NIH SIREN Emergency Trials Network

POST-ICECAP

Patterns Of Survivors' Recovery Trajectories in the ICECAP trial (POST-ICECAP)

Outcomes Manual

Version 2

Supported by:
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Table of Abbreviations

CCC	Clinical Coordinating Center
COA	Central Outcomes Assessor
COT	Central Outcomes Team
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
OHCA	Out-of-Hospital Cardiac Arrest
QA	Quality Assurance
SIREN	Strategies to Innovate Emergency Care Clinical Trials Network

1.0 SIREN Organization for POST-ICECAP Outcomes

The SIREN Clinical Coordinating Center (CCC) at the University of Michigan will serve as the Clinical Coordinating Center for the POST-ICECAP prospective, observational study. The CCC is responsible for communication with sites, training and certification of Hubs, ensuring Hub regulatory compliance, monitoring Hub performance, and providing feedback to ensure performance improvement. The Site Manager, Study Monitors, and Training Coordinators perform these tasks. Daily management of the POST-ICECAP study 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 members of the Clinical Outcomes Team (COT) housed within Columbia University and CCC oversee aspects of outcomes management. This includes tracking individual participants' follow-up visits, just-in-time training, and responding to queries from sites regarding outcomes and questionnaires. The SIREN Data Coordinating Center (DCC) at the Medical University of South Carolina will serve as the Data Coordinating Center for the POST-ICECAP study.

Approximately 65 hospitals are anticipated to participate in POST-ICECAP and enroll an average of 4 subjects per site per year. The enrollment period is anticipated to be 4 years (estimated accrual rate of 21 subjects per month).

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 365 days after Out-of-Hospital Cardiac Arrest (OHCA). The mRS score will be determined by site personnel trained to administer the mRS.

3.2 Secondary Efficacy Outcomes

Secondary efficacy measures will be administered 365 days after OHCA. All secondary measures will be administered by a trained and certified Neuropsychological Outcomes Assessor (NOA) at each site.

3.2.1 Participant-Reported Outcomes

The Neuro-QOL is a set of self-report measures (developed into item banks). The short forms of various domains that will be assessed in the POST-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 dysfunction) and Cognitive Health (i.e., Cognitive Function, Communication).

3.2.2 Neuropsychological Outcomes

Neuropsychological (NP) testing offers a unique opportunity to examine, with great sensitivity, potentially subtle yet meaningful differences in outcomes between treatment groups.

The Brief Test of Adult Cognition by Telephone (BTACT), administered at all visits, is a battery designed to reliably assess cognitive functioning via telephone. The dimensions include episodic memory, working memory, reasoning, verbal fluency, and executive function. This test consists of seven subtests, with varying scoring rules and timed parameters.

4.0 Study Team Roles and Training

All study team members conducting any outcome assessment for the POST-ICECAP study 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.

POST-ICECAP Training Links

Outcomes Training

mRS Training

Just-in-time Training

4.1 Outcome Assessor (OA) and Neuropsychological Outcomes Assessor (NOA)

While OAs can administer mRS and conduct other study assessments, NOAs are responsible for administering neuropsychological tests along with other primary and secondary efficacy measures at all visits. NOA must receive certification for BTACT. Both OA and NOA, if administering the mRS, need to be listed as having the (AB - Administer modified Rankin Scale) responsibility in the site's Delegation of Authority log and be trained on the mRS. **A site may have the same study personnel serve the roles of OA and NOA.**

NOAs will be initially 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 POST-ICECAP Regulatory Document Parameters. 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.

NOTE: To facilitate the above training process, previously certified NOAs are strongly encouraged to assist with the 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.

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 study and continue to fine-tune and calibrate their skill in administering the POST-ICECAP NTB.

4.2 Site Investigator and Other Study Coordinators

Local site investigators or other study coordinators may be asked to administer the mRS if opportunities to contact the participant are fleeting or unreliable, or the OA or NOA is not available. As mentioned above, any study team member administering the mRS must first undergo the SIREN mRS training.

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

Study team members collecting an mRS are expected to be trained in the assessment, and certifications of mRS training are being collected. Sites and study personnel should retrain as needed, at least every two years.

5.2 BTACT Assessments

NOAs can maintain certification on the BTACT by either performing the battery on a study subject at least once every 6 months or by a COT-supervised retraining process. The BTACT certification will be extended by the central outcomes team. NOAs whose BTACT certification is scheduled to expire will be notified by the central outcomes team approximately one month prior to this expiration.
NOAs who are unable to administer the BTACT for a period of more than 6 months will have to apply to extend their certifications.

6.0 Quality Assurance (QA) of Outcomes

6.1 Modified Rankin Scale

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

6.2 BTACT Assessment

To ensure maximum data quality across clinical test sites, BTACT assessments are subject to quality assurance review for completeness, accuracy, and internal consistency by the Central Outcomes Team (COT).

The COT will review testing procedures, double-score, and double-check data entry of select BTACT sessions and source 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 outcomes team.

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.

7.0 Participant Retention

A study participant will be counted as retained when the mRS is obtained at 365 days post OHCA. Study site personnel must make every effort to complete each participant's study visit within the allowable visit windows. A study participant will be counted as retained when the mRS is obtained at 365 days post OHCA. Study site personnel must make every effort to complete each participant's study visit within the allowable visit windows. described later. 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 the family and the participant (at the time of consent) fully understand what follow-ups are involved. Discuss preferred 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 all follow-up visits, 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 telephone calls at the most convenient time for 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.
- If a participant wants to come to the hospital and/or is willing to allow the NOA to visit his/her home, the mRS, BTACT, and the Neuro-QoL measures can be administered in person.
- 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 POST-ICECAP team at POST-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 POST-ICECAP Operations Committee. The Site Investigator or designee will be asked to present the case to the committee that includes the efforts exerted to locate the participant. To present the case, notify the POST-ICECAP team at POST-ICECAP-contact@umich.edu to be placed on the meeting agenda. POST-ICECAP Operations Meetings are held weekly on Monday at 4:00 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.
Please note: being unable to attend a single visit 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 follow-up assessments. All visits can be conducted by phone or in person.

On occasion, a "hard to reach" participant may be serendipitously contacted (e.g., shows up unexpectedly to a clinic appointment). In this case, mRS-trained study personnel (OA or NOA) may complete the mRS evaluation.

8.1 Telephone or In-Person Visits

Whenever possible, all visits are to be conducted via telephone. If a study participant is able or willing to come to the clinic or have the NOA come to his/her place of residence, an in-person follow-up may be scheduled.

8.2 Hospital/Assisted Living Facility Visits

Sites will need to take additional steps to schedule the telephone 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).

If the participant is still in the enrolling hospital, the site-coordinator should visit the participant in his/her room to determine the mRS score and administer other assessments, including BTACT. If the participant has been discharged to another hospital or an Assisted Living facility, the site-coordinator should contact someone very familiar with the study participant's level of functioning (e.g., caregiver, family member, LAR) to complete the mRS and find ways to administer other POST-ICECAP assessments with the participant on the phone. 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.

8.3 Patients with Disorders of Consciousness

In cases where a study participant is unresponsive, i.e., unable to follow commands, only the mRS and Disability Rating Scale will be completed for all study visits. No other outcomes, including the Neuro-QoL (even by proxy), should be attempted. Whenever possible, the mRS and Disability rating scale should be conducted by the 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. Here are the Detailed Instructions for administering the DRS questionnaire.

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

9.1 Planning and Roles

Good communication is key to 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 30-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 study by explaining the 30, 90, 180, 270, and 365 days phone call visits.

Unless it's the same team member, 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 NOA to maintain contact throughout the process.

Each site will need to decide who is responsible for contacting the participant for the phone visits. All attempts at contact (whether successful or not) should be documented. The Study Coordinator, NOA, and COT 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 in-person evaluations.

10.0 Outcomes Testing Procedures

10.1 Testing Windows

- First assessment is to be conducted 30 days after the date of cardiac arrest ± 15 days (day 15 to 45).
- Second assessment (in-person) is to be conducted 90 days after the date of cardiac arrest ± 15 days (day 75 to 105).
- The third assessment is to be conducted 180 days after the date of cardiac arrest ± 15 days (day 165 to 195).
- Fourth assessment is to be conducted 270 days after the date of cardiac arrest ± 15 days (day 255 to 285).
- Fifth and final assessment (in-person) is to be conducted 365 days after the date of cardiac arrest ± 15 days (day 350 to 380).

Ideally, the entire visit (including interviews with informants) will be conducted on the same day. When this is not possible, please email POST-ICECAP-contact@umich.edu, and subsequent visits should be conducted as soon as possible.

10.2 Informant for participants residing in Hospital/Assisted Living Facility

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 Physical Impairment Preclude Evaluation?

The mRS should be completed at **ALL** visits, 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 and 365 days visits regardless of the study participant's level of **physical impairment**. As is explained in more detail below, an informant may complete the Neuro-QoL measures on behalf of the physically impaired study participant. If the participant is able to cognitively answer the Neuro-QoL measure questions but is physically unable to read and/or respond, the NOA may read the Neuro-QoL measure questions aloud and indicate the study participant's responses on the Neuro-QoL form.

When there is uncertainty regarding the participant's mRS status and testability, 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 judgment regarding when discontinuation is necessary.

10.4 Determining English Language Proficiency

Prior to the 30-day appointment, the Study Coordinator should determine the participant's and informant's preferred language/s and whether a Spanish interpreter is needed for the interview.

The POST-ICECAP NTB will only be administered in English or Spanish. Due to the complexity of testing procedures, interpreters may not be used to administer BTACT (i.e., if the site does not have an English-Spanish bilingual NOA, the site will not be able to conduct the BTACT 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 in English is not sufficient for valid interviewing. The following can be used as an interpreter for the POST-ICECAP study: trained multilingual study team members, 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, 180, and 270 days Telephone Visit

The 30, 180, and 270-day outcomes visits include a phone evaluation of the mRS, BTACT, and other POST-ICECAP specific assessments. Whenever possible, the mRS interview should be conducted with the study participant and confirmed by a knowledgeable informant who is in close contact with the study participant. Ideally, the mRS interviews should be conducted separately so all interviewees can speak freely.

10.8 90 and 365 days Telephone or In-Person Visit

The 90-day and 365-day outcome visit includes an evaluation of the mRS, followed by the BTACT and Neuro QoL administered by the NOA.

Careful coordination and high-quality communication between all study team members, team, 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.

10.9 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 a good rapport with study participants to help maintain the participants' 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 C.) 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 can correctly answer 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.

11.0 Outcomes Descriptions, Scoring Instructions, Training, and Tips

Secondary efficacy assessments conducted for this study include the BTACT and the Neuro-QoL measures. Training for BTACT should commence within 30 days after enrollment of a site's first study participant.

In this section, the mRS, BTACT, and Neuro-Qol) measures are described in detail. Neuropsychological testing in the ICECAP trial has been limited to 45 minutes to enhance study participant compliance and minimize fatigue.

***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.**

11.1 Modified Rankin Scale (mRS)

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. All mRS evaluations should be completed by a mRS-certified, local study team member.

11.1.3 Scoring

The mRS score is determined by the 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 their 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

Simplified mRS Flow Sheet
mRS Training

SIREN mRS training is available through the CCC. 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 POST-ICECAP study, it is 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.

11.1.5 Administration Tips and Key Things to Remember

- 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.
    - mRS interviewers may access the study participant's medical record to gather additional information.
- The person administering the mRS must use good clinical judgment to determine the score based on the information s/he consider 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 on 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 disavisito 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 the 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.

- Questions regarding scores of 5, 4, and 3 are based on the participant's overall functioning, taking into consideration all disabilities, from any source.
- 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 a 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 score 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)

11.2 Neuro-QoL

The English Neuro-QoL measures can be administered in person or over the phone, available in Appendix D. There are hard copies of the test forms, but there are no printed instructions needed, since every question needs to be read verbatim. The Spanish Neuro-QoL measures are also administered via paper forms, available in Appendix E.

11.2.1 Reference

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.).

11.2.2 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.

11.2.3 Scoring

The raw score for each of the 13 Neuro-QoL measures administered in English and Spanish will be entered by the sites into WebDCU.

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

Neuro-QoL scoring is completed once uploaded onto WebDCU. No manual scoring is needed.

11.2.4 Training and Certification

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

Neuro-QoL Training

11.2.5 Administration/Scoring Tips and Administration by Proxy

- 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" 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 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) or in person.

- 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).
- When participants have completed filling out paper forms, the NOA should carefully review the forms to ensure that all questions have been clearly answered with only one response.

11.3 The Brief Test of Adult Cognition by Telephone (BTACT)

The BTACT is a battery designed to reliably assess cognitive functioning via telephone. The dimensions listed in the table below include episodic memory, working memory, reasoning, verbal fluency, and executive function. The BTACT cognitive battery is administered by the NOA over the telephone (i.e., read to the participant) using the hard copies of test forms.
The sites must store either hard or electronic copies for periodic quality review by the study monitors and the central outcomes team. You must follow NIH guidelines to determine the duration of the storage period.

This test consists of seven subtests, with varying scoring rules and timed parameters. The time to complete the entirety of the BTACT varies by participant but is approximately 10-15 minutes. This test cannot be completed by a proxy responder (i.e., an "informant").

List of BTACT Subtests	Approximate administration time (not assigned time)	Construct Tested
1. Word List Recall – Immediate	1.5 minutes	Episodic Memory
2. Digits Backward	2.5 minutes	Working Memory
3. Category Fluency	1.5 minutes	Executive Function
4. Number Series	2.5 minutes	Inductive Reasoning
5. Backward Counting	45 seconds	Processing Speed
6. Word List Recall – Delayed	1.0 minute	Episodic Memory
7. Stop and Go Task Accuracy	3.5 minutes	Attention, Inhibitory Control

The BTACT Forms A and B are to be alternated for each visit to reduce practice effect-

- FORM A English (1, 6, 12 months visits)
- FORM B English (3, 9 months visits)
- FORM A Spanish (1, 6, 12 months visits)
- FORM B Spanish (3, 9 months visits)

11.3.1 BTACT Administration and Scoring Rules

Please refer to BTACT Overall Administration and Scoring Rules for details.

General principles of Neuropsychological test administration

The skill and judgment of the NOA often affect 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 BTACT. Following these guidelines helps to ensure a valid and accurate assessment while reducing stress and discomfort for participants.

- The BTACT 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.
- 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 NOA's 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
- 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. The 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.

11.3.2 Training and Certification

NOAs can maintain certification on the BTACT by either performing the battery on a study subject at least once every 6 months or by a COT-supervised retraining process. The BTACT certification will be extended by the central outcomes team. NOAs whose BTACT certification is scheduled to expire will be notified by the central outcomes team approximately one month prior to this expiration.

NOAs who are unable to administer the BTACT for a period of more than 6 months will extend their certifications via the following procedure:

- Review BTACT Examiner's Training Manual
- Watch the Administration and Scoring Training Video
- Practice BTACT testing on at least one non-study participant

11.3.3 Reference

Lachman ME, Agrigoroaei S, Tun PA, Weaver SL. Monitoring cognitive functioning: psychometric properties of the brief test of adult cognition by telephone. Assessment. 2014 Aug;21(4):404-17. doi: 10.1177/1073191113508807. PMID: 24322011.

12.0 Outcomes CRF Completion, Data Entry, Upload, and Transfer

12.1 General

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

POST-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 Neuro-QoL

Both English and Spanish Neuro-QoL are administered on paper. After administration, the NOA will enter raw scores into the WebDCU.

12.4 BTACT

Both English and Spanish BTACT are administered on FORM A or B. After administration, the NOA will enter raw scores into the WebDCU and keep the forms as a source document for monitoring and quality check purposes..

Appendix A - POST-ICECAP Training Procedures

Training Links and Process for OA and NOA

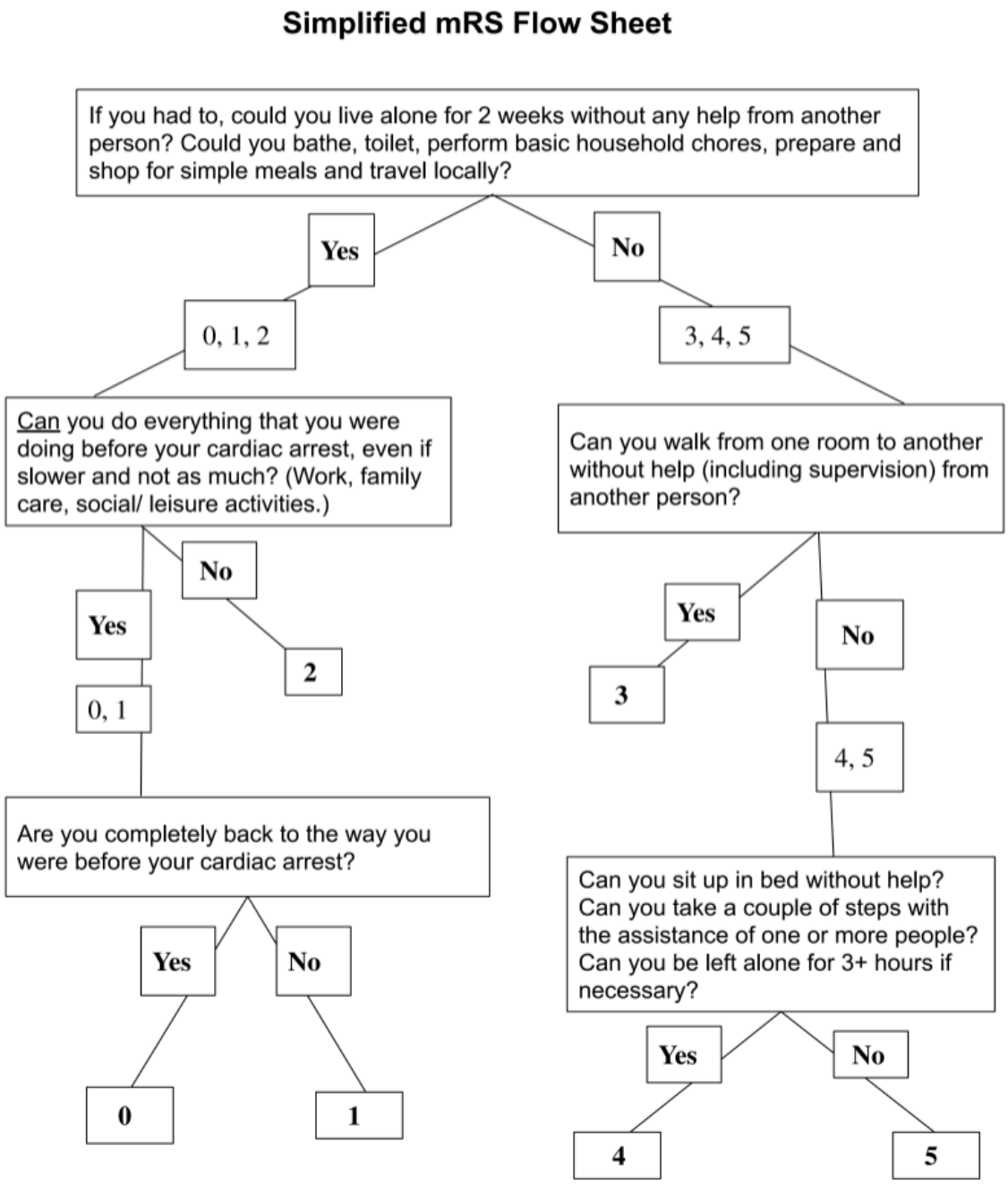
To be certified to administer the POST-ICECAP assessments, NOAs must complete the process below in order:

1) Read key POST-ICECAP documents.
    a) Study Protocol Synopsis
    b) Outcomes Manual of Procedures (this document)
2) Just-In-Time Training

*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.

Appendix B - Simplified Modified Rankin Scale Flow Sheet

Printable mRS Flow Sheet with ICECAP Header



Appendix C – POST-ICECAP BTACT Introductory Script - English

Introductions

On telephone visits, NOA will begin by explaining the outcomes procedures and letting the participant know what to expect. 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.

Appendix D - Neuro-Qol 90 and 365 days Visit Scripts, Test Instructions, and Short Forms- ENGLISH

There are no instructions for the Neuro-QoL test. The participant or administrator simply reads and answers the questions presented on the answer sheet. Both for telephone and in-person visits, the paper versions attached below are administered to study participants and are to be saved locally for monitoring purposes.

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 symptoms 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.

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

Appendix E - Neuro-Qol 90 and 365 days Visit Scripts, Test Instructions, and Short Forms - 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 symptoms 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.

List of Neuro-Qol Measures Used in the POST-ICECAP (SPANISH)
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