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A customized adherence enhancement program combined with long-acting injectable antipsychotic medication (CAE-L) for poorly adherent patients with chronic psychotic disorder in Tanzania: A pilot study methodological report

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ABSTRACT

Chronic psychotic disorders (CPDs) occur worldwide and cause significant burden including reduced quality of life and functional impairment. Care for CPD includes psychosocial and pharmacologic interventions (i.e. antipsychotic drugs) and ongoing health monitoring. This is challenging in resource-limited settings where staff are sparse and/or undertrained. Importantly, mental health human resource needs predict continued deficits compounded by increasing disease burden. A U.S. team recently developed and tested a CPD treatment approach that combines the use of long-acting antipsychotic medication (LAI) with a brief and practical customized adherence enhancement behavioral intervention (CAE-L). This report describes the methodological details of an ongoing, first-ever refinement and preliminary testing of CAE-L in poorly adherent patients with CPD in Tanzania. Additional innovative elements include: 1) a manualized curriculum that targets specific barriers and facilitators to medication adherence in Tanzanians with CPD, and 2) targeting known, high-risk individuals with CPD (those who miss ≥20% of prescribed antipsychotic medication). The study procedures are intended to pave the way for implementing a large-scale intervention trial for CPD in the Tanzanian setting. An important component of this project is capacity building to help form the next generation of care providers. Visit exchanges modeled on a successful NIH-funded Medical Education Partnership Initiative (MEPI) template will also use the U.S. and Tanzanian teams to share expertise, problem-solve, and plan iterative refinements of project deliverables. Taken together, this project has potential to advance the care of people with CPD in Tanzania and has high generalizability to Sub-Saharan Africa and other lower-resource settings.

1. Introduction

Chronic psychotic disorders (CPDs) such as schizophrenia and schizoaffective disorder occur worldwide and cause significant burden characterized by reduced quality of life, functional impairment and premature mortality due to suicide and other causes. Care for CPD includes both psychosocial and pharmacologic interventions (i.e. antipsychotic drugs) along with ongoing monitoring of health status (Patel, 2009). This may be challenging in resource-limited settings where staff are sparse and/or undertrained. Importantly, forecasts of mental health human resource demands predict continued deficits, compounded by increasing disease burden (Charlson et al., 2014).

Antipsychotic medication is a critical component of treatment for individuals with CPDs in conjunction with psychosocial approaches that support patients and families. Unfortunately, poor medication adherence is common, impedes recovery and increases burden. In Sub-Saharan Africa (SSA), poor adherence is seen in approximately half of individuals with CPD and is a major driver of relapse (Adeponle et al., 2009;

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Adewuya et al., 2009; Danladi et al., 2013; Ho Odo et al., 2014; Sariah et al., 2014). The need for effective adherence promotion approaches is extensive in SSA considering the common oral medication "stock-outs," (situations where the local medication supply has run out and hence not available at the hospital pharmacy), high-levels of stigma and limited resources to quickly intervene when individuals with CPD skip medication and begin to experience signs of relapse.

Because a major obstacle to medication adherence in CPD is difficulty with consistent medication routines (Gilmer et al., 2004; Sajatovic et al., 2011), long-acting injectable antipsychotic medication (LAI) can be an attractive treatment option for some individuals. LAI can be administered monthly or even less frequently, eliminating the daily need to take medications, which in itself can be a stigmatizing behavior (Jenkins et al., 2005). In a recent small study of patients and their caregivers conducted in Tanzania, it was identified that LAI alleviates psychotic symptoms and reduces relapse (Sariah et al., 2014). These types of drugs also make it easier for patients to adhere to the treatment regimen compared to oral antipsychotics.

While LAI can potentially improve medication treatment adherence, it is not a stand-alone care approach for CPD given the complex and long-term needs of people with CPD (Mueser et al., 2002; Zygmunt et al., 2002). Recent work by a team at Case Western Reserve University (CWRU) in Ohio, U.S.A. developed and tested a CPD treatment approach that combines LAI with a brief and practical customized adherence enhancement behavioral intervention (CAE-L) (Collins et al., 2018; Sajatovic et al., 2013). Given the availability and acceptability of LAI in Tanzania and positive U.S. outcomes findings in poorly adherent people with CPD, a combined team of Tanzanian and U.S. investigators is conducting a first-ever refinement and preliminary testing of CAE-L in poorly adherent patients with CPD in Tanzania. The overall concept for the project is that combining LAI with a behavioral approach targeted to patient-level reasons for poor adherence may modify long-term adherence behaviors and attitudes. This report describes the methodological details of the project. In addition to the novel focus, innovative elements include: 1) a manualized curriculum that targets specific barriers and facilitators to medication adherence in Tanzanians with CPD, and 2) targeting known, high-risk individuals with CPD (those who miss $\geq$20% of prescribed antipsychotic medication).

2. Methods

2.1. Overview

This 3-phase/3-aim 24-month project will refine and preliminarily test CAE-L for individuals with CPD in Tanzania. Aim 1/Phase 1 consists of an observational mixed-methods (quantitative + qualitative) assessment of reasons for poor treatment adherence among Tanzanians with CPD that will obtain information on medication adherence barriers in this setting and input from stakeholders (patients, family members, healthcare providers) on a preferred approach for optimizing adherence with evidence-based care. Aim 2/Phase 2 will develop a manualized, curriculum-driven customized adherence enhancement (CAE) approach to improve treatment adherence in CPD. Aim 3/Phase 3 will lay the groundwork that establishes a clinical trial infrastructure, adequately trained staff, and data tools/procedures preparatory to implementation of a future randomized controlled interventional trial. Commensurate with the priorities of Fogarty International/the U.S. National Institutes of Health, the project will also build critical research capacity intended to support future work in adherence promotion among highly vulnerable Tanzanians with CPD. All work is conducted consistent with local, regional and national ethical and human subjects regulatory approvals, Institutional Review Board (IRB) 05-17-16.

2.2. The CAE-L intervention

While many behavioral approaches for CPD are focused on helping individuals to engage and adhere with recommended treatments, the CAE-L approach is intended to identify and target the most common reasons for poor adherence in patients with CPD and standardize the intervention so that they could be delivered by a broad variety of healthcare providers consistently and quickly. Drawn from iterative pilot work (Jenkins et al., 2005; Sajatovic et al., 2013; Sajatovic et al., 2012a, b), the behavioral component of CAE-L is flexibly delivered as a series of up to 4 treatment modules whose use is determined based upon an individual's reasons for non-adherence (adherence barriers) identified at baseline. The modules are: 1) Psychoeducation focused on medication and consequences of missing medication; 2) Modified Motivational Enhancement Therapy (MET) to address non-adherence related to substance use; 3) Communication with Providers to facilitate appropriate treatment expectations and optimize management of feared or experienced side effects; 4) and Medication Routines intended to incorporate medication-taking into lifestyle. Prior to delivering CAE, adherence barriers are evaluated with two standardized measures, the Rating of Medication Influences (ROMI) (Weiden et al., 1994) and a slightly adapted version of the Attitudes toward Mood Stabilizers Questionnaire (AMSQ) (Adams and Scott, 2000; Harvey, 1991) which is focused on attitudes towards psychotropic drugs for CPD. CAE-L is intended to improve adherence with both LAI as well as any oral medications that individuals with CPD may be prescribed.

These investigators tested CAE-L in 2 preliminary U.S. studies. CAE-L Study 1 enrolled 30 homeless or recently homeless individuals with CPD (Sajatovic et al., 2013, 2016). Patients received monthly CAE combined with LAI (CAE-L) for 6 months. The LAI used was haloperidol decanoate, a first-generation LAI that is widely available in low-resource settings. Primary outcomes were medication treatment adherence and housing status. Secondary outcomes included psychiatric symptoms, functional status, side effects, hospitalizations and satisfaction with treatment. Mean sample age was 41.8 years (SD 8.6) with a high proportion of minorities (90% African-American) and single/never married individuals (70%).

Use of CAE-L was associated with good adherence to maintenance LAI (76% at 6 months) and dramatic improvement in concomitant orally prescribed medication, which changed from missing 46% of prescribed medication at study enrollment, to only 10% of prescribed medication at study end. Mean proportion of time in sub-optimal housing went from 56% in the 6 months prior to study enrollment to 41% in the first 3 months of the study and 14% in the last 3 months of the study ($p = .001$). There were significant improvements in psychiatric symptoms and functional status. Side effects were generally transient and mild to moderate in intensity. With respect to standardized involuntary movement and neurological rating scales, there were no significant changes except for in the Barnes Akathisia Scale (BARS) (Barnes, 1989) which reflected the emergence of akathisia.

CAE-L Study 2 was a 6-month prospective, uncontrolled trial of CAE-L in 30 recently homeless individuals with schizophrenia or schizoaffective disorder which also assessed medication adherence using the Tablets Routine Questionnaire (TRQ) (Adams and Scott, 2000; Peet and Harvey, 1991), CAE-L Study 2 refined the CAE-L approach by using social workers instead of PhD-level psychologists to deliver the behavioral intervention and used a second-generation antipsychotic drug (paliperidone palmitate) instead of a first-generation antipsychotic drug. LAI injection frequency and psychiatric symptoms measured by the Positive and Negative Syndrome Scale (PANSS) (Kay et al., 1987), Brief Psychiatric Rating Scale (BPRS) (Overall and Gorham, 1962) overall and global psychopathology (Clinical Global Impressions/CGI) (Guy, 1976). Extrapyramidal symptoms were measured with the Extrapyramidal Symptoms Scale-Abbreviated version (ESRS-A) (Chouinard et al., 1980). Social functioning was assessed via the Social and Occupational Functioning Assessment Scale (SOFAS) (Morosini et al., 2000). Mean age of the sample was 43.6 years (SD = 9.53), mainly minorities (86.7% African-American), single/never married (72.4%) with a mean of 11.55 years of education. Four individuals (13.3 %) terminated the study

prematurely. CAE-L was associated with good adherence to LAI (92.9%) and improved adherence in past-week TRQ ($p = .02$). There were significant improvements in PANSS ($p < .01$), BPRS ($p < .001$), CGI ($p = .003$) and SOFAS ($p = .005$). There were no significant changes on ESRS-A at 6-months.

2.3. Intervention site

The Department of Psychiatry at the Muhimbili National Hospital, is a 70-bed national referral hospital located in urban Dar es Salaam, Tanzania. It is the only psychiatric national referral center and serves a population of approximately 4.5 million. Patients are referred from 4 catchment zones that include 3 regional public and private hospitals. There is a large outpatient clinic that mainly serves follow-up discharged clients. Follow-up clinics are also held at the district level in 4 facilities; most are stable back-referrals from the National Hospital to clinics run by psychiatric nurses.

During 2015, there were 1,636 patients (combined inpatient and outpatient sample, 1,099 men (67.2%), 537 women) admitted to Psychiatry at Muhimbili National Hospital (MNH). Most of these patients lived within a 15-kilometer radius of the MNH clinics, a one to three bus commute which costs about US$1.20 round-trip. This is typical for urban and outlying zones of Dar es Salaam. Hospital discharge diagnoses were included schizophrenia (32.4%) and schizophreniform disorder (11%). The most commonly prescribed discharge medication was the oral version of the first-generation antipsychotic haloperidol (75% of patients). There were 16% treated with the LAI version of fluphenazine decanoate. Antipsychotic side effects were managed with trihexyphenidyl.

3. Study area

3.1. Phase 1 (Months 1–12)

In Phase 1/Aim 1 the investigators will implement a mixed-methods (quantitative + qualitative) adherence assessment battery that will identify salient barriers to treatment adherence in people with CPD defined as schizophrenia or schizoaffective disorder. Qualitative assessment will be conducted using a combination of individual and group-format methodologies. A "deliverable" of Phase 1 will be a summary report that describes barriers and facilitators to treatment for CPD from the perspective of patients, families and care providers.

3.1.1. Quantitative assessment

To better understand adherence barriers in the proposed setting, the ROMI and AMSQ will be administered to 100 individuals with CPD who self-report missing 20% or more of antipsychotic medication within the last month, an established benchmark for poor adherence (Velligan et al., 2010). Patients ages ≥18 with a clinical diagnosis of schizophrenia will be recruited from Muhimbili National Hospital and its associated ambulatory clinics.

Additional information will include demographic and clinical characteristics relevant to CPD relapse. Adherence assessments will include the Tablets Routine Questionnaire (TRQ) (Peet and Harvey, 1991; Scott and Pope, 2002) and the Drug Attitude Inventory (DAI) (Awad, 1993). CPD symptoms will be assessed with the Brief Psychiatric Rating Scale (BPRS) (Overall and Gorham, 1962). Global psychopathology will be measured with the Clinical Global Impressions (CGI) (Guy, 1976). Life and work functional status will be evaluated using the Social and Occupational Functioning Scale (SOFAS) (Morosini et al., 2000) and substance use will be measured with the Alcohol Use Disorders Identification Test (AUDIT) (Saunders et al., 1993) and Alcohol, Smoking and Substance Involvement Screening Test (ASSIST) (Group, 2002).

3.1.2. Qualitative assessment

The study team will conduct individual interviews of patients with CPD and focus groups with family members and with healthcare workers. The qualitative sample will be derived from Phase 1 quantitative survey participants and target a representative sample with respect to age and gender. Family members will be those of enrolled Phase 1 patients with CPD. Focus groups and interviews will use an adapted semi-structured guide used in NIH-funded trials conducted by this study team (Blixen et al., 2014, 2015, 2016). Consistent with the focus on broad generalizability to CPD in SSA, only individuals who are unable to provide informed consent will be excluded. Qualitative methods and thematic analysis will follow procedures outlined in previous work conducted by this team (Blixen et al., 2014, 2015, 2016).

3.1.3. Focus group format

Up to 16 adult (≥age 18) family members of individuals with CPD will be invited to participate in 2 focus groups. Family members will all have regular contact with patients (contact a minimum of 3 days/week). Family member focus groups will comprise 6–10 individuals each, and will last up to approximately 90 minutes. Focus groups will be audio-recorded and transcribed verbatim and supplemented with the addition of copious field-notes. Up to 16 health workers will be invited to participate in 2 additional focus groups, using a similar format as the family focus groups. Health workers (nurses, doctors, social workers, pharmacists) with experience interacting with patients with CPD will be recruited from clinic and hospital-based settings.

3.1.4. Individual interview format

Up to 15 patients with CPD will be interviewed regarding barriers and facilitators to medication adherence. Data recording will be the same as with focus groups.

3.1.5. Qualitative data analysis

First, the qualitative team will first independently review each transcript and highlight significant statements, sentences, or quotes. Based on review of the independently derived statements, the team will develop consensus-based "clusters of meaning" or relevant "themes and categories" (Esterberg, 2002). Researchers will further read/code each document independently and iteratively until no new insights emerge. These entries will be elaborated as coding progresses. The qualitative researchers will then construct a consensus-based coding dictionary that includes mutually exclusive definitions for each code. This coding structure will be reviewed after a preliminary analysis of a subsample of transcripts, and the dictionary will be refined through comparison, categorization, and discussion (Crabtree and Miller, 1999; Moustakas, 1994). Then, using data and codes, the qualitative team will create code-based files across all respondents. The team will further elaborate, refine, and differentiate the codes and identify similarities and differences through comparison of respondents.

3.1.6. Quantitative data analysis

Data management will be conducted using a secure online platform in concordance with approved data transfer agreement between the U.S. and Tanzanian institutions. We will conduct descriptive statistics to characterize demographic and clinical variables, including the number of barriers to adherence as represented by the number of CAE-L modules that individuals would be expected to require. Because gender differences have been documented in treatment adherence and other variables among patients with CPD (Abel et al., 2010), we will compare clinical characteristics of males and females in this sample using chi-square and two-tailed t-tests. Correlational analyses using Spearman correlations due to the non-normal distribution of lifetime hospitalizations and point-biserial correlations for dichotomous variables will be conducted to evaluate the association between TRQ and demographic and clinical variables as well as the relationship between lifetime number of psychiatric hospitalizations and demographic and clinical variables.

3.2. Phase 2 (Months 13–15)

In Phase 2/Aim 2, informed by the mixed-methods data from Phase 1, the study team will adapt the CAE-L intervention to be culturally and linguistically appropriate for the Tanzanian setting. The investigators will use a process of health promotion intervention development called "pooling and patching," in which they will pool the apparent effective elements of CAE-L with the identified barriers/facilitators from Phase 1 and, with professional judgement, then patch these pooled components create a new multi-component adherence-promotion approach. The "deliverable" of Phase 2 will include a manualized intervention that combines a psychosocial intervention to promote adherence + use of LAI.

3.3. Phase 3 (Months 16–24)

In Phase 3/Aim 3, the study team will select appropriate measures, train staff in measure implementation, and finalize CAE-L for delivery. As the second U.S. CAE-L study, social worker interventionists will be trained to deliver CAE-L. Finally, the study will roll out and evaluate CAE-L in 20 individuals with CPD in a 6-month (25-week) prospective training/proof-of-concept exercise. CAE-L will be further refined based upon input from interventionists and study participants. The "deliverable" of Phase 3 will include building capacity of a clinical trials infrastructure that includes identification of relevant tools/measures and appropriately trained staff who are capable and available to conduct research to improve health outcomes for people with CPD in Tanzania.

3.3.1. Study population

The study will enroll 20 adult patients $\geq$ age 18 with CPD who fit the same inclusion criteria noted in Phase 1. Eligible patients must agree to receive LAI and be able to participate in research activities. Exclusion criteria will include: 1) Individuals on LAI immediately prior to enrollment, or those with intolerance or resistance to LAI; 2) Medical conditions that would interfere with the patient's ability to participate in the trial; 3) Physical dependence on substances likely to lead to withdrawal reaction; 4) Immediate risk of harm to self or others, and 5) Pregnancy or lactation.

3.3.2. LAI

Patients on oral haloperidol will be switched to haloperidol decanoate. Individuals not on antipsychotic medication at the time of screening assessment or who are on a different antipsychotic medication will receive an oral tolerance test (OTT) consisting of up to 14 days of oral haloperidol 2–5 mg twice daily. If the OTT suggests good tolerability, the participant will then receive LAI (haloperidol decanoate) intramuscularly after completion of baseline assessments. Dosing of LAI will be as clinically indicated using conservative dosing to minimize drug-related adverse effects. In the U.S. CAE-L study, mean endpoint dose of haloperidol decanoate was 68.0 mg, SD 21.1, range 50–100 mg/monthly injection. It is anticipated that patients will continue on the same dose for 6 months, although dose changes will be permitted based upon clinical status. Each study participant will receive up to 8 injections during the study.

3.3.3. Concomitant treatments

Stable dose psychotropic drugs (>30 days of previous use) other than antipsychotics will be continued. New psychotropic medications will be discouraged. Medications for side effects may be given at the discretion of the treating psychiatrist and their use will be recorded.

3.3.4. Study measures

Baseline information will include previous illness history including duration of psychiatric illness, past hospitalizations, suicide attempts, medication treatment history and cumulative medical burden as evaluated by the self-reported Charlson Comorbidity Index. Primary outcomes will be change on TRQ and mean LAI injection frequency. The TRQ determines proportion of prescribed medication missed, and ranges from 0 (no medication missed/100% adherent) to 100 (no medication taken/0% adherent). For this trial, the TRQ will capture an exact proportion (%) of days with a missed medication dose for each maintenance oral psychotropic drug and derive an average combined TRQ. Full LAI adherence will be defined as receiving an injection within 7 days of scheduled time. Similar to what typically happens in clinical care settings, if an individual does not make a scheduled appointment the clinical research staff will attempt to contact the individual and reschedule him or her as quickly as possible.

Secondary outcomes will include additional information on adherence attitudes (DAI), CPD symptoms (BPRS, CGI), and Social functioning (SOFAS). The Alcohol, Smoking and Substance Involvement Screening Test (ASSIST) and Alcohol Use Disorders Identification Test (AUDIT) (Saunders et al., 1993) will assess substance use. All outcome assessments will be conducted at study baseline, Week 13, and at Week 25 follow-up.

3.3.5. Safety/laboratory evaluations

Safety evaluations will include basic laboratory evaluations (serum comprehensive metabolic panel, lipid profile, CBC with differential, and HIV as well as urine pregnancy testing for women) and EKG. Patient vital signs and weight will be collected at each study visit. Standardized measures of extrapyramidal symptoms will be assessed with Extrapyramidal Symptoms Scale-Abbreviated version (ESRS-A) (Chouinard et al., 1980). Finally, reported side effects will also be evaluated at each study visit using a standardized format.

3.3.6. Data analysis

Phase 3 quantitative analysis will be limited as the focus is on feasibility, patient acceptability, and research capacity building. However, we will assess descriptive statistics and change from baseline in the primary and secondary measures using standard pre-post techniques.

4. Discussion

The study procedures outlined above are intended to pave the way for being able to implement a large-scale intervention trial for CPD in the Tanzanian setting. A recent review of treatments for schizophrenia in SSA by Chidarikire and colleagues (Chidarikire et al., 2018) highlighted the limited mental health services related to financial constraints, lack of qualified mental health professionals and problems in care access. In the review by Chidarikire, 40 studies from eight countries demonstrated that most people with CPD were treated by both modern psychiatry and faith/traditional healers. Antipsychotic medications and psychosocial interventions were used, but were mainly available in major/urban centers. In the studies reviewed, the majority of people with schizophrenia were treated with first-generation antipsychotics (Esan, 2014; Kazadi et al., 2008; Van Rensburg and Oloruniu, 2010). However, Esan (2014) and Kazadi et al. (2008) found that many of the patients discontinued their medication. Families also reported a high level of burden associated with caring for a relative.

An important component of this project is capacity building to help build the next generation of care providers and researchers in CPD. Regular interaction using web-based conference calls between Muhimbili and CWRU senior and junior faculty, as well as with study interventionists and data collection/management staff, have been conducted for the past 12 months and facilitate the establishment of a cohesive clinical trial team. Mid and junior-level faculty at Muhimbili University and the National Hospital, who have all had early success in scholarly work with psychiatric disorders, are supported in taking the lead on implementing the project. Students at earlier phases of their training are learning research techniques and gaining expertise in the assessment and treatment of CPD patients.

In the ongoing implementation of this project, the team is in the process of reviewing and establishing consensus on such essential issues as subject recruitment/enrollment protocols, interventionist hiring and

training, selection of data collection tools, data management methods, results interpretation, and planning for initiatives that will lead to the next research initiatives. Visit exchanges modeled on a successful NIH-funded Medical Education Partnership Initiative (MEPI) template (Kaddumukasa et al., 2014) allow Muhimbili and CWRU faculty to share expertise, problem solve, and plan iterative refinements of project deliverables. Taken together, this project has potential to advance the care of people with CPD in Tanzania and has high generalizability to SSA and other lower-resource settings.

Declarations

Author contribution statement

Jessie Mbwambo, Sylvia Kaaya, Martha Sajatovic: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Isaac Lema: Performed the experiments; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Carol Blixen, Kristin A. Cassidy, Jennifer B. Levin: Conceived and designed the experiments; Wrote the paper.

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Competing interest statement

The authors declare the following conflict of interests: Martha Sajatovic MD: Research grants within past 3 years: Otsuka, Alkermes, Janssen, Reuter Foundation, Woodruff Foundation, Reinberger Foundation, National Institutes of Health (NIH), Centers for Disease Control and Prevention (CDC), International Society of Bipolar Disorders. Consultant: Bracket, Otsuka, Sunovion, Neurocrine, Supernus, Health Analytics. Royalties: Springer Press, Johns Hopkins University Press, Oxford Press, UpToDate. CME activities: American Physician's Institute, MCM Education, CMEology, Potomac Center for Medical Education, Global Medical Education, Creative Educational Concepts. The remaining authors declare no conflict of interest.

Additional information

No additional information is available for this paper.

References

Abel, K.M., Drake, R., Goldstein, J.M., 2010. Sex differences in schizophrenia. Int. Rev. Psychiatry 22 (5), 417–428.

Adams, J., Scott, J., 2000. Predicting medication adherence in severe mental disorders. Acta Psychiatr. Scand. 101 (2), 119–124. Retrieved from. http://www.ncbi.nlm.nih.gov/pubmed/10706011.

Adeponle, A.B., Thombs, B.D., Adelekan, M.L., Kirmayer, L.J., 2009. Family participation in treatment, post-discharge appointment and medication adherence at a Nigerian psychiatric hospital. Br. J. Psychiatry 194 (1), 86–87.

Adewuya, A.O., Owoeye, O.A., Erinfolami, A.R., Coker, A.O., Ogun, O.C., Okewole, A.O., et al., 2009. Prevalence and correlates of poor medication adherence amongst psychiatric outpatients in Southwestern Nigeria. Gen. Hosp. Psychiatry 31 (2), 167–174.

Awad, A.G., 1993. Subjective response to neuroleptics in schizophrenia. Schizophr. Bull. 19 (3), 609–618.

Barnes, T.R., 1989. A rating scale for drug-induced akathisia. Br. J. Psychiatry 154, 672–676. Retrieved from. http://www.ncbi.nlm.nih.gov/pubmed/2574607.

Blixen, C., Perzynski, A., Cage, J., Smyth, K., Moore, S., Sila, C., et al., 2014. Stroke recovery and prevention barriers among young african-american men: potential avenues to reduce health disparities. Top. Stroke Rehabil. 21 (5), 432–442.

Blixen, C., Perzynski, A., Cage, J., Smyth, K., Moore, S., Sila, C., et al., 2015. Using focus groups to inform the development of stroke recovery and prevention programs for younger African-American (AA) men. Top. Stroke Rehabil. 22 (3), 221–230.

Blixen, C.E., Kanuch, S., Perzynski, A.T., Thomas, C., Dawson, N.V., Sajatovic, M., 2016. Barriers to self-management of serious mental illness and diabetes. Am. J. Health Behav. 40 (2), 194–204.

Charlson, F.J., Diminic, S., Lund, C., Degenhardt, L., Whiteford, H.A., 2014. Mental and substance use disorders in Sub-Saharan Africa: predictions of epidemiological changes and mental health workforce requirements for the next 40 years. PLoS One 9 (10), e110208.

Chidarikire, S., Cross, M., Skinner, I., Cleary, M., 2018. Treatments for people living with schizophrenia in Sub-Saharan Africa: an adapted realist review. Int. Nurs. Rev. 65 (1), 78–92.

Chouinard, G., Rosschouinard, A., Annable, L., Jones, B.D., 1980. Extrapyramidal symptom rating-scale. Can. J. Neurol. Sci. 7 (3), 233–244. Retrieved from <Go to ISI>://WOS:A1980KK56700030.

Collins, C.M., Aebi, M.E., Levin, J.B., Tatsuoka, C., Cassidy, K.A., Sajatovic, M., 2018. Post-hoc analysis of two clinical trials examining Customized Adherence Enhancement plus long acting injectable antipsychotic (CAE-L) in high-risk individuals with serious mental illness. Schizophr. Res. 202.

Crabtree, B.F., Miller, W.L., 1999. Doing Qualitative Research, second ed., xvii. Sage, Thousand Oaks, CA.

Danladi, J., Falang, K.D., Barde, R.A., Jimam, N.S., Dangiwa, D.A., Jimoh, H.O., 2013. Pharmaceutical care and medication adherence in management of psychosis in a Nigerian tertiary hospital. J. Res. Pharm. Pract. 2 (2), 83–87.

Esan, O., 2014. Persistence in treatment for one year among patients in Nigeria with first-episode schizophrenia. Psychiatr. Serv. 65 (9), 1174–1176.

Esterberg, K.G., 2002. Qualitative Methods in Social Research. McGraw-Hill, Boston, MA.

Gilmer, T.P., Dolder, C.R., Lacro, J.P., Folsom, D.P., Lindamer, L., Garcia, P., et al., 2004. Adherence to treatment with antipsychotic medication and health care costs among medicaid beneficiaries with schizophrenia. Am. J. Psychiatry 161 (4), 692–699.

Group, W. H. O. A. W., 2002. The Alcohol, smoking and substance involvement screening test (ASSIST): development, reliability, and feasibility. Addiction 97, 1183–1194.

Guy, W., 1976. ECDEU Assessment Manual for Psychopharmacology. US Department of Health, Education, and Welfare (DHEW), Rockville, MD.

Harvey, N.S., 1991. The development and descriptive use of the Lithium Attitudes Questionnaire. J. Affect. Disord. 22 (4), 211–219. Retrieved from. http://www.ncbi.nlm.nih.gov/pubmed/1939930.

Ho Odo, O.S., Agbonile, I.O., Esan, P.O., 2014. Assessment of adherence to psychotropic medications among outpatients at the pharmacy department of a psychiatric hospital in Benin City, Nigeria. Asian J. Pharm. 194 (1), 86–87.

Jenkins, J.H., Strauss, M.E., Carpenter, E.A., Miller, D., Floersch, J., Sajatovic, M., 2005. Subjective experience of recovery from schizophrenia-related disorders and atypical antipsychotics. Int. J. Soc. Psychiatry 51 (3), 211–227.

Kaddumukasa, M., Katabira, E., Salata, R.A., Costa, M.A., Ddumba, E., Furlan, A., et al., 2014. Global medical education partnerships to expand specialty expertise: a case report on building neurology clinical and research capacity. Hum. Resour. Health 12, 75.

Kay, S.R., Fiszbein, A., Opler, L.A., 1987. The positive and negative syndrome scale (PANSS) for schizophrenia. Schizophr. Bull. 13 (2), 261–276. Retrieved from. http://www.ncbi.nlm.nih.gov/pubmed/3616518.

Kazadi, N.J.B., Moosa, M.Y.H., Jeenah, F.Y., 2008. Factors associated with relapse in schizophrenia. S. Afr. J. Psychiatr. 14 (2), 52. Retrieved from <Go to ISI>://WOS:000258431500007.

Morosini, P.L., Magliano, L., Brambilla, L., Ugolini, S., Pioli, R., 2000. Development, reliability and acceptability of a new version of the DSM-IV Social and Occupational Functioning Assessment Scale (SOFAS) to assess routine social functioning. Acta Psychiatr. Scand. 101 (4), 323–329. Retrieved from. http://www.ncbi.nlm.nih.gov/pubmed/10782554.

Moustakas, C., 1994. Phenomenological Research Methods. Sage, Thousand Oaks, CA.

Mueser, K.T., Corrigan, P.W., Hilton, D.W., Tanzman, B., Schaub, A., Gingerich, S., et al., 2002. Illness management and recovery: a review of the research. Psychiatr. Serv. 53 (10), 1272–1284.

Overall, J.E., Gorham, D.R., 1962. The brief psychiatric rating-scale. Psychol. Rep. 10 (3), 799–812. Retrieved from <Go to ISI>://WOS:A1962CBK8600036.

Patel, V., 2009. Integrating mental health care with chronic diseases in low-resource settings. Int. J. Public Health 54 (Suppl 1), 1–3.

Peet, M., Harvey, N.S., 1991. Lithium maintenance: 1. A standard education programme for patients. Br. J. Psychiatry 158, 197–200. Retrieved from. http://www.ncbi.nlm.nih.gov/pubmed/1707323.

Sajatovic, M., Dawson, N.V., Perzynski, A.T., Blixen, C.E., Bialko, C.S., McKibbin, C.L., et al., 2011. Best practices: optimizing care for people with serious mental illness and comorbid diabetes. Psychiatr. Serv. 62 (9), 1001–1003.

Sajatovic, M., Levin, J., Ramirez, F., al, e., 2016. A concierge model of customized adherence enhancement plus long-active injectable antipsychotic in individuals at risk for treatment non-adherence and for homelessness. Dec. 6, 2016. In: Paper presented at the 55th Annual Meeting of the American College of Neuropsychopharmacology (ACNP), Hollywood, Florida.

Sajatovic, M., Levin, J., Ramirez, L.F., Hahn, D.Y., Tatsuoka, C., Bialko, C.S., et al., 2013. Prospective trial of customized adherence enhancement plus long-acting injectable antipsychotic medication in homeless or recently homeless individuals with schizophrenia or schizoaffective disorder. J. Clin. Psychiatry 74 (12), 1249–1255.

Sajatovic, M., Levin, J., Tatsuoka, C., Micula-Gondek, W., Fuentes-Casiano, E., Bialko, C.S., et al., 2012a. Six-month outcomes of customized adherence enhancement (CAE) therapy in bipolar disorder. Bipolar Disord. 14 (3), 291–300.

Sajatovic, M., Levin, J., Tatsuoka, C., Micula-Gondek, W., Williams, T.D., Bialko, C.S., et al., 2012b. Customized adherence enhancement for individuals with bipolar disorder receiving antipsychotic therapy. Psychiatr. Serv. 63 (2), 176–178.

Sariah, A.E., Outwater, A.H., Malima, K.I., 2014. Risk and protective factors for relapse among individuals with schizophrenia: a qualitative study in Dar es Salaam, Tanzania. BMC Psychiatry 14, 240.

Saunders, J.B., Aasland, O.G., Babor, T.F., de la Fuente, J.R., Grant, M., 1993. Development of the Alcohol use disorders identification test (AUDIT): WHO collaborative project on early detection of persons with harmful Alcohol consumption–II. Addiction 88 (6), 791–804. Retrieved from. http://www.ncbi.nlm.nih.gov/pubmed/8329970.

Scott, J., Pope, M., 2002. Nonadherence with mood stabilizers: prevalence and predictors. J. Clin. Psychiatry 63 (5), 384–390. Retrieved from. http://www.ncbi.nlm.nih.gov/pubmed/12019661.

Van Rensburg, A.J., Oloruniu, S., 2010. Diagnosis and treatment of schizophrenia in a general hospital based acute psychiatric ward. Afr. J. Psychiatr. 13 (3), 204–210.

Velligan, D.I., Weiden, P.J., Sajatovic, M., Scott, J., Carpenter, D., Ross, R., et al., 2010. Strategies for addressing adherence problems in patients with serious and persistent mental illness: recommendations from the expert consensus guidelines. J. Psychiatr. Pract. 16 (5), 306–324.

Weiden, P., Rapkin, B., Mott, T., Zygmunt, A., Goldman, D., Horvitz-Lennon, M., et al., 1994. Rating of medication influences (ROMI) scale in schizophrenia. Schizophr. Bull. 20 (2), 297–310. Retrieved from. http://www.ncbi.nlm.nih.gov/pubmed/7916162.

Zygmunt, A., Olfson, M., Boyer, C.A., Mechanic, D., 2002. Interventions to improve medication adherence in schizophrenia. Am. J. Psychiatry 159 (10), 1653–1664.