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Project Protocol

Psychoeducation for patients with Bipolar Disorders in Rwanda

Project background

Mental health and neurological disorders constitute 13% of the global burden of disease(1). Alarmingly this burden has risen by 41% in the last 20 years(2). In 2016, 18.5 million years were lost to disability due to mental health problems in the African region. In comparison, the disease burden of infectious and parasitic diseases in Africa was 13.1 million years lost to disability that same year(3). Currently, three out of four people with mental health problems live in low- and middle- income countries, where fewer than 1 in 50 people with severe mental disorders receive evidence-based treatment and in most countries less than 1% of the annual health budgets is allocated to mental health(4–6). The situation has been called both a failure of humanity and one of the most neglected global health issues of our time by some of the leading experts within the field of global health(7).

Bipolar disorder (BD) is characterized by periodic episodes of elevated moods and depression, which co-occur with changes in activity or energy and is associated with cognitive, physical, and behavioural symptoms(8).

It is estimated that severe mental disorders (i.e. severe depression, BD, schizophrenia and other psychotic disorders) have a two to three times higher average mortality compared to the general population(9). Treatment rates for these disorders are low in low-and-middle-income countries (LMICs), where treatment gaps of more than 90% have been documented(10,11). This might explain why a considerable proportion – up to 50% - of individuals seeking care for mental disorders in Africa consult traditional and religious healers in their pathway to mental health care(12).
One of the major barriers in decreasing the treatment gap is the lack of human resources. In response to the shortage of health professionals, experts and WHO advocate that mental health care must therefore be delegated to non-specialist health workers, who are trained to deliver interventions for specific mental disorders(13,14).

In Rwanda, a Sub-Saharan country the size of Jutland and with around 12 million citizens, the total number of medical doctors specialized in mental health is 13 in the year of 2019. So far, no treatment guidelines on mental health disorders including BD exist in Rwanda. To date, there is no data on incidence, prevalence or prognosis for BD in Rwanda.

Rwanda's health care system is organized along the principles of the WHO on primary health care(15,16). Health Centres are the first point of contact for patients. These centres also coordinate all outreach and prevention activities held at the community level, carried out by Community Health Workers (CHWs). The next level of care is the 41 District Hospitals, which has a mental health department staffed by a permanent team of psychiatric nurses and a psychologist. At the top of the mental health care system there are two national referral hospitals. The Neuropsychiatric Hospital of Ndera and the Mental Health Department of Kigali Teaching Hospital (CHUK), where only Ndera Hospital provides inpatient care. Statistics from the 2017 annual report at Ndera Hospital and CHUK shows that the annual numbers of outpatient visits with a diagnosis of BD were 1710 and 700, respectively. No data on BD is available on district or community level.

The efficacy of psychoeducation as an add-on treatment to pharmacotherapy is well documented in the treatment of symptoms and in relapse prevention initiatives with respect to BD in western countries(17). Psychoeducation is believed to empower the patient to take an active role in the therapeutic process, thereby potentially reducing stigma, guilt, and

helplessness, as well as improving medical adherence and to engage caregivers(18). Yet, no studies on psychosocial interventions for BD have been conducted in a low-income country(19).

In September 2014, the outpatient clinic of the Mental Health Department of Kigali Teaching Hospital launched a psychoeducation program for BD. The manual for the program is entitled "Life Goals Program" (LGP) and was designed back in 1996 by Bauer and McBride(20). LGP is a manual-based structured group psychotherapy program centered on behavioural principles from social education and self-regulation philosophies. Nevertheless, the effect of the psychoeducation in Rwanda is unexplored and psychoeducation is not part of the standard treatment.

Given the enormous shortage of skilled mental health professionals in Rwanda the question that emerges is whether simple interventions such as psychoeducation could potentially be decentralized from the referral hospitals and be at least as effective and acceptable as those delivered by specialist health workers at the referral hospitals.

Project aim

The overall aim of the project is to determine the effect, feasibility and acceptability of psychoeducation for patients with BD in Rwanda at district level and referral-hospital level. Moreover, the study will explore current knowledge and practice of caregiving for individuals with BD among care providers in Rwanda.

Objectives and hypothesis

Specific objective 1: To collect descriptive data on inpatients at the only inpatient neuropsychiatric hospital in Rwanda as well as to collect data on the number of patients with BD receiving outpatient care at the referral hospitals in Rwanda. This descriptive information is crucial for understanding the service provision at the referral hospitals and the accessibility to intensive mental health care in Rwanda for patients with BD.

Hypothesis 1: We hypothesise that admission data and outpatient data will demonstrate a considerable unmet need for mental health in Rwanda.

Specific objective 2: To determine the feasibility, acceptability and effect of manual-based psychoeducation for patients with BD at the two national referral and teaching hospitals in Rwanda.

Hypothesis 2: We hypothesise that the psychoeducation at the top level of mental health care for patients with BD will improve outcomes.

Specific objective 3: To determine whether the establishment of a psychoeducation program for patients with BD at district level facilitated by district nurses, will be feasible and will show the same change over time as the psychoeducation provided by staff at hospital level.

Hypothesis 3: We hypothesise that psychoeducation conducted by district mental health nurses are feasible and will have a positive effect on patient outcome.

Specific Objective 4: To explore the perceptions and experiences with the mental health

system among patients with BD as well as their relatives to obtain information that can identify different treatment practices, and their efficacy including the use of traditional healers.

Hypothesis 4: We hypothesise that patients with BD may have sought help other places than in the health care system for reasons like accessibility, stigma and culture. Moreover, we assume that they did not receive formal and evidence-based treatment before reaching the tertiary level of the health system and that the use of psychosocial interventions was limited.

Specific Objective 5: To assess the experience, knowledge and practice of caregiving for individuals with BD among traditional and alternative healers (TAH), community health workers (CHWs) as well as the mental health nurses at the district hospital. The assessment will contribute to an understanding of the feasibility of providing treatment for patients at the district and community level.

Hypothesis 5: We hypothesise that TAH as well as religious leaders are willing to collaborate with the formal health system. Moreover, we hypothesise that the CHWs and nurses want to provide evidence-based care including psychoeducation for patients with bipolar disorder but may lack the knowledge and skills

Relevance

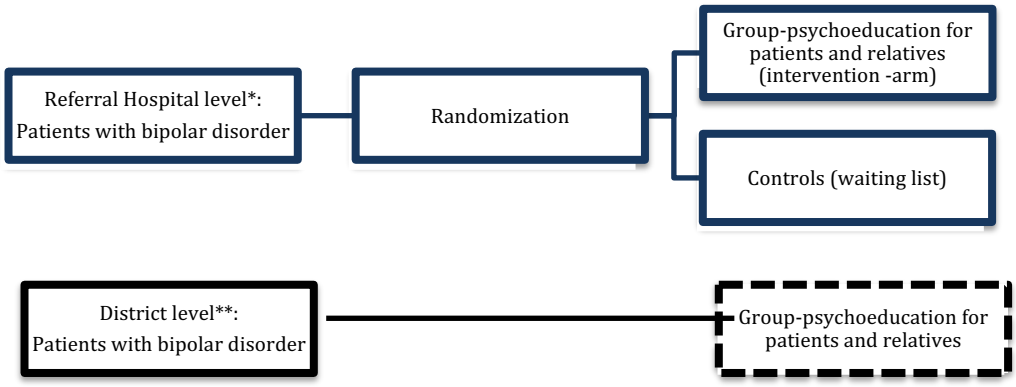
Facing the enormous treatment gap for mental health as well as the tremendous lack of human resources for health, there is an urgent need for evidence-based operationally well-documented innovations that are compatible with the realities at a population level in resource-constrained settings. Only a very limited number of studies in low- and middle-income countries have been conducted on severe mental disorders. This project is essentially this quest. Potential positive outcomes may be effected not just in Rwanda, but also in similar low-resource settings elsewhere. If proven successful, relevant next steps will include having the newly established research group expand its focus area to severe mental health disorders other than BD; or to conduct studies on the drug treatment of BD in low-income settings. Moreover, the project will serve to enhance local research capacity.

Study design

The study consists of **a quantitative part** and a **qualitative part.**

The quantitative part is divided into a prospective randomized controlled trial (RCT), and a district trial (Figure 1)

Figure 1: Project division



* A psychiatric nurse and either a psychologist or a psychiatric resident will conduct the psychoeducation.
** Two district mental health nurses will conduct the psychoeducation
___ RCT
-----The district trial

Participants

Inclusion criteria: A diagnosis of BD type I or II that meets DSM-V diagnostic criteria given by a trained psychiatrist and no episode in the preceding 4 weeks. Age ≥ 18 years.

Exclusion criteria: Exclusion criteria will be applied to obtain a sample reflecting the general patient population. The exclusion criteria include: Previous participation in any structured psychological intervention, such as psychoeducation or cognitive remediation, mental retardation, insufficient understanding of Kinyarwanda or deafness, alcohol or drug-dependence.

Intervention groups:

The RCT: Outpatients from the two-referral hospitals in Rwanda will be invited to participate and be allocated to intervention group or control group.

Intervention-arm: Manual-structured group psychoeducation. LGP is organized in two phases. Phase 1 of the LGP psychoeducation is mandatory and entails 8 sessions of 90 minutes over the course of 8 weeks (at one session per week) and has shown effect in western countries(21–23). Phase 2 will be offered after study completion. All groups will have 6-8 participants and two health professionals to conduct the sessions; a psychiatric nurse and either a psychologist or a psychiatric resident. Patients will be offered to invite their relatives for 2-3 psychoeducation-days for relatives.

Control group: Participants in the control group will be assigned to a waiting list and receive group-psychoeducation after the active intervention groups.

The district trial: This trial compares the impact of psychoeducation given at district level by district mental health nurses with the psychoeducation conducted at referral hospital (arm 1)

Randomization:

Study participants at the hospital level who meet the inclusion criteria and sign the informed consent form will be randomized individually into either intervention-arm or waiting list through block-randomization with a ratio of 1:1.

Patients at district level will not be randomized since we are unsure of the number of patients with BD at these levels fearing that the sample size will be too small. Instead all will be offered participation.

Outcome assessments:
All outcomes will be assessed at baseline, immediately post-intervention and at the 3rd and 6th month follow-up. The outcomes are based on the most commonly used measurements for trials on psychoeducation for individuals with BD in high and middle-income countries(18,19)
Baseline data: The Mini-International Neuropsychiatric Interview(24) will be used to confirm psychiatric diagnosis. Demographic information regarding the participants' living circumstances, past psychiatric history and mental health service use data will also be collected from interviews and patient files.
Primary outcomes: Relapse is defined as a new mood episode of mania (scores above or equal to 20 on the Young Mania Rating Scale (YMRS)(25)), hypomania (above or equal to 12 on the YMRS), or depression (above or equal to 17 on the Hamilton Depression Scale-17(HDRS-17(26)) or mixed episode (above or equal to 20 on the YMRS and 12 on the HDRS-17).
Secondary outcomes: The Clinical Global Impression (CGI-I /CGI-S) will be used for the clinicans to assess how much the participant's condition has improved. The Medication Adherence Rating scale (MARS) will be used to assess the adherence. All participants will fill in questions about self-stigma before and after the psychoeducation.
Tertiary outcomes: A seven-item questionnaire based on The theoretical framework of acceptability(27) will be used to access the acceptability of the intervention.

The Young Mania Rating Scale and The Medication Adherence Rating scale both needs to be cultural adapted and validated using a forward–backward translation, consensus conference and cognitive interviews (aprox. 15).

Sample size:
In the literature on group-psychoeducation, 13 out of 18 RCT's have reduction in general psychiatric symptom severity, incidence of relapse and hospitalization as main outcomes(18). We reviewed 18 RCT's on group psychoeducation for BD before we selected a study of Colom et al. as the base of our power calculation(18,28). The incidence of relapse in the study was (92%) (55 subjects) in the control group vs. 67% (40 subjects) in the psychoeducation group. For our study a sample size of 40 patients for each arm is required to achieve a level of 80% power with a 5% level of significance, when comparing the mean change in each intervention with the control arm via a two-sample t-test. Adjusting for a drop-out rate of 20%: 40/(1-(20/100))= 50 participants will be needed for each group.

Finally, for a one-year period, descriptive data on all inpatients with age > 18 years, discharged from Ndera the only inpatient psychiatric hospital, will be collected from files.

The qualitative part consists of three substudies. Each of the three substudies and their corresponding research question is outlined in Table 1, and the methodological approaches are described in further details in the following sections.

Table 1. Qualitative part

#	Substudy	Research question	Empirical data	Methods
1	**Patients**	What is the living experience of adults with bipolar disorder in Rwanda?	Semi-structured interviews (approx. 10-20)	Qualitative analysis
2	**Relatives**	How do relatives experience the mental health service system? What is the impact of caregiving on the caregiver and their living experince?	Semi-structured interviews (approx. 10-15)	Qualitative analysis
3	**Care providers**	What knowledge, experience and practice of caregiving for individuals with BD do health providers in Rwanda have? Are TAH and religious leaders willing to collaborate with the formal health system?	Focus groups (approx. 4)	Qualitative analysis

Semi-structured qualitative interviews with patients will be conducted using the methodological framework of phenomenology to explore their personal use and experiences of mental health care in Rwanda. Patients will be recruited from the group-psychoeducation program. Patients' relatives who sign up for psychoeducation-days for relatives will be asked if they want to participate in a semi-structured qualitative interview on the burden of caregiving.

Focus groups will also be conducted with CHWs as well as mental health nurses at different district hospitals and TAH and religious leaders. The interviews will be transcribed in their full length. Data will be analysed to explore the experience, knowledge and practice of treatment provided at district- and community level for patients with Bipolar Disorder.

Ethical Approval

The research protocol and study-related documents will be presented to the Rwandan National Ethical Committee (RNEC) for approval prior to study initiation. Informed consent will be obtained from participants after oral and written information.

A "twin model PhD project":

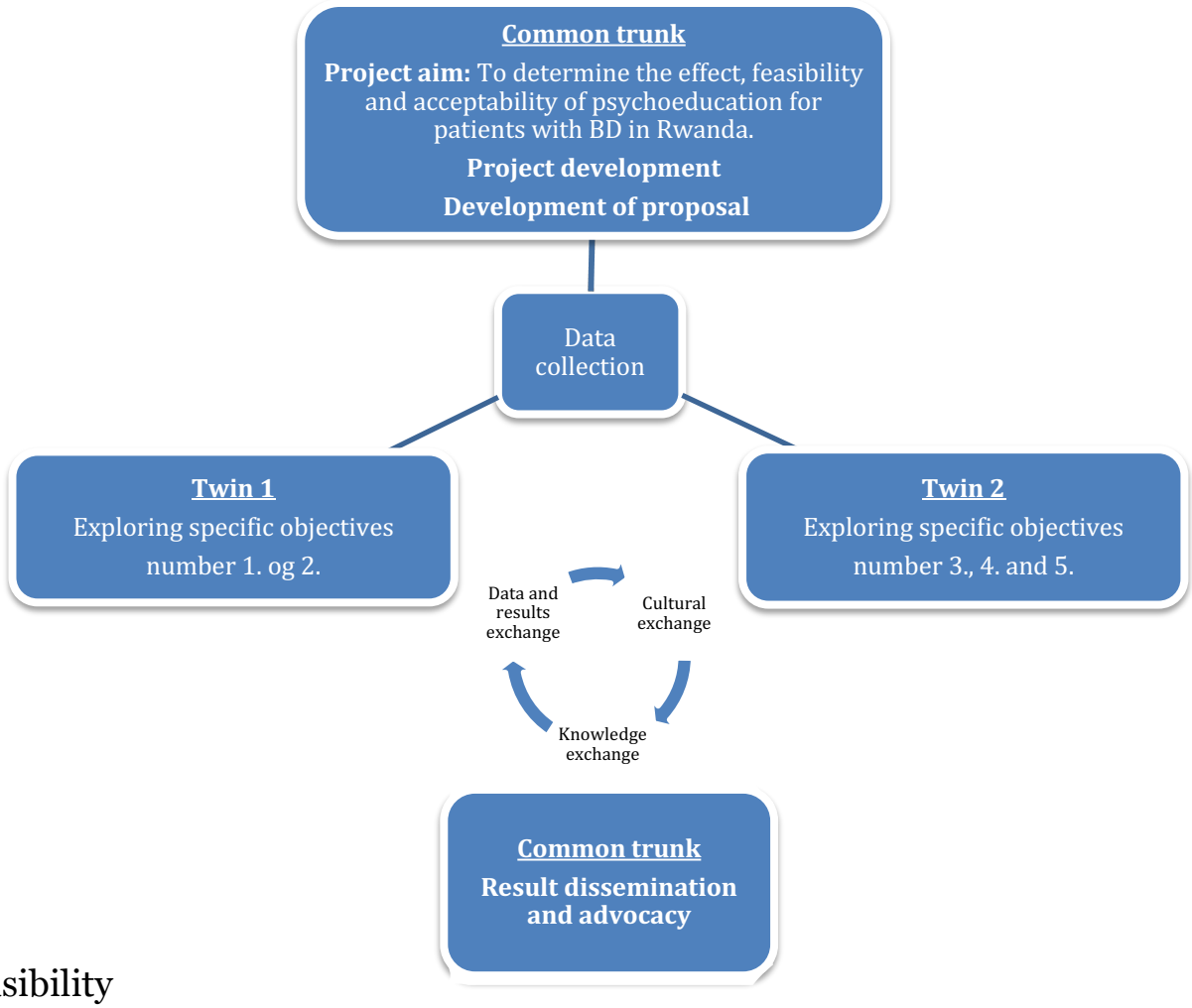
To ensure general capacity building extending further than our research team, we collaborate with a local partner institution in Rwanda – University of Rwanda. Furthermore, this research will be a 'twin model' PhD project(29) involving two PhD-students: Musoni Rwililza Emmanuel - a Rwandese psychiatrist and Caroline Juhl Arnbjerg-Nielsen – a Danish doctor. The twin model is based on the principles of local capacity building to ensure high scientific standards and participation by local stakeholders and prevents extractive research and scientific colonialism(29,30). This is in line with UN's sustainable development agenda, goal 17 on partnerships (31). The project will bring together three academic institutions in a partnership: Aarhus University (AU), University of Rwanda (UR) and Copenhagen University (Competence Centre for Transcultural Psychiatry).

Segregation of duties

The different tasks and responsibilities have been divided between the two PhD-students. Musoni Rwililza Emmanuel will mainly focus on psychoeducation at the district level and the qualitative part of the study (objective 3-4-5). Caroline Juhl Arnbjerg-Nielsen will be

responsible for the RCT and the data collection at the referral hospitals (objective 1-2). Figure 2 illustrates "The Twin PhD model" including the shared tasks and the division of responsibilities.

Figure 2: Twin-PhD-model and the segregation of duties



Feasibility

The intervention chosen – The Life Goal Programme (LGP) – is already adapted and used in a Rwandan setting. Moreover, statistics from the 2017 annual report from the two referral hospitals show that the annual numbers of outpatient visits with a diagnosis of BD were 1710 and 700 respectively, making it highly possible to include the required 150 participants from the referral hospitals. The research team is an interdisciplinary team comprised of professionals within the field of public health, transcultural psychiatry and psychology. The Rwandan PhD applicant holds professional experience in treating mental health patients in Rwanda as a trained psychiatrist; while the Danish PhD applicant has experience from DANIDA-related partnership projects in Rwanda.

Research plan and timetable

Our planned activities for the three-year project, starting in November of 2019, are presented in Table 2. We aim to initiate data-collection in the Summer of 2020.

Table 2. Activities of the three-year project.

Research activities	Year 1				Year 2				Year 3			
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
Development of the protocol and study related documents – applying for RNEC ethical approval												
Validate tools (YMRS and MARS)												
Development of focus-group questionnaire for caregivers												
Screening and enrolment of study participants for psychoeducation												
Follow-up												
Data collection on inpatients												
Data cleaning and analysis												
Authoring manuscripts												
Authoring dissertation												

Dissemination of research results

The project aims at directing research and policy attention towards mental health at the global, national and local level. For the dissemination of the outcomes of the project, we will: a) publish articles in scientific journals; b) present results at international scientific meetings and conferences; c) organise local meetings with key stakeholders during the full extent of the project.

Publications

The research project will result in several planned publications:

1. *A descriptive analysis of inpatients with mental health disorders in Rwanda*
2. *A randomized trial on the efficacy of group psychoeducation on recurrence, self-stigma and medication adherence in individuals with bipolar disorder in Rwanda*
3. *Caregiver burden in bipolar disorder: A study from Rwanda*
4. *Feasibility and impact of group psycho-education at district level on quality of life, recurrence, self-stigma and medication adherence in individuals with bipolar disorder in Rwanda*
5. *Knowledge, practices and attitudes towards bipolar disorder among traditional and religious healers in Rwanda.*
6. *Mental health professionals' perceptions of the use of traditional and alternative medicine in the care for patients with bipolar disorder in Rwanda.*
7. *Rwandan traditional and religious healers' perceptions towards western medicine.*
8. *Pathways to psychiatric care and treatment of patients with bipolar disorder in Rwanda.*

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