FULL-LENGTH ORIGINAL RESEARCH

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A home-based, primary-care model for epilepsy care in India: Basis and design

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Summary

Objectives: A cluster-randomized trial of home-based care using primary-care resources for people with epilepsy has been set up to optimize epilepsy care in resource-limited communities in low- and middle-income countries. The primary aim is to determine whether treatment adherence to antiepileptic drugs is better with home-based care or with routine clinic-based care. The secondary aims are to compare the effects of the two care pathways on seizure control and quality of life.

Methods: The home-based intervention comprises epilepsy medication provision, adherence reinforcement, and epilepsy self-management and stigma management guidance provided by an auxiliary nurse-midwife equivalent. The experimental group will be compared to a routine clinic-based care group using a cluster-randomized design in which the unit of analysis is a cluster of 10 people with epilepsy residing in an area cared for by a single accredited government grass-roots health care worker. The primary outcome is treatment adherence as measured by monthly tablet counts supplemented by two self-completed questionnaires. The secondary outcomes include monthly seizure frequency, time to first seizure (in days) after enrollment, proportion of patients experiencing seizure freedom for the duration of the study, and quality of life measured by the "Personal Impact of Epilepsy Scale," all assessed by an independent study nurse.

Results: The screening phase and neurologic evaluations and randomizations have been recently completed and follow-up is underway.

Significance: The results of the trial are likely to have substantial bearing on the development of governmental policies and strategies to provide coverage and care for patients with epilepsy in resource-limited countries.

KEYWORDS

adherence, cluster-randomized trial, community, epilepsy, primary care

1 | INTRODUCTION

Epilepsy affects over more than 50 million people worldwide and the majority of those affected live in low- and middle-income countries (LMICs).[1] Many persons with epilepsy in LMICs are deprived of appropriate treatment and support.[1–4] The provision of suitable care to such large numbers of people with epilepsy is challenging. The World Health Organization (WHO) envisages epilepsy care as a joint responsibility between primary and secondary health care providers.[1] In high-income countries, the main tasks of secondary care are to provide diagnostic and investigative services on a consultation basis, institute treatment changes, and provide counseling and follow-up when appropriate. Primary care providers are delegated the tasks of case finding, referral to secondary care and follow-up on the advice provided. Conversely, the provision of epilepsy care in LMICs using a similar model is problematic because of barriers on the supply side (eg, unavailable antiepileptic drugs [AEDs], long distances to health facilities, and insufficient expertise to treat epilepsy), as well as those on the demand side (eg, treatment costs, cultural beliefs regarding epilepsy, stigma, and faith in traditional treatment providers).[5] The paucity of trained physicians is one of reasons for the poor standards of care for epilepsy in LMICs. For example, there are an estimated 8-12 million people with epilepsy in India.[6–8] Applying the yardstick of one neurologist for 100 000 people would require at least 8000 neurologists.[9,10] The WHO estimates, however, a median of 0.07 neurologists/100 000 population in South/Southeast Asia.[11] Hence, the number of neurologists available for epilepsy care falls short of the required number and, consequently, epilepsy care has defaulted to primary care providers in this region.

The WHO recently asked member states to introduce and implement national epilepsy programs to reduce the gap in provision of care, particularly in poor and remote regions, and to integrate epilepsy management into primary care.[12] The aim is to achieve a substantial reduction in the magnitude of the treatment gap in LMICs by overcoming some of the existing barriers.[6–8]

Home-based care for epilepsy delivered by primary care personnel might overcome some of the barriers, by providing regular, cost-free AEDs, eliminating the "distance to health facility," and providing knowledge and guidance to mitigate stigma and false beliefs, and to aid self-management. India is ideally suited for testing a care model integrating specialist neurologic expertise within the existing primary care infrastructure. There are now more than 2000 qualified neurologists in the country, albeit insufficient to provide epilepsy care but enough to guide and counsel epilepsy care delivered by primary care providers. There is also a vast resource of personnel and operational infrastructure supporting primary

Key Points
- The treatment gap for epilepsy is wide in low- and middle-income countries
- Despite the provision of drugs, many people with epilepsy abandon treatment in the long term
- A pragmatic, population-based, cluster-randomized trial of home-based provision of medications by primary-care personnel has been set up
- We aim to determine the impact of home-based care on treatment adherence, seizure control, and quality of life
- We hope that the trial results will provide direction on policy regarding epilepsy care provision in low- and middle-income countries

care across the country. Hence, we have set up a pragmatic, community-based, cluster-randomized trial of home-based epilepsy care delivery by primary care health providers under the supervision of neurologists. The trial is now ongoing with enrollment and randomization completed. Herein we report on the aims, recruitment and interventional protocols, and the progress so far.

2 | MATERIALS AND METHODS

2.1 | Aims

We are aiming to determine whether a home-based intervention comprising provision of AEDs and health education emphasizing epilepsy self- and stigma-management improves treatment adherence compared with the usual clinic-based epilepsy care in the community. We will also estimate the impact of home-based care on seizure control and quality of life. Additional objectives include identification of barriers in the implementation of primary care for epilepsy in resource-limited settings.

2.2 | Setting of trial

The trial has been initiated in the urban and semi-urban rural areas of the Ludhiana district with an area of 3767 km^2 and an estimated population of 1.9 million (2011 Census India).[13] Approximately 80% of the population is literate and 30% are manual workers. The Government Health Department has divided the urban and peri-urban rural areas into nine zones to facilitate immunization coverage (Figure 1A).

2.3 | Screening for potential subjects[*]

The cluster sampling approach for evaluating vaccination coverage was used to identify individuals with epilepsy in

(A)

(B)

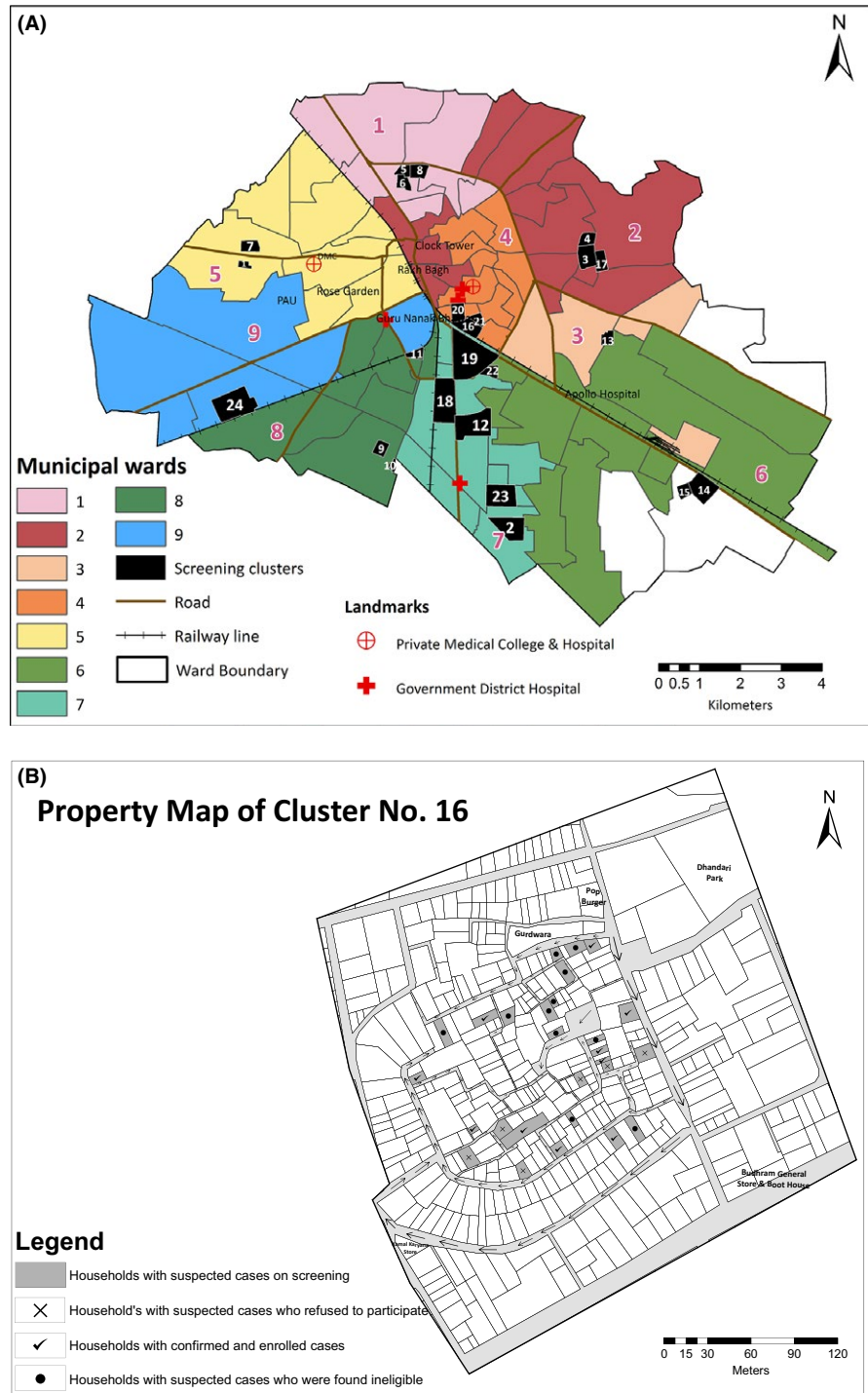## Property Map of Cluster No. 16

FIGURE 1 A, Map of the study area with division in to nine immunization zones. The primary health centers, district hospitals, and two private medical college hospitals are also mapped. B, Map of a randomly chosen screening cluster depicting the progress of door-to-door screening

the community.[14] Clusters were selected from areas with lower sociodemographic indices, for which grassroots community health workers (Accredited Social Health Activists [ASHAs]) were available and willing to assist.[15] A prevalence of 10 cases of epilepsy/1000 population was inferred from prevalence surveys in India, to which a 50% inflation was factored in to account for locked households, and for refusal to participate in screening or to enroll in the trial.[16–18] A decision was made to screen about 2000 people in each screening cluster. This amounted to 2-3

screening-clusters per immunization zone and 24 clusters in all (Figure 1A).

Beginning on December 7. 2017, study personnel accompanied by ASHAs visited door-to-door within each screening cluster using detailed geographic information system maps with household numbers superimposed on Google maps. They used a screening questionnaire, previously employed in Ecuador, and translated and validated earlier in this community (estimated sensitivity, 0.83; specificity, 0.84; predictive values, positive—59.76% and negative—60.48%).[18,19]

Subjects were classified either as "suspected epilepsy cases" or "screened negative for epilepsy" (Table S1). Screening started from a randomly chosen dwelling unit and proceeded in an orderly fashion, advancing to consecutive houses along a street and then to the adjoining street (Figure 1B). Inventories for locked, leased, and those households for which no official records exist in the municipality, as well as of all family members in any given unit, were maintained. Locked households were revisited twice before excluding them.

2.4 | Geospatial mapping[*]

The health department provided us with a current list of health facilities. The locations of these health centers were mapped using a global positioning system (GPS). Ward and immunization zone boundaries of the area were overlaid on the location map using ArcGIS 10.4 (ESRI, Redlands, CA). World View-II satellite data (spatial resolution: 0.5 m) was also used to map individual properties. Maps of each cluster thus generated were reviewed with designated ASHAs, GIS experts, and field workers prior to commencing screening. Suspected and enrolled cases were flagged on GIS maps of each cluster to assist follow-up during home-based care.

2.5 | Neurologic evaluations and treatment planning[*]

Suspected cases from the screening program were invited for neurologic assessments by study-team neurologists (two adult and one pediatric) with expertise in epilepsy. They were assessed on a conservative basis with a minimum of a 1-hour awake and sleep electroencephalography (EEG) (Nihon Kohden, Japan) and magnetic resonance imaging (MRI) (3 Tesla; Siemens, Germany) at a local academic hospital. Subsequently, treatment plans were generated and the choice of drugs and the manner of initiation were left to the judgment of the neurologists. AEDs used were restricted to those on the essential drug list with two exceptions: (a) subjects with active epilepsy who were seizure-free prior to enrollment on AED treatment are maintained on the same medication/s and (b) valproate use is avoided, when possible, in women in the reproductive age group.[20,21]

2.6 | Sample size[*]

An adherence rate of 60% in the clinic-based arm was assumed from previous Indian reports.[22,23] Good adherence was assumed when the number of remainder pills counted during monthly assessments by the study nurse was within ± 2 days' stock.[24] The sample size (n) was calculated to compare the proportion of patients with good adherence in an individual-level randomized-controlled trial to improve adherence rates from 60% to 80% with power of 0.8 and a significance level of 0.05.

In the absence of data on variance of adherence, an intracluster coefficient (ICC) (ρ) of 0.05 was initially assumed. The ICC has since been reset on the basis of data accrued during the interim (3 months after recruitment of 10 clusters) analysis to 0.000001 (95% confidence intervals, <0.000001-0.021). The number of individuals in each cluster (m) was fixed at 10.

The design effect (D) for a parallel, cluster-randomized trial was calculated using the formula:

$$D = 1 + (m - 1)\rho,^{25,26}$$

where m = number of individuals in a cluster.

The number of clusters with 10 subjects each for a parallel arm, cluster randomized trial (n_{CRT}) was calculated using the following formula:

$$n_{CRT} = D \times n/m.^{25}$$

The estimated number of subjects in each arm (n) was 91. To make up for an anticipated attrition rate of 30%, the total number of recruited subjects was fixed at 240 and number of clusters recruited (n_{CRT}) set to 24.

2.7 | Trial recruitment and randomization[*]

After neurologic assessments, subjects over 1-year old with active epilepsy were invited to enroll in the trial regardless of prior treatment status (see Box S1, for operational definitions). People with febrile seizures, neonatal seizures, single seizures not fulfilling the current operational definition for epilepsy, and acute symptomatic seizures associated with head injury, stroke, and toxic, metabolic, and acute infective conditions were excluded.[27]

The randomization-cluster (as distinct from the screening-cluster) unit was fixed at 10 subjects with confirmed active epilepsy derived from a screening-cluster (Figure 2). Clusters were randomized as soon as they were assembled according to a computer-generated, simple randomization scheme to either home-based care or usual clinic-based care. The randomization list was made previously made and is kept by a Randomization Officer (S.S.) not involved in recruitment or evaluations, who disclosed allocation only on completion of cluster assembly.

2.8 | Interventional package and control procedures[#]

Subjects in the clinic-based arm (n = 120; age range 1-80 years) are asked to attend monthly clinics at the Government District Hospital for review visits and drug dispensing. Those in the other arm (n = 120; age range 1-67 years) receive an interventional package comprising the following: (a) delivery of AEDs; (b) education and counseling about self-management, social functioning, and stigma abrogation; and (c) adherence monitoring; all provided at home on a monthly basis by study
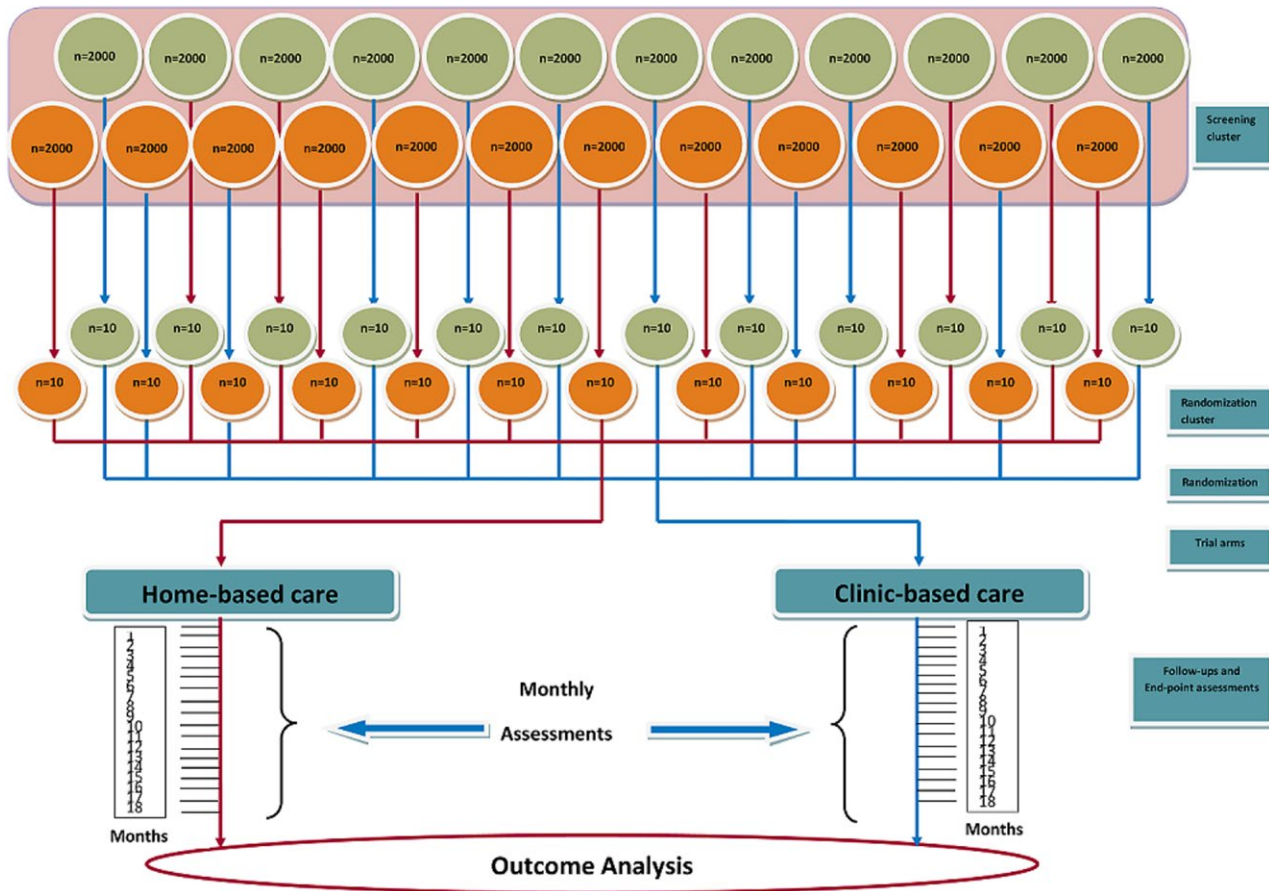
FIGURE 2 Trial flow chart depicting screening, evaluation, randomization, and assessments

personnel with qualifications equivalent to auxiliary nurse midwives (ANMs). During the first home visit, the study purpose is explained, and information about drugs, including frequency and timings of drug taking, are provided. A comprehensive brochure, a seizure diary, and prescription record are also supplied. During subsequent monthly visits, study personnel hold continued discussions regarding self-management; impart psychosocial education pertaining to schooling, marriage, and employment; inquire about medication side-effects; verify seizure diaries; and supply the scheduled stock of AEDs.

Records of home visits are reviewed at monthly meetings with the study neurologists who make changes in the treatment plan based on reports of seizure control, side-effects, and other circumstances, as necessary. Any changes in treatment plan are implemented by unscheduled home visits. Interim visits to the study neurologists take place for people with inadequate seizure control, unacceptable side-effects, or pregnancy in women with epilepsy. Likewise, subjects in the clinic-based arm can make ad hoc clinic visits or be referred to the study neurologists if they have inadequate seizure control, side-effects, or pregnancy. Medications are provided cost-free to subjects in both arms. Pediatric formulations are used for children <12 years of age.

2.9 | Outcomes[#]

The primary outcome of the trial is adherence, appraised at monthly intervals by pill counts and vernacular versions of the Self-Reporting Medication-Taking Scale (SRMS) and Brief Medication Questionnaire (BMQ).[28,29] Secondary outcomes include quality of life appraisal by the Personal Impact of Epilepsy (PIES) scale and several seizure-related parameters including monthly seizure frequency, time to first seizure (in days) after enrollment, and the proportion of subjects experiencing seizure freedom for the duration of the study.[24,30] Outcomes are assessed independently by a study nurse, who not involved in recruitment or dispensing and trained in the use of the instruments described below.

2.10 | Instruments[#]

2.10.1 | Medication adherence

Pill counts

Adherence is evaluated by counting residual dosage units of each AED dispensed during the preceding month and is assumed to be good when the number of dosage units consumed are within ± 2 days of a month's prescribed use.[24] When more

or fewer than 2 days of a month's use of dosage units are counted, adherence is deemed to be poor. When pills are not available (eg, destroyed, misplaced, or lost) for counting during the assessment visits or when subjects use pills from stocks other than those provided by the study personnel, the pill counts are classified as indeterminate.

Questionnaire-based measures

The SRMS is a 4-item scale to assess medication nonadherence.[28] It asks about different modes of medication omission associated with forgetfulness, carelessness, and stopping medications when feeling better or when feeling worse (due to side-effects of medications or failure to control seizures). The items in the questionnaire are presented in a negative structure to eliminate "yes bias."[31] The BMQ is a screening questionnaire to identify nonadherence or barriers to adherence.[29] It includes three screening questions that measure different aspects of medication-taking behavior. A positive regimen screen indicates potential nonadherence, a positive belief screen discloses beliefs that might be linked to nonadherence by inquiring about the effectiveness or bothersomeness of the medication/s and the recall screen characterizes barriers to recall (eg, due to the complexity of the regimen). Both scales are administered to the subjects or their parents (for children <18 years).

2.10.2 | Quality of life

We selected the PIES to measure quality of life as it appraises seizure burden, AED side-effects, and mood and cognition in addition to overall quality of life on a Likert scale.[30] Moreover, it can be administered to family members in case of children and illiterate subjects.

2.10.3 | Ancillary appraisals

To document fully the impact of the intervention; additional evaluations, for example, Epilepsy Self-management Scale, Kilifi Epilepsy Stigma Scale, and the Kilifi Epilepsy Beliefs and Attitudes Scales are planned.[32–35] Records are also maintained of interim visits in the home-based arm and ad hoc clinic visits and referrals in the clinic-based arm. An economic analysis of the intervention, based on governmental and societal perspectives, is also underway in a parallel study. The analytic horizon will be for the trial period.

2.10.4 | Safety assessments and monitoring

Spontaneous accounts of AED adverse events are recorded at each encounter and discussed at monthly study team meetings. Emphasis is placed on serious adverse events, pregnancy, and suicidality reporting, and standard protocols are followed to deal with the situations. Finally, a structured adverse event inventory is administered once every 6 months.[36]

All scales have been translated to the vernacular language (Punjabi) by two multilingual translators unconnected to the study team, followed by correspondence assessment.[28–30,32–36] Vernacular versions have then been back-translated to the English language and compared with the original English versions. The translated versions have been administered to 15 people with epilepsy drawn from the outpatient clinic to verify linguistic comprehension and applicability of the items. Lastly, the Likert scale has been adapted to a one Indian Rupee (=100 paisa) monetary scale (Figure S1) to quantify responses to the questions in a manner acceptable to respondents with poor literacy.

2.11 | Assessment schedules[#]

The duration of the trial will be for 24 months. The study nurse records outcomes on an android tablet (Samsung Galaxy Tablet ver. 7.0 each month. The data are then downloaded to a central server. Pill counts are performed and the SRMS and BMQ scales are administered every month (Figure 3).[28,29] The adverse effects profile questionnaire is administered once in 3 months, PIES once in 6 months, and the Epilepsy self-management, Kilifi stigma, and Kilifi Beliefs and Attitudes scales are administered in the beginning, mid-way, and at the end of the trial.[30,32–35] The data are password protected and in the keeping of the study statistician (N.B.), who validates a random 10 from paper records every month.

2.12 | Statistical analysis[#]

Baseline, individual-level analysis will compare sociodemographic characteristics including age, gender, socioeconomic status, duration of epilepsy and prior seizure frequency in the two arms. The Revised Kuppuswamy scale corrected for monetary inflation, which records education and occupation of the head of the family and family income, was used to estimate the socioeconomic status.[37] The first interim analysis was planned 3 months after recruitment of 10 clusters. The purpose of this analysis was to recalculate the ICC according to the primary outcome measure and hence reestimate the sample size and to examine the psychometric properties of SRMS, BMQ, and the PIES instruments. A second interim analysis is planned for 12 months after recruitment of the final cluster to assess attrition rates in the two groups. The analysis would require premature stopping of the trial if the attrition rate in the clinic-based arm exceeds 40%.[38]

In the final analysis after completion of all monthly assessments, cluster level summaries for each of the primary and secondary outcomes will be calculated (Figure 3). Point estimates (and their confidence intervals) of the intervention effect will be obtained from the cluster-level summaries using the 't' distribution (Table 1).[26] Hypothesis testing will use the unpaired t test for cluster level summaries in each arm. Finally,

Enrollment	Follow-up Visits																							
	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5	Visit 6	Visit 7	Visit 8	Visit 9	Visit 10	Visit 11	Visit 12	Visit 13	Visit 14	Visit 15	Visit 16	Visit 17	Visit 18	Visit 19	Visit 20	Visit 21	Visit 22	Visit 23	Visit 24
Seizure, first aid discussed																								
Adherence																								
Schooling/NA																								
Marriage/NA																								
Contraception																								
Pregnancy/NA																								
Bone Health																								
Employment																								
Driving/NA																								
Previous Pill Count																								
Seizure Diary Update																								
Follow up Visit Record																								
Pill count of medicine dispensed																								
BMQ																								
SRMS																								
Adverse Event Profile	■	■	■	■	■		■	■	■	■	■		■	■	■	■	■		■	■	■	■	■	
PIES	■	■		■	■		■	■		■	■	■	■	■		■	■	■	■	■		■	■	
Bone health screening evaluated	■	■	■	■	■	■	■	■	■	■	■		■	■	■	■	■	■	■	■	■	■	■	
PHQ 9, GAD 7	■	■	■	■	■	■	■	■	■	■	■		■	■	■	■	■	■	■	■	■	■	■	
NIDE	■	■	■	■	■	■	■	■	■	■	■		■	■	■	■	■	■	■	■	■	■	■	
ESM Scale	■	■	■	■	■	■	■	■	■	■	■		■	■	■	■	■	■	■	■	■	■	■	
Kilifi Epilepsy Beliefs and Attitude	■	■	■	■	■	■	■	■	■	■	■		■	■	■	■	■	■	■	■	■	■	■	
Kilifi Stigma Scale for Epilepsy	■	■	■	■	■		■	■	■	■	■		■	■	■	■	■		■	■	■	■	■	

FIGURE 3 Trial assessment schedules

the effect of covariates including age, gender, socioeconomic status, duration of epilepsy, prior seizure control, distance from the District Hospital, within individual correlation over time (to account for a repeated measures design for adherence) will be examined in individual-level, random-effects, logistic-regression models. The intervention effect will not be entered into the model at this stage. The residuals thus generated would constitute the summary measure for each cluster, which will then be compared between the two arms using the *t* test.[26]

Attrition rates and missing data for the outcome measures will be described. In the clinic-based arm, baseline data on subjects who withdraw after enrollment will be compared with those continuing the trial.[38] An earlier observation carried forward approach will be used to handle missing data during statistical modeling of adherence.[39] Missing data will not be imputed in the analysis of other outcomes but various sensitivity analyses under random, as well as not-at-random assumptions, will be performed. Stata version 15.1 (Stata Corp LLC, TX) will be used for the statistical analysis.

2.13 | Ethical considerations and protocol standards

The trial was approved by the local institutional ethics committee, overseen by an independent, three-member Data Monitoring and Safety Committee, and is registered with the Clinical Trials Registry of India (ref/2017/09/015380). The data sharing policy is available at http://researchatdmch.com/study-design-paper-gs/. Informed consents are recorded from all subjects older than18 years of age and from parent/legally acceptable representative in the case of children (in addition to oral assent from children 7-11 years of age and written assent from children over 12 years of age).The research methods and reporting follow Consolidated Standards of Reporting Trials criteria for extension to cluster randomized trials and for pragmatic trials.[40,41]

3 | DISCUSSION

Home-based care for epilepsy with primary care workers as the point of contact is a feasible option. Potential benefits include provision of care in the home environment using community resources in the setting of poor specialist care provision, engagement of family members as stakeholders, and reduction in direct non-medical and indirect costs of treatment (in the form of expenses incurred in traveling to clinics and wages lost). It is suited for those who find it difficult to travel (eg, elderly, those with physical disability, and children). Repeated visits and counseling by health

TABLE 1 Outcomes, endpoints, measures, and statistical approaches in the trial

S. no.	Outcome	Endpoint/s	Individual-level data	Cluster-level measure	Allocation-arm level measure	Test of hypothesis
1	Primary outcome: Treatment adherence	Pill counts	Proportion of subjects with good adherence	Mean of proportion in each cluster	Mean of cluster-level summary measure	t test
		SRMS score	Total score	Mean score within each cluster	Mean of cluster-level summary measure	t test
		BMQ score	Total score	Mean score within each cluster	Mean of cluster-level summary measure	t test
2	Secondary outcome—1: seizure control	Monthly seizure frequency	Monthly seizure frequency	Frequency means within each cluster	Mean of cluster-level summary measure	t test
		Time to first seizure	Time to first seizure (in days) after recruitment to the study	Means of time to events within each cluster	Mean of cluster-level summary measure	t test
		Seizure remission	Seizure freedom throughout trial duration	Means of proportions in each cluster	Mean of cluster-level summary measure	t test
3	Secondary outcome—2: Quality of life	PIES total score	PIES total score	Mean score within each cluster	Mean of cluster-level summary measure	t test
4	Ancillary appraisals: Participant-reported outcomes	Epilepsy-self-management	Epilepsy self-management scale	Mean score within each cluster	Mean of cluster-level summary measure	t test
		Beliefs and outcomes	Kilifi Belief and Outcomes scale	Mean score within each cluster	Mean of cluster-level summary measure	t test
		Stigma	Kilifi stigma scale	Mean score within each cluster	Mean of cluster-level summary measure	t test
		Adverse events	Adverse event questionnaire	Mean score within each cluster	Mean of cluster-level summary measure	t test

BMQ, Brief Medication Questionnaire; PIES, Personal Impact of Epilepsy.

care workers may also improve adherence, as people often discontinue treatment either in frustration over side-effects or failure of medications to control seizures, or simply after experiencing seizure freedom.[24] The approach has been undertaken before in underserved communities but has not been formally tested in a randomized-controlled trial.[42]

We chose to test home-based provision of medications and care and counseling by community health care workers against the usual clinic-based care in a cluster-randomized trial with a pragmatic design. The initial screening cluster size was fixed at 2000, as this was the population covered by one ASHA, a voluntary foundation-level social health worker. The ASHAs reside in the clusters covered by them and are hence well-informed about the health status of the residents. This helps in identifying potential participants, especially in the context of epilepsy, a stigmatized condition, which is often not disclosed during screening campaigns.[43] The randomization-cluster unit comprised people with epilepsy in the screening cluster and was adopted mainly for logistic convenience and acceptability.[26] Another justification for cluster-randomization was to prevent contamination of the counseling effects.[44] Consonant with the cluster size implemented for screening, the expected yield of potential participants with confirmed epilepsy who might consent to randomization was 10.

Medication adherence was selected over seizure control or quality of life as a primary outcome in consideration of the short duration of the trial. We thought that repeated home visits and counseling would directly impact medication adherence, epilepsy self-management, and coping with stigma. Seizure control might be a downstream effect of the intervention and, additionally, might be influenced by variables such as the characteristics of epilepsy and AEDs administered. Even so, average monthly seizure frequency, time to the first seizure after randomization, and the proportion of subjects in either arm who experienced seizure freedom throughout the trial period were chosen as (clinical) secondary outcomes. To incorporate a participant-reported outcome, we chose the PIES, a new instrument that measures seizure severity and frequency, AED-related adverse effects, and mood and cognition in addition to overall quality of life.[30] This was preferred over existing generic and epilepsy-specific quality of life scales, as it can be administered across a range of age groups and to subjects and their family members, an important consideration in its applicability in people with poor literacy.[45–49] Limitations of the scale, however, included the scant experience with its use and the lack of an established clinically meaningful difference associated with its use.

A number of measures for evaluating medication adherence have been proposed. Some, such as the electronic medication monitoring systems or serial serum AED level measurements, are highly specific and sensitive measures, but cost and impracticalities in a limited-resources setting precluded their use.[50,51] We opted for pill count as the primary measure of adherence, supplemented by two participant-completed questionnaires because of its anticipated reliability and consistency of measurement across different age groups.[51–53] Monitoring pill counts also presents unique challenges, as illustrated by a number of situations in which pill counts were found to be indeterminate, for example, due to locked houses during assessments, misplaced or lost pills, and contamination with medications acquired by subjects from other sources.

Geographic information system mapping was used for the following: (a) to aid the screening activity by mapping out households within each cluster; (b) to determine geographic correlates including spatial clustering of the epilepsy cases identified in the community survey; and (c) to aid in the analysis of the distance factor associated with treatment-seeking behavior of the control group.[54–56]

Screening, identification, and ascertainment of epilepsy are important components of any community-oriented epilepsy care program in LMICs. The present report emphasizes the interventional component as distinct from screening and case ascertainment. Other limitations include the use of simulated field staff, who, despite similar educational level and experience as existing community health workers, were commissioned solely for this project. We do not know how effective it is to delegate epilepsy care to the existing community health workers in India, initially hired mainly for mother and child care and later burdened with a variety of health-related tasks.[57] The limited geographic scope of the trial also precludes generalizability, and we do not know how effective the arrangement would be in remotely located rural areas in the country.

In the context of providing universal care for epilepsy, several issues including allocation of funds, augmenting the supply side, and dealing with competing private care need to be addressed. Our initial experience illustrates some of the challenges faced in undertaking a randomized trial in an impoverished community with poor disease- and treatment-literacy. Enrollment following the screening phase was initially modest, perhaps due to poor faith in the public health system, but later improved. We have, and will continue, to cope with heavy relocation of trial subjects within and outside the community, largely for economic reasons. In addition, it is particularly challenging to sustain medication adherence in the long term for a chronic disorder such as epilepsy in a subject population that is heavily stigmatized, has poor treatment-literacy owing to low levels of education and fragmentary access to channels of public communication, and has continuing faith in competing health care systems, for example, faith healers.[58,59]

DISCLOSURE

The authors declare no conflict of interest in relation to this work. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

ENDNOTES

* This section describes activities that have been completed

\# This section describes activities that are ongoing.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.