Standard Operating Procedure for clinical follow-up by telephone at 3 months in the CASES trial

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1. Aim

This standard operating procedures describes the process of the clinical outcome assessment by telephone at 3 months (with a margin of +/- 2 weeks) for the CASES trial. This assessment consists of the modified Rankin Scale (mRS) score (using a validated measuring instrument), the EQ5D5L, the inquiry of outcome events and serious adverse events that occurred during the follow-up period and the explanation how to complete the IMTA productivity cost and IMTA medical consumption questionnaires sent by post. This SOP will ensure the quality of the data and uniformity of the assessment of outcome.

2. Range

This SOP is intended for all qualified research assistants (including research nurses) of the National Coordinating centers (UMC Groningen for the Netherlands and UZ Leuven for Belgium) performing the centrally organized 90-day follow-up of patients included in the CASES trial.

Definitions and abbreviations:

- CASES = Carotid Artery Stenting during Endovascular treatment of acute ischemic Stroke
- eCRF = electronic Case Report Form
- FU = Follow-up
- mRS= Modified Rankin Scale
- PI = Principal Investigator
- SAE = Serious Adverse Event
- SOP = standard operating procedure

3. Responsibilities

The PI's of the National Coordinating centers (UMC Groningen for the Netherlands and UZ Leuven for Belgium) are responsible for the training of the research assistants who perform the 3-month follow-up for all centers in their own country. This SOP will therefore be discussed with each appointed research assistant individually and the procedures for the outcome assessment will be trained. This training will be documented on the training log of UZ Leuven or UMC Groningen. Each research assistant performing the 3-month follow-up by telephone for a patient of a particular center, should also be added to the delegation log of this center.

4. Procedures

Validated measurement instruments; paper versions

Every qualified research assistant should use the following questionnaires and documents as a guideline for the assessment: the “modified Rankin Scale” (algorithm and procedure in Appendix 1), the “EQ5D5L” (Appendix 2) for the follow-up by telephone and the “IMTA productivity cost questionnaire – iPCQ (Appendix 3) and “IMTA medical consumption questionnaire – iMCQ” (Appendix 4) send by post. All questionnaires should be used according to the language the patient prefers (Dutch, English and French questionnaires are available).

All questionnaires will be filled in with data acquired through the FU conversation or by post, and signed, including name, date and signature by the research assistant who performed the follow-up. The follow-up paper form will be stored at the institution where the research assistant is employed.

Immediately after the interview, or at the latest within 72 hours, the research assistant will enter the data into CASTOR.

Blinding

The appointed research assistant who assesses the 90-day follow-up by telephone, is blinded for treatment allocation. The appointed research assistant is therefore not involved in the randomization part of the trial. It is therefore crucial to create the follow-up paper form before entering the data into CASTOR, to prevent the assessor from being influenced by knowledge of the treatment allocation. Paper forms and questionnaires will be stored at the National Coordinating Center.

Logistics

At the time of a study participant's discharge from the hospital (or no more than 30 days after randomization) , the local research nurse/employee fills in the discharge form on the CASES trial website. These contact details are sent coded to the national coordinating centers (UMC Groningen for the Netherlands and UZLeuven for Belgium). With the coded information and the research assistant-specific login, the research assistant can decode the contact details via the CASES website.

The research assistant of the national coordinating center will contact the patient and/or patient's representative 2 weeks prior to the official FU date (i.e. at 10 weeks after randomization), in accordance with the study protocol. If the interview cannot take place at this moment, 4 weeks remain to plan the appointment (maximal 2 weeks after the 90 day point). During the phone call, the research assistant should state their reason for calling, and ask whether it is a convenient time to perform the interview.

Firstly, the research assistant will perform the mRS interview. This measure is the primary endpoint of the trial and therefore of most importance. Afterwards, the EQ-5D-5L and occurrence of outcomes events and SAE's will be conducted. Finally, the research nurse will explain how to fill in and return the additional questionnaires, sent to the study participants at 90 days (iPCQ and iMCQ). If the questionnaires are not received, a maximum of three attempts will be made to contact the patient.

All paper forms will be stored in a research file according to study ID at the National Coordinating Center. At the end of the trial all data will be archived as per institutions policy in accordance with all applicable laws and regulations.

The mRS, EQ-5D-5L will be entered in the CASTOR database of the CASES trial, immediately after completion of the follow-up paper form. Upon reception of the iPCQ and iMCQ questionnaires, this information will also be entered manually into the CASTOR database by the appointed research assistant. If during the telephone interview it emerges that outcome event or SAE's have occurred and that these were not registered in the CASTOR database, the local PI will be informed accordingly. The local PI will be asked to follow up, collect and register the appropriate data regarding these events in the CASTOR database. Additionally, the SAE will be documented in the patient file by the local site staff.

Aftercare

The follow-up assessment should also be considered as aftercare. The research assistant will gain more trust from the patient/patient's representative by being understanding and showing flexibility with scheduling (considering the patient is in rehabilitation and their representative's busy schedule). This way, the patient/their representative will be more predisposed to sharing information.

The research assistant will also take the following into account:

- Introduce yourself (name, position)
- State the aim, duration and procedure of the interview
- Emphasize the confidentiality of the interview
- Conduct the interview with proper care (be understanding, question further, summarize, check answers, etc.)
- Structure the interview
- Communicate clearly and carefully. If necessary, refer the patient to their treating physician.

5. Modified Ranking Scale

The mRS should be scored according to the 'short' version. First ask general questions as mentioned above, then continue with the algorithm in Figure 1 on the mRS form in Appendix 1**.** Depending on which level is scored on the mRS, specific questions will follow. These questions belong to the level scored on the algorithm, including one level above and one below. E.g. the algorithm indicates a score of mRS 3; the research assistant then continues with the questions regarding independence. This either confirms the score, or rejects it (if the patient answers 'no' to all). In that case, the rest of the questionnaire should be completed, in closed-ended questions, starting with question 1. This ensures uniformity, continuity and completion. If a patient/representative answers 'yes' to a question, the item just below should still be answered. After, the follow-up is scored accordingly. If not done so already, add a notation explaining how this score was achieved.

6. EQ5D5L

The EQ5DL questionnaire consists of 5 items and a thermometer question (Appendix 2). It is essential to capture the patient's own thoughts. The question on pain/other discomforts may also pertain to speech or language impairments, and motor/sensory deficits. Offering this clarification might help the patient with their answer.

7. IMTA productivity cost questionnaire (iPCQ) & IMTA medical consumption questionnaire (iMCQ)

For the purpose of health economic evaluation, additional questionnaires will be sent to the study participants at 90 days for measuring loss of productivity (IMTA productivity cost questionnaire (iPCQ)) and medical consumption (IMTA medical consumption questionnaire (iMCQ)).

These questionnaires will be sent to home address the participant (or representative as stated in the discharge form). During the telephone interview, the participant will be explained how to complete these forms and return them to the central coordinating centre with the enclosed addressed and stamped envelope. A letter of explanation will also be sent along with the questionnaires.

8. Outcome events and SAE's during the FU period

The local research team is responsible for monitoring of outcome events and SAEs during FU period. However the research assistant should verify if any outcome events or SAE's occurred during the FU period.

Should such an event be reported by the study participant, the local research will be informed. This will allow the local research team to follow up on the event and to complete the corresponding outcome events and/or SAE forms in CASTOR.

9. Appendices

Appendix 1. Structured interview for the modified Rankin Scale

The modified Rankin Scale (mRS) is used commonly as a measure of functional outcome following a stroke. The goal of the structured interview is to systematically assign an mRS score to patients. The interview consists of 5 sections that corresponding to the levels of the mRS. (see table)

Modified Rankin Scale	
0	No symptoms
1	No significant disability. Able to carry out all usual activities, despite some symptoms.
2	Slight disability. Able to look after own affairs without assistance, but unable to carry out all previous activities.
3	Moderate disability. Requires some help, but able to walk unassisted.
4	Moderate severe disability. Unable to attend to own bodily needs without assistance, and unable to walk unassisted.
5	Severe disability. Requires constant nursing care and attention, bedridden, incontinent.
6	Dead

Procedure

You start with explaining the purpose of several general questions. Allow the patients themselves to tell what their condition is, how their recovery went and what their home situation currently looks like. The algorithm in Figure 1 will help you to determine quickly at which level of functioning the patient is. After, you continue to ask the questions that correspond to that level.

For sections 1, 2, 3, & 5 ask about current daily activities.

For Section 4 ask about ability to perform the activity before stroke and then ask about a change in ability after the stroke. If the person did not participate in an activity (e.g. work) before stroke then move to the next question as indicated on the questionnaire. Sometimes it can be difficult to establish whether or not someone could do an activity before stroke (particularly if the person had one or more previous strokes) - in this case use your judgement.

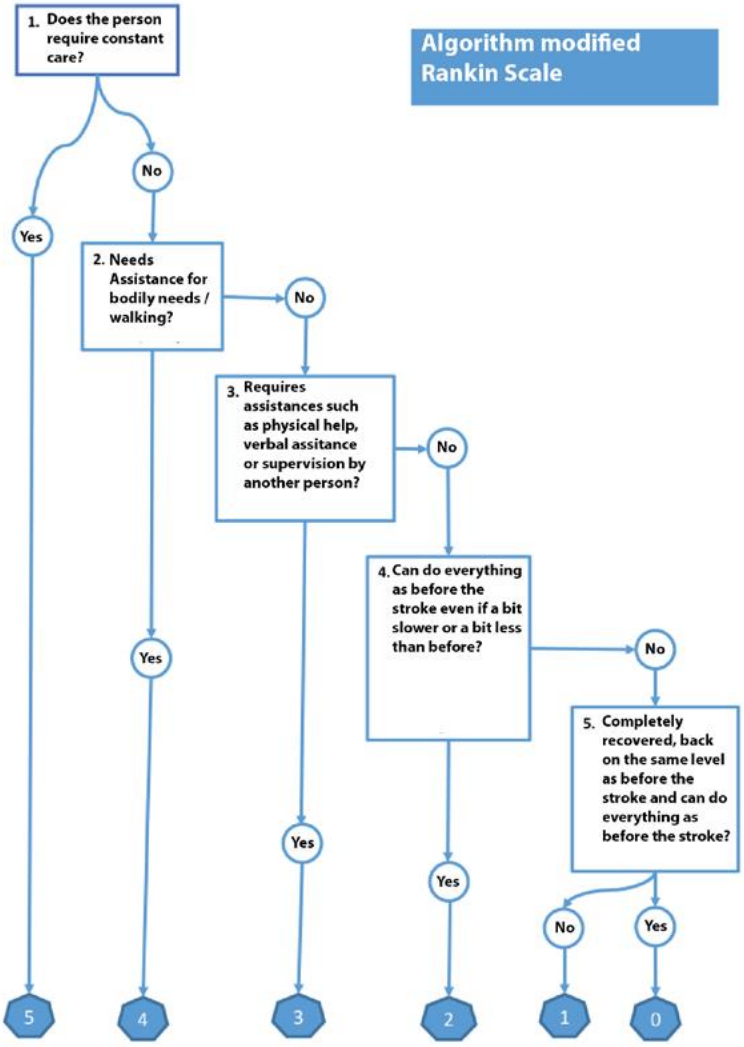


Figure 1: Algorithm modified Rankin Scale

Appendix 2: EQ-5D-5L

It is recommended that the interviewer follows the text of the EQ-5D. While there is some room for the interviewer's own choice of words, one should stick as closely as possible to the wording of the questionnaire's directions.

It is recommended that the interviewer has a copy of the EQ-5D in front of them during the telephone interview. This allows the respondent's answers to be recorded directly by the interviewer on the EQ-5D. If the respondent asks for an explanation, the interviewer can help by repeating the question word for word. The interviewer should not offer his or her own explanation, but should suggest that the respondent interprets the question himself. If the respondent has difficulty identifying which box to tick, the interviewer should repeat the question word for word and ask the respondent to give the answer that most closely reflects his or her thoughts about his or her health today.

EuroQol 5D-5L – English (French and Dutch questionnaires are available)

Under each heading, please tick the ONE ban that best describes your health TODAY

MOBILITY
I have no problems in walking about
I have slight problems in walking about
I have moderate problems in walking about
I have severe problems in walking about
I am unable to wall about

SELF-CARE
I have no problems washing or dressing myself
I have slight problems washing or dressing myself
I have moderate problems washing or dressing myself
I have severe problems washing or dressing myself
I am unable to wash or drees myself

USUAL ACTIVITIES {e.g. *work, study, housework, family or leisure activities)*
I have no problems doing my usual activities
I have slight problems doing my usual activities
I have moderate problems doing my usual activities
I have severe problems doing my usual activities
I am unable to do my usual activities

PAIN / DISCOMFORT
I have no pain or discomfort
I have slight pain or discomfort
I have moderate pain or discomfort
I have severe pain or discomfort
I have extreme pain or discomfort

ANXIETY / DEPRESSION
I am not anxious or depressed
I am slightly anxious or depressed
I am moderately anxious or depressed
I am severely anxious or depressed

I am extremely anxious or depressed ❑

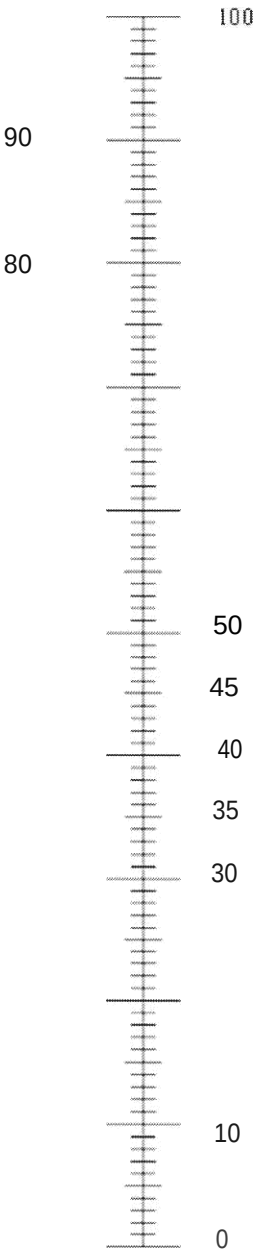
EuroQoL 5D-5L — continued

We would like to know how good or bad your health is TODAY. You will see a scale numbered from 0 to 100.

100 means the best health you can imagine 0
means the worst health you can imagine.
Please indicate on the scale how your health is TODAY.

YOUR HEALTH TODAY =

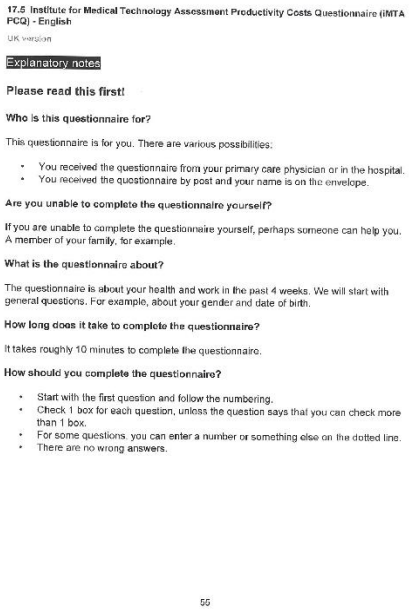
The best health you can imagine



The worst health you can imagine

Appendix 3 : IMTA productivity cost questionnaire (iPCQ)

English, Dutch and French versions available



17.5 Institute for Medical Technology Assessment Productivity Costs Questionnaire (iMTA PCQ) - English

UK version

Explanatory notes

Please read this first!

Who is this questionnaire for?

This questionnaire is for you. There are various possibilities:

- You received the questionnaire from your primary care physician or in the hospital.
- You received the questionnaire by post and your name is on the envelope.

Are you unable to complete the questionnaire yourself?

If you are unable to complete the questionnaire yourself, perhaps someone can help you. A member of your family, for example.

What is the questionnaire about?

The questionnaire is about your health and work in the past 4 weeks. We will start with general questions. For example, about your gender and date of birth.

How long does it take to complete the questionnaire?

It takes roughly 10 minutes to complete the questionnaire.

How should you complete the questionnaire?

- Start with the first question and follow the numbering.
- Check 1 box for each question, unless the question says that you can check more than 1 box.
- For some questions, you can enter a number or something else on the dotted line.
- There are no wrong answers.

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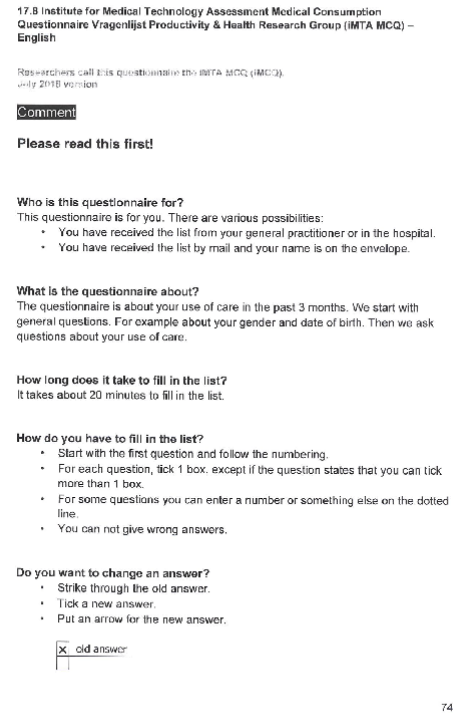
Appendix 4 : IMTA medical consumption questionnaire (iMCQ)

English, Dutch and French versions available



17.8 Institute for Medical Technology Assessment Medical Consumption Questionnaire Vragenlijst Productivity & Health Research Group (iMTA MCQ) – English

Researchers call this questionnaire the iMTA MCQ (iMCQ).
July 2018 version

Comment

Please read this first!

Who is this questionnaire for?
This questionnaire is for you. There are various possibilities:

- You have received the list from your general practitioner or in the hospital.
- You have received the list by mail and your name is on the envelope.

What is the questionnaire about?
The questionnaire is about your use of care in the past 3 months. We start with general questions. For example about your gender and date of birth. Then we ask questions about your use of care.

How long does it take to fill in the list?
It takes about 20 minutes to fill in the list.

How do you have to fill in the list?

- Start with the first question and follow the numbering.
- For each question, tick 1 box, except if the question states that you can tick more than 1 box.
- For some questions you can enter a number or something else on the dotted line.
- You can not give wrong answers.

Do you want to change an answer?

- Strike through the old answer.
- Tick a new answer.
- Put an arrow for the new answer.

x old answer

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