Title

A COVID-19 pandemic adapted framework for translation and cross-cultural adaptation of questionnaires on Quality of Life, disability, stigma, self-esteem, and wealth into Kinyarwanda using a mixed multistep approach with early involvement of patients living with epilepsy and healthy volunteers

Names protocol contributors

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Abstract

Background: Rwanda has a very high prevalence of epilepsy at 49 per 1000 and an important diagnosis and treatment gap has been observed. Understanding the contribution of influencing factors such as stigma and self-esteem, may provide better guidance to reduce this gap. However, in these low resource settings there is equally a data gap.

Access to structured scales and questionnaires offers an opportunity to standardize data collection and accelerate a broader use. Validated and cross-culturally adapted questionnaires in the endogenous language are pivotal. A solid cross-cultural translation process is critical to ascertain the face and content validity and precedes formal validation studies. This protocol provides the framework for the translation of validated scales on stigma, self-esteem, disability and (health-related-) Quality of Life, and wealth into Kinyarwanda with a methodology adapted to the COVID pandemic allowing remote collaboration and data collection.

Methods: This is a mixed forward-backward translation approach, broken down into three phases and nine steps. The process will be driven by an expert panel including the principal investigator, linguistic experts, physicians familiar with epilepsy, patients living with epilepsy, healthy volunteers, three forward translators and two back translators. In phase 1, a single reconciled forward translation is developed by the panel based on the forward translation from English to Kinyarwanda from three forward translators. In this phase, the panel also assesses the cultural content validity of the proposed forward translation. In phase 2, an independent group of volunteers performs a comparability/similarity assessment of two English back translations against the respective original version. In case of inconsistencies, the panel reviews and adapts the reconciled forward translation. In phase 3, the panel approves the final versions in Kinyarwanda after assessing the output of in-depth interviews of patients, volunteers and physicians. The protocol allows for repetition of steps as needed based on outcomes of previous steps.

Discussion: Cross-culturally adapted, translated scales will enable measurement of different influencing

factors of epilepsy in Rwanda. Ultimately, disentangling the relationship between epilepsy and its related disability, depression, stigma and self-esteem, will inform public health interventions to address the most important factors and close the treatment gap.

Trial registration: ISRCTN17123528, retrospectively registered

Keywords

WHOQOL-BREF, QOLIE-10P, cross cultural adaptation, Kinyarwanda, Translation

Administrative information

Note: the numbers in curly brackets in this protocol refer to SPIRIT checklist item numbers. The order of the items has been modified to group similar items (see http://www.equator-network.org/reporting-guidelines/spirit-2013-statement-defining-standard-protocol-items-for-clinical-trials/).

Title {1}	A COVID-19 pandemic adapted framework for an international collaboration on cross-cultural translation of questionnaires on Quality of Life, disability, stigma, self-esteem, and wealth into Kinyarwanda using a mixed multistep approach with early involvement of patients living with epilepsy and healthy volunteers
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Introduction

Background and rationale {6a}

Epilepsy is a chronic neurological disorder that results in a substantial disease burden on patients, their families and the society.(1, 2) Of the estimated 70 million. The incidence, prevalence and disease burden associated with epilepsy are highest in low- and middle-income countries, accounting for 80% of people living with epilepsy (PwE) globally.(3, 4)

Rwanda has a very high prevalence of epilepsy estimated of 49 per 1000 and an important treatment gap (encompassing diagnosis and treatment) of epilepsy and its comorbidities has been observed in different Rwandan regions.(5) In rural areas, the epilepsy diagnosis gap amounts to 62.5% and the total treatment gap amounts to 91.4%. For depression, only 1% of PwE in rural areas is diagnosed with depression in clinical practice, compared to observations of depressive symptoms in 48% and 63% of PwE in a rural Rwanda setting and an Indian hospital setting, respectively.(6, 7) A more profound understanding of possible influencing factors may provide better guidance to close this gap.

A recent psychosocial model demonstrated the complex relationship between a condition, resulting disability, depression, stigma, and self-esteem.(8) The stigma of chronic conditions can create depression on one hand and lower self-esteem on the other.(9-11) Furthermore, it has been shown that depression and self-esteem are interconnected.(12) Ultimately disentangling the different determinants that affect disability, depression, stigma and self-esteem, will inform public health interventions and allow a focus on the most impactful factor.

Several interventions addressing depression, stigma and reintegration of PwE in their communities have proven effective.(10)

Validated and reliable scales and questionnaires in the endogenous language are primordial to drive this research in a low-resource setting. During the translation process, it is crucial to ascertain the face validity and content validity before moving to validation studies. Face validity ascertains whether “on its face” the version in the new language seems like a good translation of the construct (comparability). Content validity refers to the operationalization of the translation against the relevant content domain for the construct (similarity).

This protocol provides a framework for the translation of different validated scales addressing to measure and quantify stigma, self-esteem, disability, wealth, and (health-related-) Quality of Life for use in Rwanda, with a methodology adapted to the COVID pandemic allowing remote collaboration and data collection.

Objectives {7}

To translate of scales related to disability, (HR-)QoL, self-esteem and economic evaluation into a Kinyarwanda version, using a mixed multistep approach to ensure face validity (comparability) and content validity (similarity):

A) Quality of Life, Health-Related Quality of Life and Disability
    a. WHOQOL-BREF: World Health Organization Quality of Life – brief version
    b. QOLIE-10P: Quality of Life in Epilepsy -10P
    c. WG-SS: Washington Group – Short Scale

B) Stigma
    a. ESS: Epilepsy Stigma Scale

C) Self-esteem
    a. RSE: Rosenberg self-esteem questionnaire

D) Economic evaluation and wealth
    a. EquityTool

Trial design {8}

This is an international collaboration, single-center study using a mixed approach of an expert panel combined with forward and backward translation in a multistep process focused on face validity and content validity through early patient involvement, adapted from guidelines for the process of cross-cultural adaptation of self-report measures.(13)

The process will be driven by the principal investigator, assisted by an expert panel composed of a linguistic expert, medical doctors, two patients living with epilepsy, two healthy volunteers, three forward translators and

two back translators. The task of the panel is to approve intermediate deliverables at each phase in the study, discuss discrepancies of forward and backward translations and the backward translation comparative study. It is ultimately accountable for the final versions in Kinyarwanda after assessing the input of the prefinal interviews from PwE, VOLUNTEER and HCPs.

The multistep process including forward translation, backward translation, translation validity testing and in-depth interviews is summarized in table 1, broken down into 3 phases and 9 steps. Step 3, 4 and steps 7, 8, 9 may be reiterated based on assessment outcomes.

Phase 1 : Forward translation						
		Step	***Action/Intervention***	***tool***	***Deliverable***	***Who***
	1	***FT translation***	Translation English to Kinyarwanda		FT1 and FT2 Kinyarwanda version	FT1, FT2 and FT3
	2	***FT1, FT2 and FT3 reconciliation***	Panel evaluates FT1, FT2 and FT3	consensus	reconciled FT Kinyarwanda version (rFT)	FT1, FT2, FT3, expert 1, expert 2, moderator, PI, PwE, HV
	3	***rFT version evaluation***	content validity assessment using CASI	content validity questionnaire	content validity index for items and scales	FT1, FT2, FT3, expert 1, expert 2, PwE, HV
	4	***final FT creation***	Panel evaluates CVI assessment of rFT version	consensus	final FT version	FT1, FT2, FT3, expert 1, expert 2, moderator, PI, PwE, HV
Phase 2 : Backward translation						
	5	***BT translation***	Translation		BT1 and BT2 Kinyarwanda version	BT1 and BT2
	6	***OV vs BT1 and OV vs BT2 assessment***	CASI assessment	comparability/similarity questionnaire	comparability/ similarity scores by item	HV
	7	***Prefinal version creation***	Panel evaluates BT 1 and BT2, identifies differences based on similarity assessment, discusses between translators	consensus	Kinyarwanda prefinal version	FT1, FT2, FT3, BT1, BT2, expert 1, expert 2, moderator, PI, PwE, HV
Phase 3 : prefinal version testing						
	8	***prefinal version evaluation***	Complete Kinyarwanda prefinal version followed by CAPI (PwE/HV) or CASI (HCP)	in depth interviews, CAPI assisted and HCP CASI questionnaire	single item observations	PwE, HV, HCP
	9	***prefinal version evaluation***	Panel evaluates early testing and integrates feedback in prefinal version. May request repeat testing of second prefinal version signs off and reiterate this process. Signs off on final version	consensus	final version	FT1, FT2, FT3, BT1, BT2, expert 1, expert 2, moderator, PI, PwE, HV

Figure 1: study diagram

FT= forward translation; BT= Backward translation; FT1 = forward translator 1; FT2 = forward translator 2; FT3 = forward translator 3; BT1= Backward translator 1; BT2 = Backward translator 2; PI = principal investigator, PwE = patient with epilepsy; HV = healthy volunteer, HCP= healthcare professional; CAPI= computer assisted personal interview; CASI= Computer-Assisted Self Interviewing; OV= original version

Step 1: Forward Translation: three forward translators provide translation from English to Kinyarwanda of all items, including response options.

Step 2: Forward translation reconciliation: the expert panel creates a single Kinyarwanda translation based on the forward translations from step 1, reviews and approves the version

Step 3: Content Validity Assessment: the expert panel assesses all items of each questionnaire in terms of relevance both conceptually and culturally, using a content validity questionnaire

Step 4: Final Forward translation: the expert panel reviews the content validity indices by item and by the scale and discusses items that perform weakly, amend as necessary and approve the final forward translation versions after review.

Step 5: Back-translation: two back translators provide translation from Kinyarwanda to English of all items, including response options.

Step 6: comparability/similarity assessment: both English back translations are compared to the original English version for comparability/similarity using a comparability/similarity questionnaire

Step 7: prefinal version creation: the expert panel, including back translators, discuss the results of the back translations and amend the Kinyarwanda versions as needed. In case of major changes, steps 5-7 are repeated.

Step 8: prefinal version testing: early patient, healthy volunteer, and HCP testing to assess problems in understanding of items and response categories, possible pitfalls

Step 9: Final version creation: expert panel review of the prefinal testing with possible amendments. Approval of the final versions after review. Final versions will then proceed in a validation study, defined in a different protocol.

Methods: Participants, interventions and outcomes

Study setting {9}

This is a single center study at the CARAES Neuropsychiatric Hospital (Kigali, Rwanda), a tertiary referral center for neurology and psychiatry. Enrolment logs will be kept at the site trial master file.

Interviewers for CAPI will be recruited among the hospital staff. CAPI will be performed at the site. CASI will be performed online. Data collection will be digital through CAPI and CASI in all steps, using the Kobotoolbox.

Panel meetings will be organized online as video meetings as a collaboration between investigators from the CARAES Neuropsychiatric Hospital, Kigali, Rwanda and University Hospital of Ghent, Belgium, translators possibly residing outside of Rwanda.

Eligibility criteria {10}

Study participants

Expert panel members

Experts and panel members will be selected upon recommendation of the principal investigator, the lead site investigator and the clinical trial assistant. Final approval is provided by the principal investigator upon review of their qualifications as outlined under eligibility criteria.

Translators will be selected according to the required competences and may have a residence outside of Rwanda or Belgium. Three forward translators will be selected: a professional translator, a translator without exposure to clinical practice or medicine and a translator familiar with the use of questionnaires. Two backward

translators will be selected: a translator without exposure to clinical practice or medicine and a translator familiar with the use of questionnaires.

Patients, healthy volunteers and healthcare professionals

During the projects patients, healthy volunteers and healthcare professionals will be enrolled with different roles: two PwE (A) and two volunteer (B) to be included in panel discussions. Volunteers (C) will be enrolled for assessment of similarity/comparability of the original version (OV) and Backtranslations (BT1 and BT 2). For early testing of the prefinal version, PWE, volunteer and healthcare professionals each will be recruited.

Interviewer for prefinal version testing at center of Ndera:

Inclusion criteria

1. Having attended a pre-interview training on use of questionnaire, probing questions and reporting of verbal comments
2. Understanding of purpose, procedures and methods of all questionnaires

In case of doubt regarding inclusion/exclusion criteria, a consensus between PI and lead investigator Ndera will be reached through phone conversation.

Eligibility criteria

A) PwE (N=2) included in panel discussions

Inclusion criteria

1. definite clinical diagnosis of epilepsy, defined as two epileptic seizures, unprovoked, with a minimum interval of 24 hours
2. able to read self-administered questionnaires and able to write
3. bilingual English and Kinyarwanda, preferably trilingual French, English, Kinyarwanda
4. able to attend/complete computer assisted personal interviewing
5. willing to attend videoconferencing and CASI
6. ≥ 18y of age
7. providing signed informed consent

Exclusion criteria:

1. presence of cognitive deficit hampering interview, comprehension of questions
2. presence of neurological deficit that hinders answering of questions, reading or understanding
3. presence of hallucinations, psychosis

B) HVs (N=2) included in panel discussions

Inclusion criteria

1. able to read
2. ≥ 18y of age
3. willing to attend videoconferencing and CASI
4. provide signed informed consent

Exclusion criteria:

1. presence of any medical condition unless treatment provides total symptom control for at least 6

months or unless judged healthy by the enrolling investigator
2. presence of cognitive deficit, possibly hampering participation or reading, understanding or answering of questions,
3. presence of hallucinations, psychosis

C) volunteers (N=30) for similarity/comparability assessment of original version (OV) and Backtranslation (BT)

Inclusion criteria

1. Fluent in English
2. able to attend/complete CASI
3. ≥ 18y of age
4. providing signed informed consent

Exclusion criteria:

1. presence of physical condition hampering reading, understanding or answering
2. presence of hallucinations, psychosis

D) Patients (N=5) for testing of prefinal version

Inclusion criteria

1. definite clinical diagnosis of epilepsy, defined as two epileptic seizures, unprovoked, with a minimum interval of 24 hours
2. able to understand and respond to questionnaire
3. ≥ 18y of age
4. provide signed informed consent

Exclusion criteria:

1. presence of cognitive deficit hampering interview, comprehension of questions
2. presence of neurological deficit that hinders answering of questions, reading or understanding
3. presence of hallucinations, psychosis

E) Healthy Volunteers (N=5) for testing of prefinal version

Inclusion criteria

5. able to understand and respond to questionnaire
6. ≥ 18y of age
7. provide signed informed consent

Exclusion criteria:

1. presence of any medical condition unless treatment provides total symptom control for at least 6 months or unless judged healthy by the enrolling investigator
2. presence of cognitive deficit, possibly hampering participation or reading, understanding or answering of questions,
3. presence of hallucinations, psychosis

F) Healthcare Profession (N=5) for testing of prefinal version

Inclusion criteria

1. ≥ 18y of age
2. Board certified healthcare professional in Rwanda
3. Fluent in Kinyarwanda
4. provide signed informed consent

Exclusion criteria:

1. presence of any medical condition unless treatment provides total symptom control for at least 6 months or unless judged healthy by the enrolling investigator
2. presence of cognitive deficit, possibly hampering participation or reading, understanding or answering of questions

Who will take informed consent? {26a}

All study participants, including the panel members will sign an informed consent.

In particular, patients, healthy volunteers and healthcare professionals participating in different steps will be enrolled:

A) Two patients and two healthy volunteers included in expert panel. Informed consent will be obtained by principal investigator.

B) 30 volunteers for comparability/similarity assessment. Informed consent will be obtained by principal investigator.

C) Patients, healthy volunteers and physicians, 5 each, included in testing of prefinal version: Informed consent will be obtained by lead site investigator or co-investigator

A signed version of the informed consent will be stored at the study site.

Additional consent provisions for collection and use of participant data and biological specimens {26b}

Not Applicable

Interventions

Explanation for the choice of comparators {6b}

Not Applicable. This is not a comparative study.

Intervention description {11a}

A) Expert panel meetings

Experts, forward translators and backward translators as well as patients and HVs:

1. Participate in panel discussion for reconciliation of forward translation 1 (FT1) and forward translation 2 (FT2) into a single forward translation (rFT) version. Advice is sought on how to adapt differences in translations in a single version, from a face validity and content validity

perspective, taking into account the perspective of PwE.

2. Complete the scale content validity questionnaire for all Kinyarwanda rFT using CASI
3. Participate in panel discussion for reconciliation of the results of the comparability/similarity assessment of the two backward translations to the original English versions
4. Participate in panel discussion and provide input in reconciliation of prefinal version

B) similarity/comparability of English backtranslations and original versions

Volunteers (N=30) complete the similarity/comparability questionnaire for each Kinyarwanda backward translated scale using CASI

C) testing of prefinal version

Patients (N=5), healthy volunteers (N=5) and healthcare professionals (N=5) for testing of prefinal version

1. Patients and healthy volunteers complete the Kinyarwanda prefinal version, either self-administered using CASI, either healthcare professional administered, if applicable
2. Patients and healthy volunteers complete the in-depth interview for each Kinyarwanda forward translated scale using CAPI.
3. Healthcare professionals complete the Kinyarwanda prefinal version, either self-administered, either healthcare professional administered, if applicable to healthy volunteers
4. Healthcare professionals complete the content validity questionnaire for each Kinyarwanda forward translated scale using personal interview by investigator.

Criteria for discontinuing or modifying allocated interventions {11b}

At the request of participant, study participation can be interrupted as stated in the informed consent.

Strategies to improve adherence to interventions {11c}

Not Applicable

Relevant concomitant care permitted or prohibited during the trial {11d}

Any treatment for any ongoing condition will be continued during the study as per physician guidance.

Provisions for post-trial care {30}

Not Applicable.

Outcomes {12}

Outcomes of all steps of the translation process will be documented.

1. Translations will be collected in excel format, on a by item basis for all individual forward and

backtranslations as well as reconciled versions. Intermediate and final versioning of the questionnaires will be created reflecting the original format of the questionnaires.

2. Panel expert meetings: detailed minutes of the meetings will be compiled in a meeting report in Word format
3. Content validity assessment will be performed by CASI, using Kobo Tools. Data and calculations will be tabulated in excel format.
4. Content validity assessment will be performed by CASI, using Kobo Tools. Data and calculations will be tabulated in excel format.
5. Prefinal testing will be performed on paper and transferred into a Kobo Tools form
6. Demographic data are collected using Kobo Tools and transferred to an Microsoft Excel file. in case of paper-based collection, data will be single data entered in the Kobo Tool form.

Participant timeline {13}

Given the involvement of different study participants, different timelines apply for different groups

TIMEPOINT	enrolment	*FT1 and FT2 reconciliation into FT version*	*FT version evaluation*	*OV vs BT1 and OV vs BT2 assessment*	*BT version reconciliation*	*Patient/healthy volunteer evaluation*	*Final version sign off*
Possibly reiterative step?			yes	yes	yes	yes	
Eligibility screen	A,B,C,D,E						
Informed consent	A,B,C,D,E						
Demographics	A,B,C,D,E						
Epilepsy Characteristics	A,C						
Panel meeting		A,B			A,B		A,B
Complete questionnaires FT version			A,B				
CAPI assessment FT version			A,B				
Comparability/ similarity questionnaire				C			
Complete prefinal version						D,E,F	
Complete structured personal interviews						D,E,F	

Table 1: participant type by action
A= PwE included in panel discussions; B= HVs included in panel discussions, C= healthy volunteers (N=30) enrolled for assessment of similarity/comparability of OV and BT; D= PwE (N=5) for testing of prefinal version; E= Healthy Volunteers (N=5) for testing of prefinal version; F= Healthcare professionals (N=5) for testing of prefinal version

Sample size {14}

PwE and HC included in panel discussions

The number of patients is will account for 25% of the panel discussion for forward translation reconciliation and 20% for the backward translation and the final sign off expert panel meeting. The proportions result from calculation after composing the panel with required stakeholders and are not powered.

HVs (N=30) enrolled for assessment of similarity/comparability of OV and BT

Number of HVs has been recommended by Sperber et al(14)

PwE (N=5), HVs for testing of prefinal version

Number has been recommended in the literature as a minimal sample size.(13, 15)

Recruitment {15}

PwE and volunteers included in panel discussions

PwE will be recruited upon personal invitation by the lead site investigator, based on the profile required to participate in online meetings and discuss complex linguistic issues.

Volunteers will be recruited amongst members of the Rwandan Organization of Epilepsy, the Rwandan ILAE Chapter.

Volunteers for assessment of similarity/comparability of OV and BT

Volunteers will be recruited from the English classes, Kigali University

PwE and Healthy Volunteers for testing of prefinal version

PwE will be recruited, according to presentation in the Neurology outpatient clinic at the CARAES Neuropsychiatric Hospital, Ndera, Rwanda and after signing informed consent.

HVs will be recruited among persons accompanying PwE to the Neurology outpatient clinic at the CARAES Neuropsychiatric Hospital, Ndera, Rwanda.

HCPs for testing of prefinal version

HCPs will be recruited among the staff of the CARAES Neuropsychiatric Hospital, Ndera, Rwanda and amongst members of the Rwandan Organization of Epilepsy, the Rwandan ILAE Chapter.

Assignment of interventions: allocation

Sequence generation {16a}

Not Applicable

Concealment mechanism {16b}

Not Applicable

Implementation {16c}

Not Applicable

Assignment of interventions: Blinding

Who will be blinded {17a}

Not Applicable

Procedure for unblinding if needed {17b}

Not Applicable

Data collection and management

Plans for assessment and collection of outcomes {18a}

For the assessment and collection of outcomes, different forms will be used.

	intervention	***primary outcome***	***secondary outcome***
Kinyarwanda FT version evaluation	*Content validity questionnaire, using a Likert scale 1-4, 1= not relevant to 4 highly relevant*	*s-CVI/ave; s-CVI/UA; I-CVI (item level); proportion relevance*	*Identification of single Items with I-CVI below threshold*
OV vs BT1 and OV vs BT2 assessment	*CASI assessment similarity/comparability questionnaire using a 7-point likert scale*	*mean score for similarity and comparability by item**	*mean score on a 7-point Likert scale for interpretability by item **
Prefinal Kinyarwanda version evaluation testing with PwE, HV and HCP	*In depth interview assessing the Kinyarwanda prefinal version questionnaires using CAPI assessment*	*By item observations reported by each interviewee reflecting difficulty on understanding, item response options or emotional reactions*	*By item observations by the interviewer reflecting difficulty on understanding, item response options or emotional reactions*
Demographic data	*Demographic data form*	*Descriptive analysis*	

Table 2: assessment plans
CVI= content validity index; s-CVI/ave= scale-CVI/average; I-CVI= Item-CVI; UA= universal agreement score
** Any mean score ≥3 necessitates a formal review of the translation. Any mean score between 2.5 and 3 in the similarity column is also considered problematic and is reviewed for possible correction.*

A) CASI Tools

1. Form 1: for use in step 3: content validity assessment

	Response options			
Item	Not relevant	Somewhat relevant	Quite relevant	Highly relevant
how much does the following question/item relate to '*'?				

Table 3: form 1 – content validity questionnaire
(*) to be added, as per questionnaire construct: quality of life, disability, stigma, self-esteem, epilepsy

2. Form 2: for use in step 6: comparability and similarity of backtranslation

Please circle the response which most closely represents how you would rate the following pairs of items in terms of:
(A) Comparability of language (how comparable is the formal wording?) and
(B) Similarity of interpretation (would the paired items be interpreted similarly, even if the wording is different?).
Please circle only one response for (A) and one response for (B) for each pair of items.

original wording	back translated wording	(A) COMPARABILITY OF LANGUAGE
		EXTREMELY COMPARABLE 1 2 3 MODERATELY COMPARABLE 4 5 6 NOT AT ALL COMPARABLE 7
		(B) SIMILARITY OF INTERPRETATION
		EXTREMELY SIMILAR 1 2 3 MODERATELY SIMILAR 4 5 6 NOT AT ALL SIMILAR 7

Table 4: form 2 – comparability/similarity questionnaire

3. Form 3: for use in step 8: questionnaire for HCP

		strongly agree	agree	disagree	strongly disagree
1	The questions were clear and easy				
2	The questions covered all the problem areas of (*)				
3	I would like the use of this questionnaire for future assessments				
4	The questionnaire lacks important questions regarding (*)				
5	Some of the questions violate subject's privacy.				

After completion of the overall scale content validity, please note below the item you have any remark on. Please elaborate your remark for discussion in the expert panel. Please indicate the class you experienced difficulty with.

Item number	Description of remark	Incorrect wording	Difficulty level	Response options	Other

(*) to be added, as per questionnaire construct: quality of life, disability, stigma, self-esteem, epilepsy
Table 4: form 3–questionnaire for HCP

4. Form 4: for use in step 8: content validity questionnaire for PwE/HV

Structured interviews after signed informed consent are conducted face to face by a trained interviewer, using CAPI.

The interviews are structured into three parts:

(a) demographic data collection

(b) the respondent completes the questionnaire using CAPI

(c) the cognitive interview, in which the researcher review the questionnaire with the study participant, question by question, inquiring about any points that might have generated difficulties or were unclear while completing the questionnaire and at the same time, assessing the respondent's comprehension of the questions.

The interviewer will complete the questionnaire below, adapted from Tsang et al:(16)

please indicate your findings per item													
item number	did the subject understand/comprehend the item? Probing question: please tell me in your own words what this question was asking? What came to mind when reading this question?				did the subject request explanation of the item? From observation: did patient request additional information or seek clarification on an item?	did the subject experience any difficulty to answer? Probing questions: do you have any difficulty answering this question?			difficulty to answer? From observation: did the patient hesitate in his answer?	did the subject experience any emotional barrier to answer? Probing questions: do you have any emotional objection to answer this question?			difficulty to answer? Probing question: do you feel this item violates your privacy ?
	very good	good	poor	very poor	yes/no	no difficulty at all	some difficulty	a lot of difficulty	yes/no	no difficulty at all	some difficulty	a lot of difficulty	yes/no
1													
…													

Table 5: form 5–in-depth interview for patients and HVs

5. Form 5: demographics and baseline characteristics for any study participant

Family Name
First name
phone number
Emailaddress
Village
Sector
District
Province
date of birth
marital status (single, living together with partner, married, divorced, seperated, widower/widow, co-habitation with family or friends)
educational level (options: primary not started; primary not completed; primary completed; secondary completed; university/bachelor/master)
Profession/professional status
medical history trauma yes/no
medical history depression yes/no
medical history other mental health disorder yes/no
medical history infectious disease yes/no
medical history non-communicable disease yes/no
date of first seizure*
date of diagnosis of epilepsy*
time since last seizure*

current treatment for any condition (list generic names and indication)

Table 6: demographics

(*) for PwE only

Plans to promote participant retention and complete follow-up {18b}

A compensation will be provided for study subjects as following:

A= patients, included in panel discussions

Patients will receive compensation for participation in panel discussions and for completion of the measures and time dedicated to the CAPI assisted content validity questionnaire assessment, estimated at 24 working hours, or 3 working days in total. Remuneration will be provided according to function at time of enrolment and according to the function equivalent daily remunerations from the latest publication of the official gazette, Rwanda, https://www.minijust.gov.rw/.(17)

B= HVs (N=30) enrolled for assessment of similarity/comparability of OV and BT

HVs will receive compensation for participation for comparison of OV and BT1 and BT2, estimated at 3 working hours in total. Remuneration will be provided according to function at time of enrolment and according to the function equivalent daily remunerations from the latest publication of the official gazette, Rwanda, https://www.minijust.gov.rw/

C= PwE (N=5) for testing of prefinal version

PwE will receive compensation for completion of the measures and time dedicated to the content validity questionnaire assessment, estimated at 8 working hours in total or 1 working day in total.

In addition, they will receive reimbursement of transportation fee at the day of visit to the site. They will also receive remuneration for drinks and one hot meal at the site.

Remuneration will be provided according to function at time of enrolment and according to the function equivalent daily remunerations from the latest publication of the official gazette, Rwanda, https://www.minijust.gov.rw/

D= Healthy Volunteers (N=5) for testing of prefinal version

HVs will receive compensation for completion of the measures and time dedicated to the content validity questionnaire assessment, estimated at 8 working hours in total or 1 working day in total.

In addition, they will receive reimbursement of transportation fee at the day of visit to the site. They will also receive remuneration for drinks and one hot meal at the site.

Remuneration will be provided according to function at time of enrolment and according to the function equivalent daily remunerations from the latest publication of the official gazette, Rwanda, https://www.minijust.gov.rw/

Data management {19}

At end of study, all study related documents will be stored on a cloud server from the Sponsor.

Data collection

A) Forward translations

Forward translations will be exchanged between PI and translators (FT1 and FT2). Files will not be encrypted and exchanged by email.

B) Panel meeting minutes
Panel meeting minutes will be taken by the assigned person. Panel meeting minutes will be documented in MS Word. Meeting minutes will contain detailed analysis and methods of data analysis. Files will not be encrypted and exchanged by email to participants to the meeting.

C) panel member FT testing and content validity questionnaire testing
This step will be CAPI assisted, supported by a questionnaire developed using the KOBO toolbox. Data collection will be performed on the KOBO toolbox platform, https://www.humanitariandatasolutions.com/
Files are encrypted on the platform and only accessible to the CAPI organizer

D) Backward translations
Backward translations will be exchanged between PI and translators (BT1 and BT2). Files will not be encrypted and exchanged by email.

E) Comparability/similarity testing
This step will be CAPI assisted, supported by a questionnaire developed using the KOBO toolbox. Data collection will be performed on the KOBO toolbox platform, https://www.humanitariandatasolutions.com/
Files are encrypted on the platform and only accessible to the CAPI organizer

F) Patient and HV prefinal version testing
Patient and HV prefinal testing and interview will be performed using pencil and paper. Data will be entered into an electronic database using the KOBO toolbox platform, https://www.humanitariandatasolutions.com/
Files are encrypted on the platform and only accessible to the CAPI organizer

Data Entry:
Data from patient and HV prefinal testing and interview will be entered into an electronic database using the KOBO toolbox platform. After single data entry, a check on 10% of datapoints (estimated at 150 datapoints) will be performed.

Data analysis:
A statistical analysis plan will be created before end of data cleaning.
Data subject to statistical analyses are:

1. Demographic data and epilepsy characteristics, as applicable for descriptive statistics.
2. Data from Comparability/similarity testing: descriptive statistics of comparison of the mean scores of each item score.
3. Data from patient and HV completion of the prefinal version according to each questionnaire scoring system, for detection of differences between patients and HVs and for early testing of construct validity

Data checks:

Some questionnaires (e.g. RSE) contain negative and positive questions. In case the order for answering is not respected (e.g. maximum scores for negative AND positive questions), the participants data will not be considered for any of the questionnaires.

Confidentiality {27}

A= Patients included in panel discussions

Patients will have a crucial role in the early development stage. An enrolment log, anonymizing patient data, will be kept with name and contact details at the study site. Patients will be offered the possibility to be acknowledged in the acknowledgement section of relevant publications, which will lift the anonymity of the participant.

B= HVs (N=30) enrolled for assessment of similarity/comparability of OV and BT

An enrolment log, anonymizing patient data, will be kept with name and contact details at the study site.

C= PwE (N=5) for testing of prefinal version AND D= Healthy Volunteers (N=5) for testing of prefinal version

PwE and HVs will have a crucial role in the late development stage. An enrolment log, anonymizing PwE and HV data, will be kept with name and contact details at the study site.

Plans for collection, laboratory evaluation and storage of biological specimens for genetic or molecular analysis in this trial/future use {33}

Not Applicable

Statistical methods

Statistical methods for primary and secondary outcomes {20a}

Demographics and Epilepsy characteristics will be analyzed using descriptive statistics only.

Step 3: content validity assessment

Data from the content validity questionnaire will be analyzed as follows:

a. conversion of Likert scale responses to ‘0’ and ‘1’. Scores ‘not relevant =1’ and ‘somewhat relevant = 2’ will be converted to ‘0’ and scores ‘quite relevant =3’ and ‘highly relevant = 4’ will be converted to ‘1’
b. content validity by item calculations on converted scores (Table 6)

The CVI indices Definition Formula			
abbreviation	definition	description	formula
I-CVI	item-level content validity index	The proportion of content experts giving item a relevance rating of 3 or 4	(agreed item)/ (number of expert)
item S-CVI/Ave	scale-level content validity index by items	The average of the I-CVI scores for all items on the scale	(sum of I-CVI scores)/(number of item)
expert S-CVI/Ave	scale-level content validity index by expert	The average of proportion relevance judged by all experts.	(sum of proportion relevance rating)/ (number of expert)
proportion relevant	proportion relevance	proportion relevant is the average of relevance rating by individual expert.	
UA	Universal agreement score	Universal agreement (UA) score is given as 1 when the item achieved 100% experts in agreement, otherwise the UA score is given as 0.	
S-CVA/UA	scale-level content validity index based on the universal agreement method	The proportion of items on the scale that achieve a relevance scale of 3 or 4 by all experts. Universal agreement (UA) score is given as 1 when the item achieved 100% experts in agreement, otherwise the UA score is given as 0.	(sum of UA scores)/(number of item)

Table 7: content validity definitions, descriptions and calculations

Step 6: Data from Comparability/similarity testing:

a. descriptive statistics of comparison of the mean scores of each item.
b. By item individual scores on the 7-point Likert scale indicating ' EXTREMELY COMPARABLE/SIMILAR (score 1)' to 'NOT AT ALL COMPARABLE/ SIMILAR (score 7)': any individual score of 6 or 7 will trigger a formal review of the translation
c. Mean score of each item on comparability/similarity: Any mean score ≥3 (7 is worst agreement; 1 is best agreement) necessitates a formal review of the translation. Any mean score between 2.5 and 3 in the interpretability column is also considered problematic and is reviewed for possible correction.
d. By item analysis for differences on agreement: any difference > 3 will trigger a formal analysis of the translation.

Data from early patient, HV and HCP testing:

e. Total scores of questionnaires: questionnaire sum score from PwE and HV
f. For HCP testing: analysis of usability for each questionnaire
g. For patients and HV: by item analysis of individual scores.
h. Given the low number of study participants, we will address in the panel discussion any item that does not have any congruent positive score defined as 'totally agree' or 'agree' compared to any negative score defined as 'disagree' or 'totally disagree'. We will also address those non-continuous items that collected an answer 'no' on >50% of patients.

Data checks:

Some questionnaires (eg RSE) contain negative and positive questions. In case the order for answering is

not respected (eg maximum scores for negative AND positive questions), the participants data will not be considered for any of the questionnaires completed.

Interim analyses {21b}

As this is a stepwise approach design, analyses as outlined above will be conducted at the specific timepoints and may trigger repeat sequences of evaluation and repeat analysis until desired congruence levels are achieved. These analyses are not considered interim analysis as they are phase/step related.

Methods for additional analyses (e.g. subgroup analyses) {20b}

Not Applicable

Methods in analysis to handle protocol non-adherence and any statistical methods to handle missing data {20c}

Missing data from questionnaire on comparability/similarity will not be imputed. Statistical analysis will be conducted on the number of responses obtained.
Missing demographic data will not be imputed except for unknown day or month of birth. They will be imputed to 01 and Jan respectively.
Missing data on epilepsy characteristics will not be imputed, but every attempt will be made to obtain these data from paper medical records and electronical medical records, if any.

Plans to give access to the full protocol, participant level-data and statistical code {31c}

Requests for full protocol and anonymized participant data need to be submitted to the principal investigator, Peter Dedeken, MD (peter.dedeken@ugent.be), and will only be disclosed after approval by the study team. Notice of approval status will be provided within 14 of first confirmed reading of the request.

Access to statistical code, only applicable to the PwE and HV prefinal version testing stage, will only be granted upon approval of the validation of the respective measure. Requests for statistical code need to be submitted to the principal investigator, Peter Dedeken, MD (peter.dedeken@ugent.be), and will only be disclosed after approval by the study team. Notice of approval status will be provided within 14 of first confirmed reading of the request.

Oversight and monitoring

Composition of the coordinating centre and trial steering committee {5d}

Not Applicable

Composition of the data monitoring committee, its role and reporting structure {21a}

This study does not have a data monitoring committee. No longitudinal follow-up is performed.

Adverse event reporting and harms {22}

We do not anticipate adverse events for study participants.
Sense of a possible breach of personal space/privacy by the questionnaires is addressed in the content validity questionnaire.

Possible indirect costs such as loss of economic activity, are compensated through the remuneration as stipulated above.

Frequency and plans for auditing trial conduct {23}

No longitudinal follow up is planned. The stepwise approach with possible reiterative actions is self-controlling. Decisions on versions that allow protocol progress are taken through panel discussion agreement and are documented in reports.

Plans for communicating important protocol amendments to relevant parties (e.g. trial participants, ethical committees) {25}

The need for protocol amendments will be evaluated as per study conduct deviation and anticipated deviation. Major study conduct deviations will trigger a major protocol amendment which will be submitted to the EC for approval within 10 days of the first observation of a major planned or observed study conduct deviation. Minor study deviations will not trigger a protocol amendment and, if any occurring, will be added in case of major protocol amendments only.
After EC approval of the major protocol amendment, all investigators will be asked to countersign the new ICF and protocol, if applicable.

Dissemination plans {31a}

A) Publication plans:
   - The study protocol will be published in Trials, BMC, Springer Nature
   - The final versions of the questionnaires will be made available on the website of the CARAES Neuropsychiatric Hospital after additional validation.
   - Manuscript on the results of different steps as a learning for cross-cultural translation and adaptation

B) Communication to study participants
   Study participants will have access to the final versions of the questionnaires through the website of the CARAES Neuropsychiatric Hospital after additional validation.

Discussion

Trial status

Protocol version 2.2

Version date 27 Sep 2021

Planned start enrolment: 06 July 2021

Completed enrolment: 31 Dec 2021

Abbreviations

BT	Backtranslation
BT1	Backtranslation 1
BT2	Backtranslation 2
CAPI	Computer Assisted Personal Interview
CASI	Computer Assisted Self Interview
ESS	Epilepsy Stigma Scale
FT	Forward translation
FT1	Forward translation 1
FT2	Forward translation 2
FT3	Forward translation 3
HV	Healthy Volunteer
HCP	Healthcare Professional
ESS	Epilepsy Stigma Scale
OV	Original Version
PwE	Patient living with epilepsy
QOLIE-10P	Quality of Life in Epilepsy, 10 item patient questionnaire
RSE	Rosenberg Self Esteem Scale
WG-SS	Washington Group Short Scale on disability
WHOQOL-BREF	World Health Organization- Quality of Life abbreviated questionnaire

Declarations

Acknowledgements

We acknowledge J. Umwiringirwa for her input on possible patient recruitment strategies.

Authors' contributions {31b}

PD is the principal investigator. FS is the lead site investigator. DET and PAJMB are program supervisors PD conceived the study design. FS performed the feasibility assessment locally for execution and composed the local expert panel. PD led the protocol development, review and approval. All authors read and approved the final manuscript

Funding {4}

This study is supported by an unrestricted grant. The funder provides an unrestricted grant but does not have any role or authority in the study design, data collection and analysis, study conduct and management, decision to publish, or preparation of an abstract or manuscript.

Availability of data and materials {29}

Anonymized meeting reports of panel discussions will be available upon request to Peter Dedeken, MD (peter.dedeken@ugent.be) after completion of the final version for validation.
Data from VOLUNTEER and patients assessing BT and prefinal version, will be accessible upon publication of the validation studies of the respective measures/questionnaires.

There are no contractual obligations possibly limiting full data access.

Ethics approval and consent to participate {24}

IRB approval from the Ethical Committee of CARAES Neuropsychiatric clinic, Ndera, Kigali (Rwanda), has been obtained, with reference 025/CNEC/2021.

Written, informed consent to participate will be obtained from all participants

Consent for publication {32}

1. Purpose of the study

The purpose of this study is to create a Kinyarwanda translated version of different questionnaires, which have been created abroad for assessment of Quality of Life (QoL), disability, self-esteem, perceived stigma and self-esteem. The purpose in the future is to use these questionnaires in future research and clinical practice.
The translation of scales into Kinyarwanda is a multistep process which requires feedback from patients, healthy volunteers and physicians to ensure accurate translations. This project is an international collaboration between researchers from the University of Ghent (Belgium) and CARAES Neuropsychiatric Hospital, Ndera (Rwanda). Together with experts in epilepsy, linguistic experts and translators, we aim to provide highly accurate translated scales.

2. What will happen during the study and how the study will be conducted?

We recruit healthy volunteers, patients living with epilepsy and healthcare profession to participate in this study.
You participate as a: (tick which apply)
☐ Panel member with the role of patient or healthy volunteer: you are member of a panel with experts, forward translators and back translators, which convenes to reach consensus on the translation of scales

and signs off on intermediate and final versions. You commit to complete the initial forward translation version of the questionnaires and answer questions for each item using a computer assisted self-interview. You commit to attend all panel meetings and participate actively to achieve an optimal translation.

☐ Panel member with the role of expert: you are member of a panel with experts, forward translators and back translators, which convenes to reach consensus on the translation of scales and signs off on intermediate and final versions. You commit to attend all panel meetings and participate actively to achieve an optimal translation.

☐ Panel member with the role of translator: as a translator, you are responsible for timely delivery of forward translation or backtranslation. You are member of a panel with experts, forward translators and back translators, which convenes to reach consensus on the translation of scales and signs off on intermediate and final versions. You commit to attend all panel meetings and participate actively to achieve an optimal translation.

☐ Validator of English backtranslation: you agree to participate in a survey on similarity/comparability of English version of the questionnaires, using an online questionnaire for each item, called computer assisted self-interview

☐ Patient or healthy volunteer for testing of the prefinal version: You agree to complete prefinal version of the Kinyarwanda translated questionnaires. Second, you also agree to an in-depth interview for each item which will be conducted, called computer assisted personal interview.

☐ as a healthcare professional for testing of the prefinal version: you agree to an online questionnaire, called computer assisted self-interview, which assesses the content validity for each scale and user preference questions.

3. Study participation.

Your participation in this study is voluntary and you may choose to withdraw from participation at any time. You will not be penalized if you don't wish to participate in this study. Participation will have no effect on the medical care you receive.

4. Risks/Disadvantages.

The study doesn't require any invasive procedure. We do not anticipate any risks for patients participating in this study. If you have any health problem, please feel free to contact by phone the Principal Investigator Dr Fidèle SEBERA at (+250)788486102 or the president of ethic committee

5. Confidentiality.

Your data will be anonymised. Your data are analysed anonymously. An enrolment log will be kept at the study site of Ndera for 10 years, after which it will be destroyed.

The results of our research will be revealed as soon as they will be available.

6. Acceptation to participate

My questions about this study have been answered by …… (name of investigator).

I have read and I have understood my role in this study and I have heard that any time I want to withdraw I can do so without explanations and this has no impact to my health care.

Informed consent form

I……. (name) confirm that I have read (has been read to me) and I understand the provided information about the current study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.
I understand that my participation is voluntary, and I am free to withdraw at any time without my medical care or legal rights being affected.
I understand that relevant sections of my medical notes and data will be collected during the study. I give permission for relevant individuals to have access to my records.
I agree to take part in the above-mentioned study.

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Name of Participant Signature Date

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Name of the principal Investigator Signature Date

Competing interests {28}

PD received consultancy fees from UCB Pharma, Merck and Novartis.
PAJMB received speaker and consultancy fees from UCB Pharma, LivaNova, and Medtronic, and research grants from the same companies through his institution.
FS received an unrestricted educational grant from UCB S.A. (Brussels, Belgium) as part of the Corporate Societal Responsibility support provided to the neurology department of the CARAES neuropsychiatric hospital at Ndera, Kigali (Rwanda).

Authors' information (optional)

PAJMB (MD, PhD, Prof, FEAN) is president elect of the EAN and lead of the African activities of the EAN. He is promotor of several PhD projects in Rwanda.
DET was the head of the Corporate Societal Responsibility at UCB Pharma and has lead several educational projects in China, Myanmar, Rwanda, Democratic Republic of Congo, Mozambique and Madagascar
PD is a clinical neurologist, wanting to bring epilepsy in Africa out of the shadows. As a principal investigator, please feel free to contact him: peter.dedeken@ugent.be.
FS was the first neurologist in Rwanda and will lead a sub-Saharan African curriculum in Neurology.

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