA compliant storage system controlled by the University of Michigan).

a) Each site will have its own MDropbox subfolder. The Site Manager will send relevant site personnel invitations to their subfolders to provide access.
b) The source documents and CRFs should be combined into one .pdf file.
c) The naming format of both the training video and the CRFs is NOAFirstnameLastname_SubjectID_DDMMMYYYY (e.g., AngelaCaveney_1234_24MAR2020).

5) A member of the Central Outcomes Team will review the video, CRFs and data entry in WebDCU™ using the same pass/fail criteria as used in the initial certification process. Feedback will be provided.

a) If the assessment is passed, the COT will notify the NOA that no additional videos are required until further notice.

b) If the assessment is not passed
   i) The COT will conduct individualized training with the NOA.
   ii) The next 90 Day assessment conducted by this NOA will be video recorded and submitted to the COT for review.
   iii) This review process continues until the rater passes one visit. In cases where there are multiple failures, the COT has full discretion to determine whether to replace or to allow the NOA to continue to perform ICECAP NTB assessments for the ICECAP trial.

c) Once the recertification video has passed, the Site Manager at the CCC will extend the NOAs expiration date by 6 months (from the date of recertification) in WebDCU™.

d) The member of the COT reviewing a particular assessment is responsible for raising and resolving data clarification requests (DCRs).

6.0 Quality Assurance (QA) of Outcomes

6.1 Modified Rankin Scale

The 30 and 90 Day mRS interviews will not be recorded or reviewed for quality assurance (QA).

6.2 ICECAP NTB

To ensure maximum data quality across clinical test sites, all components of the ICECAP NTB are subject to quality assurance review for completeness, accuracy and internal consistency by the Central Outcomes Team.

The QA procedure for the ICECAP NTB is detailed in Appendix B. In summary, the NOA will be required (if the participant agrees) to video record:

- His/her first ICECAP NTB 90 Day evaluation
- Remedial reviews resulting from performance issues
    - NOA will be notified by COT when this is necessary
- A ~10% random sample of assessments
    - NOA will be notified by Site Manager when an assessment has triggered a random review

As soon as possible, but no later than 1 week following the study visit, site personnel should upload the video and source documents associated with the assessment to the COT.

The COT will review testing procedures, double score, and double-check data entry of select sessions and materials. Feedback will be given on all reviewed sessions, regardless of whether errors were made. Whenever possible, feedback will be provided within 1 week of the date study visit assessment materials are received by the CCC.

Questions and/or clarifications will be requested in WebDCU™ through the established data clarification process so sites can make corrections and respond to the questions posed by the COT. Any unusual cases will be further discussed within the COT to assist in scoring/rating consistency.

6.3 Remedial Training

Remedial reviews and remedial retraining of NOAs will be conducted when there are recurring errors of any kind (e.g., test administration, scoring) and/or for persistent transgressions from clinical standardization guidelines. Retraining will be conducted by the COT and will include, at a minimum, a discussion and a review of the study material specific to the problem area. Additional training procedures will be dictated (as needed) by the COT on a case-by-case basis. In all cases, the Site Manager will notify the site of additional required reviews so arrangements may be made for video recording.

7.0 Participant Retention

A study participant will be counted as retained when the mRS is obtained at 90 days post cardiac arrest. Study site personnel must make every effort to complete each participant's study visit within the allowable visit window (90 days ± 15 days). High rates of participant retention must be maintained throughout the study. Each site should strive for 100% retention.

7.1 Study Participant Retention Plan

Site Investigators at each study site are responsible for establishing a specific study participant retention plan. At a minimum, this plan should incorporate the following points to maximize participant retention:

- Ensure that family and the participant (at the time of consent) fully understand what follow up is involved. Discuss location and timing of follow up, what will be covered and how long it will take.
- Emphasize the value of the participant's involvement in the study during the informed consent process and as frequently as possible throughout subsequent interactions.
- Collect contact information from the family prior to discharge. This should include detailed information for the participant including home address, home phone, work phone, cell phone and email address. Also collect names and contact information for people who would know how to locate and contact the participant in the future if s/he should move.
- At the time of hospital discharge and at the 30 Day visit, collect detailed information regarding where the participant will be living and update other contact information.
- Set up follow up appointments in the required visit windows and make every effort to schedule at the most convenient time for the participant. When possible, schedule the 90 Day visit at a time that coincides with another hospital appointment so only one trip is needed.
- Assist participants with making transportation arrangements (if necessary) and working out the logistics of travel, including identifying (and if necessary contacting) the person who will accompany the participant.
- Use appropriate and timely visit reminder strategies (e.g., phone calls) a few days before a scheduled visit and/or on the morning of the appointment.
- Send a confirmation letter prior to the visit that includes the appointment date, time, where the participant should go and how long the appointment will take. Remind participants to bring eyeglasses and/or hearing aids if needed.
- Offer in-person contact with a participant in his/her home or other community location if the participant does not want to come to the hospital for the appointment.
    - If a participant does not want to come to the hospital and is not willing to allow the NOA to visit his/her home, the mRS and the Neuro-QoL measures can be administered over the telephone.
        - Neuropsychological measures will not be completed over the phone.
- Make all visits as short and as pleasant as possible for the participant. Do not keep participants waiting.
- If an appointment is missed, attempt to re-contact and reschedule as soon as possible. Continue these efforts per the local retention plan until contact is made.
- If a participant is difficult to reach, attempt to contact him/her at different times of the day and the week, including evenings and weekends.
    - Use all available methods to contact the participant (e.g., phone, mail, e-mail, texting, calling other people). Also, make use of publicly available information such as phone and post office directories and other public registries.
- Make every effort to complete the assessment during the test window and to complete all tests on the testing day. If the entire assessment cannot be completed within one day, make every attempt to finish the visit within 3 days of the initial appointment.
- If the assessment cannot be completed within the test window, the site should email the ICECAP team at ICECAP-contact@umich.edu to request an extension of the test window.
    - The email should include the dates of the participant's test window, a brief description of the circumstances that led to the delay, and the outcome measures that were not completed.

7.2 Lost to Follow Up

All participants deemed "lost to follow up" will be reviewed by the SIREN Operations Committee. The Site Investigator or designee will be asked to present the case to the SIREN Operations Committee that includes

the efforts exerted to locate the participant. (To present the case, notify the ICECAP team at ICECAP-Contact@umich.edu to be placed on the meeting agenda. SIREN Operations Meetings are held weekly on Wednesday at 2:00 PM ET.) The Operations Committee may ask the Site Team to make further efforts to find the participant and be asked to undergo further review. Unable to attend an in-person outcomes assessment does not constitute a “lost to follow up”.

8.0 SCHEDULING THE APPOINTMENTS

A member of the site study team will contact the participant and his/her mRS informant (e.g., Legally Authorized Representative, caregiver, family member) to schedule the 30 and 90 day follow up assessments. The 30 Day visit is to be conducted by phone. (This visit does not need to be recorded.) The 90 Day visit should be conducted in person whenever possible.

The 90 Day mRS should be scheduled at the same time as the regular study visit. The Central Outcomes Team has established a web-based ICECAP Central Outcomes Assessor Google Calendar. Access to this calendar is provided by the COT. It is the site’s responsibility to consult the Central Outcomes Google Calendar to determine the availability of the Central Outcomes Assessor prior to scheduling with the participant and informant (i.e., to avoid double booking).

To schedule the appointment on the Central Outcomes Assessor Google Calendar, the NOA will enter his/her site’s name, Participant ID, calling information (e.g., conference room invitation, phone number) and the language in which the interview will need to be conducted.

If there is a change in the schedule more than 2 days before, the local team member may just remove it from the ICECAP Central Assessor Calendar. Within 2 days, the SC must both remove the appointment from the calendar and notify the COA by email at joypink@umich.edu.

Study team members at the individual sites are responsible for confirming the appointment with participants and their informant. The mRS interviews conducted by the COA (with the informant and/or the study participant) may need to occur on a different date from the in-person visit or the follow up phone visit. If separate calls need to be scheduled, these should occur as close to the 90 Day ICECAP NTB assessment as possible.

In the majority of cases, the mRS interview will be scheduled in advance using the central calendar described above. However, on occasion, a “hard to reach” participant may be serendipitously contacted (e.g., shows up unexpectedly to a clinic appointment). In this case, the site study staff should first attempt to contact the COA. If the COA is not available, other blinded, mRS trained study personnel (e.g., the NOA) may complete the 90 Day mRS evaluation. When this occurs, the local mRS interviewer must contact the COA to discuss the information collected and the 90 Day mRS scoring.

8.1 Telephone Only Visits

Whenever possible, the 90 Day visit is to be conducted in-person. If a study participant is unable or unwilling to come to the clinic or have the NOA come to his/her place of residence, a telephone follow up may be scheduled. When this occurs, the COA will administer the mRS and the NOA will administer (only) the Neuro-QoL measures (the rest of the ICECAP NTB is not to be administered by phone) over the telephone. This visit does not need to be recorded. Site study staff will facilitate the call between the study participant and the COA. As is the case when the visit is in-person, every effort should be made to schedule the mRS and Neuro-QoL interviews on the same day.

8.2 Hospital/Assisted Living Facility Visits

Sites will need to take additional steps to schedule the 30 and 90 Day appointments if the study participant is still hospitalized or in an assisted living facility (e.g., nursing home, group home, adult home or skilled nursing facility).

In cases where a study participant is unresponsive, only the mRS will be completed for the 90 Day visit. No other outcomes, including the Neuro-QoL (even by proxy) should be attempted.

8.2.1 30 Day Visit

If the participant is still in the enrolling hospital, the blinded study member administering the 30 Day mRS should visit the participant in his/her room to determine the mRS score. If the participant has been discharged to another hospital or assisted living facility, the person conducting the mRS should contact someone very familiar with the study participant's level of functioning (e.g., caregiver, family member, LAR) to complete the mRS. If information will be collected from the study participant's medical caregivers, a copy of the signed study consent form should be first sent to the facility.

8.2.2 90 Day Visit

If the participant is still an inpatient at the enrolling hospital, a study team member should visit the participant in his/her room to determine feasibility of completing the ICECAP NTB. The ICECAP NTB (with the exception of the Neuro-QoL. See sections 10.3 and 11.9 for more detail.) should not be attempted on study participants who are bedridden (i.e., an mRS of 5. See section 11.1 for more detail). If the participant has been discharged to another hospital or assisted living facility, the SC or NOA should contact someone very familiar with the study participant's level of functioning (e.g., caregiver, family member, LAR) to determine testability (defined roughly as an mRS of 4 or better).

Whenever possible, the 90 Day mRS should be conducted by the COA by phone with both the study participant (if s/he is able to communicate by phone) and an informant who is very familiar with the study participant's level of functioning. If information will be collected from the study participant's medical caregivers, a copy of the signed study consent form should first be sent to the facility.

For study participants who are able to be tested, the NOA should administer the ICECAP NTB in person at the facility.

9.0 Communication Between Study Coordinator, Neuropsychological Outcomes Assessor and Central Outcomes Assessor

9.1 Planning and Roles

Good communication is key for the successful completion of the outcome evaluations. The Study Coordinator, being the first to interact with the participant and his/her family will have the most information regarding the initial situation and be the first to begin developing rapport. During hospitalization, the Study Coordinator should attempt to obtain the following in preparation for the 90 Day follow up:

- Pre-injury information
- Contact information
- Testing/interview language preference

The study coordinator, if possible, should begin to orient the family to the expectations of the clinical trial by explaining the 30 Day phone call and 90 Day in-person visit.

If a site finds it useful to do so, the Study Coordinator can introduce the NOA to the participant and family members before hospital discharge, but this is not necessary. It is always important for the Study Coordinator and the Neuropsychological Outcomes Assessor to maintain contact throughout the process.

Each site will need to decide who is responsible for contacting the participant for the 30 Day phone visit and to schedule the 90 Day in-person visit. All attempts at contact (whether successful or not) should be documented. The SC, NOA and (if applicable) Outcomes Assessor should keep each other informed if there is expected to be (or is any history of) difficulty with locating and contacting the participant so a plan is developed that includes ample time to find and schedule the participant's 90 Day evaluation.

9.2 Maintaining Blinding

Anyone administering the 90 day mRS and/or the ICECAP NTB should be blinded to the study treatment to which the participant was allocated, and to that the participant received. To maintain the blind, Study Coordinators and Site Investigators must not reveal this information and must keep all material that potentially could reveal this out of view of these individuals. NOAs and COAs should tell study participants and/or their informants that they do not know which treatment the participant received and should not be provided any information about the study treatment. If an NOA, OA or COA becomes unblinded during any outcome assessment, s/he should alert the Site Investigator immediately. This should be reported to the ICECAP leadership team.

Blinding is preferred, but not necessary for the 30 day phone visit, which may be done by the Study Coordinator if trained in the mRS. If, while arranging the 90 day visit (during the window for that visit), the Study Coordinator contacts the participant or care-giver, but becomes concerned that subsequent contact may be lost, the unblinded Study Coordinator trained in the mRS may assess a mRS as a contingency to protect against loss to follow up and missing data. Even if this is done, every attempt is required to schedule follow up with the COA and the NOA.

10.0 Outcomes Testing Procedures

10.1 Testing Windows

The 30 Day telephone visit is to be conducted 30 days (± 15 days) after the date of randomization. The 90 day in-person visit is conducted 90 days (± 15 days) post randomization. Ideally, the entire visit (including interviews with informants) will be conducted on the same day. When this is not possible, subsequent visits should be conducted as soon as possible (within the visit window).

10.2 Informant

An ideal informant is someone who was familiar with the participant before the injury and has knowledge of his/her current functional level. Informants should be very familiar with participants' level of independence and any difficulties with functioning. The informant is typically a caregiver, family member or close friend. If the participant is living in an assisted care facility or other medical setting, it is permissible to speak with a caregiver or member of the care team, even if this person did not know the participant prior to the injury.

10.3 Does Impairment Preclude Evaluation?

The mRS should be completed at the 30 day telephone visit and 90 day in-person visit, regardless of the study participant's level of impairment. Every effort should be made to collect information from multiple sources. This should include, whenever possible, observation of and conversation with both the participant (if s/he is able) and the informant (e.g., caregivers, family members and/or close friends).

Similarly, the Neuro-QoL measures should be completed at the 90 day visit regardless of the study participant's level of impairment (unless the participant is unresponsive). No other outcomes, including the Neuro-QoL (even by proxy) should be attempted. As is explained in more detail below, an informant may complete the Neuro-QoL measures on behalf of the study participant. If the participant is able to cognitively answer the Neuro-QoL measure questions, but is physically unable to read and/or respond (on the iPad), the Neuropsychological Outcomes Assessor may read the Neuro-QoL measure questions aloud and indicate the study participant's responses on the iPad.

As a general guideline, the ICECAP NTB (with the exception of the Neuro-QOL by proxy) should not be attempted with study participants whose mRS score is 5, or "bedridden". Bedridden is loosely defined as someone who is unable to move him/herself into a sitting position (in bed), unable to walk any steps (even with others helping) and unable to be left alone for more than 3 hours. When scheduling the 90 day evaluation, the study member scheduling the appointment should ask questions to determine if ICECAP NTB administration is feasible (either by getting an estimate of the mRS score or by determining the participant's mental status).

If it is clear that the study participant cannot be tested in-person, only the mRS and the Neuro-QoL may be conducted by phone. When there is uncertainty regarding the participant's mRS status and testability, an in-person visit should be scheduled and the NOA should attempt to test the participant. As always, the NOA should enter comments into the "General Comments" section regarding the participant's ability to complete testing and use clinical judgement regarding when discontinuation is necessary.

10.4 Determining English Language Proficiency

Prior to the 30 Day appointment, the Study Coordinator should determine the participant and informant's preferred language/s and whether an interpreter is needed for the mRS interview. The mRS and the Neuro-QoL may be administered in any language for which there is an appropriate, available interpreter.

The ICECAP NTB (with the exception of the Neuro-QoL) will only be administered in English or Spanish. Due to the complexity of testing procedures, interpreters may not be used to administer the neuropsychological outcomes included in the ICECAP NTB (i.e., If the site does not have an English-Spanish bilingual NOA, the site will not be able to conduct the ICECAP NTB in Spanish). It is up to the site to determine, on a case by case basis, whether the patient's level of proficiency with English (or Spanish) is sufficient enough to understand testing. It is not absolutely necessary to test in the participant's native language. If English (or Spanish) proficiency is determined to be insufficient for valid testing, the NTB will not be administered.

10.5 Working with an Interpreter

Interpreters must be used to interview study participants whose proficiency with English is not sufficient for valid mRS interviewing. The following can be used as an interpreter for the ICECAP study to administer the mRS and Neuro-QoL: trained multilingual study team members (if blinded), on-staff interpreters, contract interpreters and telephone interpreters. Other individuals, including (but not limited to) the study participant's family and friends, other study participants or untrained volunteers cannot be used as interpreters. For detailed

information regarding other considerations and best practices when working with a translator please review this website.

10.6 Notes on Documentation

General documentation instructions include:

- Writing must be legible.
- Errors should be noted with a single strike through, initials and date.
- In the “General Comments” section of the CRF, note anything relevant about test administration. It is important to note when the study participant exhibited poor comprehension or effort during testing. Also note if there were any variations from standard testing procedures.

10.7 30 Day Telephone Visit

The 30 Day outcomes visit includes a phone evaluation of the mRS. This visit is not to be audio recorded. The 30 Day mRS may be conducted by any mRS trained study site member who is (preferably, but not required to be) blinded to the treatment group assignment for the study participant. Whenever possible, the 30 Day mRS interview should be conducted both with the study participant and a knowledgeable informant who is in close contact with the study participant. Ideally, the mRS interviews should be conducted separately so all interviewed can speak freely.

10.8 90 Day Outcome In-Person Visit

Careful coordination and high quality communication between all study team members, the Central Outcomes Assessor, the study participant and the informant are essential to optimizing the conditions for quality outcomes assessments and to minimizing inconvenience to the participant. Each site should develop its own strategy and plan.

If a study team member suspects that the study participant and/or informant is in an altered state of consciousness due to alcohol or illicit drugs, the visit must be rescheduled.

It is critical that an informed caregiver or family member attend the 90 Day in-person outcomes visit. The mRS requires an informant interview. In the unusual circumstance where an informant cannot attend the visit, this person should be separately contacted by telephone to complete the mRS informant interview. As the primary outcome, the mRS should be conducted first whenever possible.

10.8.1 ICECAP NTB Required Materials

An ICECAP NTB “testing kit” will be mailed to each site by the Clinical Coordinating Center. This kit includes:

- iPad
- iPad External Keyboard
- “Examination in Progress” Sign
- English Test Instructions Booklet
- Spanish Test Instructions Booklet
- Trail Making Test Forms
- English Stroop Test Forms
- Oral Symbol Digit Examination Sheet (Double sided)
- NIH Toolbox Home Base Form
- Answer Key for NIH Toolbox List Sorting Test (Double sided)

*If replacement materials or additional forms are ever needed, sites may contact the Clinical Coordinating Center.

In addition to the equipment listed above, the site will need access to video recording equipment. Video recorders will not be provided by the CCC. Sites may use any appropriately secure video recording device (e.g., laptop webcam, encrypted smartphone) available to the research team that meets the site's local, institutional standards. The NIH Toolbox iPad is not to be used for video recording.

Printable, electronic versions of English and Spanish test instructions are found in Appendix D and Appendix E, respectively. English and Spanish test forms (those that are not shipped to sites as part of the test kit) and additional English and Spanish stimulus materials required to administer the NIH Toolbox are available in Appendix F and Appendix G, respectively. All documents included in or linked to in this manual may be printed by site study personnel. (Only the Trail Making Test forms and Stroop forms may not be printed or copied in any way due to copyright restrictions and/or potential for test invalidation.) CRFs are located in the CRF section of the ICECAP website.

Tests that are not sent by the Clinical Coordinating Center and must be printed at each site are:

- Rey Auditory Verbal Learning Test (RAVLT) in English and Spanish
- Controlled Oral Word Association Test (COWAT) in English and Spanish
- Category Fluency Test (CFT) in English and Spanish
- English Pronunciation Guide for the NIH Toolbox Oral Reading Recognition Test
- Spanish Pronunciation Guide for the NIH Toolbox Oral Reading Recognition Test

10.8.2 ICECAP NTB Testing Environment

Throughout the ICECAP outcomes assessment process, standardized procedures must be used to objectively and reliably assess the study participant's functional status, cognitive abilities and perceived health-related quality of life 90 days after cardiac arrest. The NOA must work to create a comfortable and supportive testing environment that elicits optimal performance from the study participant without compromising the integrity of test data.

- Testing should take place at a desk or at a table that is comfortable and appropriately sized for the study participant.
    - Straight backed chairs are ideal.
    - Study participants may remain in their wheelchairs.
- Testing must be conducted in a private, quiet, well-lit, and uncluttered room that is free of distractions.
    - Distractions both inside and outside of the room should be considered.
    - Mobile phones, televisions and other distractions must be put away and/or turned off. Neither the study participant nor the NOA should be checking his/her phone at any time.
- An "Examination in Progress" sign should be placed on the door (to minimize interruptions).
- Study participants requiring hearing or visual aids (to attain optimal performance) must be wearing them.
- Family members, friends and caregivers are not permitted to observe neuropsychological testing.
- Study participants should be asked if they need to use the restroom before the visit begins.

10.8.3 ICECAP NTB Standard Administration

The skill and judgment of the NOA often affects participants' willingness to be tested, the effort they invest and the overall quality of the data collected. NOAs are required to simultaneously administer tests correctly,

observe and assess participant behavior, and make necessary adjustments. They must work to elicit optimal performance from the examinee, while ensuring that the interaction does not compromise the data obtained.

The following guidelines are provided to maintain inter-rater reliability and ensure standard administration of the ICECAP NTB. Following these guidelines helps to ensure valid and accurate assessment while reducing stress and discomfort for participants.

- The ICECAP NTB measures must be administered in the order specified.
    - The test sequence is designed to ensure the fluency of the assessment battery, facilitate completion of the measures that are most instrumental to the study aims.
- Standard administration procedures must be followed EXACTLY according to the instructions provided.
    - All deviations from standard procedures must be reported to the Central Outcomes Team.
- ICECAP NTB test instructions must be read verbatim.
    - Memorization of instructions is not required, however, instructions must be practiced several times to develop familiarity and fluency.
    - It is the NOAs responsibility to ensure that the participant understands the instructions before each test is started and that understanding is maintained throughout the test.
    - Following the initial reading, repetition, clarification and paraphrasing of instructions is allowed (only if needed) to help the participant understand what to do.
        - Additional information must reflect the standard instructions.
        - No new information, suggestions or hints may be provided at any time.
- Recording of responses and timing of tests must be accurate and precise.
    - A digital stopwatch must be used
    - Cellphone timing is not permitted
- For the ICECAP study, testing will be completed using a pen rather than a (more traditional) pencil. This is due to practical issues with the study's quality assurance procedures. Pencil marks do not copy well.
- Except when indicated (e.g., many of the practice trials of the NIH Toolbox), feedback provided during test administration must be non-directive and focus on effort rather than accuracy of performance.
- Brief breaks (in between tests) may be given if needed. Timing of the breaks must consider both the study participant's needs and the test requirements.
    - Except under extenuating circumstances, breaks should be given only between tasks.
    - If the study participant requests a break during a task, the NOA should ask him/her if s/he can wait until the task is completed.
        - If a break must be taken during a timed task (invalidating that test's data in most cases), this must be both noted in the "General Comments" section and the Central Outcomes Team must be notified.
- Sound clinical judgment must be exercised when deciding when battery discontinuation is necessary.
- Scoring should be done immediately to improve accuracy.
    - The NOA may listen to the recorded visit to verify the answers.
    - Tests should be double-scored, preferably by a second person.

10.8.4 ICECAP NTB Testing Rapport & Feedback

The degree to which a study participant is put at ease before an evaluation can have a significant effect on his/her performance. It is imperative that the NOA work to establish good rapport with study participants to help maintain the participant's level of motivation and engagement.

The NOA should begin the assessment by introducing him/herself by name and explaining his/her role. The NOA should next describe the purpose of testing, what the test(s) will be like, how long testing will take and the

fact that the participant may take breaks (in between tests) if needed. (An example script of this introduction is provided in Appendix D.) The participant should be given an opportunity to ask questions and every effort should be made to build rapport and put the participant at ease. Testing should not commence until the participant indicates readiness to begin.

Tips to build rapport include:

- Casual, appropriate conversation should be used to relax the study participant.
- The NOA should be enthusiastic and encouraging by using neutral reassurances throughout the testing, such as:
    - "I appreciate how hard you're working on these tests"
    - "You're doing fine"
    - "Just do the best you can"
- If the study participant asks for feedback about his/her performance on a particular item (e.g., "Did I get that one correct?") the NOA should reply that answering these questions is not allowed as part of the rules for this study.
- If the participant expresses or exhibits signs of frustration or requests that testing be discontinued, the NOA should empathically acknowledge the participant's concerns and also add notes to "General Comments" regarding any reported symptoms (e.g., pain, fatigue) that could impair test performance.
    - Many times, these challenges can be overcome with short breaks (e.g., visit the restroom, a drink of water) or a brief conversation about something about which the participant is interested (e.g., the weather, a hobby, a local sports team or a television show).
        - It is inappropriate to discuss sensitive topics such as politics or religion.
    - If it is possible to continue testing, an attempt should be made to do so.
- Study participants should be assured that the tests are designed so that no one correctly answers all the questions. Participants should not leave with the impression that they "failed" in any way.
- At the end of the session, NOAs should thank the participant for his/her effort and participation in the study. The participant should leave the visit feeling successful.

10.8.5 Test Battery Order

Ideally, the mRS will be administered first, however, this is flexible, particularly if there is no question regarding whether the study participant is able to undergo ICECAP NTB testing or risk that the study visit will not be completed. It is important, however, that the mRS not, in any way, disrupt or be "inserted into" the ICECAP NTB portion of the assessment. The Central Outcomes Assessor's interview with the study participant's informant/s, however, may occur simultaneously with the NOAs administration of the ICECAP NTB (as long as this is done in another room and does not disrupt ICECAP NTB testing in any way).

The ICECAP NTB outcome measures are administered in the following order:

1. Rey Auditory Verbal Learning Test (Learning Trials, Interference Trial, Immediate Recall)
2. NIH Toolbox Tests
    a. Touch Screen Tutorial
    b. Picture Vocabulary Test
    c. Flanker Inhibitory Control and Attention Test
    d. List Sorting Working Memory Test
    e. Dimensional Change Card Sort Test
    f. Pattern Comparison Processing Speed Test
    g. Picture Sequence Memory Test
    h. Oral Reading Recognition Test
    i. Oral Symbol Digit Test

3. Rey Auditory Verbal Learning Test (30 Minute Delay and Recognition)
4. Trail Making Test
5. Stroop Test
6. Controlled Oral Word Association Test
7. Category Fluency Test
8. Neuro-QoL Measures

Please review this NOA Testing Flowchart for additional information.

10.8.6 Consent and Procedure for Video Recording the ICECAP NTB Administration

When (and only when) required for training and quality assurance purposes (Appendix B), all components of the ICECAP NTB should be video recorded. It is necessary to obtain the study participant's verbal permission prior to recording the 90 Day visit since the participant him/herself did not sign the initial consent form.

The camera should be focused on the NOA and testing table, not the study participant. Only the participant's hands and arms should be visible in the video.

The script to obtain consent for video recording can be found in Appendix D.

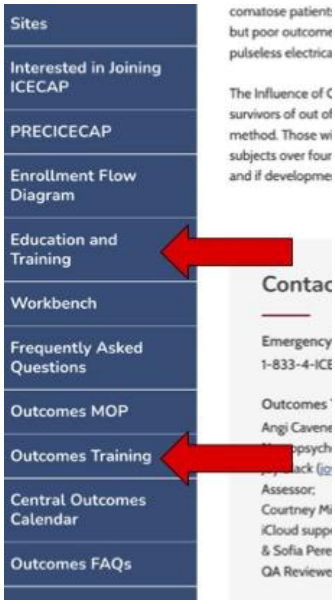
11.0 Outcomes Descriptions, Scoring Instructions, Training and Tips

The term ICECAP Neuropsychological Test Battery ("NTB") encapsulates all secondary efficacy assessments conducted for this study. This includes the Neuro-QoL measures, the NIH Toolbox tests and all of the traditional neuropsychological paper and pencil tests. Training on the ICECAP NTB should commence within 30 days after enrollment of a site's first study participant.

In this section, the modified Rankin Scale and all of the ICECAP NTB outcome (neuropsychological and participant-reported) measures are described in detail. Neuropsychological testing in the ICECAP trial has been limited to approximately one and a half hours to enhance study participant compliance and minimize fatigue. Participants who cannot tolerate the complete battery in one session may be scheduled for a second session.

***Note. In order to access the University of Michigan's training modules, you will need a UMICH Friend Account.** Please visit the UM Friend Account page on the SIREN website. This page provides detailed instructions on requesting, using, and recovering your password for your Friend account. When you have read through the instructions you can request your account by clicking the link on that page.

Once you have a Friend account, you will be able to access the ICECAP training page. You must log in using your Friend account and the "Education and Training" and "Outcomes Training" menu items will appear in the navigation bar on the left side of your screen. **If you do not see these menu items, you are not logged in.**



mRS Training
ICECAP NTB Training

See Appendix D for all English test instructions.
See Appendix E for all Spanish test instructions.
See Appendix F for all English test forms.
See Appendix G for all Spanish test forms.

11.1 Modified Rankin Scale (mRS)

Simplified mRS Flow Sheet
mRS Training

11.1.1 Reference

Rankin J. “Cerebral vascular accidents in patients over the age of 60.” Scott Med J 1957;2:200-15

11.1.2 Description

The modified Rankin Scale (mRS) is a stroke outcome scale used to assess a participant’s current functional status. It consists of six levels. Zero indicates no residual symptoms at all and 5 indicates severe disability (bedridden). The mRS is always assessed using the level of function at the current time and should never be retrospective.

For the ICECAP study, the 30 day mRS evaluation should be completed by a blinded, mRS certified, local study team member. Except in rare cases, the 90 day mRS evaluation will be completed by the Central Outcomes Assessor. If the 90 day mRS evaluation must be completed by someone other than the COA, the local mRS interviewer must contact the COA to discuss the information collected and the 90 day mRS scoring.

11.1.3 Scoring

The mRS score is determined by the blinded, trained, certified study staff member conducting the interview. The score is not “self-report”. To determine the score, the mRS interviewer uses his/her clinical judgment and all available information (e.g., patient interview and exam, caregiver interview). The outcome categories (scores) of the mRS include:

- 5 - Bedridden
- 4 - Needs assistance (or supervision) from another person to walk
- 3 - Needs assistance from another person to look after own affairs
- 2 - Substantial reduction in work, family responsibilities and/or social and leisure activities
- 1 - Mild, residual symptoms
- 0 - No symptoms

11.1.4 Training and Certification

mRS Training

SIREN mRS training is available through the Clinical Coordinating Center. Training consists of watching a training video, then watching and scoring five vignettes. Four of five vignettes must be scored correctly to pass. The process repeats until a passing score is achieved. A certificate will be sent automatically via email upon passing. For the ICECAP study, it is not necessary to send this certificate to the CCC or to upload it to WebDCU™.

The SIREN mRS certification is valid for two years. mRS certified individuals are required to track their own certification and recertify when needed.

11.1.5 Administration Tips and Key Things to Remember

- The 30 day mRS evaluation will be completed by a blinded, mRS certified, local study team member. Whenever possible, the 90 day mRS evaluation will be completed by the Central Outcomes Assessor.
    - In the rare case when the 90 day mRS evaluation is completed by someone other than the COA, the person completing the 90 day mRS must contact the COA to discuss the information collected and the mRS scoring.
- It is extremely important to gather information from multiple sources via separate interviews whenever possible.
    - Study participants often lack insight and are likely to deny psychological problems.
    - Informants are often overly cautious. Questioning must determine what the person could do, not what s/he has actually done or is “allowed” to do.
    - Due to the risk of unblinding, mRS interviewers may NOT access the study participant’s medical record (without specific, written consent from the ICECAP Outcomes Committee) to gather additional information.
- The person administering the mRS must use good clinical judgment to determine the score based on the information s/he considers to most accurately reflect the status of the study participant at the time of the examination.
    - Therefore, information obtained from the informant or the study participant may be relied upon more or less heavily, depending what the mRS interviewer determines is the reliable source of information for any given question.
- All contradictory information should be explored. Contradictions may occur within an interview with a person (e.g., says s/he cannot make a simple meal, but is back to work part-time) or between interviews with the study participant and informant.
- In all cases, additional questioning (and sometimes additional interviews) is required. It is permissible to return to and rephrase previously asked questions.
- mRS interviewing is fluid and does not have to go in the exact order presented on the form. Generally, it is least awkward to begin with items regarding the highest level of impairment and work down from there.
- mRS questions should be first asked generally as worded on the form itself, but then may be expanded upon in any way needed to ensure the correct score is obtained.
- In general, once a score is determined, the remaining questions do not need to be asked. Despite this, however, it is ok to ask additional questions to be sure all needed information is obtained. If there is any uncertainty regarding the score, additional questions should be asked. Too many questions is far better than too few.
- The person administering the mRS may NOT discuss the score with the Neuropsychological Outcomes Assessor and/or use data from the ICECAP NTB as guidance.
- The person administering the mRS may NOT look at the study participant’s medical record (due to risk of unblinding) or discuss the score with a study member who is unblinded (due to risk of unintended bias).

- Questions regarding scores of 5, 4 and 3 are based on the participant's overall functioning, taking into consideration all disabilities, from any source.
- Questions regarding scores of 0, 1 and 2 consider only disability related to the cardiac arrest that led to the study participant's enrollment in the ICECAP study.
- Changes resulting from extraneous factors (socioeconomic, weather, flu pandemic) are disregarded. Study participants are asked what they "could do" if these issues were resolved.
- Preventative driving restrictions (e.g., due to history of seizures) per se' should not be considered a disability in this study. The question is whether the person can do, not what s/he is allowed to do.
- There are three key questions when deciding between an mRS score of 5 vs 4. To be scored a 4, a participant must be able to:
    - Be left alone for at least 3 hours
    - Sit him/herself up in bed
    - Walk a few steps (with or without the assistance of another person or people)
- When deciding between an mRS score of 4 vs 3, the ability to operate a wheelchair independently (without the assistance of another person) is scored as "able to walk" independently.

11.2 Rey Auditory Verbal Learning Test (RAVLT) - Learning, Interference and and Immediate Delay

RAVLT English Forms
RAVLT Spanish Forms
RAVLT Learning and Immediate Delay English Instructions
RAVLT Learning and Immediate Delay Spanish Instructions
RAVLT Training

11.2.1 Reference

Rey Auditory Verbal Learning Test. Adapted from Taylor, E.M. (1959). The Appraisal of Children with Cerebral Deficits. Cambridge, MA: Harvard University Press, and Lezak, M.D. (2004) Neuropsychological Assessments (4th ed.). New York: Oxford University Press.

11.2.2 Description

The RAVLT Learning and Immediate Delay Trials evaluate verbal learning and memory during a multiple-trial list-learning task. Participants are read a list (List A) of 15 common words and asked to recall as many of the words as possible. This process repeats 5 times. Following the 5th Trial, a second set of 15 words (List B) is read and the participant is asked to recall as many as possible. Following this Trial, the study participant (without repetition of List A) is again asked to recall the words from List A.

11.2.3 Scoring

Scoring for the RAVLT is manual. The scores collected include:

- The total number of words recalled during each Learning Trial (i.e., Trials 1 through 5)
- The total number of words recalled on the Interference Trial (i.e., List B)
- The total number of words recalled on the Immediate Delay Trial

11.2.4 Training and Certification

The RAVLT training module and quiz can be found on the ICECAP NTB Training web page. In brief, the training for the RAVLT includes:

- Observation of the RAVLT training video

- Passing the RAVLT quiz
- Practice test administration (minimum of 5 times)
- Submission of a passing test video

At the discretion of the Central Outcomes Team, and in accordance with the training and certification procedures in Appendix A, additional, remedial practice and video submissions may be required.

11.2.5 Administration Tips and Key Things to Remember

- The words for every Trial should be read at the rate of one word every second.
- It is not necessary to read the full instructions for Trials 3 through 5 if the participant clearly understands what to do.
- The NOA must practice this test until s/he is able to keep up with a participant who recalls words very quickly. It is NOT acceptable to ask the participant to slow down or repeat him/herself, nor is it acceptable to miss recording words.
    - The NOA may later go back and listen to the recording to verify that all words were recorded.
- The participant should not be allowed to give up too easily. The NOA should not discontinue a Trial until the participant has indicated that s/he can not think of any other words AND at least 10-15 seconds have passed since the last correct response was given. The NOA can encourage participants by saying something like “just think for a few more seconds to see if any more words come to you”.
- If the study participant asks, “Did I already say that?” the NOA should inform him/her that s/he cannot provide this information.
- Repetitions and intrusions (saying words that are not on the list) are not recorded or scored. There is no need to comment on or to document these.
- This test can be intimidating for many participants. Acknowledging that it is a difficult task and that the participant is not expected to remember all of the words is often helpful.
- If a participant seems to be neglecting words from previous Trials (i.e., misunderstanding the instructions to repeat the entire list each time), the NOA should re-explain that the participant should include words from prior Trials.
- Pluralization of a stimulus word is counted as correct (drums for drum).
- The study participant is NOT informed that there will be a 30 Minute Delay Trial.
- The 30 Minute Delay Trial must be administered 30 ±5 minutes after the Immediate Delay Trial is completed (i.e., right before beginning administration of the NIH Toolbox tests). To facilitate timing, the NOA should note the time finished with the Immediate Delay.

11.3 NIH ToolBox of Neurological and Behavioral Functioning

ICECAP NIH Toolbox Administrator’s Manual
Link to General NIH Toolbox Training
Picture Vocabulary and Oral Symbol Digit Instructions (English Only)
NIH Toolbox Home Base
Oral Symbol Digit Examination Sheet
Answer Key for NIH Toolbox List Sorting Test
English Pronunciation Guide for the NIH Toolbox Oral Reading Recognition Test
    - English Pronunciation Audio
Spanish Pronunciation Guide for the NIH Toolbox Oral Reading Recognition Test
    - Spanish Pronunciation Audio (Only required for NOAs planning to test in Spanish)
NIH Toolbox SetUp and Data Download Module
Oral Symbol Digit Training Module
NIH Toolbox Training Checklist

11.3.1 Reference

Gershon, R.C., Wagster, M.V., Hendrie, H.C., Fox, N., Cook, K.F., & Nowinski, C.J. (2013). NIH Toolbox for Assessment of Neurological and Behavioral Function. Neurology, 80(11 Supplement 3), S2-S6.

11.3.2 Description

The NIH Toolbox of Neurological and Behavioral Functioning is a set of integrated assessment tools for measuring cognitive, emotional, motor, and sensory health with enough flexibility to be appropriate for a wide range of ages. The Toolbox was developed with the ultimate goal of improving communication within and between fields of biomedical research and to advance knowledge by using common data elements (CDEs). The combined NIH Toolbox Battery examines various cognitive (episodic memory, language, processing speed, working memory, executive functions, attention), emotional (negative affect, psychological well-being, stress and coping, social relationships), sensory (vestibular, audition, olfaction, taste, vision), and motor (dexterity, strength, locomotion, endurance, balance) functions. The NIH Toolbox is designed to measure these domains in individuals aged 3 through 85 years and has been normed for both English and Spanish speakers.

In the ICECAP trial, tests from the Core Battery for the NIH Toolbox Cognition Battery, as well as one supplemental Cognitive Toolbox test (Oral Symbol Digit) will be administered. The chosen tests measure episodic memory, language, processing speed, working memory, executive function, and attention. Administration time for the NIH Toolbox Cognition Battery is approximately 30 minutes.

Below is the list of NIH Toolbox Cognitive tests that will be administered in the ICECAP trial in the order of administration. Prior to shipping the iPad to a site, individuals at the Clinical Coordinating Center will install the NIH Toolbox App and configure the ICECAP Toolbox battery in the correct order.

Cognitive Domain	NIH Toolbox Test	Approximate Admin Time
Familiarization with iPad Touch Screen	Touch Screen Tutorial	<1
Language - Vocabulary Comprehension	Picture Vocabulary Test	4
Executive – Inhibition	Flanker Inhibitory Control and Attention	3
Working Memory	List Sorting Working Memory Test	7
Executive – Flexibility	Dimensional Change Card Sort Test	4
Processing Speed	Pattern Comparison Processing Speed	3
Memory – Episodic	Picture Sequence Memory Test	7
Language - Reading Decoding	Oral Reading Recognition Test	3
Processing Speed - Working Memory	Oral Symbol Digit Test	3

11.3.3 Scoring

NIH Toolbox scoring is completed by the NIH Toolbox App. No manual scoring is needed.

11.3.4 Training and Certification

To complete Toolbox training NOAs must follow the process outlined in Appendix A.

NIH Toolbox Training Notes:

- The demonstration videos of the NIH Toolbox eLearning Course are a valuable training tool and all should be watched. NOAs only need to watch the 8 modules that go with the tests being administered in this trial. (i.e., Visual Reasoning, Speeded Matching, Rey Auditory Verbal Learning and Face Naming should not be watched.)

- The NIH Toolbox eLearning Course training instructs users to practice 8-10 times. For purposes of the ICECAP study, NOAs are asked to practice 5 times.

- As part of training, the NOA should practice the "Administrator's Gesture" to be sure s/he knows how to pause the battery before working with a study participant. This should be demonstrated in the certification video (i.e., 5th practice test) submitted to the Central Outcomes Team for review.

- As part of training, the NOA should listen to the Word Reading Recognition Test Pronunciation audio recording multiple times and submit a recording of him/herself pronouncing the words. Feedback on the NOAs pronunciation will be provided by the COT and additional (full or partial) recordings may be requested if needed.
    - English Pronunciation Audio
    - Spanish Pronunciation Audio (Only required for NOAs planning to test in Spanish)

11.3.5 Administration Tips and Key Things to Remember

- The ICECAP NIH Toolbox Administrator's Manual is an edited version of the much larger NIH Toolbox Administrator's Manual that is referred to in the eLearning Course. This manual provides detailed information about administering the NIH Toolbox tests as well as step-by-step instructions to setting up participants, choosing the ICECAP battery, pausing the battery, uploading data and much more.
- The iPAD and NIH Toolbox passcodes will be sent to sites by the CCC.
- When setting up a new participant, the following fields are required:
    - Identifier (4 digit subject number)
    - Gender
    - Race
    - Ethnicity
    - Age
    - Handedness
    - Highest Education Level Completed
- Do NOT complete the "Name" or "Birthdate" fields
- The List Sorting Working Memory Test and the Oral Reading Recognition Test require the use of an external keyboard. The NOA should practice connecting and disconnecting this keyboard several times before testing a study participant.
- The Picture Vocabulary Test and Oral Symbol Digit Test are the only ones for which the NOA has to read the instructions. These are found both in the NIH Toolbox Assessor's Manual and below in Appendix D. The rest are presented on the iPad to be read by the NOA or presented by NIH Toolbox app itself.
- The below supplemental (i.e., in addition to the iPad) materials are needed for the following NIH Toolbox tests:
    - Flanker Inhibitory Control and Attention Test - Home Base
    - List Sorting Working Memory Test - Answer sheet. External Keyboard
    - Dimensional Change Card Sort Test - Home Base

    - Word Reading Recognition Test - Pronunciation Guide. External Keyboard
    - Oral Symbol Digit Test - Stimulus Card
- When using the external keyboard: Yes = 1. No = 0.
- Do not pause the battery during a task. See detailed instructions regarding how to pause a task in the ICECAP NIH Toolbox Administrator's Manual.
- Immediately after the visit, the Neuropsychological Outcomes Assessor must download the participant's test data from the ipad and transfer it to the CCC.
- Pay close attention to the timing of the RAVLT Delay (30 ±5 minutes). The NIH Toolbox may be paused in between tests to administer the RAVLT Delay and Recognition tests if necessary.
- NIH Toolbox testing is available in Spanish via a separate app entitled "NIH Toolbox en Español".
    - To administer the NIH Toolbox in Spanish, the NOA must be both bilingual (English and Spanish) and certified to give the ICECAP NTB.
        - The Spanish NTB may not be administered by an English (only) speaking NOA with the help of a translator (certified or otherwise).
    - There is no separate, Spanish NIH Toolbox manual.
    - Printed Spanish instructions are not available for the NIH Toolbox. These are available only through the NIH Toolbox en Español app.
    - The only external (i.e., outside the app) Spanish document is the Spanish Pronunciation Guide for the NIH Toolbox Oral Reading Recognition Test.

11.4 Rey Auditory Verbal Learning Test (RAVLT): 30 Minute Delay and Recognition

RAVLT Delay English instructions
RAVLT Delay Spanish instructions

11.4.1 Reference

Rey Auditory Verbal Learning Test. Adapted from Taylor, E.M. (1959). The Appraisal of Children with Cerebral Deficits. Cambridge, MA: Harvard University Press, and Lezak, M.D. (2004) Neuropsychological Assessments (4th ed.). New York: Oxford University Press.

11.4.2 Description

The 30 Minute Delay and Recognition portions of the RAVLT assess delayed verbal memory. After administration of the NIH Toolbox tests, the assessor again asks the participant to recall the words from the RAVLT List A. Finally, the assessor reads a longer list of 52 words and asks him/her to identify the words from List A. The scores collected include the number of words recalled on the Delay Trial as well as the number of true and false positives on the recognition portion of the test.

11.4.3 Scoring

Scoring for the RAVLT 30 Minute Delay and Recognition trail is manual. There are three scores derived for the 30 Minute Delay and Recognition parts of the RAVLT test.

- Total number of List A words recalled on the 30 Minute Delay
- The total number of correct answers/true positives (the words the participant stated were on List A that were actually on List A) on the Recognition Trial
- The total number of false positives (words the participant stated were on List A that were not on List A) on the Recognition Trial

11.4.4 Training and Certification

Training for the 30 Minute Delay and Recognition portion of the RAVLT is included as part of the training for the RAVLT as is outlined in section 11.2.4. No additional training is required.

11.4.5 Administration/Scoring Tips and Key Things to Remember

- The 30 Minute Delay should occur 30 ±5 minutes after the Immediate Delay Trial is completed.
    - To maintain this timing, the NOA may need to pause in between NIH Toolbox tests or the Neuro-QoL. If this occurs, the NOA should immediately return to the paused test and complete the Toolbox tests and Neuro-QoL before beginning the Trail Making Test.
- List A words are NOT read again before the 30 Minute Delay.
- If the study participant asks for any kind of help or feedback, the NOA should inform him/her that s/he cannot provide this information.
- Repetitions and intrusions (saying words that are not on the list) are not recorded or scored. There is no need to comment on or to document these.
- Pluralization of a stimulus word is counted as correct (drums for drum).

11.5 Trail Making Test (Trails)

Forms may not be reproduced by sites. They will be sent by the CCC.
English instructions
Spanish instructions
Trails Training

11.5.1 Reference

Army Individual Test Battery. (1944). Manual of Directions and Scoring. Washington, DC: War Department, Adjutant General's Office.

11.5.2 Description

The Trail Making Test is a two-part test of attention, mental flexibility and processing speed. Trail Making Part A (Trails A) requires the study participant to draw lines to connect 25 numbered circles in consecutive order. Trail Making Part B (Trails B) requires the study participant to alternate between numbered and lettered circles (1-A, A-2, 2-B, B-3, 3-C, etc.). The test is timed and the study participant is urged to connect the circles "as fast as you can". The maximum time allowed is 100 seconds for Trails A and 300 seconds for Trails B. The score collected for each part of this test is the total time to completion.

11.5.3 Scoring

Scoring for the Trails is manual. The time to completion in seconds should be recorded separately for Parts A and B. Time to complete is rounded to the nearest second. The maximum score for Part A is 100". The maximum score for Part B is 300 seconds.

11.5.4 Training and Certification

Trails training can be found on the ICECAP Training web page. Training for Trails includes:

- Observation of the Trails training video
- Passing the Trails quiz

- Practice test administration (minimum of 5 times)
- Submission of a passing test video

At the discretion of the Central Outcomes Team, and in accordance with the training and certification procedures in Appendix A, additional, remedial practice and video submissions may be required.

11.5.5 Administration/Scoring Tips and Key Things to Remember

- Valid administration of Trails can be challenging and requires the full, undivided attention of the NOA throughout the entire test.
- The participant and NOA will each need a pen.
- The Sample portions of this test are used to ensure the participant understands the task. The NOA can explain further if needed until the participant understands or it becomes clear that s/he cannot complete the test.
- Timing starts as soon as the NOA says to begin.
- Timing is not stopped until the test is complete or the discontinuation time point has been reached.
    - Timing is not stopped during error correction. Errors should be corrected very quickly.
        - The NOA should not correct the participant until s/he actually reaches the incorrect circle since many participants will correct themselves before reaching the wrong location.
- Part A is discontinued at 100 seconds. Part B is discontinued at 300 seconds. If the participant is close to finishing it is permissible, and often desirable, to allow him/her to finish.
- Occasionally the NOA may not catch an error before the participant quickly continues on to another circle. If this happens, the NOA should mark the error as quickly as possible and draw the participant's attention back to the circle preceding the mistake.
- It is not necessary that a participant actually touch the circle, if it is clear to the NOA that the participant intended to touch it. However, if this occurs during the Sample parts of this test the NOA should remind the participant to touch each circle so that this situation may be avoided on Part A and Part B (the real tests).
- If the participant draws a line through another circle on the way to the correct circle, this is not an error as long as it is clear to the NOA that the participant did not intend the incorrect circle as the target.
- All instructions must be read exactly as they are written, no matter how repetitive they seem or if the participant expresses that s/he understands what to do and wishes to begin.
- If the participant asks what circle is next, the NOA must not provide the answer. Instead, the NOA should instruct the participant to draw a line to the circle that s/he thinks comes next.
    - Additional help may be given in a graduated manner when the participant cannot figure out where to go next, however, help should be given only gradually and conservatively and only when absolutely necessary.
- It is not required that the participant keep the pen on the paper at all times, however, picking up the pen should be discouraged if a participant has trouble keeping track of where s/he is on the form.
- When rounding seconds, tenths of .50 or greater round up whereas .49 or less rounds down. (e.g., 21.49 = 21 seconds. 21.50 = 22 seconds)
- If a participant is unable to understand Sample A, Part A (real test) is not given. Similarly, if the participant is unable to understand Sample B, Part B is not given.
- If a participant is unable to complete Part A before the 100" time limit, Sample B and Part B are not given.
- This NOA "cheat sheet" for Trails B is available to help with administration, however, the ultimate goal is to become so familiar with this test that this guide is not necessary.

11.6 The Stroop Test

Forms may not be reproduced by sites. They will be sent by the CCC.
Link to English instructions
Stroop Training

11.6.1 Reference

Golden, C. J. (1975a). A group version of the Stroop Color and Word Test. Journal of Personality Assessment, 39 (4), 386–388.

11.6.2 Description

The Stroop Test is a three-part test of executive functioning, specifically inhibition. This test is comprised of three trials, each lasting 45 seconds. On the “Word Reading” trial, participants are asked to read a list of words printed in black ink as quickly as they can. On the “Color Naming” trial, participants are asked to quickly identify the color of ink that “XXXX” is printed in. Finally, on the “Interference” (aka “Color-Word”) trial, participants are presented with a page where the names of colors (e.g., green) are printed with ink of a different color (e.g., the word green is printed in blue ink). Participants are asked to name the color of the ink that the word is printed in as quickly as possible. The score of most interest on this test is the number of colors correctly named on the Interference trial.
*Note. No Spanish version of the Stroop Test will be administered in the ICECAP study.

11.6.3 Scoring

The Stroop Test is manually scored. There are three scores derived for this test. They include the total number of correct responses (within 45 seconds) on each of the three trials: 1) Word Reading, 2) Color Naming and 3) Color-Word/Interference.T

11.6.4 Training and Certification

Stroop Test training can be found on the ICECAP Training web page. Training for the Stroop includes:

- Observation of the Stroop training video
- Passing the Stroop quiz
- Practice test administration (minimum of 5 times)
- Submission of a passing test video

At the discretion of the Central Outcomes Team, and in accordance with the training and certification procedures in Appendix A, additional, remedial practice and video submissions may be required.

11.6.5 Administration/Scoring Tips and Key Things to Remember

- The participant sees only one test page one at a time.
- The Stroop booklet is placed directly in front of the participant on the table (or other flat surface) and cannot be lifted.
- The booklet can be rotated by the participant (up to 45 degrees to either the right or left).
    - The Color and Color-Word pages must be viewed at the same angle as was the Word Reading page.
- None of the pages may be covered in any way.
- After initial reading, instructions may be repeated and rephrased as much as needed to ensure that the participant understands what to do.

- The participant may keep his/her place by pointing to the items with a finger; however, no part of a word may be covered.
- Administration of the Stroop may be stopped and started over for a variety of reasons.
    - If on any page, the participant hesitates and does not give an initial response within three seconds, then the examiner should say "Stop. Did you understand the instructions?" Instructions should be repeated as necessary and the page started over.
    - If the participant does not appear to be responding as quickly as possible, the examiner should say " Stop. Remember you are to repeat the words/color names as quickly as you possibly can. Let's start over again, doing the page as quickly as you can."
    - If the participant covers up parts of the word/stimulus, say, "Stop. You can point to the words with your hand if you like, but you cannot cover any of the items or letters. We will begin again, but remember not to cover any of the items or letters."
- Timing begins as soon as the participant begins speaking, not when the NOA says begin.
- Errors are not corrected or counted.
- When 45 seconds is done, the NOA should circle the last correct item read by the participant. If the participant finished the page and began again, the NOA should write a "1" by the circle.
- The "Color-Word" trial is sometimes also called the "Interference" trial. It is the total correct on this trial (not an equation) that is entered onto the CRF as the "Number correct on interference trial" variable.
- This NOA "cheat sheet" for the Color-Word Trial is available to help with administration, however, the ultimate goal is to become so familiar with this test that this guide is not necessary.

11.7 Controlled Oral Word Association Test (COWAT)

Link to English Form
Link to Spanish Form
Link to English instructions
Link to Spanish instructions
COWAT Training

11.7.1 Reference (Benton, Hamsher, and Sivan, 1994).

Benton, A. L., Hamsher, K. de S. & Sivan, A. B. (1994). Multilingual Aphasia Examination (3rd ed.): Manual of Instruction. Iowa City, IA: AJA Associates.

11.7.2 Description

The Controlled Oral Word Association Test assesses phonemic verbal fluency in three word-naming trials. For each one-minute trial, the study participant is asked to say as many words as he/she can think of that begin with a given letter of the alphabet (excluding proper names and the same word with a different ending). The score collected is the sum of all acceptable words for the three combined trials.

11.7.3 Scoring

Scoring for the COWAT is manual. The score is the sum of all acceptable words for the three letters combined.

11.7.4 Training and Certification

COWAT training can be found on the ICECAP Training web page. Training for the COWAT includes:

- Observation of the COWAT training video
- Passing the COWAT quiz
- Practice test administration (minimum of 5 times)
- Submission of a passing test video

At the discretion of the Central Outcomes Team, and in accordance with the training and certification procedures in Appendix A, additional, remedial practice and video submissions may be required.

11.7.5 Administration/Scoring Tips and Key Things to Remember

- The letters used in English are F, A and S. The letters used in Spanish are P, M and R.
- If the study participant starts providing words beginning with the wrong letter, the NOA should remind him/her of the correct letter. This correction is allowed only once for each letter trial.
- The NOA should legibly record all words (in full) in the order that they are produced. If production is too rapid for immediate, verbatim recording, the NOA may write down the first few letters of a word and go back as soon as possible and complete the word.
- If repetitions occur that may be accepted if an alternate meaning was intended by the study participant ("four" and "for", "son" and "sun"), the NOA should ask what was meant by these words at the end of the 1-minute period.
- No credit is given for any names, including products such as Lexus or Nike, or for the names of the days or months.
- Slang terms, curse words, and foreign words that are commonly known (e.g., taco, faux pas, lasagna) are acceptable.
- Numbers are accepted unless they violate the "same word, different ending" rule (e.g., "four" and "forty" are acceptable words, however, "forty-one" and "forty-two" are the same word as "forty", just with a different ending).
- Words that have the same ending, but have entirely different meanings (e.g., appoint and appointment) are acceptable.
- Different verb tenses of the same word do not count (e.g., sank, sunk) unless they are separated in the list and could have different meanings (e.g., sink, other word, sank).
- When scoring, place an "X" to the right of words that do not count.

11.8 Category Fluency Test (CFT)

Link to English Form
Link to Spanish Form
Link to English instructions
Link to Spanish instructions
CFT Training

11.8.1 Reference

Goodglass, H. & Kaplan, E. Assessment of aphasia and related disorders. Philadelphia: Lea & Febiger: 1972.

11.8.2 Description

The Category Fluency Test assesses semantic verbal fluency in one animal naming trial. In this one minute trial, participants are asked to list as many animals as possible within one minute. The score collected is the sum of all acceptable animals named.

11.8.3 Scoring

Scoring for the CFT is manual. The total score is the number of acceptable animals named within 1 minute.

11.8.4 Training and Certification

CFT training can be found on the ICECAP Training web page. Training for the CFT includes:

- Observation of the CFT training video
- Passing the CFT quiz
- Practice test administration (minimum of 5 times)
- Submission of a passing test video

At the discretion of the Central Outcomes Team, and in accordance with the training and certification procedures in Appendix A, additional, remedial practice and video submissions may be required.

11.8.5 Administration/Scoring Tips and Key Things to Remember

- Mythological animals, cartoon characters and fictitious animals do not score.
- Extinct animals are scored as correct.
- Superordinate (e.g., insect) and subordinate (e.g., ant, moth, fly) items all score.
- Sex based (e.g., mare and stallion) variants all score.
- Age based (e.g., foal, horse) variants all score.
- Animals with the same stem score only for the first word (e.g. cock, cocks, cockerel, etc.) unless they are two entirely different animals (e.g., ant, anteater).
- When scoring, place an "X" to the right of any animals that do not count.

11.9 Neuro-QoL

The English Neuro-QoL measures are presented entirely on the iPad via the NIH Toolbox app. There are no hard copies of test forms or printed instructions needed. The Spanish Neuro-QoL measures are administered via paper forms, available in Appendix E.

Neuro-QoL Training

11.9.1 Reference

Cella, D., Nowinski, C. J., Peterman, A., Victorson, D. E., Miller, D., Lai, J-S., & Moy, C. (2011). The neurology quality-of-life measurement initiative. Archives of physical medicine and rehabilitation, 92 (10 SUPPL.).

11.9.2 Description

The Neuro-QOL (Quality of Life in Neurological Disorders) is a measurement system including carefully developed and rigorously calibrated comprehensive item banks of participant-reported outcomes that assess multiple aspects of health-related quality of life. The Neuro-QoL is specific to people with neurological disorders. The item banks include: Physical Health (Mobility, Fine Motor/ADL, Fatigue, Sleep Disturbance), Social Health (Ability to Participate in Social Roles & Activities, Satisfaction with Social Roles & Activities), Mental Health (Depression, Anxiety, Stigma, Positive Affect & Well-Being, Emotional-Behavioral Dyscontrol) and Cognitive Health (Cognitive Function, Communication). These self-report measures can be completed by a proxy responder (i.e., an "informant") when necessary.

In English, the Neuro-QoL measures are available through the same platform as the NIH Toolbox. The specific item banks and scales to be administered for the ICECAP study have been pre-configured by the Clinical Outcomes Team at the CCC. In the Toolbox App, the Neuro-QoL measures ICECAP battery is entitled "ICECAP-Neuro-QoL", needs to be selected in addition to the "ICECAP-NTB" battery and is to be administered last, after all other ICECAP NTB tests have been completed.

List of (English) Neuro-QoI Measures Used in the ICECAP Trial
Neuro-QoL Item Bank v1.0 – Ability to Participate in Social Roles and Activities
Neuro-QoL Item Bank v1.0 – Anxiety
Neuro-QoL Item Bank v1.0 – Depression
Neuro-QoL Item Bank v1.0 – Emotional and Behavioral Dyscontrol
Neuro-QoL Item Bank v1.0 – Fatigue
Neuro-QoL Item Bank v1.0 – Lower Extremity Function – Mobility
Neuro-QoL Item Bank v1.0 – Positive Affect and Well-Being
Neuro-QoL Item Bank v1.0 – Stigma
Neuro-QoL Item Bank v1.0 – Upper Extremity Function – Fine Motor, ADL
Neuro-QoL Item Bank v1.1 – Satisfaction with Social Roles and Activities
Neuro-QoL Item Bank v2.0 – Cognitive Function
Neuro-QoL Scale v1.0 – Communication
Neuro-QoL Short Form v1.0 – Sleep Disturbance

11.9.3 Scoring

English Neuro-QoL scoring is completed by the NIH Toolbox App. No manual scoring is needed.

Spanish Neuro-QoL scoring is done manually. The raw score for each of the 13 Neuro-QoL measures administered in Spanish will be calculated by the CCC.

11.9.4 Training and Certification

Training of the Neuro-QoL measures is minimal and involves only reading the below information and watching a brief video explaining how to start and introduce the measures.

11.9.5 Administration/Scoring Tips and Key Things to Remember

- The Neuro-QoL self-report measures are ideally completed by the respondent without help from anyone else.
    - If the participant is able to complete the test independently, the NOA should be available to answer questions or assist with technical issues, but respect the study participant's privacy by not "hovering" or closely watching the iPad screen as s/he completes this test
        - It is acceptable for the NOA to define a term (e.g., "nausea"), but not to define a concept where the participant's subjective interpretation is the goal of the question (e.g., "quality of life").
    - The NOA or an interpreter may read and/or record Neuro-QoL responses if needed.
    - If the participant is unable to complete the Neuro-QoL measures, a proxy (e.g., close family member) responder may answer on behalf of the participant.
        - When using a proxy responder, the NOA should begin by stating "The following questionnaires will ask about your care recipient's symptom and activity levels; his/her ability to think, concentrate and remember things; questions specific to his/her condition, and questions related to his/her quality of life. Please answer the following questions based on what you think your care recipient would say."

    - The Neuro-QoL measures may be administered by phone (i.e., read to the participant or informant) if a 90 day in-person visit is not possible.
- The NOA should encourage participants to answer all items to the best of their ability. If a participant indicates the item asks about an activity s/he does not do, the NOA should instruct the participant to consider what that activity would be like, and imagine or predict how it would be.
- The time to complete the Neuro-QoL varies by participant, but is approximately eight minutes (English version).
- The “Go Back” and “Skip” buttons may be used to navigate through questions if needed.
- When participants have completed filling out paper forms (Spanish only), the NOA should carefully review the forms to ensure that all questions have been clearly answered with only one response.

12.0 Outcomes CRF Completion, Data Entry, Upload and Transfer

12.1 General

ICECAP Case Report Forms must be accessed via WebDCU™ (ICECAP database home page → Project Setup → CRF Collection Schedule) directly to ensure use of the most current version.

ICECAP Case Report Form Completion Guidelines.

Fields common to all outcomes CRFs (Must be completed on all forms)

- Header. Subject ID
- Qa "Data collected". Indicate whether the data were collected. If "No", a comment should be added in "General comments" to explain why.
- Qb "Date of assessment". In dd-mmm-yyyy format
- General comments. Open field for useful information including deviations from standardized testing procedures and behavioral observations.
- Footer. The study team member conducting testing enters his/her printed name, signature and date of testing in dd-mmm-yyyy format.

12.2 Modified Rankin Scale

The mRS score is added to CRF 144.

- The overall mRS score is entered into field Q01 "Modified Rankin Scale".
- The role of the person completing the mRS evaluation (either "Blinded central assessor" or "Site personnel") is entered into field Q02 "Assessor".

12.3 Paper and Pencil Tests

On the Trail Making Test, study participants will mark directly on the response forms. For all other tests, the Neuropsychological Outcomes Assessor will record participants' performance/responses on the forms. Immediately following the visit, the NOA will score (and double score) all of the tests and write the score on the CRFs. The NOA will then transfer the data from the CRF to WebDCU™ electronic case report forms within 5 calendar days after the visit. All source documents and CRFs requiring review for quality assurance purposes must be combined into a single .pdf and uploaded to the COT (via MDropbox) for review. The file name format is NOAFirstnameLastname_SubjectID_DDMMMYYYY.

Paper forms must be maintained by the sites.

12.3.1 Rey Auditory Verbal Learning Test

Ten variables are collected for the RAVLT Test. All variables are added to CRF 298.

- The total number of correct words the participant recalls on Trial 1 (List A) is entered into field Q01 "Trial 1."
- The total number of correct words the participant recalls on Trial 2 (List A) is entered into field Q02 "Trial 2."
- The total number of correct words the participant recalls on Trial 3 (List A) is entered into field Q03 "Trial 3."

- The total number of correct words the participant recalls on Trial 4 (List A) is entered into field Q04 “Trial 4.”
- The total number of correct words the participant recalls on Trial 5 (List A) is entered into field Q05 “Trial 5.”
- The total number of correct words the participant recalls on the Interference Trial (List B) is entered into field Q06 “Interference Trial”
- The total number of correct words the participant recalls on the Immediate Recall Trial (List A) is entered into field Q07 “Immediate delay.”
- The total number of correct words the participant recalls on the 30 Minute Delay Trial (List A) is entered into field Q08 “Delayed recall.”
- The total number of correct answers/true positives (the words the participant stated were on List A that were actually on List A) on the Recognition Trial is entered into field Q09 “Recognition Trial - True positives.”
- The total number of false positives (words the participant stated were on List A that were not on List A) on the Recognition Trial is entered into field Q10 “Recognition Trial - False positives.”

There are two additional fields on CRF 298. These fields are used to determine the frequency of test administration for a given NOA. It is very important that these fields are completed consistently (i.e., same name and/or nickname used each time the same NOA) with the name of the person who administered the ICECAP NTB.

- Q11 “Assessor first name”
- Q12 “Assessor last name”

12.3.2 Trail Making Test

Five variables are collected for the Trail Making Test. All variables are added to CRF 154.

- Q01 “Part A completed within 100 seconds” should be answered “Yes” if Part A was completed in 100 seconds or less and “No” if it was not.
- The total number of seconds a study participant took to complete Part A (real test only - do not include sample) is entered into Q02 “Time in seconds Part A”. If Part A was not completed within 100 seconds, the NOA should leave this field blank.
- Q03 “Part B completed within 300 seconds” should be answered “Yes” if Part A was completed in 300 seconds or less and “No” if it was not.
- The total number of seconds a study participant took to complete Part B (real test only - do not include sample) is entered into Q04 “Time in seconds Part B”. If Part B was not completed within 300 seconds, the NOA should leave this field blank.
- In field Q05 “Hand used”, the NOA enters whether the participant used his/her dominant or non-dominant hand to complete the Trail Making Test.

Note: If Part B is not administered because the participant could not complete Part A within 100 seconds, Q03 and Q04 on CRF 154 should be left blank.

12.3.3 Stroop Test

Three variables are collected for the Stroop Test. All variables are added to CRF 152.

- The number of words correctly read on the “Word Reading” trial is entered into field Q01 “Number correct on word reading trial”.
- The number of colors correctly named on the “Color Naming” trial is entered into field Q02 “Number correct on color naming trial”.

- The number of colors correctly named on the “Interference” (aka “Color-Word”) trial is entered into field Q03 “Number correct on interference trial”.

12.3.4 Controlled Oral Word Association Test

Only one variable is collected for the Controlled Oral Word Association Test. The total number of acceptable words for all 3 letters combined is summed and entered into field Q01 “Total score (FAS)” on CRF 136.

*Note. The letters used in Spanish are PMR (not FAS), however, the same CRF field is used.

12.3.5 Category Fluency Test

Only one variable is collected for the Category Fluency Test. The total number of acceptable animals named is entered into field Q02 “Total score for animals” on CRF 136.

12.4 NIH Toolbox

Neuropsychological data from tests performed using the NIH Toolbox will be collected on the iPAD via the NIH Toolbox App. Immediately after the visit, the NOA must upload the participant’s test data from the iPad to the CCC using the steps outlined in the ICECAP NIH Toolbox Administrator’s Manual. The CCC will house the data on a secure, compliant storage service such as MDropbox. MDropbox is a secure University of Michigan cloud collaboration and storage service. It provides a safe and easy way to store and share files and collaborate with others at UM and at outside institutions. It is approved for protected data and ePHI (HIPAA). The information is then transferred to WebDCU™ by the CCC.

It is not necessary for site personnel to complete any CRFs for the NIH Toolbox data. CRF 513 will be completed by the CCC.

12.5 Neuro-QoL

The NIH Toolbox App will be used to collect the English Neuro-QoL data. The information is stored on the iPad as a separate file (i.e., not with the NIH Toolbox data). The English Neuro-QoL data are to be uploaded separately, but using the same process described above in Section 12.4.

The Spanish Neuro-QoL is administered on paper. After administration, the NOA will upload copies of all Spanish Neuro-QoL forms to MDropbox. All raw scores for the 13 Neuro-QoL measures administered in Spanish will be calculated by the CCC. The CCC will also directly enter all Spanish Neuro-QoL scores into WebDCU.

It is not necessary for site personnel to complete any CRFs for the NIH Toolbox data. CRF 512 will be completed by the CCC.

13.0 References

Army Individual Test Battery. (1944). Manual of Directions and Scoring. Washington, DC: War Department, Adjutant General’s Office.

Becker, L. B., T. P. Aufderheide, R. G. Geocadin, C. W. Callaway, R. M. Lazar, M. W. Donnino, V. M. Nadkarni, B. S. Abella, C. Adrie, R. A. Berg, R. M. Merchant, R. E. O'Connor, D. O. Meltzer, M. B. Holm, W. T. Longstreth

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Appendix A - Detailed ICECAP NTB Training Procedures

Training Links

General ICECAP Education and Training Page

ICECAP mRS and Secondary Outcome Training Page

NIH Toolbox eLearning Course

Training Process

To be certified to administer the ICECAP NTB, Neuropsychological Outcomes Assessors must complete the below process in order:

1) Read key ICECAP documents.
    a) Study Protocol Synopsis
    b) Outcomes Manual of Procedures (this document)
    c) ICECAP specific NIH Toolbox Administrator's Manual

2) Watch all (10) ICECAP training modules and pass quizzes at the end of each module.
    a. Intro to Outcomes
    b. Testing Tips
    c. RAVLT
    d. NIH TB Setup & Data
    e. Oral Symbol Digit
    f. Trail Making Test
    g. Stroop Test
    h. COWAT
    i. CFT
    j. Neuro-QoL

3) Complete the NIH Toolbox eLearning modules that are relevant to the ICECAP Trial.
    a) Print a copy of the ICECAP NIH Toolbox Training Checklist
    b) Watch all modules listed on the Checklist
        i) The How To Videos are here (Scroll down a bit)
        ii) The Cognition Domain Videos are here
    *Note - not all training videos on these web pages are required - just the ones listed on the Checklist.

    c) Complete the ICECAP NIH Toolbox Training Checklist
    d) Check off modules as they are completed.
    e) Add printed name and date of completion of the last module.
    f) Sign the form indicating understanding and completion of modules.
    g) Upload completed Checklist as a People Document in WebDCU.

    h) Listen to the English (and Spanish if applicable) Word Reading Recognition Test Pronunciation audio recording multiple times. Submit a recording of him/herself pronouncing the words as part of the certification video submission.

i) Practice the "Administrator's Gesture" several times. (Be sure to demonstrate proficiency with this movement in the certification video submitted to the CCC - Step 7 below).

4) Read the FAQ page of the ICECAP website (updated throughout the study).

5) Practice all ICECAP NTB testing (including the NIH Toolbox tests and Neuro-QoL) with a non-study participant at least four times.

   a) Optional: Watch this example of a mock testing session

   b) Optional: Review this helpful NOA Testing Flowchart.

6) Participate in a Q&A meeting conducted by a member of the COT.
   a) The exact timing of this call is at the discretion of the NOA, but will likely be most helpful after the first or second.
   b) Must be completed before the certification video is recorded.
   c) At the discretion of the COT, this requirement may be waived for NOAs at sites where a fully certified NOA is available to help with the training process of additional, new NOAs.

7) Submit a passing "certification video", (a video recording of a 5^{th+} practice session), source documents, mock CRFs and pronunciation audio to the COT via the appropriate folder in MDropbox (a secure, HIPAA compliant storage system controlled by the University of Michigan). Submit the "Test" NIH TB/Neuro-QoL data to the iCloud folder.
   a) Each site will have its own MDropbox folder. The COT will send site personnel invitations to their MDropbox folder to provide access.
   b) The source documents and mock CRFs should be combined into one .pdf file.
   c) The naming format of both the training video and the mock CRFs is NOAFirstnameLastname_0000_DDMMMYYYY (e.g., AngelaCaveney_0000_24MAR2020).

8) A member of the COT will review the certification video, source documents, mock CRFs and pronunciations. (For planning - allow 1 week turnaround for all reviews.)
   a) If the assessment is failed, the COT will conduct individualized training with the NOA.
      i) Failure is defined as 2 or more minor errors or 1 or more major errors. A major error is defined as any error that indicates a lack of understanding of the proper standardized administration of any test OR any scoring error that is large enough to change the interpretation of the data.
   b) If the assessment is failed, the NOA will practice a 6th time and submit a new certification video and mock CRFs.
      i) A member of the COT will review the new certification video and mock CRFs.
         (1) If the assessment is failed again, the COT will conduct additional, individualized training with the NOA.
            (a) The NOA will practice a 7th time and submit a 3rd video and mock CRFs.
            (b) A member of the COT will renew the new video and CRFs and provide feedback to the NOA.
               (i) If the 3rd certification video submitted is not yet passing, the COT will discuss whether additional attempts will be allowed for this NOA.
                  1. If not allowed, the NOA will be notified that s/he will not be certified on the ICECAP NTB.
                  2. If allowed, it is up to the discretion of the COT to determine the next steps based on the particular difficulties observed.

c) Once a certification has been passed, the COT will issue the ICECAP NTB Certification. The site will upload this certification as a People Document in WebDCU.

*Note. For planning purposes, it is suggested that NOAs begin the certification process shortly after the 30 Day visit of the first participant they will test. It is each NOA's responsibility to manage the steps of this process for him/herself and ensure certification is in place prior to beginning testing. NOAs should allow a minimum of 1 week for the COT to review and provide feedback regarding a certification video. NOAs should keep in mind that additional certification videos may be requested (and allow extra time for this possibility).

Appendix B - Quality Assurance of 90 Day ICECAP NTB

Below is the process by which the Central Outcomes Team will ensure the integrity of the administration, scoring and data entry of all components of the ICECAP NTB.

First 90 Day Visit Conducted by an NOA

Neuropsychological Outcomes Assessors will follow the below QA procedure for their first 90 Day assessments:

1) Video record the first 90 Day ICECAP-NTB outcome assessment conducted

2) Submit the video, source documents and CRFs to the COT via the appropriate folder in MDropbox. Submit the NIH TB/Neuro-QoL data to the iCloud folder.
    a. The same MDropbox folder that is used for the certification process is used for QA.
    b. The source documents and CRFs should be combined into one .pdf file (preferred, not required).
    c. The naming format of both the training video and the CRFs is NOAFirstnameLastname_0000_DDMMMYYYY (e.g., AngelaCaveney_0000_24MAR2020).

3) A member of the COT will review the video, source documents and data entry in WebDCU™ using the same pass/fail criteria as used in the initial certification process. Feedback will be provided.
    a. If the assessment is passed, the COT will notify the NOA that no additional videos are required until further notice.
    b. If the visit is failed, the COT will conduct individualized training with the NOA.
        i. The next 90 Day assessment conducted by this NOA will be video recorded and submitted to the COT for review.
            1. This review process continues until the rater passes one visit. In cases where there are multiple failures, the COT has full discretion to determine whether to replace or to allow the NOA to continue to perform ICECAP NTB assessments for the ICECAP trial.

4) The member of the COT reviewing a particular assessment is responsible for raising and resolving data clarification requests (DCRs).

*Note. The COT has full discretion to vary the above process on a case-by-case basis (e.g., when errors are with data entry and data entry errors were made by another study member).

Random Reviews

Sites will be proactively notified by the ICECAP CCC Site Manager when a pending visit has triggered a random review. When this occurs, the NOA will follow the below procedure:

1) Video record administration of the ICECAP NTB assessment
2) Submit the video and source documents to the COT using the same process as was used for the first 90 day visit review.
    a) A member of the COT will review the video, source documents and data entry in WebDCU™ using the same pass/fail criteria as used in the initial certification process. Feedback will be provided.

i) If the assessment is passed, the COT will notify the NOA that no additional videos are required until further notice.
ii) If the visit is failed, the COT will conduct individualized training with the NOA.
(1) The next 90 Day assessment conducted by this NOA will be video recorded and submitted to the COT for review.
a. The above process repeats until the COT is satisfied that the NOA can competently administer and score the ICECAP NTB.

5) The COT has full discretion to vary the above process on a case-by-case basis (e.g., when errors are with data entry and data entry errors were made by another study member).

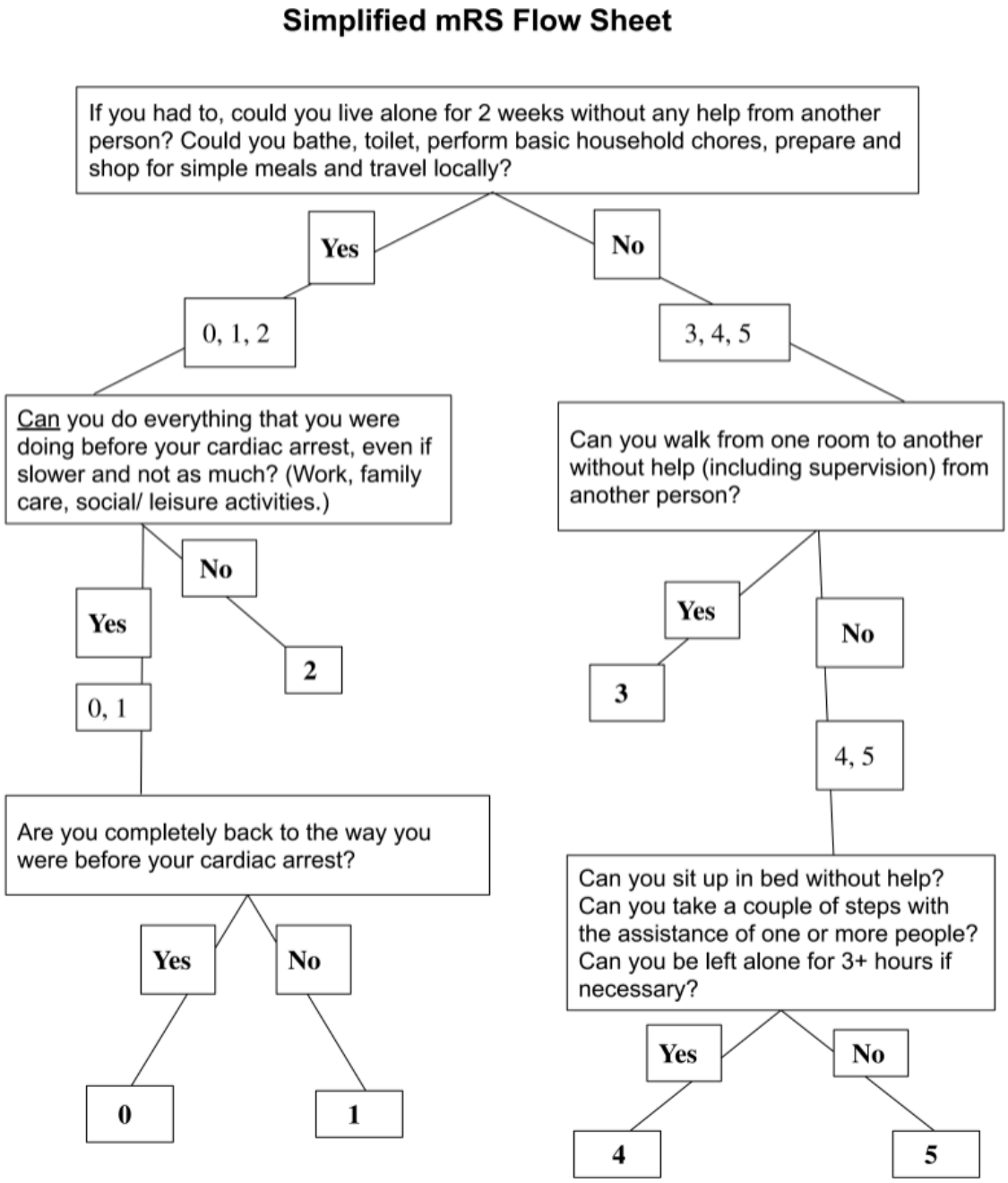
6) The member of the COT reviewing a particular assessment is responsible for raising and resolving data clarification requests (DCRs).

Remedial Reviews

Remedial reviews (in addition to those outlined above) of all or part of the ICECAP NTB may be requested at the discretion of the COT and will follow a similar review process as outlined above. In all cases, the ICECAP Site Manager will notify the site of additional reviews so arrangements may be made for video recording.

Appendix C - 30 & 90 Day Simplified Modified Rankin Scale Flow Sheet

Printable mRS Flow Sheet with ICECAP Header



Appendix D - 90 Day ICECAP NTB Scripts and Test Instructions - English

Introductions

On the day of the 90 Day visit the Neuropsychological Outcomes Assessor will begin by explaining the outcomes procedures and letting the participant know what to expect. This will include an introduction to the Central Outcomes Assessor and his/her role in the study. Each NOA is welcome to develop his/her own introduction. Below is an example of what might be said as an introduction.

Hello _____. My name is _____. I'm going to be working with you to complete the last phase of the study you have been helping with. Today I'm going to be asking you some questions about your recovery and how you are doing in your day to day life. We are also going to be completing some tasks that look at how well you can remember, concentrate and problem solve. Some of those tasks will seem easy for you, others may be more challenging. No one is expected to get them all correct. Just do the best you can. The appointment today should take about an hour to an hour and a half. You can take a break if you need to.

Also, today, another member of the study team will be joining us by phone to ask you some more questions about your recovery. Her name is _____. I'm going to call her and together we will complete a few of the measures I just told you about.

Video Consent

The following script should be used when obtaining consent from a participant to record a session.

I am requesting your permission to video record this session. This recording will be reviewed by specially trained investigators to evaluate the quality of my assessment. The recording will capture your voice, however, we will make sure your face is not recorded. You don't have to agree to the recording. If you do not agree, this will not affect your study participation in any way. Do you agree to be recorded?

If the study participant does not agree to be recorded, the NOA should then proceed with testing without additional dialogue or recording.

If the study participant agrees to be recorded, the NOA should state, ***When I turn on the recording, I will ask you if you agree to be recorded. Please say "Yes, I agree to be recorded."***

The NOA next turns on the recording and says, ***Do you agree to have your voice recorded?***

Rey Auditory Verbal Learning Test - Learning, Interference and Immediate Delay

Learning Trials (List A)

I am going to read you a list of words. Listen carefully, for when I stop, you are to say back as many as you can remember. It doesn't matter in what order you repeat them. Just say as many as you can. Any questions? [If no questions, start reading the List A]

Read through the list slowly, saying approximately one word per second. Once you have finished, say: ***Now, tell me as many of those words that you can remember, in any order.***

As the participant is naming words, mark the words recalled in the boxes next to the corresponding word. If the participant asks you if s/he has already said a word, respond: ***I cannot tell you, but there is no penalty for repeating words.*** If the participant names a word that is not on the list, you do not need to write the word in the empty boxes below the list. Do not let the participant give up, and do not move on until at least 10-15 seconds have passed since s/he has said a new correct word. Then, continue on to the next Trial.

Once the first Trial is completed, say**:** ***Now I am going to read the same list again. Once again, when I stop, I want you to tell me as many words as you can remember, including words you already said. It doesn't matter in what order you say them, just say as many as you can. Any questions?*** [If no questions, start reading List A]

Read through the list slowly, saying approximately one word per second. Once you have finished, say: ***Now, tell me as many of those words that you can remember, in any order.***

As the participant is naming words, mark the words recalled in the boxes next to the corresponding word.

Repeat this process with List A for Trials 3-5. It is not necessary to read the full instructions for Trials 3 through 5 if the participant clearly understands what to do.

Interference Trial (List B)

Now I am going to read you a <u>new</u> list of words. Again, when I stop, you are to say back as many words from this new list as you can remember. Again, the order in which you say the words does not matter. Any questions? [If no questions, start reading List B]

Read through List B at the same speed. Once you have finished, say: ***Now, tell me as many of those words that you can remember, in any order.***

As the participant is naming words, mark the words recalled in the boxes next to the corresponding word.

Immediate Delay

After the Interference Trial (List B) is completed, administer the Immediate Delay (List A). <u>DO NOT read List A again.</u>

Say: ***Now tell me all the words you can remember from the first list.***

NIH Toolbox - Picture Vocabulary and Oral Symbol Digit Tests

Only the Picture Vocabulary and Oral Symbol Digit Instructions are included here because these are the only two Toolbox tests that require the assessor to read them. All other Toolbox instructions are presented on the screen to be read by the NOA or read aloud by the NIH Toolbox app itself.

NIH Toolbox Picture Vocabulary Test Instructions Age 3+

Say: You are going to be asked the meaning of some words. For each item, you will hear a word and see four pictures on the screen. Touch the picture that you think best matches the meaning of the word that was said. If you are not sure, make your best guess. If you need to hear the word again, touch the button that has a picture of an EAR, also called the PLAY AGAIN button. After you touch a picture, you will hear a new word and see more pictures.

You will keep hearing words and touching pictures until you are done. If you want to change your last answer, touch the button with the HAND that says GO BACK. The pictures you just saw will reappear and you will hear the word again. Touch your choice, and then more words and pictures will appear. Tell me when you are ready to start.

Practice item 1:

An audio recording says: **Let's try one for practice: Banana. Touch the picture of Banana.** If correct, the audio recording says: **That's right!** The program will automatically go to the next practice item. If incorrect, the Banana picture will light up and an audio recording will say: **This is a banana. Let's try again.** The examiner should allow the participant up to three chances to answer this practice item correctly. After three unsuccessful attempts by the participant, the examiner should touch the picture of the banana and say: **This is a banana.** The next practice item will appear automatically.

Practice item 2:

An audio recording says: **Let's try another one: Spoon. Touch the picture of Spoon.** If correct, an audio recording says: **That's right!** If incorrect, the Spoon picture will light up and an audio recording will say: **This is a spoon. Let's try again.** The examiner should allow the participant up to three chances to answer this practice item correctly. After three unsuccessful attempts by the participant, the examiner should touch the picture of the spoon and say: **This is a spoon.**

The introduction to the test items will appear automatically.

Test items:

Read: Now, you're going to do some more. Remember, you will hear a word and then you will see four pictures. One of the pictures will show what the word means. Touch that picture and you will hear a new word and see four more pictures. Again, touch the picture that shows what the word means. If you don't know, make your best guess. Any questions?

When participant is ready, touch button that says ***Touch and Hold Here to Continue***.

An audio recording will introduce each word with the instructions. The items will continue in this format until the test is completed.

NIH Toolbox Oral Symbol Digit Test

The first screen will be an instructional screen to be read by the examiner. The examiner should put the laminated sheet in front of the participant, *with the side with the practice items (SIDE 1) facing up*.

The examiner should point to this sheet and SAY: **Please look at the symbols at the top of the page. Each symbol is paired with a number.** (Point to the pairs and show how they are arranged across the row.) **Now look here.** (Point to the row of symbols without numbers.) **Here there are symbols but no numbers. I would like you to tell me the number that goes with each symbol like this: You see this symbol** (point to the O), **it is matched with the number 6** (point to the key)**, so you would say or tell me "6"; this next symbol** (point to the X), **is paired with an 8** (point), **so you would say or tell me 8. Does this make sense?**

Answer any questions if the participant is unsure. **Now you try the rest of the row for practice. Remember to say each number out loud so that I can hear you.**

The examiner should provide feedback after each response, indicating whether the response is correct with, "**That's right**," or correcting the response when it is wrong. Repeat practice items as necessary until the participant can answer them correctly.

After the participant has completed the practice row, say, **Good. Now that you know how to do this, I am going to ask you to do some more. Now I will turn over this sheet and you will see more rows which have symbols, but not the numbers that go with them.**

At the bottom of the screen is a button *Touch and Hold Here to Continue*. Touch and hold that button to continue to the next screen.

The examiner should turn over the laminated sheet to SIDE 2 to reveal the test items.

SAY: **When I tell you to begin, I want you to do the rows on this page the same way – tell me the number that goes with each symbol. I want you to work as quickly as you can without skipping any of the boxes or making mistakes. When you are finished with the first row, move on to the next one. Continue working until you hear a bell sound on this iPad and I tell you to stop. If you make a mistake, just tell me the correct answer and keep going. Ready?**

At the bottom of the screen is a button *Touch and Hold Here to Continue*. Touch and hold that button to move to the next screen, where you will begin the test.

On the next screen, the examiner should touch *START TEST* and immediately, say, **Begin.**

As soon as the examiner touches *START TEST*, a timer will begin counting down from 120 seconds at the bottom of the screen (for the examiner's information only). All items with the correct answers (144 in total) will appear in "scoring boxes" on the iPad screen. As the participant calls out answers to each item, the examiner should touch each item to mark it as correct, or leaves it unmarked if it is incorrect. Touching the item on the iPad screen adds a check mark by the number. If the examiner makes an error, he/she should

simply touch the item again to deselect it.

As needed, the examiner should slide his/her finger on the screen to scroll to more items and to score each of them (for legibility, not all 144 items appear on the iPad screen at once, but all are accessible via scrolling).

At the end of 120 seconds, a tone will sound to alert the examiner and participant that time is up. The examiner should instruct the participant to stop. After the tone, a window will pop up on the iPad screen that says: “Are you finished marking the correct answers from the participant? If you choose no, please touch *NEXT* when you are finished marking correct answers.” The examiner should touch *YES* if he/she has finished scoring items. Otherwise, the examiner should touch *NO* and continue recording any items that need to be scored. When finished scoring, the examiner should touch *NEXT* to end the test.

Rey Auditory Verbal Learning Test - 30 Minute Delay and Recognition

30 Minute Delay (List A)

After the designated delay time period (30 minutes ± 5), administer the Delayed Recall Trial of List A. You may say:

A short while ago I read a list of words to you several times, and you were trying to learn these words. Tell me the words from this list again.

If needed, you may clarify that this was the first list read to the participant.

Recognition

I am going to read a list of words to you, one at a time. If the word was on the first list, say "Yes," and if it wasn't, say "No".

Read the words at a comfortable pace, giving the participant as much time as needed to indicate whether s/he believes each word was on List A or not. Circle the words to which the participant answered "yes".

Trail Making Test

Trails A

Give the study participant a pen and the test page and say:

> ***On this page are some numbers (point). Begin at number 1*** **(point to 1)** ***and draw a line from 1 to 2*** **(point to 2)**, ***2 to 3*** **(point to 3)**, ***3 to 4*** **(point to 4)** ***and so on, in order, until you reach the end*** **(point to the circle marked "end").** ***Draw the lines as fast as you can. Ready ------- Begin!***

If the study participant completes the sample item correctly demonstrating he/she understands what to do, say: ***Good! Let's try the next one.***

Turn the paper over and give Part A (Real Test) of the test.

If the study participant makes a mistake on Sample A, point out the error and explain it.
The following explanations of mistakes serve as illustrations:

- ***You started with the wrong circle. This is where you start*** **(point to number 1)**
- ***You skipped this circle*** **(point to the circle the participant omitted).** ***You should go from number 1*** **(point)** ***to 2*** **(point)**, ***2 to 3*** **(point to 3)**, ***and so on, until you reach the circle marked "end"*** **(point).**

If it is clear that the study participant intended to touch a circle but missed it, do not count it as an omission, however, remind the study participant to be sure to touch each of the circles when drawing the connecting lines.

Do not correct the study participant until he/she actually touches the wrong circle (i.e., do not assume a mistake will be made).

If the study participant cannot complete Sample A, take his/her hand and guide the pen, **using the non-ink end**, through the trail. Then say: ***Now you try it.***

Return the pen to the participant with the point down and say:

> ***Remember, begin at number 1*** **(point to 1)** ***and draw a line from 1 to 2*** **(point to 2)**, ***2 to 3*** **(point to 3)**, ***3 to 4*** **(point to 4)** ***and so on, in order, until you reach the circle marked "end"*** **(point).**
>
> ***Do not skip around, but go from one number to the next in the proper order. Remember to work as fast as you can. Ready --- Begin!***

If the study participant succeeds this time proceed to Part A. If the study participant still has difficulty, repeat the above procedure until the task is completed successfully or it becomes evident that the participant cannot do the task.

After the study participant has completed Sample A, turn the paper over to Part A and say:

> ***On the page are numbers from 1 to 25. Do this the same way. Begin at number 1 (point 1) and draw a line from 1 to 2 (point to 2), 2 to 3 (point to 3), 3 to 4 (point to 4), and so on, in order, until you reach the end (point). Remember to work as fast as you can. Ready ---Begin!***

Using a stopwatch, start timing as soon as the instruction is given to begin. The examiner must watch the study participant closely in order to catch any errors as soon as they are made. If the study participant makes an error, call it to his/her attention immediately, return the study participant's pen to the last correct circle, and continue the test from that point. Do not stop timing while correcting the participant's error.

After the study participant completes Part A, take the test sheet and record the time in seconds. Errors contribute to evaluation of performance principally by increasing the total performance time.

Trails B

Next, tell the study participant:

> ***That's fine. Now we'll try another one.***

Place the sample side of Part B on the table in front of the study participant, in the same position as the sheet for Part A was placed. Point to the sample and say:

> ***On this page are some numbers and letters. Begin at 1 (point) and draw a line from 1 to A (point to A), A to 2 (point to 2), 2 to B (point to B), B to 3 (point to 3), 3 to C (point to C), and so on, in order, until you reach the end (point to the circle marked "end").***
>
> ***Then say: Remember, first you have a number (point to 1), then a letter (point to A), then a number (point to 2), then a letter (point to B), and so on. Draw the lines as fast as you can. Ready--- Begin!***

If the study participant completes the Sample B correctly say: ***Good! Let's try the next one.***

Proceed immediately to Part B (Real Test).

If the study participant makes a mistake on Sample B, point out the error and explain why it is incorrect. The following explanations of mistakes serve as illustrations:

- ***You started with the wrong circle. This is where you start (point to number 1).***
- ***You skipped this circle (point to the circle the participant omitted). You should go from 1 (point to 1) to A (point to A), A to 2 (point to 2), 2 to B (point to B), B to 3 (point to 3), and so on until you reach the circle marked "end" (point).***

If it is clear that the study participant intended to touch a circle but missed it, do not count it as an omission. Remind the study participant, however, to be sure to touch each of the circles when drawing the connecting lines.

If the study participant cannot complete Sample B, take his/her hand and guide the pen, **using the non-ink end**, through the circles. Then say:

> ***Now you try it. Remember, you begin at number 1*** **(point)** ***and draw a line from 1 to A*** **(point to A)*****, A to 2*** **(point to 2)*****, 2 to*** **B (point to B)*****, B to 3*** **(point to 3),** ***and so on until you reach the circle marked "end"*** **(point)*****. Ready --- Begin!***

If the study participant succeeds this time, go on to Part B. If not repeat the procedure until the task is performed successfully or it becomes evident that the study participant cannot do the task.

After the study participant has completed the sample, turn the paper over to Part B and say:

> ***On this page are both numbers and letters. Do this the same way. Begin at number 1*** **(point to 1)** ***and draw a line from 1 to A*** **(point to A)*****, A to 2*** **(point to 2),** ***2 to B*** **(point to B)*****, B to 3*** **(point to 3)*****, 3 to C*** **(point to C)*****, and so on, in order, until you reach the*** **end (point to the circle marked "end")*****.***
> ***Remember, first you have a number*** **(point to 1)*****, then a letter*** **(point to A)*****, then a number*** **(point to 2)*****, then a letter*** **(point to B),** ***and so on. Do not skip around, but go from one circle to the next in the proper order. Draw the lines as fast as you can. Ready--- Begin!***

Using the stopwatch, start timing as soon as the participant is told to begin. Remember to be alert for mistakes. If the participant makes an error, point it out immediately, return the participant to the last correct circle, and continue the test from that point. Do not stop timing.

After the study participant completes Part B, take the test sheet and record the time in seconds. Errors contribute to the evaluation of the performance principally by increasing the total performance time.

ICECAP Discontinue Rules: The time limit for Trails A is 100 seconds. The time limit for Trails B is 300 seconds.

Stroop Test

Word Task

Place the first stimulus page in front of the participant (flat on the table, no more than 45-degree rotation) and say:

This is a test of how fast you can read the words on this page. After I say begin, you are to read down the columns starting with the first one (point to the left-most column) **until you complete it** (run hand down leftmost column) **and then continue, without stopping, down the remaining columns in order** (run your hand down the second column, then the third, fourth and fifth columns).

If you finish all the columns before I say "Stop," then return to the first column and begin again (point to the first column).

Remember, do not stop reading until I tell you to "Stop" and read out loud as quickly as you can. If you make a mistake, I will say "No" to you. Correct your error and continue without stopping. Are there any questions?

Instructions may be repeated or paraphrased as often as necessary so that the participant understands what is to be done.

Then continue. **Ready?... Then begin.** As soon as the participant says the first response (whether right or wrong), begin timing.

After 45 seconds, say **Stop.**

Circle the last item read by the participant. If the participant finished the page and began again, write a "1" by the circle.

Color Task

Turn the page over so only the 2nd page is showing and say:

This is a test of how fast you can name the colors on this page. You will complete this page just as you did the previous page, starting with this first column. Remember to name the colors out loud as quickly as you can.

If the participant has any trouble following the instructions, they should be repeated in their entirety.

When the participant is ready, say: **Ready? Then begin.**

As soon as the participant starts, begin timing on a stopwatch. After 45 seconds, say: **Stop.**

Circle the last item read by the participant. If the participant finished the page and began again, write a "1" by the circle.

Color-Word Task

Turn to the 3rd page and say:

This Word page is like the page you just finished. I want you to name the color of the ink the words are printed in, ignoring the word that is printed for each item. For example, (point to the first item of the first column), **this is the first item: what would you say?**

If the participant is correct, continue with the instructions.

If the participant is incorrect, say: **No, that is the word that is spelled there. I want you to say the color of the ink the word is printed in. Now,** (pointing to the same item) **what would you say to this item?** (If correct say) **That's correct** (point to second item). **What would the response be to this item?** If the participant is correct, proceed; if incorrect, repeat above as many times as necessary until the participant understands or it becomes clear that the participant is unable to complete this test.

Next say: **Good. You will do this page just like the others, starting with the first column** (pointing) **and then going on to as many columns as you can. Remember, if you make a mistake, just correct it and go on. Are there any questions?**

When the participant is ready, say: **Ready? Then Begin**. As soon as the participant starts, begin timing on a stopwatch. After 45 seconds, say: **Stop.**

Circle the last item read by the participant. If the participant finished the page and began again, write a "1" by the circle.

Controlled Oral Word Association Test (COWAT)

Have a stopwatch ready before giving the following instructions:

> ***I am going to say a letter of the alphabet, and I want you to say, as quickly as you can, all the words you can think of that begin with that letter. You may say any word at all except proper names, such as names of people or places. So you would not say "Boston" or "Bob." Also, do not use the same words again with a different ending, such as "eat" and "eating. For example, if I say "L," you could say, "light," "lay," "lion," or "lunch." Can you think of other words beginning with the letter "L?"***

Wait for the participant to give a word, indicate if the word is correct, and ask the participant to give another word beginning with the letter "L".

Once two appropriate words beginning with the demonstration letter are given, say:

> ***That is fine. Now I'm going to give you another letter. Again say all the words beginning with that letter that you can think of. Remember, no names of people or places, just ordinary words. Also, if you should draw a blank, I want you to keep on trying until the time limit is up. You will have a minute for each one. The first letter is "F." Begin!***

Begin timing immediately.

Repeat the same instructions for the letters A and S.

Allow **1 minute** for each letter. Say ***"Fine"*** or ***"Good"*** after each 1-minute performance. If the study participant discontinues before the end of the minute, encourage him/her to try to think of more words. If there is a silence of 15 seconds, say:

Can you think of other words beginning with the letter --? (Say the letter appropriate for that particular Trial.)

Record the participant's responses in the spaces provided on the worksheet form.

Category Fluency Test (CFT)

Have a stopwatch ready before giving the following instructions:

I want to see how many different types of animals you can say in one minute. Try not to repeat yourself. Begin.

Begin timing immediately.

Allow **1 minute** for animal naming.

Record the participant's responses in the spaces provided on the worksheet form.

Neuro-QoL

There are no instructions for the Neuro-QoL test. The participant simply reads and answers the questions presented on the screen of the iPad.

If a participant is unable to complete the Neuro-QoL measures, a proxy (e.g., close family member) responder may answer on behalf of the participant. When using a proxy responder, the NOA should begin by stating:

The following questionnaires will ask about your care recipient's symptom and activity levels; his/her ability to think, concentrate and remember things; questions specific to his/her condition, and questions related to his/her quality of life. Please answer the following questions based on what you think your care recipient would say.

In English, Computer Adaptive Test (CAT) versions of the Neuro-QoL measures are administered via the NIH Toolbox App on the iPad. Below are links to the full .pdf versions (if needed) for IRB use only. When administered as a CAT, each participant will only receive a few questions from each measure. These paper versions are not to be administered to study participants.

List of Neuro-Qol Measures Used in the ICECAP Trial
Neuro-QoL Item Bank v1.0 – Ability to Participate in Social Roles and Activities
Neuro-QoL Item Bank v1.0 – Anxiety
Neuro-QoL Item Bank v1.0 – Depression
Neuro-QoL Item Bank v1.0 – Emotional and Behavioral Dyscontrol
Neuro-QoL Item Bank v1.0 – Fatigue
Neuro-QoL Item Bank v1.0 – Lower Extremity Function – Mobility
Neuro-QoL Item Bank v1.0 – Positive Affect and Well-Being
Neuro-QoL Item Bank v1.0 – Stigma
Neuro-QoL Item Bank v1.0 – Upper Extremity Function – Fine Motor, ADL
Neuro-QoL Item Bank v1.1 – Satisfaction with Social Roles and Activities
Neuro-QoL Item Bank v2.0 – Cognitive Function
Neuro-QoL Scale v1.0 – Communication
Neuro-QoL Short Form v1.0 – Sleep Disturbance

Appendix E - 90 Day Visit Scripts and Test Instructions - Spanish

mRS, Introductions & Video Consent

No Spanish scripts are needed because these are all flexible interviews and conversations, not validated tests.

NIH Toolbox

Printed Spanish instructions are not available for the NIH Toolbox. These are available only through the NIH Toolbox en Español app.

Stroop Test

The Stroop Test is not being administered in Spanish as part of the ICECAP trial. Individuals who are tested in Spanish will not take the Stroop Test.

Rey Auditory Verbal Learning Test - Learning, Interference and Immediate Delay - Spanish

Learning Trials (List A)

Le voy a leer una lista de palabras. Escuche con cuidado, porque cuando yo pare, tiene que repetir todas las que pueda recordar. No importa en qué orden las repita. Solo diga todas las que pueda decir. ¿Alguna pregunta? [If no questions, start reading the List A]

Read through the list slowly, saying approximately one word per second. Once you have finished, say: ***Ahora, dígame todas las palabras que pueda recordar, en cualquier orden.***

As the participant is naming words, mark the words recalled in the boxes next to the corresponding word. If the participant asks you if s/he has already said a word, respond: ***No puedo decírselo, pero no hay penalidad por repetir palabras.*** If the participant names a word that is not on the list, you do not need to write the word in the empty boxes below the list. Do not let the participant give up, and do not move on until at least 10-15 seconds have passed since s/he has said a new correct word. Then, continue on to the next Trial.

Once the first Trial is completed, say**:** ***Ahora voy a leer la misma lista de nuevo. Una vez más, cuando yo pare, quiero que me diga todas las palabras que usted pueda recordar, incluyendo las palabras que ya dijo. No importa en qué orden las diga, solo diga todas las que pueda decir. ¿Alguna pregunta?*** [If no questions, start reading List A]

Read through the list slowly, saying approximately one word per second. Once you have finished, say: ***Ahora, dígame todas las palabras que pueda recordar, en cualquier orden.***

As the participant is naming words, mark the words recalled in the boxes next to the corresponding word.

Repeat this process with List A for Trials 3-5.

Interference Trial (List B)

Ahora le voy a leer una lista nueva de palabras. De nuevo, cuando yo pare, usted tiene que repetir todas las palabras que pueda recordar de esta lista nueva. De nuevo, el orden en que usted diga las palabras no tiene importancia. ¿Alguna pregunta? [If no questions, start reading List B]

Read through List B at the same speed. Once you have finished, say: ***Ahora, dígame todas las palabras que pueda recordar, en cualquier orden.***

As the participant is naming words, mark the words recalled in the boxes next to the corresponding word.

Immediate Delay

After the Recall of List B is completed, administer the Immediate Delay Recall Trial of List A. DO NOT read List A again. Say: ***Ahora dígame todas las palabras que pueda recordar de la primera lista.***

Rey Auditory Verbal Learning Test - 30 Minute Delay and Recognition - Spanish

30 Minute Delay (List A)

After the designated delay time period (30 minutes ± 5), administer the Delayed Recall Trial of List A. You may say:

Hace un ratito le leí una lista de palabras varias veces, y usted estaba tratando de aprender estas palabras. Dígame las palabras de esta lista de nuevo.

If needed, you may clarify that this was the first list read to the participant.

Recognition

Le voy a leer una lista de palabras, de una en una. Si la palabra estaba en la primera lista, diga "Sí", y si no estaba, diga "No".

Trail Making Test - Spanish

Trails A

Give the study participant a pen and the test page and say:

> ***En esta página hay algunos números (señalarlos). Comience con el número 1*** **(señale el 1)** ***y dibuje una línea de 1 a 2*** **(señale el 2)**, ***2 a 3 (señale el*** **3)**, ***3 a 4 (señale el*** **4)** ***y así sucesivamente, en orden, hasta que llegue al final (señale el círculo marcado*** **"final")**. ***Dibuje las líneas lo más rapido que pueda. Listo ------- ¡Comience!***

If the study participant completes the sample item correctly demonstrating he/she understands what to do, say: ***¡Bien! Intentemos con el próximo.***

Turn the paper over and give Part A of the test.

If the study participant makes a mistake on Sample A, point out the error and explain it.
The following explanations of mistakes serve as illustrations:

- ***Usted comenzó con el círculo incorrecto.*** **Aquí es donde comenzó (señale el número 1)**
- ***Usted se omitió este círculo (señale el círculo que se omitió). Debe ir del número 1*** **(señalar)** ***al 2*** **(señalar)**, ***2 a 3*** **(señalar el 3)**, ***etc., hasta llegar al círculo marcado "final"*** **(señalar)**.

If it is clear that the study participant intended to touch a circle but missed it, do not count it as an omission, however, remind the study participant to be sure to touch each of the circles when drawing the connecting lines.

Do not correct the study participant until he/she actually touches the wrong circle (i.e., do not assume a mistake will be made).

If the study participant cannot complete Sample A, take his/her hand and guide the pen, **using the non-ink end**, through the trail. Then say: ***Ahora, inténtelo.***

Return the pen to the participant with the point down and say:

> **Recuerde, comience con el número 1 (señale el 1) y dibuje una línea de 1 a 2 (señale el 2), 2 a 3 (señale el 3), 3 a 4 (señale el 4) y así sucesivamente, en orden, hasta que llegue al círculo marcado "final" (señalar).**
>
> **No se mueva de una parte a la otra al azar, sino que debe ir de un número al siguiente en el orden adecuado. Recuerde trabajar lo más rápido que pueda. Listo ------- ¡Comience!**

If the study participant succeeds this time proceed to Part A. If the study participant still has difficulty, repeat the above procedure until the task is completed successfully or it becomes evident that the participant cannot do the task.

After the study participant has completed Sample A, turn the paper over to Part A and say:

> **En la página hay números del 1 al 25. Haga esto de la misma manera. Comience con el número 1 (señale el 1) y dibuje una línea de 1 a 2 (señale el 2), de 2 a 3 (señale el 3), de 3 a 4 (señale el 4) y así sucesivamente, en orden, hasta que llegue al final (señalar). Recuerde trabajar lo más rápido que pueda. Listo ------- ¡Comience!**

Using a stopwatch, start timing as soon as the instruction is given to begin. The examiner must watch the study participant closely in order to catch any errors as soon as they are made. If the study participant makes an error, call it to his/her attention immediately, return the study participant's pen to the last correct circle, and continue the test from that point. Do not stop timing while correcting the participant's error.

After the study participant completes Part A, take the test sheet and record the time in seconds. Errors contribute to evaluation of performance principally by increasing the total performance time.

Trails B

Next, tell the study participant:

> **Eso está bien. Ahora, probaremos otro más.**

Place the sample side of Part B on the table in front of the study participant, in the same position as the sheet for Part A was placed. Point to the sample and say:

> **En esta página hay algunos números y letras. Comience con el 1 (señalar) y dibuje una línea del 1 a A (señale A), de A a 2 (señale el 2), de 2 a B (señale el B), de B a 3 (señale el 3), de 3 a C (señale el C), y así sucesivamente, en orden, hasta llegar al final (señale el círculo marcado "final").**
>
> **Luego diga: Recuerde, primero tiene un número (señale el 1), luego una letra (señale la letra A), luego un número (señale el 2), luego una letra (señale la B), y así sucesivamente. Dibuje las líneas lo más rapido que pueda. Listo ------- ¡Comience!**

If the study participant completes the Sample B correctly say: **¡Bien! Intentemos con el próximo.**

Proceed immediately to Part B.

If the study participant makes a mistake on Sample B, point out the error and explain why it is incorrect. The following explanations of mistakes serve as illustrations:

- **Usted comenzó con el círculo incorrecto. Aquí es donde comenzó (señale el número 1).**
- **Usted se omitó este círculo (señale el círculo que se omitió). Usted debería ir de 1 (señale el 1) a A (señale A), de A a 2 (señale el 2), de 2 a B (señale B), de B a 3 (señale el 3), y así sucesivamente hasta llegar al círculo marcado "final" (señalar).**

If it is clear that the study participant intended to touch a circle but missed it, do not count it as an omission. Remind the study participant, however, to be sure to touch each of the circles when drawing the connecting lines.

If the study participant cannot complete Sample B, take his/her hand and guide the pen, **using the non-ink end**, through the circles. Then say:

> ***Ahora, inténtelo usted.*** **Recuerde, usted comenzó en el número 1 (señale el 1) y dibuje una línea desde el 1 hasta la A (señale A), de A a 2 (señale el 2), de 2 a B (señale B), de B a 3 (señale el 3), y así sucesivamente hasta llegar al círculo marcado "final" (señalar).** ***Listo ------- ¡Comience!***

If the study participant succeeds this time, go on to Part B. If not repeat the procedure until the task is performed successfully or it becomes evident that the study participant cannot do the task.

After the study participant has completed the sample, turn the paper over to Part B and say:

> ***En esta página hay números al igual que letras. Haga esto de la misma manera.*** **Comience con el 1 (señalar el 1) y dibuje una línea del 1 a A (señale A), de A a 2 (señale el 2), de 2 a B (señale el B), de B a 3 (señale el 3), de 3 a C (señale el C), y así sucesivamente, en orden, hasta llegar al final (señale el círculo marcado "final").**
>
> **Recuerde, primero tiene un número (señale el 1), luego una letra (señale la letra A), luego un número (señale el 2), luego una letra (señale la B), y así sucesivamente.** ***No se mueva de una parte a la otra al azar, sino que debe ir de un círculo al siguiente en el orden adecuado. Dibuje las líneas lo más rapido que pueda. Listo ------- ¡Comience!***

Using the stopwatch, start timing as soon as the participant is told to begin. Remember to be alert for mistakes. If the participant makes an error, point it out immediately, return the subject to the last correct circle, and continue the test from that point. Do not stop timing.

After the study participant completes Part B, take the test sheet and record the time in seconds. Errors contribute to the evaluation of the performance principally by increasing the total performance time.

ICECAP Discontinue Rules: The time limit for Trails A is 100 seconds. The time limit for Trails B is 300 seconds.

Controlled Oral Word Association Test (COWAT) - Spanish

Have a stopwatch ready before giving the following instructions:

> ***Voy a decirle una letra del abecedario y quiero que diga, lo más rápido que pueda, todas las palabras que pueda pensar que comienzan con esa letra. Puede decir todas las palabras que pueda pensar, excepto nombres propios, como los nombres de personas o lugares. Por ejemplo, "Boston" o "Bob". Además, no use la misma palabra nuevamente con un final diferente, como por ejemplo: "encanto" y "encantado". Por ejemplo, si digo "S," usted puede decir: "sol", "sentarse", "sandalia" o "santo".*** **¿Puede pensar otras palabras que comiencen con la letra "S"?**

Espere a que la persona le diga una palabra, indique si la palabra es correcta y solicite a la persona que le diga otra palabra que empiece con la letra "S".

Once two appropriate words beginning with the demonstration letter are given, say:

> ***Eso está bien. Ahora, le voy a decir otra letra. Una vez más, diga todas las letras que comienzan con esa letra que usted puede pensar. Recuerde, no diga nombres de personas ni lugares, solo sustantivos comunes o palabras corrientes. También, si nada le viene a la mente, quiero que siga intentándolo hasta que finalice su tiempo. Usted tendrá un minuto para cada uno. La primera letra es la "P". ¡Comience!***

Begin timing immediately.

Repeat the same instructions for the letters M and R.

Allow 1 minute for each letter. Say ***"Correcto"*** or ***"Bien"*** after each 1-minute performance. If the study participant discontinues before the end of the minute, encourage him/her to try to think of more words. If there is a silence of 15 seconds, say: ***¿Puede pensar en otras palabras que comiencen con la letra "--"?*** **(diga la letra adecuada para esa prueba en especial).**

Category Fluency Test - Spanish

Have a stopwatch ready before giving the following instructions:

Quiero saber cuántos tipos de animales diferentes puede decir en un minuto. Trate de no repetirlos. Puede empezar.

Record the participant's responses in the spaces provided on the worksheet form.

Neuro-QoL - Spanish

There are no instructions for the Neuro-QoL test. The participant simply reads and answers the questions presented on the paper.

If a participant is unable to complete the Neuro-QoL measures, a proxy (e.g., close family member) responder may answer on behalf of the participant. When using a proxy responder, the NOA should begin by stating:

The following questionnaires will ask about your care recipient's symptom and activity levels; his/her ability to think, concentrate and remember things; questions specific to his/her condition, and questions related to his/her quality of life. Please answer the following questions based on what you think your care recipient would say.

In Spanish, the Neuro-QoL measures will be administered via paper forms. Links to .pdfs of the 13 Neuro-QoL measures are included in the table below.

List of Spanish Neuro-Qol Measures Used in the ICECAP Trial
Neuro-QoL Short Form v1.0 – Ability to Participate in Social Roles and Activities
Neuro-QoL Short Form v1.0 – Anxiety
Neuro-QoL Short Form v1.0 – Depression
Neuro-QoL Short Form v1.0 – Emotional and Behavioral Dyscontrol
Neuro-QoL Short Form v1.0 – Fatigue
Neuro-QoL Short Form v1.0 – Lower Extremity Function – Mobility
Neuro-QoL Short Form v1.0 – Positive Affect and Well-Being
Neuro-QoL Short Form v1.0 – Stigma
Neuro-QoL Short Form v1.0 – Upper Extremity Function – Fine Motor, ADL
Neuro-QoL Short Form v1.1 – Satisfaction with Social Roles and Activities
Neuro-QoL Short Form v2.0 – Cognitive Function
Neuro-QoL Scale v1.0 – Communication
Neuro-QoL Short Form v1.0 – Sleep Disturbance

Appendix F - Test Forms and Stimulus Materials - English

Test Forms

English test forms for the Trail Making Test and the Stroop Test will be shipped to sites from the CCC. These forms are not to be photocopied. To request additional test forms, contact the CCC. There are no test forms needed for the NIH Toolbox tests or the Neuro-QoL.

The English ICECAP study test forms may be downloaded and printed for the following tests:

- Rey Auditory Verbal Learning Test (RAVLT)
- Controlled Oral Word Association Test (COWAT)
- Category Fluency Test (CFT)

Stimulus Materials

No additional stimulus materials are required for administering the RAVLT, Trail Making Test, Stroop Test, COWAT, CFT or Neuro-QoL.

Hard copies of the required stimulus materials required for the NIH Toolbox tests will be shipped to sites in the testing kit. Additional copies may be accessed via the links below printed by sites. These materials include:

- NIH Toolbox Home Base
- Oral Symbol Digit Examination Sheet
- Answer Key for NIH Toolbox List Sorting Test
- English Pronunciation Guide for the NIH Toolbox Oral Reading Recognition Test

Appendix G - Test Forms and Stimulus Materials - Spanish

Test Forms

The English version of the Trail Making Test form will be used for Spanish speaking individuals in the ICECAP study. The Spanish test form of the Stroop Test and the English form of the Trail Making Test will be shipped to sites from the CCC. These forms are not to be photocopied. To request additional test forms, contact the CCC.
There are no test forms needed for the NIH Toolbox tests or the Neuro-QoL.

The Spanish ICECAP study test forms may be downloaded and printed for the following tests:

- Rey Auditory Verbal Learning Test (RAVLT)
- Controlled Oral Word Association Test (COWAT)
- Category Fluency Test (CFT)

Stimulus Materials

No additional stimulus materials are required for administering the RAVLT, Trail Making Test, Stroop Test, COWAT, CFT or Neuro-QoL.

Hard copies of the required stimulus materials required for the NIH Toolbox tests will be shipped to sites in the testing kit. Additional copies may be accessed via the links below and printed by sites. These materials are the same for as the English versions with the exception of the Pronunciation Guide for the NIH Toolbox Oral Reading Recognition Test

- NIH Toolbox Home Base
- Answer Key for NIH Toolbox List Sorting Test (English and Spanish Keys are the same)
- Spanish Pronunciation Guide for the NIH Toolbox Oral Reading Recognition Test